1. Introduction

Anaphylaxis is a severe, life-threatening, generalized or systemic hypersensitivity reaction. Anaphylaxis may be divided into ‘allergic anaphylaxis’ and non-allergic anaphylaxis’. The clinical features of allergic and non-allergic anaphylaxis may be identical.

Antibiotics are the most common trigger for anaphylaxis, followed by muscle relaxants, chlorhexidine and Patent Blue dye.

The severity-grading of hypersensitivity reactions depends on signs and symptoms. Minor or moderate reactions (Grade 1 and Grade 2) are correctly termed ‘hypersensitivity’, and should not be called ‘anaphylaxis’ as only Grade 3, 4 and 5 hypersensitivity can correctly be termed anaphylaxis.

Grade 1: is characterized by cutaneous features such as rash, itch or peripheral swelling.

Grade 2: mild hypotension or wheeze (usually not requiring treatment), with or without Grade 1 features.

Grade 3: hypotension or wheeze are severe, and may include airway swelling.

Grade 4: fulfils the requirements for initiating cardiopulmonary resuscitation.

Grade 5: is a fatal reaction.

Perioperative anaphylaxis is a clinical diagnosis, and presenting features may have many other causes that are more frequent than anaphylaxis. Despite this, early recognition and treatment of anaphylaxis during anaesthesia is essential for avoiding harm.
2. Scope

The guidance applies to all anaesthetists who are responsible for the clinical management and/ or care of these patients.

3. Guideline Standards and Procedures

Anaphylaxis is likely when all the following criteria are met:

Sudden onset and rapid progression of symptoms

   Life threatening Airway and/or Breathing and/or Circulation problems,

   HYPOTENSION being the most frequent presenting feature

Skin and/or mucosal changes (flushing, urticarial, angioedema) are uncommon presenting features.

Under Anaesthesia Common Signs include:

- HYPOTENSION
- BRONCHOSPASM

Immediate Management

- Use ABCD approach
- Adrenaline is the mainstay of the treatment of anaphylaxis
- Remove Causative Agent
- Elevate Legs
- CALL FOR HELP AND INVESTIGATION BOX.
- IF SYSTOLIC BLOOD PRESSURE LESS 50mmHG start CRP as ALS guidelines
Anaphylaxis during Anaesthesia
Immediate Management

IF Adult CARDIAC ARREST
Pulseless Electrical Activity, PEA or SBP<50mmHg

- ALS GUIDELINES for non-shockable rhythms.
- 1mg i.V ADRENALINE.
- Start CPR if SBP< 50mmHg.
- Elevate legs. 2L Crystalloids.

DIAGNOSIS
REMOVE

- Unresponsive hypotension or bronchospasm.
- Remove triggers: chlorhexidine, synthetic colloid.
- Stop procedure. Use minimal volatile if GA.

CALL FOR HELP AND ANAPHYLAXIS BOX

AB

- Maintain Airway/100% O2.
- Consider early intubation.
- Delay may lead to complete obstruction.

CIRCULATION

ADULT iV ADRENALINE: 50 mcg 1-2 min
1:10.000 100mcg/ml 0.5 ml.
ADULT IM ADRENALINE: 500mcg
1:1.000 1mg/ml 0.5 ml lateral thigh
PAEDIATRIC iV ADRENALINE: 2-10mcg/kg
1:10.000 100mcg/ml
PAEDIATRIC IM ADRENALINE
1:1.000 1mg/ml
< 6 YEARS 150 mcg (0.15ml)

Rapid iv fluid bolus 20ml/kg
Crystalloids
Elevate legs

Hydrocortisone 200mg iv
PAEDIATRIC 2-4 mg/Kg iv
Anaphylaxis during Anaesthesia

Refractory Management

- Request more help
- Call for Senior help
- May require assistance with fluids

- Triggers removed?
- Chlorhexidine including impregnated CVP.
- Colloids
- Latex remove from theatre

- Monitoring
- Arterial line.
- CVP
- Consider TTE/TOE

RESISTANT HYPOTENSION
- Adrenaline Infusion
- Additional iv fluids 50ml/Kg
- Add second vasopressor
- Consider CVP

Vasopressin: 2 units iv.
Dilute 20units (1ml) in 20ml of NaCl 0.9%.
Consider in patients taking ACE Inhibitors.
Repeat if necessary.

