NHS Tayside

Penicillin Allergy, De-labelling and Anaphylaxis

PADL SLWG

December 2023

Learning Outcomes

1. Understand the underpinning principles of allergy, anaphylaxis and Penicillin Allergy De-Labelling (PADL)
2. Demonstrate ability to differentiate between allergies, intolerances and misconceptions by assessing information taken from a drug allergy focused history
3. Identify situations where an antibiotic challenge is safe and clinically appropriate either as inpatient or day case
4. Identify and manage patients who develop anaphylaxis
5. Implement a safe management plan for a patient who has developed anaphylaxis following PADL in the inpatient setting

What is Allergy?

- Allergy is an abnormal immune response to typically innocuous environmental stimuli; examples including foods, venom such as honeybee, wasp, drugs, latex & aeroallergens such as pollen
- Allergic reactions can be:
  - Immediate; IgE-mediated; within 2 hours of exposure
  - Delayed; cellular/T-cell mediated; many hours to weeks later
- Timing of onset of allergic reaction to exposure relate to the manner of exposure and allergen involved. E.g. iv drug should cause reaction within seconds. Oral drug could take 2 hours.
- Allergic reactions typically have classical presenting signs
- Both immediate and delayed reactions can result rarely in life-threatening reactions
- Often the risk of allergy can be determined by a careful history
- The frequency of allergic reactions to drugs is probably over-estimated
- Multiple adverse reactions to drugs can occur that do not have an allergic basis. E.g. GI upset

Penicillin Allergy

- True anaphylactic reactions (which can be fatal) occur in less than 0.05% of treated patients
- General hypersensitivity reactions (e.g. rashes) to penicillin occur in between 1 and 10% of exposed patients
- Mild cutaneous reactions can occur days to weeks after such as rash.
- Symptoms of nausea, vomiting or diarrhoea – likely to be side effects and not true allergy
- Symptoms of side effects such as GI upset can be treated with anti-emetics and/or anti-diarrheals if needed so that appropriate treatment can take place.
- Scottish Antimicrobial Prescribing Group have published on the safety and efficacy of penicillin allergy de-labelling

RESEARCH LETTER

An algorithm for safe de-labelling of antibiotic allergy in adult hospital in-patients

Jacqueline Sneddon, Lesley Cooper ✉, Neil Ritchie, Cathal Steele, Mark Spears, Jo McEwen, Zoey Dempsey, Rebecca Sutherland, Elham Khatamzas, R Andrew Seaton

First published: 02 April 2021 | https://doi.org/10.1111/cea.13878

Safety and efficacy of de-labelling penicillin allergy in adults using direct oral challenge: a systematic review

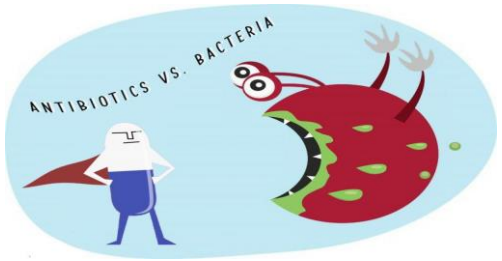
Lesley Cooper ✉, Jenny Harbour, Jacqueline Sneddon, R Andrew Seaton

