13 Allergy clinic baseline survey: provision of specialist allergy clinic services


William Egner


Tim Cook


Nigel Harper


Tomaz Garcez

Key findings

- We describe self-declared provision and practice of specialist perioperative allergy services in the UK and compare this to national recommendations.
- An on line questionnaire was distributed to providers of allergy services in the UK in 2016.
- Over 1200 patients were investigated in 44 centres annually.
- 21 adult centres saw >20 patient per year, twelve <20 adults and eleven only children.
- Variation in workload, waiting times, access, staffing, and diagnostic approach was noted. Geographical variation was marked.
- Paediatric centres reported the longest routine waiting times (most wait >13 weeks) in contrast to adult centres (most <12 weeks).
- Service leads are allergists/immunologists (91%) or anaesthetists (7%).
- Potentially important differences were seen in:
  - Testing repertoire [10/44 (23%) lacked BSACI-compliant NMBA 'panels'
  - 17/44 (39%) lacked a NAP6 defined minimum NMBA panel
  - 19/44 (43%) failed to screen all cases for chlorhexidine
  - 21/44 (48%) failed to screen all cases for latex
  - 26/44 (59%) had specialist nurses
  - 18/44 (41%) clinics included an anaesthetist
  - 18/44 (41%) gave immediate information to patients in clinic, and 5/44 (11%) on support groups.
- Diagnostic testing is not harmonised, with marked variability in the NMBA panels used to identify safe alternatives.
- Poor access to services and patient information provision require attention.
- Harmonisation of diagnostic approach is desirable, particularly with regard to a minimum NMBA panel for identification of safe alternatives.
- These baseline data provide a valuable resource for comparision to data collected during the NAP6 project

Introduction

National Guidelines exist for the investigation and management of drug allergy, including in the perioperative setting (Ewan 2010, Harper 2009, NICE 2014). The incidence of perioperative anaesthetic anaphylaxis is uncertain, and access to specialist allergy services in the UK outside of London and the South East of England has been noted to be patchy and poorly harmonised in the approach to diagnosis and management (Finlay 2014). There are also NHS national specialist services definitions for allergy B09 and E09 (NHS Commissioning Board 2013a, NHS Commissioning Board 2013b). This survey of the provision of specialist perioperative allergy centres was conducted as part of NAP6 studying perioperative anaphylaxis. It aims to describe the self-reported provision and practice of specialist allergy services for perioperative anaphylaxis in the UK.

Methods

A SurveyMonkey™ questionnaire to ascertain availability, workload and practice in centres providing the specialist assessment of perioperative allergy in the UK was devised (Appendix 1) and distributed to all potential providers of perioperative allergy services in the UK. Sixty-five potential providers were contacted through triangulation of clinic lists from the British Society for Clinical Immunology and Allergy (BSACI), the British Society for Immunology (BSI), Allergy UK, the Anaphylaxis Campaign, Royal Colleges of Pathologists and Physicians and the professional networks known to the panel and the UK Immunology and Allergy Nursing Group. Of these, 44 separate centres declared such activity, and there are no other known UK specialist clinics with a significant workload who have not responded yet are known to the panel. This survey was distributed between December 2015 and April 2016, and services were asked to provide data relating to the previous 12 months. Where discrepancies or uncertainties were identified in the data, the centres were contacted again for clarification by email.

The SurveyMonkey™ data was exported to a spread sheet for descriptive analysis. No formal statistical analysis was undertaken.

Based on responses, adherence to recommendations derived from the BSACI (Ewan 2010), the Association of Anaesthetists of Great Britain and Ireland (Harper 2009), and the National Institute for Health and Care Excellence CG183 (NICE 2014) guidance was assessed as follows:

National Institute for Health and Care Excellence (NICE) CG183 recommendations (N)

N1 Allergy specialists should give the following written information to people who have undergone specialist drug-allergy investigation:
- N1.1 the diagnosis – whether they had an allergic or non-allergic reaction
- N1.2 the drug name and a description of their reaction
- N1.3 the investigations used to confirm or exclude the diagnosis
- N1.4 drugs or drug classes to avoid in future
- N1.5 any safe alternative drugs that may be used.

N2 Providing information and support to patients:
- N2.1 provide structured written information on person's suspected drug allergy.

British Society for Clinical Immunology and Allergy (BSACI) recommendations (B)

B1 Referral should be made to a major allergy centre with expertise in drug allergy and high throughput of anaesthetic anaphylaxis because of the need for experience in interpreting tests and the serious consequences of diagnostic error.

B2 The centre should be able to investigate all potential causes. This involves a range of drug classes/substances, including:
- B2.1 neuromuscular blocking agents (NMBAs)
- B2.2 intravenous (IV) anaesthetics
- B2.3 antibiotics
- B2.4 opioid analgesics
- B2.5 non-steroidal anti-inflammatory drugs (NSAIDs)
- B2.6 local anaesthetics (LAs)
- B2.7 latex
- B2.8 skin antiseptics (we used chlorhexidine as a surrogate for this).

B3 Investigation should be in a dedicated drug-allergy clinic.

B4 Stepwise investigation is necessary and depends on the likely cause, but a suspected IgE-mediated reaction (eg. NMBAs, IV anaesthetics, antibiotics, latex) requires:
- B4.1 skin testing and
- B4.1 in some cases, drug challenge.

B5 The aim of the investigation should be to identify the cause of anaphylaxis and to recommend a range of drugs/agents likely to be safe for future use.

B6 The allergist is responsible for a detailed report to the referring doctor and GP, and a shorter report and provision of 'medical alert' wording to the patient.

B7 Role of the anaesthetist – Report to Medicines and Healthcare products Regulatory Agency (MHRA).

B8 Role of the allergist.
- B8.1 Identify the cause of the reaction
- B8.2 Identify drugs likely to be safe for future anaesthesia
- B8.3 Provide a written report to referring consultant, copied to GP and surgeon
- B8.4 Provide patient with a brief 'to whom it may concern' letter (listing the above)
- B8.5 Provide patient with an 'Alert' application and the specific wording to be inscribed
- B8.6 Report to MHRA.

B9 The presence of a clinic nurse with specialist allergy experience.

Association of Anaesthetists of Great Britain and Ireland (AAGBI) recommendations (A)

A1 Cases of anaphylaxis occurring during anaesthesia should be reported to the Medicines Control Agency (Note: MHRA has now superseded the Medicines Control Agency (MCA)).

We arbitrarily defined 'larger' adult centres as those seeing ≥20 patients referred for investigation of perioperative hypersensitivity per year, and 'smaller' centres as those seeing <20, to examine whether there were any differences in the services provided that clearly correlated with workload for standard B1.

Some of the text of the guideline recommendations above are open to interpretation. The guidelines state that the clinic should be able to investigate all causes, but are not specific about whether testing should occur in all cases to demonstrate lack of sensitisation or detect potential hidden exposure. Therefore, the NAP6 panel agreed that for antiseptics (chlorhexidine in most cases) the compliant clinic would be able to test, but we have also noted where the testing was applied to all, or only selected cases since this is often a hidden allergen. The same approach was used for latex testing. We have noted where centres were able to test to B2.1–2.8 inclusively as evidence of full repertoire testing.