Glucagon 1mg iv. Consider in patients on
Beta-blockers. Repeat dose if necessary at
5min intervals.

Noradrenaline infusion.

RESISTANT BRONCHOSPASM
- Adrenaline Infusion
- Consider tension pneumothorax
- Add alternative bronchodilators

Salbutamol:
- Metered dose inhaler max 12puffs.
- PAEDIATRIC 6 puffs<6Y 12puffs>6Y
- Slow iv 250 mcg.
- PAEDIATRIC DOSE: >2 YEARS 15mcg/Kg iv
  1month-2YEARS 5mcg/Kg iv

Magnesium Sulphate 50% I.V
- 2g during 20min.
- PAEDIATRIC DOSE 50mg/kg iv max 2g over 20min.
Recommendation/ Cautions

- **Treatment**

1- Adrenaline is the primary treatment of anaphylaxis and should be administered immediately if anaphylaxis is suspected. In the perioperative setting this will usually be IV.

2- A rapid IV crystalloid (not colloid) fluid challenge of 20 ml/kg should be given immediately. This should be repeated several times if necessary.

3- If an IV colloid is being administered at the time of the anaphylactic event, it should be discontinued, and the IV administration set replaced.

4- During anaphylaxis with a systolic blood pressure <50 mmHg in adults, even without cardiac arrest, CPR should be started simultaneously with immediate treatment with adrenaline and liberal IV fluid administration.

5- Vasopressin and glucagon for the management of intractable perioperative anaphylaxis should be available within 10 minutes, wherever anaesthesia is administered.

Details of locations are in RARE EMERGENCY DRUGS LOCATIONS CHART WITHIN THEATRES AREAS UHL.

6- Administration of IV vasopressin 2 Units, dilute 20 units (1ml) in 20 ml of Sodium Chloride 0.9%, repeated if necessary, should be considered when hypotension due to perioperative anaphylaxis is refractory.

7- During perioperative anaphylaxis in patients taking beta blockers early administration of IV glucagon 1 mg should be considered, repeated as necessary.

8- A corticosteroid should be administered as part of resuscitation of perioperative anaphylaxis.

9- Chlorphenamine may be given as part of the resuscitation process, but NAP6 found no evidence of either benefit or harm. It may reduce angioedema and urticarial.
10-There remains uncertainty about the benefits or potential harm of administering sugammadex during resuscitation of perioperative anaphylaxis and for management of rocuronium induced anaphylaxis specifically. Clinical trials would provide valuable evidence.

11.-When anaphylaxis occurs following recent insertion of a chlorhexidine coated central venous catheter, this should be removed, and if appropriate replaced with a plain one.

12-Patients with severe anaphylaxis should be admitted to critical care.

13-All patients with suspected anaphylaxis should be closely monitored in PACU/SACU/HDU for a minimum of 6 - 12 hours in case of late deterioration from a biphasic response.

14-Non-essential surgery should not be started after severe perioperative anaphylaxis.

15-Where pulse oximeter saturations fall during anaphylaxis in a patient who has received Patent Blue dye, hypoxia should be assumed to be real. A blood gas sample should be taken, when the patient is stable enough for this.

16-Latex related anaphylaxis – atypical late presentation often occurs 30-60 minutes after contact. This is due to airborne exposure or mucous membrane contact.

17-If an adverse reaction to blood or blood components is suspected, return all components to the laboratory where possible and inform the blood transfusion laboratory as per protocol.

- **Departmental Organization**

-All cases of severe perioperative anaphylaxis, including fatalities, should be discussed with an allergy clinic at the first available opportunity.

-All cases of Grades 3–5 perioperative anaphylaxis should be
presented and discussed at local Morbidity and Mortality meetings for purposes of education and familiarization.

- Operating theatres should have an accessible list of chlorhexidine-containing items. Appropriate alternatives should be available for patients with suspected or confirmed chlorhexidine allergy.

