University Hospitals of Derby and Burton NHS Foundation Trust

Guideline for Medication Challenge on Paediatric Day Case
Full Clinical Paediatric Guideline – Derby & Burton

Reference no.: CH CLIN G132/Feb 24/v3

Aim and Scope

To give guidance on how to undertake medication challenges in children with possible allergy including immediate or delayed reactions.

Introduction

All drugs have the potential to cause 'adverse drug reactions but not all of these are caused by a drug allergy. A drug allergy is a reaction caused by an immunological reaction. The majority of drug allergies arise from antibiotics, anaesthetic agents and NSAIDS. It can be a challenge just from the clinical history alone to identify whether someone has had an allergic reaction to a medication and so further investigations maybe required.
A drug provocation test (DPT) is considered the gold standard test to confirm or refute the diagnosis of allergy in individuals at low risk of an IgE-mediated type 1 immediate hypersensitivity reaction.

This guideline mainly looks at DPT for antibiotics but the same principles might be applied for other medications. This will be guided by the paediatric allergy team.

Beta Lactam allergy

5.6% of the general population claim to have a penicillin allergy. About 95% of penicillin allergy labels are incurred when tested. True allergic reactions to beta-lactams are less common in children than adults. There are no predisposing risk factors for beta-lactam allergy in children, and only a minority (7-16%) of children with suspected beta-lactam hypersensitivity are found to be allergic following investigation.

Beta-lactam allergy is frequently over-diagnosed and may lead to an increase in health costs and antibiotic resistance. A diagnosis of penicillin allergy increases the risk of MRSA, C.difficile or VRE infections and death; presumably through increased use of alternatives to beta-lactam antibiotics.

True allergic reactions to penicillin are less common in children. Children treated with beta-lactams, particularly those under 4 years of age, frequently develop urticarial or maculopapular skin rashes. These reactions are rarely reproduced with challenge testing. De-labelling provides reassurance that penicillin use is safe in the future. Less than 7% of children react on re-exposure. Reactions, if they develop, are usually mild–moderate and occur 3– 4 days from the start

of the *challenge.*

Risk Stratification

A detailed drug allergy history, including review of prescription records where possible, will allow the clinician to stratify the risk of allergy.

Patients may report symptoms and/or signs:

1. Non- immunological side effects from Beta lactams (see table 1). These patients would be **LOW RISK**. Patients may or may not be suitable depending on the history.
2. Consistent with type 1 (IgE mediated) immediate hypersensitivity or type 4 (t cell mediated) delayed reactions (see table 2). **NOT SUITABLE for DPT.**
3. Entirely in keeping with side effects and other non-allergic phenomena, in whom no allergy testing is indicated (see table 1). However, such patients may require reassurance from a test as proof of tolerance and in this situation, a DPT could be considered.

Conduction of the DPT.

1. Where a child / family reports a reaction to an antibiotic resulting in symptoms in table 1 and there are no exclusion criteria as in table 2, a direct DPT with the **low risk pathway** can be performed.
2. Specific referrals for DPT may come from the allergy team for those with more significant or unclear symptoms. They will request the specific medication (may also be non-beta lactam antibiotic) and the type of DPT (single/graded/prolonged). This might be the **low risk** or **medium risk pathway** and might include a delayed DPT (see below).
3. Written informed consent is required and should be completed prior to the challenge.
4. If the index antibiotic is not unknown, then Amoxcillin should be used.

Table 1: Low Risk Symptoms

- Minor gastro- intestinal symptoms (nausea, abdominal pain, diarrhoea)
- Candidiasis (thrush)
- Minor symptoms unrelated to any form of allergic reaction, for example headache, arthralgia, strange taste in mouth
- Family history of penicillin allergy but without personal history of allergy
- Patient has taken and tolerated the same penicillin subsequent to the index reaction.
- Patient reports “benign” rash * which developed more than 1 h after the first dose of a course of penicillin.
- Patient reports a childhood rash with no other history available.
- Patient/Parent cannot remember what happened during index reaction but was told it was not serious and did not require hospital treatment

*Benign= non-urticarial, non- itchy, non-blistering, short-lived (less than 24 h) and did not require treatment.