Similarly, where NMBA use was assessed (standard B2.1), the centre was deemed compliant where the ability to test for NMBAs was offered, and we separately assessed if panels of NMBAs included all of the following (the agreed NAP6 minimum NMBA panel (see below) and referenced to standard N1.4, N1.5, B2.1, B5, B8.2).

The 'NAP6 minimum NMBA panel' was defined as: the suspected NMBA, at least one alternative in the same class, inclusion of suxamethonium and rocuronium (to identify a safe agent for rapid sequence induction), and inclusion of atracurium or cisatracurium. If the suspected culprit drug is one of those agents, then the minimum panel would consist of four agents. Vecuronium, pancuronium and mivacurium have either not been available at times during the survey period or are so infrequently used that their use was not deemed mandatory for compliance with the 'NAP6 minimum NMBA panel.'

For MDT related data (mandated in the National Specialist Services Contracts for Allergy B9 and E9) (NHS Commissioning Board 2013a, NHS Commissioning Board 2013b), we defined an MDT as a face-to-face or telephonic/video-conferenced multidisciplinary meeting with at least two medical and/or nursing specialties present. We did not count clinics where two or more specialties were present but where the respondents did not report an MDT in the MDT specific question.

Results

We identified approximately 50 centres providing adult, paediatric or mixed perioperative allergy testing services. The survey was sent to all centres and 47 evaluable responses were received. One respondent submitted no data so was excluded from analysis, and two other services submitted duplicate entries which were excluded, leaving 44 evaluable responses. Eleven services provided paediatric services alone. Adult services were available in 33 centres, of which five also saw a small number of children.

Workload

Sixteen adult centres and two paediatric centres reported actual numbers of patients seen, and other centres estimated activity for the previous twelve months.

Adult Centre Workload

The 33 adult centres evaluated an estimated 1271 adult patients in the previous twelve months. Of these, 21 (64%) investigated ≥20 patients per year (range 21–136, median 57 cases), and twelve (36%) saw <20 (median 10). Eleven (33%) adult centres saw ≥50 patients per year. Ninety per cent (1,149/1,271) of adult cases were investigated in larger centres (>20) and 10% (122/1,237) in smaller centres (<20).

Paediatric Centre Workload

All paediatric centres saw <20 patients per year, with a median of 4 (range 1-9). Fifty-three children were investigated for suspected perioperative anaphylaxis over the previous twelve months; 46 in specialist paediatric centres and seven in the five combined adult/paediatric centres.

Access

Considerable geographical variability in distribution of services is shown in Figure 1.

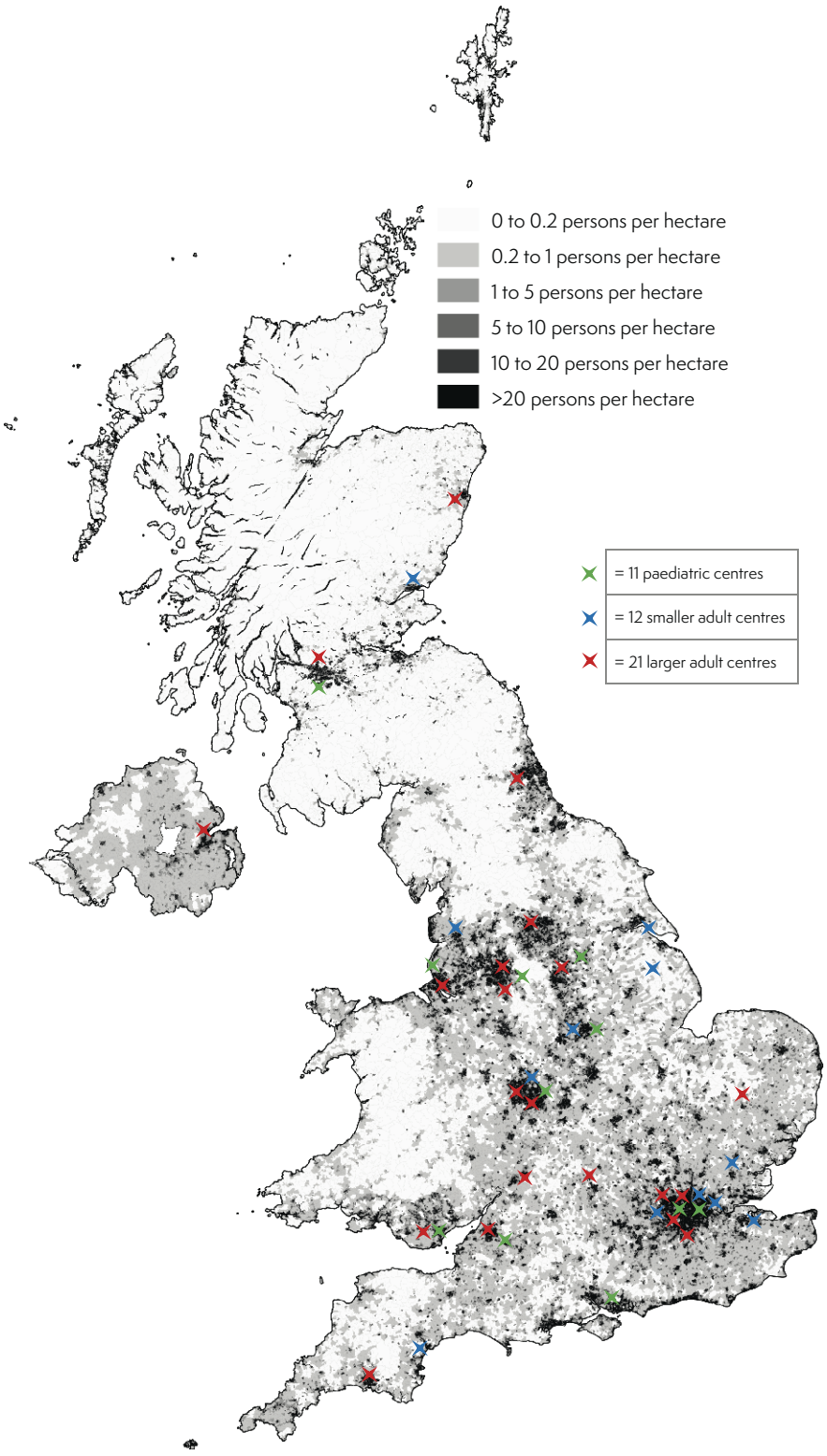
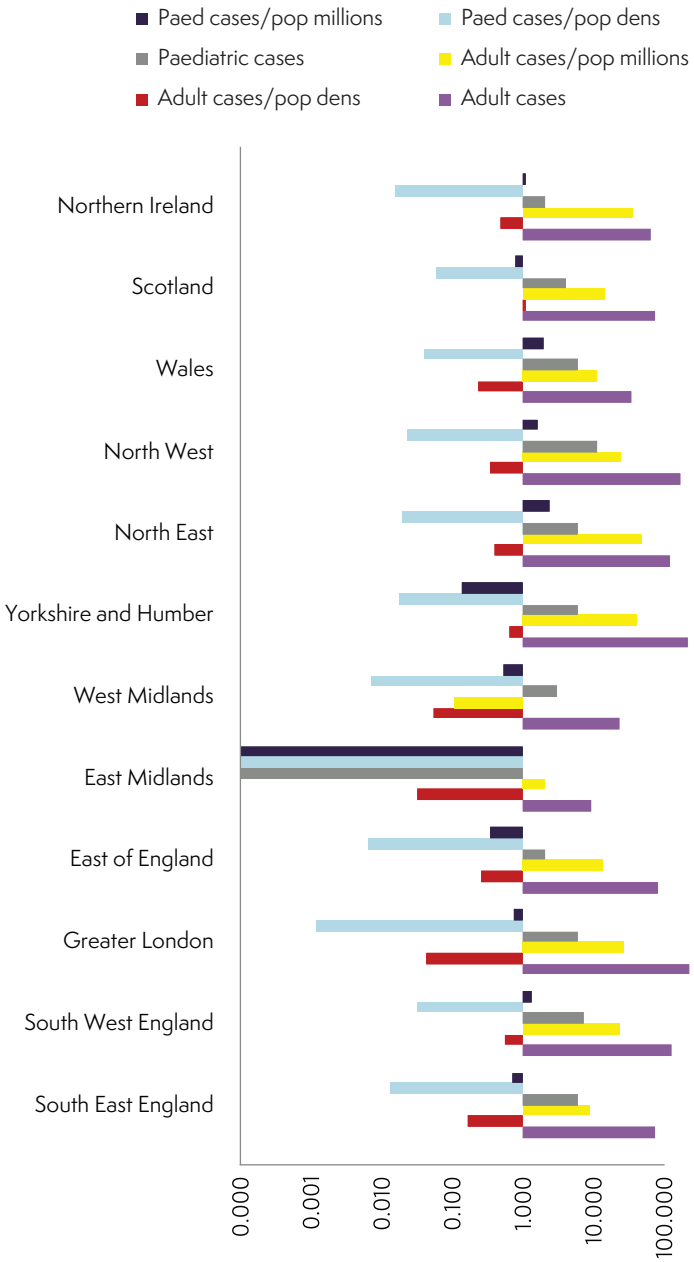