- If administration of Patent Blue dye is planned during surgery, the surgical team should discuss the risk of anaphylaxis as part of the consent process for surgery.

- Investigation of perioperative anaphylaxis should include follow-up, either in hospital or in primary care, to detect adverse sequelae such as new anxiety, impairment of cognition or activities of daily living or deterioration in cardiorespiratory or renal function. The anaesthetic department lead should coordinate this.

Investigations and referral to Allergy Clinic.

ANAESTHETIC ANAPHYLAXIS INVESTIGATION BOX CHECKLIST

Boxes should be in Recovery areas, ICUs, Maternity Suite, MRI, CTscan and Catheter Suite Laboratory.

This pack contains:
1.- Guideline of the management of suspected anaphylaxis during anaesthesia
2.- Details of where to find glucagon and vasopressin with details of doses. Less than 10 minutes away.
3.- Instructions on taking three timed blood samples for mast cell tryptase and forms.
4.- Stickers Anaesthetic Anaphylaxis Check List.
5.- Template for letter to be given to the patient.
6.- Template for letter to be sent to the GP.
7.- Referral form to be sent to the Allergy Clinic.
8.- Urgent surgery management plan.
MAST CELL TRYPTASE

<table>
<thead>
<tr>
<th>MAST CELL TRYPTASE (Blood test) SENT TO IMMUNOLOGY AT</th>
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<tbody>
<tr>
<td>0 hours</td>
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Brown (serum) Bottle: Labelled with times

- It is anaesthetist responsibility to ensure the samples are taken, including 24h sample
- Ensure you date and time the tubes. There is no need to refrigerate the samples.
  - 1st sample as soon as the patient is stable.
  - 2nd sample as close as 1-2 hours as possible after the event. (No more than 6h)
  - 3rd baseline at least 24 hours after the event.
- Phone Immunology (6710) when you have taken the 2nd sample so they expect a group of 3 samples.

COMMUNICATION AND FOLLOW UP
- Record full details of the anaphylaxis and resuscitation in the patient’s medical record.
- Anaesthetic Anaphylaxis Check List Sticker (Investigation box) to be added to patient notes.
- Suspected medication stopped and an alternative prescribed on drug chart.
- Document potential allergens on wristband and drug chart.
- Explain to the patient what has happened as soon as practicable and record your conversation in the medical record. Give the patient the completed Patient Letter (Appendix 2)
- Report the event in Datix System.
- Inform Perioperative Anaphylaxis Lead and Allergy Consultant about suspected/anaphylaxis via Anaphylaxis Anaesthetic Mailbox. (Anaesthanaphylaxis@uhl-tr.nhs.uk)

- Ensure the event is reported to the MHRA though the Yellow Card system and keep a note of the MHRA Reference Number to update with the Allergy Clinic diagnosis. You will need this number for the Allergy Clinic Referral Form.
- Complete all parts of the Allergy Clinic Referral Form (Appendix 1) and send together with photocopies of
anaesthetic record, drug chart and other relevant documentation to Allergy Consultant.

- Inform patient’s GP using **GP letter.** *(Appendix 3)*
- If postponed surgery is urgent, refer to **Urgent Surgery Management Plan.** *(appendix 4)*
- Ensure the patient is followed up for adverse physical and or psychological effects.
- Follow this link for Appendix 1, 2 and 3
  https://www.leicestershospitals.nhs.uk/aboutus/departments-services/allergy/

All patients experiencing suspected perioperative anaphylaxis should be referred for specialist investigation in an allergy clinic. This is the responsibility of the **Consultant Anaesthetist** in charge of the patient at the time of the event, i.e. the consultant anaesthetizing or supervising the case.

Patients should be ideally seen by Allergy Clinic within 6 weeks. The case should be discussed with the allergist prior the appointment.
ANAESTHETIC ANAPHYLAXIS INVESTIGATIONS

1. Document in Medical Notes
2. Anaesthetic Anaphylaxis Check List Sticker.
3. Stop and document suspected medication in drug chart and on wristband.
4. Datix Form.
5. Email Anaesthetic Anaphylaxis Mailbox (Anaesthanaphylaxis@uhl-tr.nhs.uk)
7. Complete all parts of the Allergy Clinic Referral Form and with photocopies of anaesthetic record, and drug chart.