Table 2 : Exclusion criteria for a drug challenge (for any drug)

- Rash occurring within 1 h of the first dose of penicillin*.
- Rash lasting more than 24 h and/or affecting more than 10% of body surface.
- Rash associated with blisters, skin peeling, mucosal inflammation (eyes, mouth, genitals), purpura.
- Symptoms suggestive of a type 1 immediate hypersensitivity reaction -, including swelling, urticaria, angioedema, shortness of breath, wheeze, loss of consciousness, or collapse.
- Patients who required hospital treatment and /or adrenaline due to their reaction
- Patients who cannot remember what happened during the index reaction but were told it was serious and/or required medical intervention.
- Severe or uncontrolled asthma or Severe chronic obstructive airways disease
- Severe aortic stenosis
- Patients who, at the time they are being considered for DPT, are acutely unwell or clinically unstable. This includes patients with respiratory and/or cardiac compromise
- Previous penicillin allergy testing which concluded that the patient was allergic to penicillin.

* The exception to this is if the allergy team feel the history is not convincing or unclear.

Examples of reactions

1. Low Risk: A child presents with a recent/historical history of a **mild** maculopapular, **more than one hour** after the dose. A **single dose** challenge is appropriate.

2. Medium Risk: A child presents with **immediate** symptoms at **< 1 hour** post dose,the history is historical and not quantifiable BUT NOT anaphylaxis or severe delayed reaction.

3. High Risk: A child has immediate angioedema, wheeze or other systemic symptoms then skin tests, RASTS and consideration of BAT may be appropriate followed by high risk challenge **OR** significant asthma/chronic urticaria **OR** other co-morbidities.- **(We are not doing these in Derby as yet but this might be considered in the future**)

4. Severe delayed hypersensitivity reactions are never challenged

Location/Type of the challenge

	Single dose DPT	Graded DPT	
Risk level	Low	High	Medium
Location	OP/ward/Daycase	Day Case	
Nurse : patient	1:4	1: 1 consultant present	1:2
Number of doses	Single full dose for age	5	3 split doses
Observation period	1 hour	1 hour post last dose	

Challenge Protocols

1. Low Risk: **Single Dose**: age appropriate dose of the antibiotic given as a single dose.Further doses may be required on discharge depending on the history.

2. Medium Risk: An age appropriate dose of the antibiotic is **divided into three aliquots at 10%, 50 % dose and then remainder** to be given 30 minutes apart. Further doses may be required on discharge depending on the history.

3. High Risk: An allergy consultant may wish to devise a protocol (appendix 1) for an individual child but usually 3-5 doses will be used. Two further total doses are to be taken once a day at home.

Planning the challenge

Antibiotic challenges must be under the care or discussed with an allergy consultant / allergy nurse – **They will let the team know which challenge protocol to use.**

- The parents must be informed, before arrangements made that:
    - Their child will be taking the treatment which they had a reaction to before.
    - There is a chance they may develop a similar reaction.
    - Depending on the protocol, the procedure might give increasing doses to minimise any reaction
    - Family will need to sign a consent form on or before the day of challenge..
- Explain it will need to be postponed if unwell and they will be contacted about the date.