Figure 1a. Geographical distribution of centres providing specialist assessment of perioperative allergy in the UK

This map is modified from https://commons.wikimedia.org/wiki/File%3APopulation_density_UK_2011_census.png By Skate Teir CC BY-SA 3.0 (http://creativecommons.org/licenses/by-sa/3.0) under the GNU Free Document Licence http://www.gnu.org/copyleft/fdl.html The original data is from the ONS: Office for national statistics licensed under the Open Government Licence v3.0

Figure 1b. Regional variation in the number of services and referral patterns related to population size and density
(Note that the longer bars to the left of 1.0 are the smallest values, but to the right are larger values. Case/pop million = survey-reported cases per million of population in the 2011 UK Census data. Case/pop dens = survey-reported cases divided by the population density per km² in the 2011 UK census data.)



Compliance with standards

Compliance with published standards for each aspect of patient care is presented in (Figures 2a–c). Overall the results showed little difference in compliance between larger, smaller or paediatric centres (Figures 2a–c) for most elements, but notable differences in approach to paediatric cases due to a perception of rarity of neuromuscular blocking agent (NMBA) allergy in paediatric cases in some, or a wish to avoid or limit distressing testing (like IDT (intradermal testing)) in most. As a result, few paediatric centres would strictly meet the BSACI standard of investigating all administered drugs or identifying several or a range of (herein assumed to be at least 2) alternatives.

Figure 2a. Clinic adherence to BSACI guidance (%)

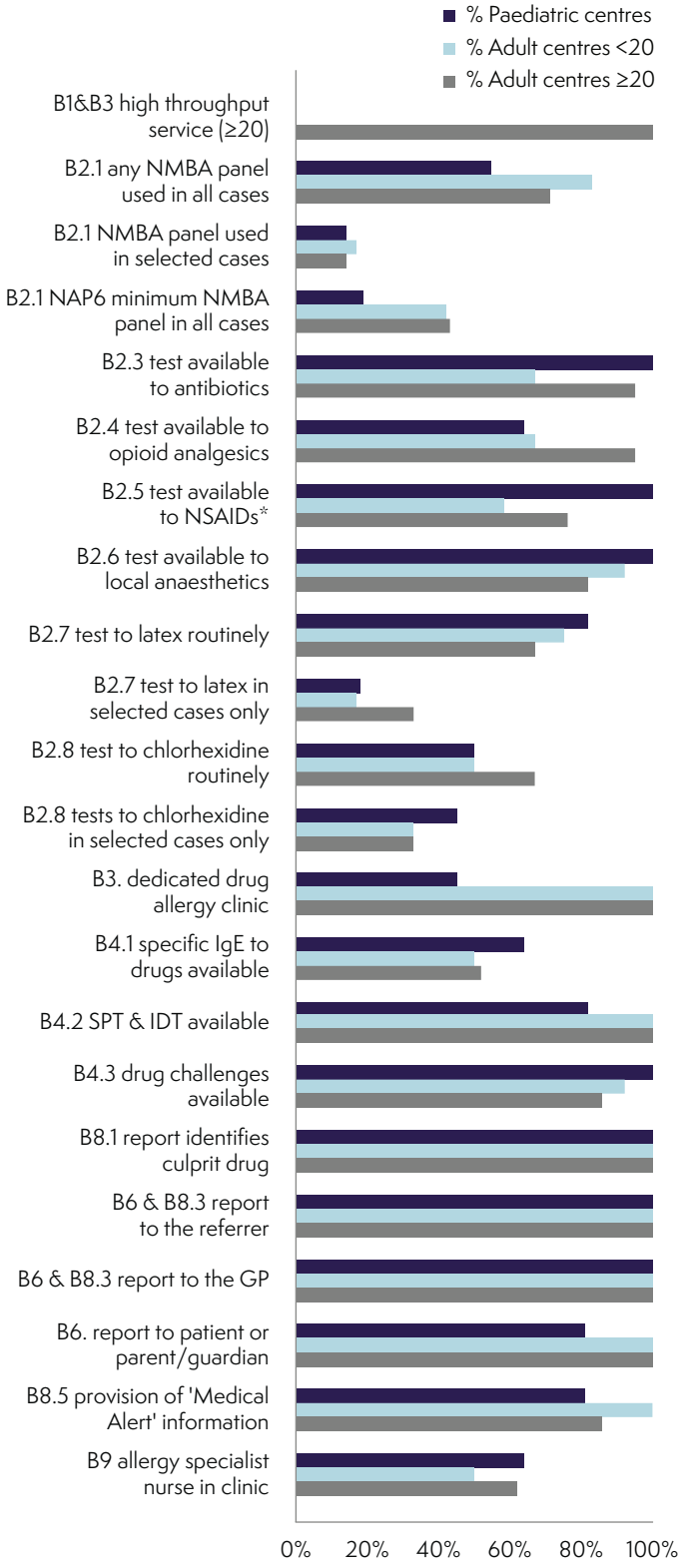


Figure 2b. Adherence to NICE CG 183 and BSACI communication guidance (%)