Respiratory Medicine
Dr Nasreen Khan
Glenfield Hospital Leicester 0116 287 1471

8. Explain to patient and complete Patient Letter.
4. Education and Training

All anaesthetists responsible for perioperative care should be trained in recognition and management of perioperative anaphylaxis and relevant local arrangements. Clinical Directors of anaesthetic departments should ensure their anaesthetists have been trained in the management of perioperative anaphylaxis.

5. Monitoring and Audit Criteria

<table>
<thead>
<tr>
<th>Element to be Monitored</th>
<th>Lead</th>
<th>Method</th>
<th>Frequency</th>
<th>Reporting Arrangements</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anaphylaxis events</td>
<td>ITAP Q&amp;S Lead</td>
<td>Datix Incidents and Audits</td>
<td>All Incidents</td>
<td>ITAPS Q&amp;S Board</td>
</tr>
<tr>
<td>Referral Compliance</td>
<td>Anaesthetic Anaphylaxis Lead</td>
<td>Email to Anaesthetic Anaphylaxis Mailbox and Allergy Clinic Follow Up</td>
<td>Every 6 months</td>
<td>ITAPS Q&amp;S Board and Immunology Lead</td>
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</tbody>
</table>

6. Supporting References


- AAGBI resources Allergies and Anaphylaxis where you can find NAP 6 report, Quick Reference Handbook Card, link to the yellow card, and link to British Society of Allergists and Clinic Immunologists in the UK. https://www.aagbi.org/safety/allergies-and-anaphylaxis


- Australian and New Zealand College of Anaesthetists (ANZCA) and Australian and New Zealand Anaesthetic Allergy Group (ANZAAG). Perioperative Anaphylaxis Management Guidelines.

7. **Key Words**

Anaesthetic anaphylaxis; perioperative anaphylaxis; suspected adverse drug reaction; drug allergy; suspected drug allergy; mast cell tryptase, NAP 6.

8.

<table>
<thead>
<tr>
<th>CONTACT AND REVIEW DETAILS</th>
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<tbody>
<tr>
<td><strong>Guideline Lead (Name and Title)</strong></td>
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<tr>
<td>Patricia Romero, Consultant Anaesthetist</td>
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<tr>
<td>Prea Ramasamy, Consultant Anaesthetist</td>
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| **Date of Next Review by Approval Committee:** | **Details of Changes made during review:** |
| April 2022 | Anaesthesia anaphylaxis investigation pack. |
| | -IV crystalloid 20 ml/kg repeated. |
| | -CPR if systolic BP<50mmHg(adults). |
| | -Vasopressin 2 units in refractory hypotension, repeat PRN. |
| | -Early glucagon 1mg in beta-blocked patients, repeat PRN. |
| | -Harmonization of clinic diagnostic pathways. |
| | -Links provided for better accessibility to Appendix documents |
| | - Mailbox for anaesthetic anaphylaxis |
Patient details
Name............................................................................................................................................
Date of birth .../.../...... Hospital / NHS Number .........................................................
Address ..............................................................................................................................................
........................................................................................................................................................... Telephone .................................................................

Referring consultant anaesthetist (for clinic correspondence)
Name............................................................................................................................................
Address..............................................................................................................................................
........................................................................................................................................................... Telephone.............................................. Secure Email .................................................................

Patient's GP (for clinic correspondence)
Name............................................................................................................................................
Address..............................................................................................................................................
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Surgeon (for clinic correspondence)
Name............................................................................................................................................
Address..............................................................................................................................................
........................................................................................................................................................... Telephone.............................................. Secure Email .................................................................

Date of the reaction...../...../20....
Time of onset of Clinical Features ....../.....h (24h clock)

Suspected cause of the reaction (most likely first)
1) ........................................ 2) ........................................ 3) ........................................