Prior to starting challenge

- Check the child is well. It should NOT go ahead if any upper respiratory symptoms, fever or worsening of asthma.
- Perform examination (including documentation of any underlying eczema) and undertake baseline observations.
- Explain procedure to family and sign consent form if not already done.
- Prescribe emergency drugs as per table below:

Drug	Age	Dose
Adrenaline IM	< 5 years	150 microgram (Jext/Epipen Jr)
	6 - 11 years	300 microgram (Jext/Epipen)
	12 -17 years	500 microgram
Chlorphenamine PO (Piriton)	< 5 years	1mg (12 hourly for <2 years and 4-6 hourly for 2-5 year)
	6 - 11 years	2mg 4-6 hourly
	12 years and older	4mg 4-6 hourly

Procedure of the challenge

- Record the baseline observations.
- Observe for any symptoms for 30 minutes between doses (when applicable).

- Continue if free from symptoms and observations are stable for an hour after the last dose.

Use of Prolonged DPT

- Not all patients will need a prolonged DPT. This is based on the clinical history. Some children will have a reaction up to 7 days after an antibiotic and this needs to be challenged .
- The Allergy team will highlight if the patient needs a prolonged DPT and how long for.

Following the challenge

- If the child completes the antibiotic challenge without a reaction, **if required**, provide them with the appropriate number of doses of antibiotics so they can to assess for delayed reaction from history. Ask allergy consultants if not sure.
- Ask the family to contact Dr Starkey's (86826), Dr Traves/ Sinha secretary (86441) or Dr Goels secretary (Burton EXT 3271) if any reactions after discharge. Give the family a copy of the information sheet (see appendix).
- A discharge letter following the challenge is needed the family and inform the GP with the results of the initial challenge.
- Email to Dr Starkey /Dr Traves/Dr Sinha/Dr Goel once the day case admission and discharge summary are completed, so that they are aware of the challenge and they can update the family following the challenge.
- They will complete a letter to the parents and GP once the course antibiotics has finishedexplaining whether the child still needs to avoid that group of antibiotics.

Appendix 1:

Affix Patient label here

Drug Challenge Documentation

Complete and then fill or scan into notes

Which Antibiotic protocol is the patient having (please tick)

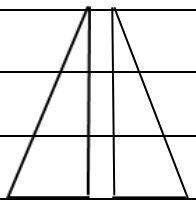
Low Risk: Single Dose: ☐

Medium Risk: An age appropriate dose of the antibiotic is divided into three aliquots at 10% 50% and then remainder to be given 30 minutes apart. ☐

High Risk: An allergy consultant may wish to devise a protocol (appendix 1) for an individualchild but usually 3-5 doses will be used. ☐

1.Day of the antibiotic challenge **DATE:**	
1. Nurse/Doctor assess child fit for antibiotic challenge	
2. Senior Doctor aware of the challenge (to be contacted if concerns/queries : Dr ……..	
3. Baseline observations taken and listen to chest – risk of wheeze and breathing difficulty	

Temp		Pulse	
O2 Sats		Blood Pressure	
Respiration rate		Weight	

2.Assessment prior to antibiotic challenge	
History surrounding antibiotic reaction	
Past medical history	
Known allergies:	Drug History
Patients condition today:	
Examination findings:	
CVS:	Pulse: BP:
Chest 	Wheeze/No wheeze
	Respiration rate
	Any Breathing Problems
Skin	Any rash/urticaria
Oral mucus membranes	
Other Comments:	

Fit for challenge: yes		No		Emergency prescription written: Yes		No		
Parental Consent:Yes		No		Signed: Print name & designation				