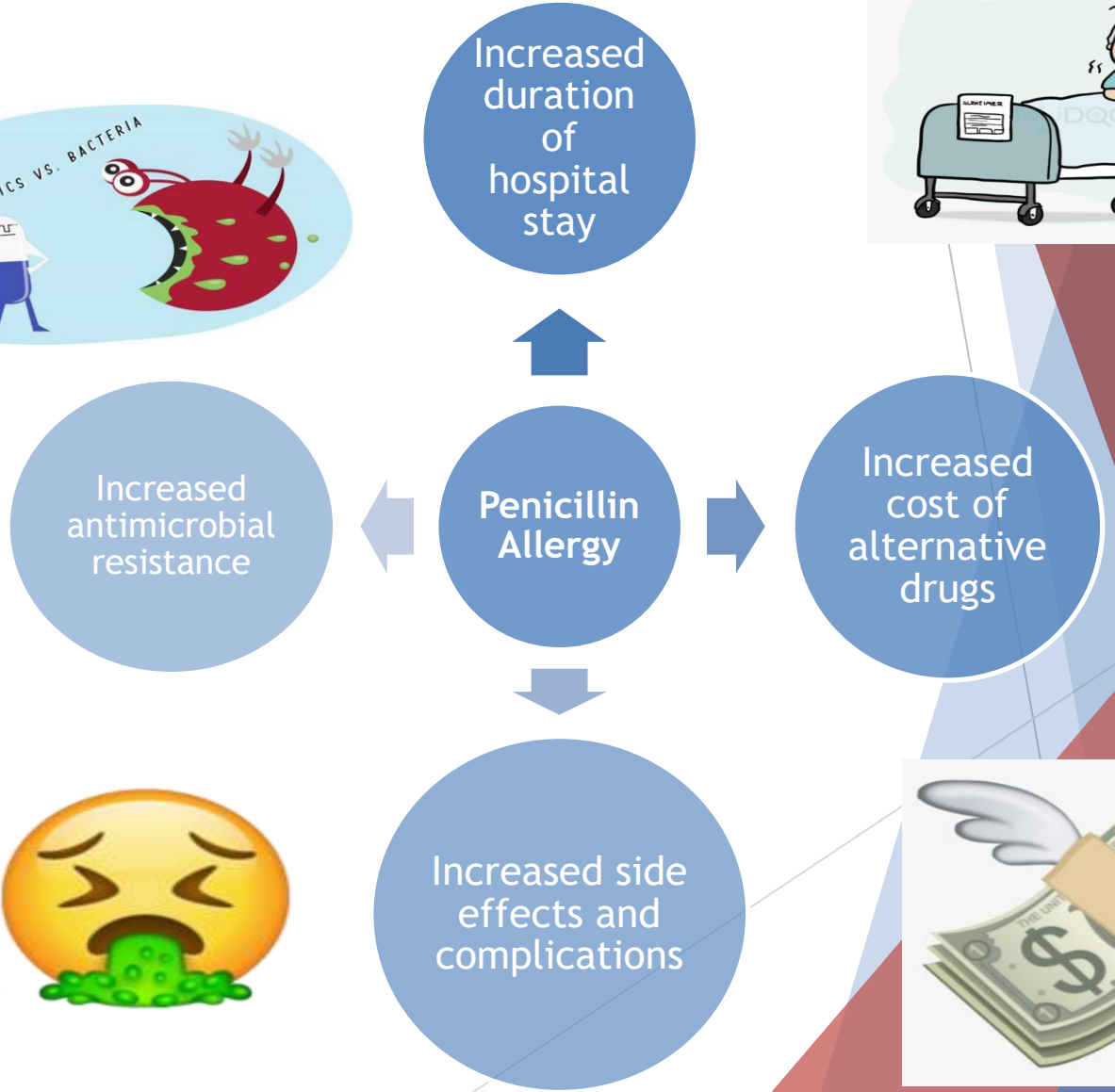
JAC-Antimicrobial Resistance, Volume 3, Issue 1, March 2021, dlaa123, https://doi.org/10.1093/jacamr/dlaa123

Published: 27 January 2021 **Article history** ▾

Why does it matter?

If there was a system of removing false allergy labels, then many of these effects could be avoided





J Hosp Infect. 2020 Sep;106(1):35-42. doi: 10.1016/j.jhin.2020.05.042. Epub 2020 Jun 3.

Impact of penicillin allergy records on antibiotic costs and length of hospital stay: a single-centre observational retrospective cohort

N Powell [1], K Honeyford [2], J Sandoe [3]

J Clin Pathol. 2014 Dec;67(12):1088-92. doi: 10.1136/jclinpath-2014-202438. Epub 2014 Sep 2.

A real-time prospective evaluation of clinical pharmaco-economic impact of diagnostic label of 'penicillin allergy' in a UK teaching hospital

M Li [1], M T Krishna [2], S Razaq [3], D Pillay [1]

3522 excess bed-days (3.87% of annual bed-days)

Excess antibiotic spend of £10,637 (2.61% of annual antibiotic drug spend)

JAMA. 2018 Nov 13;320(18):1846-1848. doi: 10.1001/jama.2018.14358.

Overdiagnosis of Penicillin Allergy Leads to Costly, Inappropriate Treatment

Rita Rubin

Total cost of antibiotics for patients with penicillin allergy 1.82-2.58-fold higher than for first-line antibiotics.