Proposed surgical or other procedure: .............................................................................................
Was surgery/procedure completed? Yes □ No □
If ‘no’, has another date for surgery being scheduled? Yes □ No □
Urgency/Date of future surgery...........................................................................................................
**TIMELINE 1:** Drugs administered in the hour before the reaction. Please include any other relevant exposures, e.g. chlorhexidine, iv colloids, Patent Blue dye.

<table>
<thead>
<tr>
<th>Drugs and other exposures</th>
<th>Time [24 hour clock]</th>
<th>Route of drug administration</th>
<th>Comments</th>
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Please continue on a separate page if you need to add more details.

**TIMELINE 2:** Clinical features of the reaction and other relevant events. Please include lowest BP, SpO2 and expired CO2.

<table>
<thead>
<tr>
<th>Clinical Features and Events</th>
<th>Time [24 hour clock]</th>
<th>Comments</th>
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Neuraxial blockade

Spinal □   Epidural □   Epi-spinal □

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<thead>
<tr>
<th>Drug/Procedure</th>
<th>Time (24 hr clock)</th>
<th>Route</th>
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Peripheral nerve/regional block

Type of block(s) ........................................

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<th>Drug</th>
<th>Time (24 hr clock)</th>
<th>Route</th>
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Latex free environment? Yes □ No □

Chlorhexidine skin prep (by anaesthetist) Yes □ No □ Time(s) ...............

Chlorhexidine skin prep (by surgeon) Yes □ No □ Time .........................

Chlorhexidine medical lubricant gel Yes □ No □ Time ...........................

Chlorhexidine-coated intravascular catheter Yes □ No □ Time ..........................

**TIMELINE 3: Drugs and IV fluids given to treat the reaction**

<table>
<thead>
<tr>
<th>Drug /IV fluid</th>
<th>Time (24 hour clock)</th>
<th>Route</th>
<th>Comments on response to treatment</th>
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**CPR REQUIRED?**  Yes ☐  No ☐  Time started ....../......h (24h clock)
**Duration of CPR (minutes) ..............**

**ADVERSE SEQUELAE from this reaction e.g. cardiac, renal, neurological, respiratory, anxiety**


**Investigations performed prior to referral (please give results)**

N.B. It is the anaesthetist’s responsibility to obtain the results from the laboratory

Were blood samples taken for Mast Cell Tryptase?  Yes ☐  No ☐
First MCT sample  Time___:__  Date__/__/____ Result............................
Second MCT sample  Time___:__  Date__/__/____ Result............................
Third MCT sample  Time___:__  Date__/__/____ Result............................
Other bloods tests:
Test:..............................  Time___:__  Date__/__/____ Result............................
Test:..............................  Time___:__  Date__/__/____ Result............................
Case discussed at a multidisciplinary meeting?  Yes ☐  No ☐
Reported to the MHRA  Yes ☐  No ☐
By whom? ...........................................  MHRA Reference Number ...........................................

**Please send the completed form to the allergy clinic together with:**

- Photocopy of the anaesthetic record and any previous anaesthetic records
- Photocopy of the prescription record if relevant
- Photocopy of relevant recovery-room documentation
- Photocopy of relevant ward documentation

Please file a copy of this form in the patient’s casenotes
LETTER TO THE PATIENT FOLLOWING PERIOPERATIVE ANAPHYLAXIS

Date: 
Patient’s name: 
Patient’s address: 
Hospital Number: 
NHS Number: 
Planned Procedure: 
Consultant Surgeon: 
Consultant Anaesthetist: 

Dear 

You had a suspected severe allergic reaction (anaphylaxis) during anaesthesia on 
To find out the cause of the reaction I will refer you to the anaesthetic allergy clinic at: 

Dr. Nasreen Khan 
Respiratory Consultant  Allergy Clinic 
Glenfield Hospital Leicester 0116 287 1471 

They will contact you with an appointment – this normally takes a few weeks. 

- If you have not heard in six weeks or if you have any queries please contact me (details below).

- It is important you attend the allergy clinic to prevent a further severe allergic reaction.