3. Emergency Medication **Weight:**

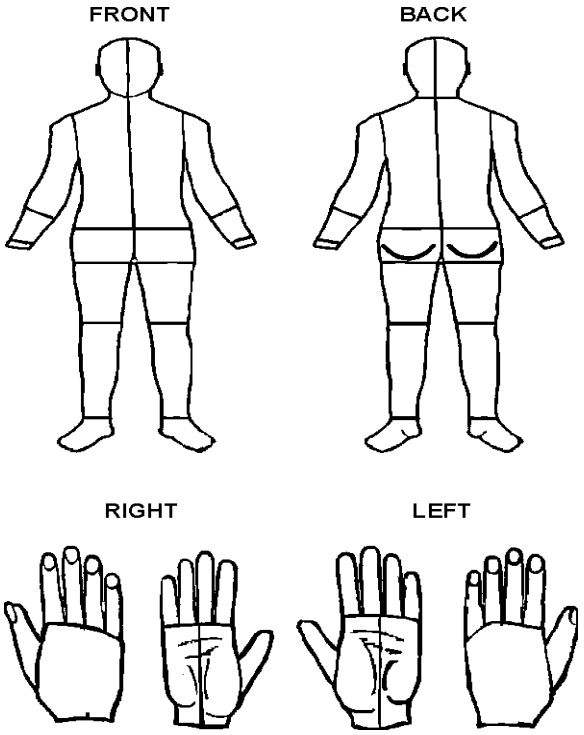
Date	Drug approved Name	Dose	Route	Signature	Given By	Time
	Chlorpheniramine (Piriton) Up to 2 year: 1 mg 2 – 6 years: 1-2 mg 6-12 years: 2 mg 12-18 years: 4 mg		Oral			
	Epinephrine (adrenaline) 1 in1000 Under 6 year: Adrenaline autoinjector 150 micrograms (0.15ml) 2 – 6 years: Adrenline autoinjector 300 micrograms (0.3ml) 6-12 years: 1:1000 Adrenaline IM 500micrograms (0.5ml)		IM			

Carefully read the following instructions before starting the challenge

1. Ensure the details above are completed before commencing the challenge.
2. A Doctor must always be available during the active part of the challenge in case of any medical emergency.
3. The procedure overleaf must be strictly followed.
4. The child can eat and drink normally throughout the challenge as long as they have tolerated if before.

4. Drug Challenge Procedure **Drug being challenged ……**

Time	**Drug:**		**Observations**					
	Fraction	Dose	Time	Pulse	Resp	SaO_2	BP	Comments



Details of any reactions and actions

Document rash on the chart

5. On completion of the challenge					
Result of challenge	**Negative / mild reaction/systemic symptoms**				
Outcome of thechallenge					
Observe 1 hour post challenge			Time left ward		
If passed challenge; are further doses needed ? If so sort		Yes		No	
Is the information sheet given to parents		Yes		No	
Email result to consultant and scan/fill notes		Sent to			
Comments on reactions and actions taken					
Nurse Print Name:		Doctor Print Name			
Signature:		Signature:			
Date:		Date:			

Appendix 2:

Classification of reactions

MILD	Spreading hives or rash. Tingling/ itching mouth Swelling of lips or face Significant itching	If unclear seek advice Stop challenge Given oral antihistamines
SEVERE	Tightness of throat Breathlessness or wheezing Severe dizziness or imminent collapse Abdominal pain/diarrhoea Any difficulty in breathing or swallowing Floppiness Pale, loss of colour Loss of consciousness	Lie child flat and administer IM Adrenaline (Adrenaline Auto-injector ifavailable). Will need to be observed for 6 hours **Call: CRASH TEAM -2222**

Appendix 3:

Resuscitation Council UK

GUIDELINES 2021

Anaphylaxis

Anaphylaxis?

A = Airway **B** = Breathing **C** = Circulation **D** = Disability **E** = Exposure

Diagnosis – look for:

- Sudden onset of Airway and/or Breathing and/or Circulation problems[1]
- And usually skin changes (e.g. itchy rash)

Call for HELP

Call resuscitation team or ambulance

- Remove trigger if possible (e.g. stop any infusion)
- Lie patient flat (with or without legs elevated)
  - A sitting position may make breathing easier
  - If pregnant, lie on left side

Give intramuscular (IM) adrenaline[2]

Inject at **anterolateral aspect** – middle third of the thigh

- Establish airway
- Give high flow oxygen
- Apply monitoring: pulse oximetry, ECG, blood pressure

If no response:

- Repeat IM adrenaline after 5 minutes
- IV fluid bolus[3]