Delabelling 50% of patients would save an estimated £5501 in antibiotic costs and £503,932 through reduced excess bed-days.

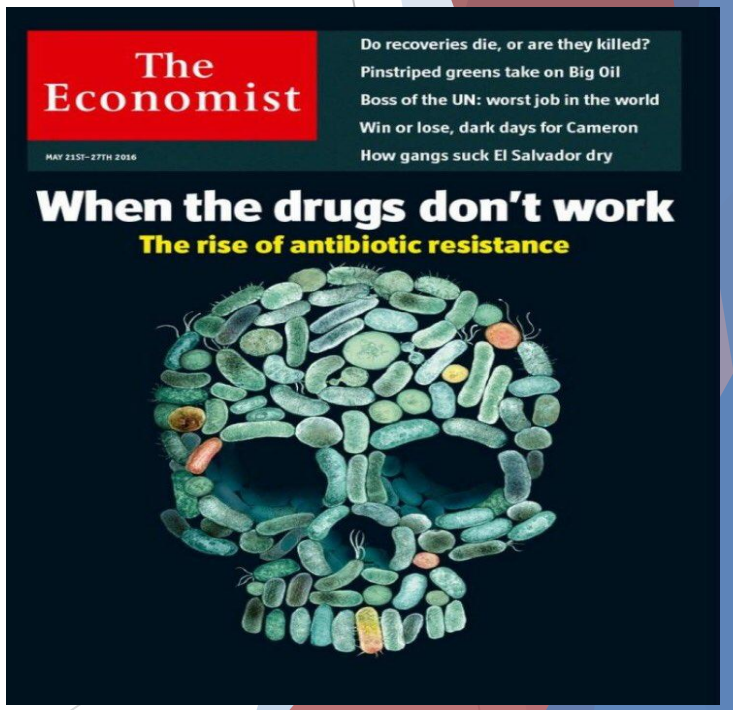
New report calls for urgent action to avert antimicrobial resistance crisis

International organizations unite on critical recommendations to combat drug-resistant infections and prevent staggering number of deaths each year

World Health Organization

AMR will result in 10 million deaths each year by 2050

Current COVID-19 death toll in excess of 6 Million



Currently 700,000 people die/year due to drug resistant diseases

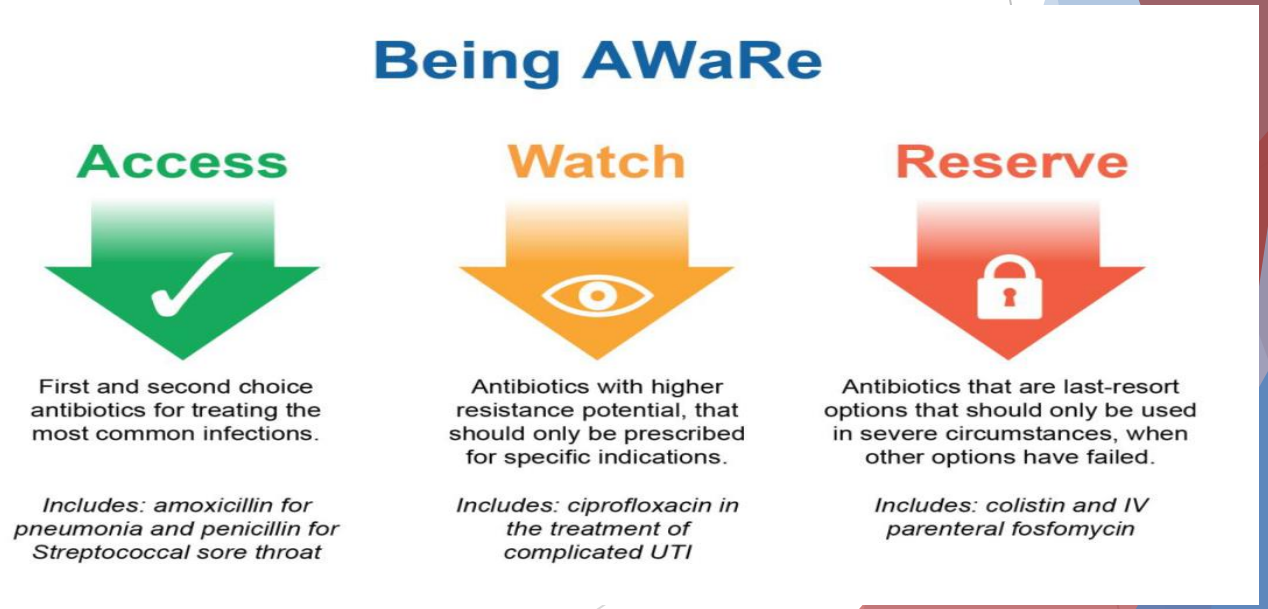
De-labelling wrongly identified penicillin allergies can reduce the resistance occurring