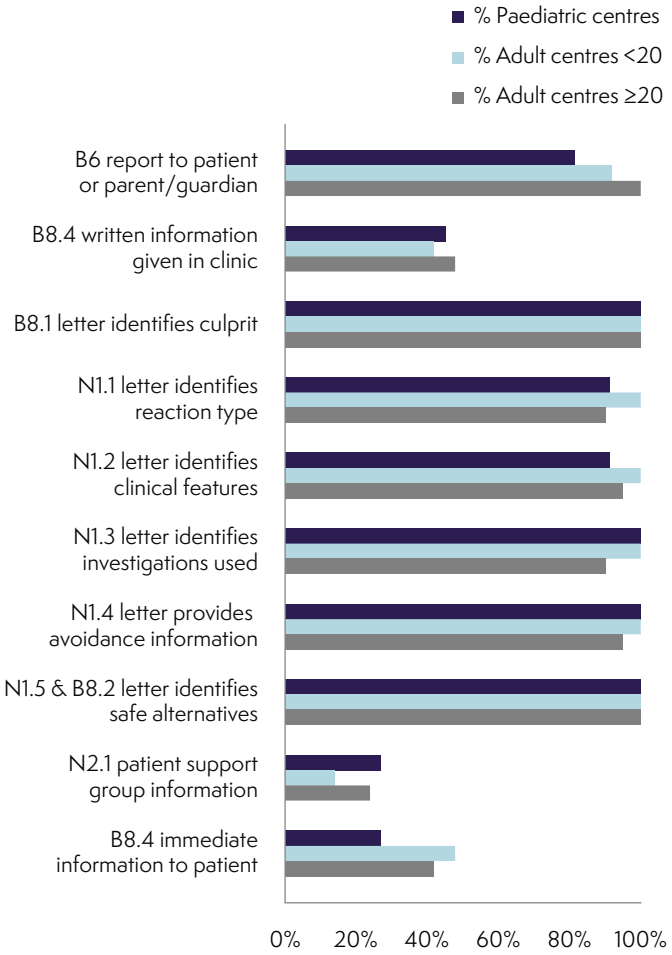
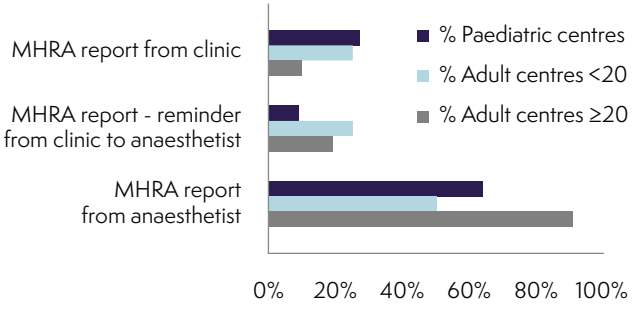


Figure 2c. Compliance with AAGBI guidance on MHRA reporting by clinic and anaesthetist



Figures 2a–c show clinic compliance with the standards assessed. For NMBA compliance we have shown those centres which routinely use a panel in all vs those which use panels in selected cases only; both would be deemed complaint with BSACI guidance as written (since stepwise investigation is allowed). Compliance with NAP6 minimum NMBA panel specification is also shown in contrast to those who routinely use panels. The availability of all routine test modalities – sIgE (specific IgE blood test), SPT (skin prick testing), IDT is also shown, as these are required both for expert allergy centre status and to meet the requirements of BSACI guidance.

Standards with greatest variations in practice were the use of NMBA panels and anaesthetists in paediatric clinics, issuing of written and verbal information at the clinic visit, provision of information on patient support groups, availability of blood testing for drug-specific IgE, routine use of testing to latex or chlorhexidine and direct reporting to MHRA by the clinic.

Waiting times

Waiting times are shown in Figures 3a–c.

Adult centres

Urgent appointments were available to most within five weeks (Figures 3a & b). Most adults were seen within 12 weeks routinely. Two centres breached current national waiting time targets of 18 weeks – both were larger centres.

There were no major differences in waiting times between larger and smaller centres.

Figure 3a. Outpatient waiting times in 12 smaller adult centres

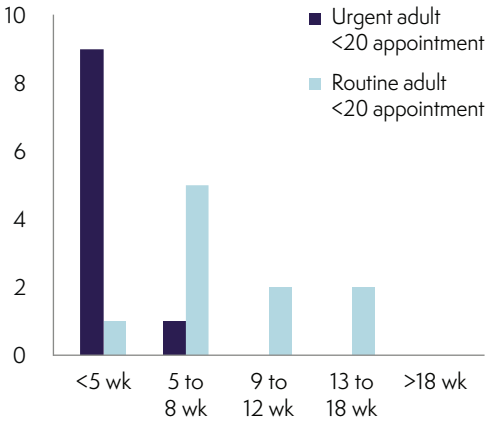
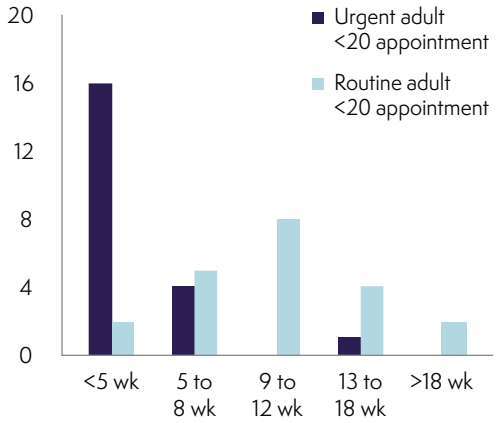


Figure 3b. Outpatient waiting times in 21 larger adult centres

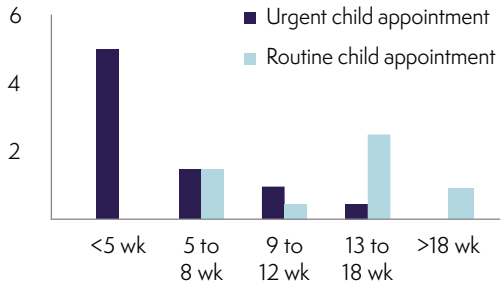


Paediatric centres

Urgent appointments were available to most within eight weeks. Routine paediatric appointment waiting times were longer than adults, with most waiting >13 weeks (Figure 3c).

One centre breached current national targets with a wait of >18 weeks.

Figure 3c. Outpatient waiting times for children in 11 paediatric centres



Staffing and leadership

Leadership

Adult centres

The majority of services (28/33) are led by an allergist or immunologist, with three led by an anaesthetist, one by a respiratory physician and one did not declare a specialty lead.

Of the 21 larger adult centres, 18 were allergist/immunologist-led, and three led by an anaesthetist with drug allergy experience. Of the 12 smaller adult centres, nine are allergist/immunologist-led, one led by an anaesthetist with allergy experience, and one by a respiratory physician experienced in allergy and one did not declare a specialty lead.

Paediatric centres

All eleven centres are led by a paediatric allergist.

Involvement of an anaesthetist

Adult centres

Nine of 21 larger centres and five of 12 smaller centres reported involvement of an allergy-experienced anaesthetist in the clinic. A total of 675/1,271 (53%) adults were seen in a clinic including an allergy-experienced anaesthetist, of whom 626 (93%) were seen in the nine larger centres. Two further centres (both larger centres) had an anaesthetist without extensive anaphylaxis experience and one reported both.

Paediatric centres

One of eleven paediatric centres reported the involvement of an allergy-experienced anaesthetist.

Overall, eighteen of 44 (41%) centres can be deemed to have appropriate anaesthetist involvement.

Involvement of a nurse with drug allergy experience

Sixty per cent of all centres (26/44) had at least one nurse with drug allergy experience.

Adult centres

Thirteen of 21 larger adult and six of twelve smaller adult centres had a drug allergy-experienced nurse.

Paediatric centres

Seven of eleven paediatric centres had a drug allergy-experienced nurse.