If no improvement in Breathing or Circulation problems[1] despite TWO doses of IM adrenaline:

- Confirm resuscitation team or ambulance has been called
- Follow REFRACTORY ANAPHYLAXIS ALGORITHM

1. Life-threatening problems

Airway
Hoarse voice, stridor

Breathing
↑work of breathing, wheeze, fatigue, cyanosis, SpO_2 <94%

Circulation
Low blood pressure, signs of shock, confusion, reduced consciousness

2. Intramuscular (IM) adrenaline
Use adrenaline at 1 mg/mL (1:1000) concentration

Adult and child >12 years:	500 micrograms IM (0.5 mL)
Child 6–12 years:	300 micrograms IM (0.3 mL)
Child 6 months to 6 years:	150 micrograms IM (0.15 mL)
Child <6 months:	100–150 micrograms IM (0.1–0.15 mL)

The above doses are for IM injection **only**.
Intravenous adrenaline for anaphylaxis to be given **only by experienced specialists** in an appropriate setting.

3. IV fluid challenge
Use crystalloid

Adults:	500–1000 mL
Children:	10 mL/kg

Appendix 4:

University Hospitals of Derby and Burton NHS Foundation Trust

What to do after your child's drug challenge

This leaflet explains what happens now that your child has had an oral medication challenge in hospital. If you have any further questions or concerns, please do not hesitate to contact Dr Traves secretary (01332 786441) or Dr Starkey's Secretary (01332 786826) or Dr Goel secretary (01283 566 333 ext 3271)

1.What medicines has my child had today?

Today (__//__), your child has had a drug challenge to……
……and received a total dose of……

2. What did today show?

Your child did not show any signs or symptoms of an immediate type allergic reaction whilst ondaycase unit today.

3.What happens now?

Depending on the history of your child's reaction , they may need further doses to take home. Your doctor will have decided this and will have been discussed.

In order to capture any signs of a delayed allergic reaction, it is important to take the antibiotic for a **further …… days** at home. Antibiotics will finish on ……/……/….

What happens if my child has an allergic reaction at home?

If any signs of an allergic reaction occur during the next three days at home, such as itching, redness,swelling or a rash, **STOP** the medication and treat with an antihistamine such as chlorphenamine (piriton) or cetirizine as on the medicine packaging.

If you are able, please take some photos of the rash that occurs.

Do not give any more doses of the antibiotic.

Once your child is settled, please call the consultants to report the reaction.

What happens if my child has a more severe allergic reaction?

If your child shows any signs or symptoms of a more severe allergic reaction such as coughing, wheezing, breathlessness, throat tightening or collapse (known as anaphylaxis) **dial 999 for anambulance immediately.**
If your child has ever been issued an adrenaline autoinjector (epipen, Jext or Emerade) for this type of allergicreaction, follow your emergency plan.

References (including any links to NICE Guidance etc.)

1. Savic, et al. BSACI guideline for the set- up of penicillin allergy de-labelling services by non-allergists working in a hospital setting Clin Exp Allergy. 2022;52:1135–1141.

2. Drug allergy (nice.org.uk)

3. Sheffield Guideline , Drug Allergy in children 2020

4. https://bnfc.nice.org.uk/drugs

Documentation Controls

Reference Number CH CLIN G 132	**Version:** V3		**Status** Final	
Version / Amendment History	Version	Date	Author	Reason
	V1	Dec 2021	Dr L Starkey	Review and update
	V3	Feb 2024	Dr L Starkey	
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Training and Dissemination: Cascade the information via BU newsletter and address training				
Development of Guideline: Dr L Starkey Paediatric Consultant				
In Consultation with: Allergy Paediatric Consultants, Pharmacy, Allergy nurse, Sunflower team				
Linked Documents: (Nice guidance/Current national guidelines)				
Keywords: Antibiotic, Daycase				

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