Until you have attended the allergy clinic, you should avoid all drugs and other potential causes you were exposed to the hour prior the allergy reaction. These include:

  - Latex
  - Chlorhexidine, including medical, dental and household products
  - Anaesthetics drugs (specify)
  - Antibiotics (specify)
  - Analgesics (specify)
  - Other drugs (specify)

It is important that you show this letter if you have any medical appointments between now and the time of your clinic appointment. I will write to your GP with this information. 
LETTER TO THE PATIENT’S GP FOLLOWING PERIOPERATIVE ANAPHYLAXIS

Date:

GP’S name and Address:

Dear Dr

Your patient:
Address:
Hospital Number:
NHS Number:
Planned Procedure:
Consultant Surgeon:
Consultant Anaesthetist:

**Had a suspected severe allergic reaction (anaphylaxis) during anaesthesia on**

Your patient has been referred for investigation to the anaesthetic allergy clinic at
Dr Nasreen Khan,
Respiratory Consultant
Allergy Clinic
Glenfield Hospital, Leicester, LE3 9QP
01162871471

Until the patient has attended the allergy clinic, they should avoid all drugs and potential allergens to which they are exposed during the hour prior the allergic reaction. These include:

- Latex
- Chlorhexidine, including medical, dental and household products
- Anaesthetics drugs (specify)
- Antibiotics (specify)
- Analgesics (specify)
- Other drugs (specify)

I have given the patient a letter providing the same information as here.

Yours sincerely,
Urgent surgical intervention after suspected perioperative anaphylaxis and prior to allergy investigations: suggested management.

It is possible to provide a safe anaesthesia in almost every case and unnecessary to postpone surgery.

- It is important to discuss the case with a consultant Allergist or Clinical Immunologist as soon as possible after the suspected anaphylactic event.

- Regional anaesthesia, where practical may be a sensible option to enable avoidance of most drugs suspected to have caused anaphylaxis during previous general anaesthesia.

- If anaesthesia was induced with propofol and general anaesthesia is required, the choice of induction agents include inhalational agents, thiopental, etomidate (non-lipid formulation) and ketamine.

- If tracheal intubation is required and a NMBA is contraindicated:
  - A remifentanil infusion, magnesium sulphate and topical anaesthesia are helpful adjuncts to deep anaesthesia in facilitating laryngoscopy and intubation.
  - Where remifentanil was used in the previous anaesthetic, consider the use of alfentanil.
  - Awake intubation under topical anaesthesia is an alternative

- If local anaesthetics are not contraindicated, sufficient surgical muscle relaxation can usually be provided if necessary with adequate depth of anaesthesia and adjunct neuroaxial block, transversus abdominis blocks, rectus sheath blocks or other peripheral nerve block.
✓ Pre-warn the theatre team beforehand, and be prepared to diagnose and treat anaphylaxis promptly.

✓ Premedication with antihistamines and steroids may reduce the severity of reactions caused by non-specific histamine release but will not prevent anaphylaxis.

**Avoid the following** if administered/exposed during the 60 minutes prior to the suspected anaphylactic event:

- All drugs to which the patient was exposed, with exception of inhalational anaesthetist agents.
- All antibiotics of the same class that was administered (beta lactams; macrolides; fluoroquinolones; aminoglycosides; monobactams; carbapenems). The surgical and anaesthetic team should discuss antibiotic choice with a microbiologist.
- If an NMBA was administered during this period, all NMBAs should be avoided unless it is impossible to do so, due to the risk of cross-sensitivity.
- Chlorhexidine (including chlorhexidine, antiseptic wipes, medical gel and chlorhexidine-coated intravascular lines/catheters)
- IV colloids
- Radiological contract and dyes used for lymph node identification
- Latex.
- Local anaesthetics of the same class.
- Histamine-releasing drugs (morphine and codeine) as the previous reaction may have been due to non-specific histamine release

If past anaesthetic records are not available, in addition to the above:

- Assume that the patient previously received an antibiotic. Antibiotics are the most common cause of perioperative anaphylaxis in the UK. Discuss antibiotic prophylaxis with a microbiologist beforehand.
- Assume that the patient was previously exposed to propofol, morphine, chlorhexidine, latex, IV colloid and NMBA.