Involvement of a pharmacist to prepare drug dilutions

Four centres reported the availability of pharmacy-led drug preparation for clinical investigations; in three larger adult centres and one paediatric centre.

Operation of the service

Adult centres

Face-to-face multi-disciplinary team meetings (MDTs) were more common in larger centres (12/21, 57%) than smaller centres (4/12, 33%). Two centres (one larger, one smaller) had an alternative arrangement to ensure MDT discussion (eg. a telephone MDT before, during or after the clinic). Three larger and one smaller adult centres reported presence of an anaesthetist in clinic, but no formal MDT.

While 55% complied with a face-to-face or telephone MDT, if the presence of two specialties in a clinic is judged to be equivalent to an MDT then overall provision rises to 67%.

Paediatric centres

Five paediatric centres had a face-to-face MDT arrangement (5/11, 45%). Two additional services performed clinics jointly with a paediatric allergist. Only one clinic was staffed by an anaesthetist experienced in drug allergy.

Overall compliance with a face-to-face MDT standard in paediatric clinics was 45% and if the presence of two specialties in a clinic is judged to be equivalent to an MDT then overall compliance rises to 64%.

Clinic assessment

Most adult patients (1,262/1,271, 99%) and all 53 paediatric cases were assessed by face-to-face clinic visits. Some larger centres offered additional remote diagnostic interpretation and triaging of cases. Two larger adult centres reported additional initial laboratory interpretative investigation of acute reactions for 203 patients, some of whom may have subsequently been triaged to face-to-face clinic visits (information not available).

Database

Sixty-four per cent of all centres reported keeping a database of anaesthetic adverse reaction cases: thirteen larger adult centres (62%), eight smaller adult centres (67%) and seven paediatric centres (64%).

Referral pathways

All but one clinic reported that they accept consultant-to-consultant referrals to enable rapid and direct assessment.

Investigations

Considerable variation in practice was revealed both in the repertoire and testing modalities across the survey centres. Centres should be able to investigate all potential culprits in line with the standards above.

Pholcodine testing

Six larger adult centres, one smaller centre and one paediatric centre routinely query pholcodine exposure (8/44, 18%). There is no specific standard for testing against pholcodine, but it would be expected to be part of an expert centre's repertoire.

Chlorhexidine testing

Fifty-seven per cent (25/44) of centres reported testing for chlorhexidine in all cases. A further 16 (36%) reported testing only those with known exposure. Thus, 93% were compliant with the guidance for being able to assess this antiseptic. Compliance is summarised in Figure 2.

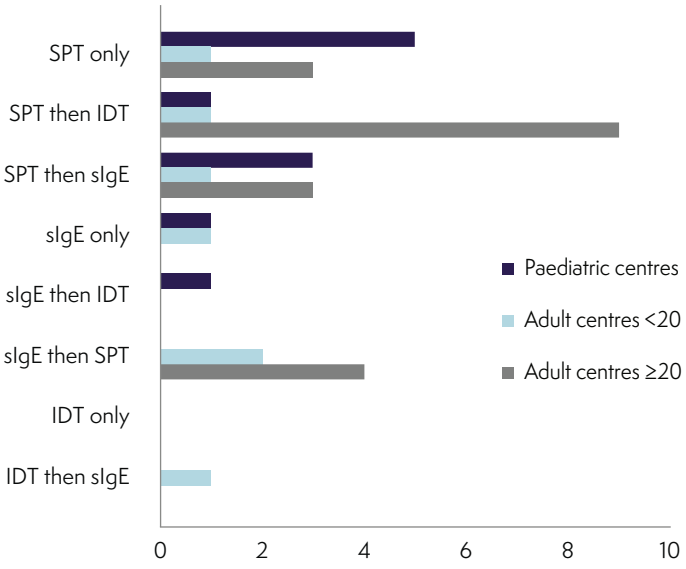
Fourteen (67%) larger adult centres routinely tested for chlorhexidine and seven in selected cases only. Six smaller (50%) adult centres routinely tested for chlorhexidine and four in selected cases only. Five (45%) paediatric centres routinely tested and five only in selected cases.

Reported testing protocols (Figure 4) varied. Skin prick testing (SPT) was the most common first-line test (26/44) followed by serum specific immunoglobulin E (sIgE) (9/44), with intradermal testing (IDT) or sIgE commonly used for second-line testing in adults (IDT was rarely used in children). One centre reported performing chlorhexidine challenges. Nine centres reported the use of chlorhexidine sIgE blood tests as a first-line test (seven of which would then do SPT as a second-line test). Only one larger adult clinic used IDT as a first-line test (with sIgE test as a second-line test).

Latex

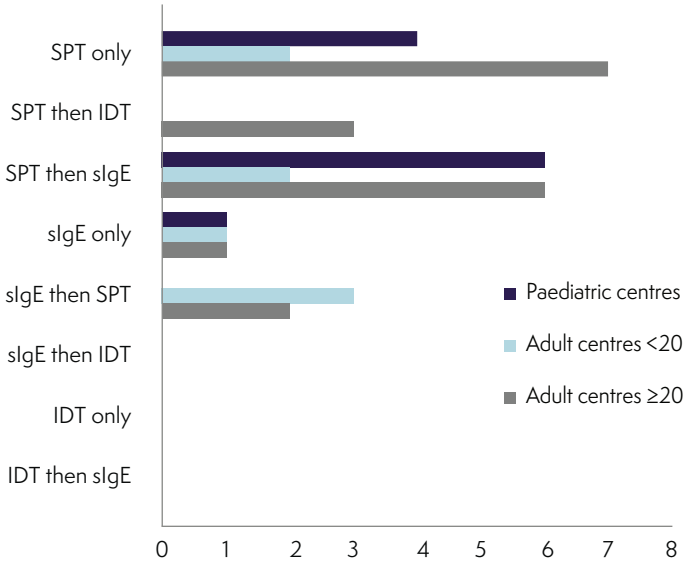
Twenty-three adult centres (14 larger; nine smaller, 70% overall) reported always testing for latex, and nine more in selected cases. SPT was the preferred first test for 20 (16 larger,; four smaller) and sIgE for five (three larger; two smaller) centres. Secondary testing was predominantly sIgE (eight centres) and IDT (three centres). Only larger adult centres used IDT for latex. Compliance is summarised in Figure 2.

Figure 4. Testing sequence for chlorhexidine



Nine of eleven paediatric centres reported that they always test for latex and two in selected cases. Ten reported using SPT as first line testing, six reported using sIgE as a second line test and none reported using IDT. Five apparently only use a single modality of testing (four SPT, one sIgE) (Figure 5).

Figure 5. Testing sequence for latex



Neuromuscular blocking agents (NMBA)

Panel testing and safe identification of alternative NMBA

Practice was highly variable. Compliance is summarised in Figure 2 and Table 1.

Table 1. Comprehensive panels of NMBA are not used in all centres *Any use of an NMBA Panel initially or sequentially. Two additional centres said that cisatracurium would be tested but only where it had been administered at time of the reaction. **Panel including suxamethonium, rocuronium and either atracurium or cisatracurium as defined by NAP6 (see Methods)

Panels which include this drug(s) routinely	Larger adult centres ≥20 n=21 (%)	Smaller adult centres <20 n=12 (%)	Paediatric centres n=11 (%)
Compliant with BSACI NMBA panel*	**13 (62%)**	**5 (43%)**	**2 (18%)**
Compliant with NAP6 minimum NMBA panel**	**9 (43%)**	**5 (43%)**	**2 (18%)**
Atracurium	15 (71%)	10 (83%)	6 (54%)
Cisatracurium*	12 (57%)	5 (42%)	2 (18%)
Mivacurium	10 (48%)	7 (58%)	4 (36%)
Pancuronium	10 (48%)	5 (42%)	3 (27%)
Suxamethonium	14 (67%)	8 (83%)	5 (46%)
Vecuronium	14 (67%)	9 (75%)	5 (46%)
Rocuronium	9 (43%)	4 (33%)	3 (27%)

Adult centres

Most adult centres (32/33) reported using a 'panel' of agents containing many of the routinely available drugs when testing for NMBA allergy (Table 1), but the majority would only do so where the suspected NMBA was positive in initial skin testing. There is no definition of an appropriate panel in existing guidance, but the NAP6 panel agreed a harmonised NAP6 minimum NMBA panel definition to meet the requirement of safe identification of alternative agents (see methods).

Compliance is summarised in Figure 2 and Table 1. Most adult centres initially test to the suspected culprit agent only, and all reported use of a panel of NMBAs, however one specifically would only test to a couple of alternatives rather than the full panel or the NAP6 minimum panel. A small number of larger centres reported that they routinely test extended NMBA panels in all, but most appeared to only use the panel where one of the suspected culprits was positive on initial screening.

Paediatric centres

Five of eleven paediatric centres initially test to the suspected culprit agent only, while six reported use of a limited panel of NMBAs sequentially, of which only two included rocuronium and suxamethonium routinely. However, all would only proceed to use the panel where the initial test was positive, and one centre specifically stated that NMBA was rarely tested in children. Compliance is summarised in Figure 2a.

Suxamethonium was routinely used in panels by five paediatric centres, but another commented that suxamethonium is rarely used in children and is therefore rarely part of the panel (Table 1).

Testing strategies appeared consistent for NMBAs, with most reporting use of SPT first and then IDT if negative; two specified SPT only (Figure 6). Several centres noted the need to minimise distressing IDT testing in children. Few centres used sIgE to thiocholine, suxamethonium, and quaternary ammonium groups. One centre reported using sIgE followed by sequential SPT and IDT.

Drug challenges

No centre performed challenges to NMBAs. Twenty-five of 44 (57%) centres perform challenges to anti-emetics, eleven (25%) to hypnotics, 24 (55%) to anxiolytics, 34 (77%) to NSAIDs, 29 (66%) to opioids, and 41 (93%) to local anaesthetics.

Other challenges on offer include: heparin, latex, chlorhexidine, and paracetamol.

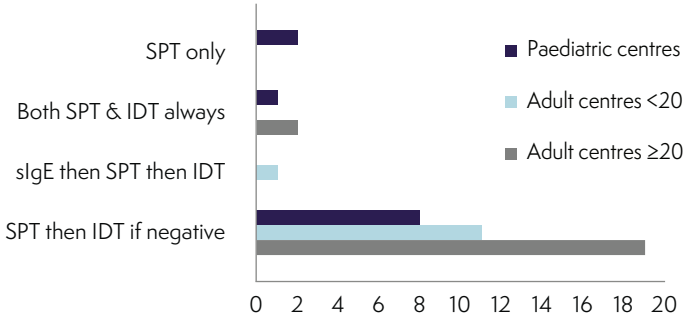
All paediatric centres offered NSAID and local anaesthetic challenges.

Antibiotic challenges

Forty centres (91%) provide antibiotic challenges (20/21 larger adults centres, 8/12 smaller centres, 11/11 paediatric centres).

Waiting times for antibiotic challenges were reported to be under nine weeks for 21/44 (48%), more than three months in 12/43 (28%) of centres and were similar in all types of centre (Figure 7).

Figure 6. Testing sequence for NMBAs



Information

Adherence to relevant guidelines is shown in Figure 2a.

Only half of adult centres give immediate information to the patient (10/21 larger, 5/12 smaller and 3/11 paediatric centres). All centres, however, stated that the patient receives a copy of the clinic letter. Only five of 44 centres (11%) reported giving additional information on patient support groups (two smaller adult centres and three larger ones).

Thirty-nine (89%) centres (19/21 larger adult, 11/12 smaller adult, 9/11 paediatric) issued Medical alert/hazard warning information to the patient.

All adult and paediatric centres sent a clinic letter to the referring clinician, and all also sent this to the general practitioner.

Copy letters to the surgeon where applicable (Figure 2a) were sent by 36 (82%) centres (18/21 larger, 10/11 smaller, 8/11 paediatric centres).

All centres reported that the clinic letter identified the culprit drug when found and all but one identified the nature of the reaction (Figure 2a and 2b). Two (5%) centres did not routinely describe the clinical features of the reaction or the clinical tests performed in the clinic letters (Figure 2b).

All adult clinic centres reported identifying the drugs or drug groups to avoid and suitable alternatives.

Only six centres reported that they provide details of the alternative diagnosis where IgE-mediated allergy was excluded (Figure 2b).

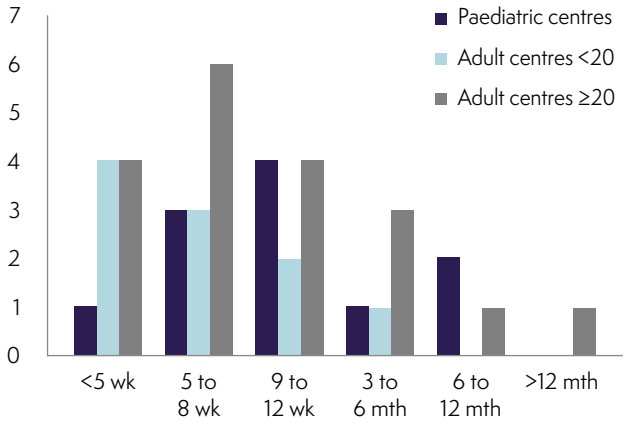
Medicines and Healthcare products Regulatory Agency (MHRA) reporting

Eleven (25%) centres overall (5/21 larger adult, 3/12 smaller adult and 3/11 paediatric) reported directly to MHRA, the rest relying on the referring clinician to do this (Figure 2c).

Discussion

This is the first UK survey of specialist allergy centres evaluating perioperative anaphylaxis and provides important information on the availability and self-reported practice in these services, prior to NAP6 case data collection. Where possible, practice has been mapped to UK recommendations (Ewan 2010, Harper 2009, NICE 2014). Most activity occurred in adult centres, but we do not know if this reflects differences in adult or paediatric referral patterns or incidence of anaphylaxis or surgery. Future analysis of cases reported to NAP6 will provide data on this.

Figure 7. Waiting times for antibiotic challenge



Forty-four widely distributed UK centres (33 adult and 11 paediatric) were identified, of which 21 saw more than 20 adult patients per year, but paediatric services were small and inequitably distributed. Two smaller adult centres subsequently ceased providing service in 2017 due to staff retirements (workload approximately 30 patients per annum) and one more may also have ceased operation. There was wide variation in the number of cases seen in each region with respect to total regional population and population density (Figure 1).

London and the Midlands have the greatest concentration of services and, in contrast to many other reports on allergy services, the urban areas of northern England appear to be well served.

Provision of services is limited in Northern Ireland, Wales, Scotland, the East of England, the South West, the South East of England and the West Midlands. Scotland has three adult centres and Wales and Northern Ireland only one each. Wales and Scotland appear to have only one paediatric centre and Northern Ireland none. No services submitted paediatric returns from the South West or East of England.

Paediatric centres and a few larger adult centres reported the greatest problems with access waiting times, and therefore the relationship of staffing and resources appropriate to the workload may need to be explored further. Two thirds of children had to wait more than twelve weeks to be seen, while more than half of adults waited more than eight weeks to be seen, which may impact on test sensitivity. Drug sensitisation to chlorhexidine is known to be transient (Opstrup 2016), so these delays in assessment run the risk of missing important sensitisations and compromising the diagnostic algorithm.

Access to drug challenge services was also poor, with fewer than half the centres able to challenge to antibiotics within eight weeks.

Both BSACI and AAGBI guidance strongly recommend a sufficient workload to maintain expertise and 20 cases was designated by our NAP6 panel to be a reasonable minimum to achieve this (Ewan 2010, Harper 2009). Future guidelines should agree a definition of the minimum workload. Our pragmatic definition enabled a review of compliance with recommendations by workload. Only one third of centres see more than 50 patients each year. No paediatric service saw more than ten cases in a year. Of note, we found no clear evidence that self-reported compliance with published guidance varied markedly between adult centres with larger and smaller workload except for the less frequent use of extended NMBA panels, or between adult and paediatric centres, with the exception of the provision of more limited range of testing in smaller centres and the fact that testing is limited in children to minimise painful investigations like IDT, as well as the perception that NMBA allergy is rare in children. NAP6 minumum NMBA panel use is the exception rather than the rule. Separate paediatric guidance may be needed in future, since most centres would therefore not be adherent to the suggested NAP6 minimum NMBA panel.

The NHS England National Specialist Service Definitions for allergy (B09 and E09) mandate hub and spoke networking, accreditation and working to NICE, BSACI, RCPCH and AAGBI guidance. Smaller clinics and all paediatric clinics might benefit from being part of these governance networks where this is not already the case.

As almost two thirds of centres already keep a record of their cases in a spreadsheet or database (a requirement of the Specialist Allergy Service Specifications), this provides the opportunity to support research in allergy. A minimum dataset could usefully be defined by professional societies. Improved coordination of data collected would offer the opportunity of improved research in specialist allergy.

Adherence to guidelines for testing modalities appears good overall in adults and most services appeared comprehensive in repertoire, consistent with current recommendations. However, there was room for harmonisation of approach to NMBA, latex and chlorhexidine testing, and better patient information. The current guidelines are not very specific regarding minimal acceptable test repertoire and the authors analysed several additional requirements (NAP6 minimum NMBA panel and routinely testing for chlorhexidine) specifically to enable robust evaluation. Future iterations of guidelines should consider being more specific to advance harmonisation of practice.

The purpose of perioperative drug allergy testing is to identify the culprit drug, plus any cross-reacting drugs to which the patient may also be allergic, thereby to identify safe drugs, particularly when several drugs were co-administered. This should enable the centre to provide a list of drugs to avoid, a list of safe alternatives and a list of drugs that have been excluded as the cause of the allergic reaction. Not all centres used harmonised protocols for NMBA and routine testing for chlorhexidine and latex, but paediatric centres may have some valid reasons for differences.

We noted marked variability in the adequacy of the NMBA panels used (Ewan 2010, Harper 2009, NICE 2014) when judged against the NAP6 minimum NMBA panel suggestions and this may raise concerns about adequacy of testing – especially the identification of safe alternative NMBAs for rapid sequence induction of anaesthesia. Most centres reported they would only test an extended panel if the putative culprit was positive, consistent with current guidance, but this may create a risk of failure to identify NMBA allergy through false negative testing should all other culprits be negative, or if the clinical picture was highly suspicious for NMBA allergy. It was not clear if all would proceed to panel testing if the original suspected culprit was negative, but several centres specifically commented that they would do so in those circumstances.

Half of the centres apparently omitted some common drugs (particularly cisatracurium and suxamethonium). This could be a risk to patients, since not testing prevents detection of relevant sensitisations or cross-reactivity to select safe alternatives, or restricts future anaesthetic options for rapid sequence induction. Practice in children may however be different for practical reasons, and separate guidance may be needed.

It is likely that specific guidance on this matter would be of benefit in future for adults too. The NAP6 panel developed a minimum NMBA panel that met the requirements of safe future anaesthesia in all circumstances. Only 20 to 43% of centres met the NAP6 minimum NMBA panel definition. This panel could be considered for future adoption (potential culprit, an NMBA from a different class, and two agents with specific utility: rocuronium and suxamethonium). Auditing and understanding the best diagnostic algorithm will require harmonised practice in future.

Communication with colleagues appears generally good. Communication with patients may be less good. Most centres reported that they were fully compliant with the recommendations of NICE CG183 regarding specific written information, however supply of immediate information to patients, written information to patients and information on patient support groups was incomplete on their returns (Figure 2b).

Reporting of allergy testing results to the MHRA by clinics is rare and this is usually deferred to the anaesthetist (Figure 2c).

While MDT working is not in guidelines it is a national specialist commissioning standard. Only half of the services had a face-to-face MDT to discuss cases. Of concern, anaesthetists were involved in fewer than half of the specialist centres and very rarely in paediatric clinics. Three adult services were led by anaesthetists. Anaesthetists have a key role in detecting non-allergic causes for the clinical presentations, understanding the normal adverse event profile of the drugs given, the confounding effects of polypharmacy and patient co-morbidity, advising on suitable future strategies for anaesthesia and ensuring that all likely causes have been considered (Harper 2009). More anaesthetists with an interest in allergy are needed to promote learning and enhance service quality. Networking arrangements could be used to ensure anaesthetist involvement in MDT case discussions.

The staffing of clinic services was very variable and may not meet specialist service recommendations and guidance. Specialist nurses with allergy experience were missing in 36–50% of clinics. Pharmacist involvement in preparation of drug dilutions for skin tests or challenges was very infrequent, but would be desirable.

Diagnostic testing practice must be harmonised. Definitive and translatable predictive values for any testing strategy or sequence remain unknown. Skin prick testing remains the initial test of choice for most centres, but follow-up testing and the indications to do so are variable. Intradermal testing appears to be under-used in comparison to international recommendations overall (Ewan 2010, Opstrup 2014, Simon 2014) and this was particularly so in paediatric centres.

Chlorhexidine appeared to be under-investigated and not part of routine testing in many centres, in spite of its ubiquitous (and at times unrecognised) presence in the perioperative environment. Despite many publications and a suspicion of increasing prevalence of this potentially hidden allergen, many centres did not screen routinely, although all claimed to assess potential exposures. No guideline explicitly states that chlorhexidine testing is mandatory in the investigation of perioperative anaphylaxis, but the variability in testing and the ubiquity of chlorhexidine make this worthy of consideration. In contrast, latex allergy may be becoming less prevalent, yet is still routinely included by most.

From a patient's and clinician's perspective, variability of care is a concern. Our patient representative authors were concerned about low-volume services that rarely see this type of event, or services that do not have harmonised protocols in place for testing of culprit agents and safe alternatives.

It was reassuring that no major differences were noted that obviously correlated with service size other than breadth of NMBA panel and fewer MDT discussions. However, this survey did not evaluate differences in the diagnostic accuracy or quality of advice provided by centres, more data on this will be available through NAP6 data analysis. Therefore, the recommendations regarding hub and spoke networking to improve harmonisation and quality assurance merit consideration. As recommended in NICE CG183 (NICE 2014), it was noted that consultant-to-consultant referrals remain an important source of referral.

This survey provides an important snapshot of UK provision and practice in perioperative allergy testing before the main phases of NAP6.

References

Ewan 2010: Ewan PW, Dugue P, Mirakian R, Dixon TA, Harper JN, Nasser SM, BSACI guidelines for the investigation of suspected anaphylaxis during general anaesthesia. Clin Exp Allergy 2010;40: 15-31.

Harper 2009: Harper NJ, Dixon T, Dugue P, *et al.*, Suspected anaphylactic reactions associated with anaesthesia. Anaesthesia 2009;64: 199-211.

NICE 2014: CG183 N. Drug Allergy: Diagnosis and Management of Drug Allergy in Adults, Children and Young PeopleNICE: London 2014. https://www.nice.org.uk/guidance/cg183?unlid=34921046120163510161 3 (accessed 8 February 2017).

Finlay 2010: Finlay I, Egner W. Allergy - will we ever meet the unmet need? J R Soc Med 2010; 103: 430-1.

NHS Commissioning Board 2013a: Specialised allergy services (all ages) B09/S/b [internet]. NHS England Specialist Services. 2013 https://www.england.nhs.uk/wp-content/uploads/2013/06/b09-spec-allergy.pdf (accessed 8 February 2017).

NHS Commissioning Board 2013b: Paediatric Medicine: Specialised Allergy services E03/S/j [internet]. NHS England Specialist Services. 2013. https://www.england.nhs.uk/wp-content/uploads/2013/06/e03-paedi-medi-allergy.pdf (accessed 8 February 2017).

Opstrup 2016: Opstrup MS, Poulsen LK, Malling HJ, Jensen BM, Garvey LH. Dynamics of plasma levels of specific IgE in chlorhexidine allergic patients with and without accidental re-exposure. Clin Exp Allergy 2016; 46: 1090-8.

Opstrup 2014: Opstrup MS, Malling HJ, Krøigaard M, *et al.* Standardized testing with chlorhexidine in perioperative allergy--a large single-centre evaluation. Allergy 2014; 69: 1390-6.

Simons 2014: Simons FE, Ardusso LR, Bilo MB, *et al.* International consensus on (ICON) anaphylaxis. World Allergy Organization 2014; 7: 9.

Appendix 1:

The Survey Questions

Q1 Please enter the full name of the hospital Trust where the allergy clinic is situated:

Q2 Please enter the postcode of your Trust:

Q3 Please enter the email address of the person completing the Survey:

Q4 How many cases of suspected perioperative anaphylaxis has your clinic investigated in the past 12 months?

Q5 Is this figure: Estimate or Actual?

Q6 How many cases do you see by each of the methods below?

Please provide the number of cases for each method in the past 12 months:

- Face to face clinic appointment
- Laboratory investigation only
- Other - please specify the method and number of cases

Q7 Is this figure: Estimate or Actual?

Q8 What is the current perioperative allergy clinic waiting time for:

- for CHILDREN
- An URGENT clinic
- A ROUTINE clinic
- for ADULTS
- An URGENT clinic
- A ROUTINE clinic
- Choices
- <5 weeks
- 5-8 weeks
- 9-12 weeks
- 13-18 weeks
- 18 weeks
- N/A (laboratory only service)

Q9 How is your perioperative allergy clinic normally staffed and supported? Please include all staff who are routinely involved in the clinic. Please tick all options that apply:

- Allergist or immunologist in clinic
- Anaesthetist with drug allergy experience in clinic
- Anaesthetist without specific drug allergy experience in clinic
- Nurse with drug allergy experience in clinic
- Pharmacy drug preparation for clinic
- Face to face multidisciplinary team meeting pre/post clinic
- Telephone multidisciplinary team meeting pre/during/post clinic
- Other (please specify)

Q10 Do you have a spreadsheet or database of the cases seen in your suspected perioperative allergy clinic?

- Yes or No

Q11 Do you routinely ask about exposure to pholcodine?

- Yes or No

Q12 Which of these are tested as part of your routine panel for perioperative allergy?

- Chlorhexidine
- Latex
- Other

Frequency?

- Never
- Always
- Selected cases

Initial test

- Skin Prick Test
- Intradermal Skin Test
- Allergen Specific IgE
- N/A

Subsequent test

- Skin Prick Test
- Intradermal Skin Test
- Allergen Specific IgE
- N/A

Q13 When investigating Neuromuscular Blockade (NMB) anaphylaxis, what is your testing pathway?

- Skin Prick Test only
- Intradermal Skin Test only
- Skin prick Test first and Intradermal Skin Test if negative
- Both Skin Prick Test and Intradermal Skin Test, regardless of either result
- Other (please specify)

Q14 Do you test for the suspected culprit only or alternatively a panel of NMBs?

- Culprit (if you select this option please progress to Q16 - please skip Q15)
- Panel (if you select this option please complete Q15 onwards)

Q15 Which of the following drugs are in your panel? Please tick all that apply:

- Atracurium
- Cistatracurium
- Mivacurium
- Pancuronium
- Suxamethonium
- Vecuronium
- Other (please specify)

Q16 Do you provide a challenge testing service for the following? Please tick all that apply:

- Antibiotic
- Antiemetic
- Hypnotic (excluding benzodiazepines)
- Anxiolytic
- Muscle relaxants
- NSAID
- Opioids
- Local anaesthetic
- Other

Q17 If an antibiotic is suspected and initial tests are negative, what is the average additional time to complete the challenge testing?

- Less than 5 weeks
- 5-8 weeks
- 9-12 weeks
- 3-6 months
- 6-12 months
- Greater than 12 months

Q18 What information do you provide to the PATIENT following the assessment and diagnosis of perioperative anaphylaxis? Please tick all that apply:

- Immediate written information
- Information regarding patient support groups
- Clinic letter
- Written information as per NICE guidance (NICE GC183 – https://www.nice.org.uk/guidance/cg183)
- Medical alert application
- Other (please specify)

Q19 What information do you provide to REFERRERS/OTHERS following the assessment and diagnosis of perioperative anaphylaxis? Please tick all that apply:

- Clinic letter to referrer
- Clinic letter to GP
- Clinic letter to Surgeon (if applicable)
- Other (please specify)

Q20 What information do you include in the clinic letter/ documentation to the referrer and patient? Please tick all that apply:

- Name of culprit agent
- Nature of reaction (allergic versus non-allergic)
- Clinical features of reaction
- Details of tests performed
- Drugs/groups to avoid
- Suitable/safer alternatives
- Details if allergy excluded
- Other (please specify)

Q21 Reporting to the MHRA – who does this?

- Us – the suspected perioperative anaphylaxis clinic
- The referrer/anaesthetist – we remind them to do it
- Not us – we leave this at the discretion of the referrer/ anaesthetist involved at the event

Q22 Do you accept consultant to consultant referrals for perioperative anaphylaxis?

- Yes
- No, referral must come from GP