Policy paper

UK 5-year action plan for antimicrobial resistance 2019 to 2024

Ambitions and actions for the next 5 years, supporting the 20-year vision for antimicrobial resistance (AMR).

- The AWaRE list is a Traffic light system for antimicrobials. Many first line treatments such as amoxicillin or flucloxacillin belong to the ACCESS list which should be promoted
- Most alternatives used where there is penicillin allergy belong to either the Watch or Reserve list and are more likely to promote resistance development



Healthcare Improvement Scotland | SAPG

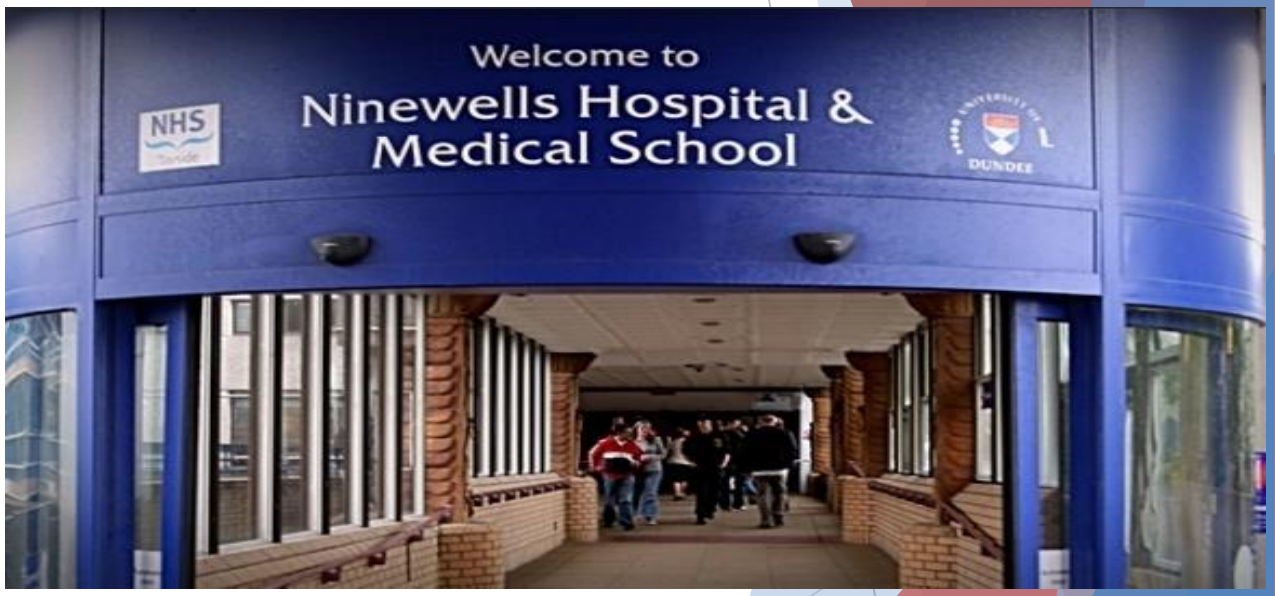
- Multi-professional PADL Steering Group set up in 2018

Purpose of the group was to:

- Explore safety and efficacy of PADL
- Develop PADL toolkit for Board implementation

NHS Tayside PADL Point Prevalence Survey (PPS)

- PPS carried out across 3 receiving units
- 351 patients screened
- 28 patients found to have documented penicillin allergy
- Overall prevalence 7.9%
  - AMU 9.4%
  - ASRU 7.8%
  - Paediatrics 3.5%
- 82% eligible for PADL risk assessment



SAPG PADL Toolkit

- Draws on contemporary evidence
- Risk stratification algorithm developed
- Piloted across 5 Boards
- Intended for use by non-allergy specialists
- Supporting documents available

Healthcare Improvement Scotland | SAPG

About us | Guidance & QI Tools | Publications

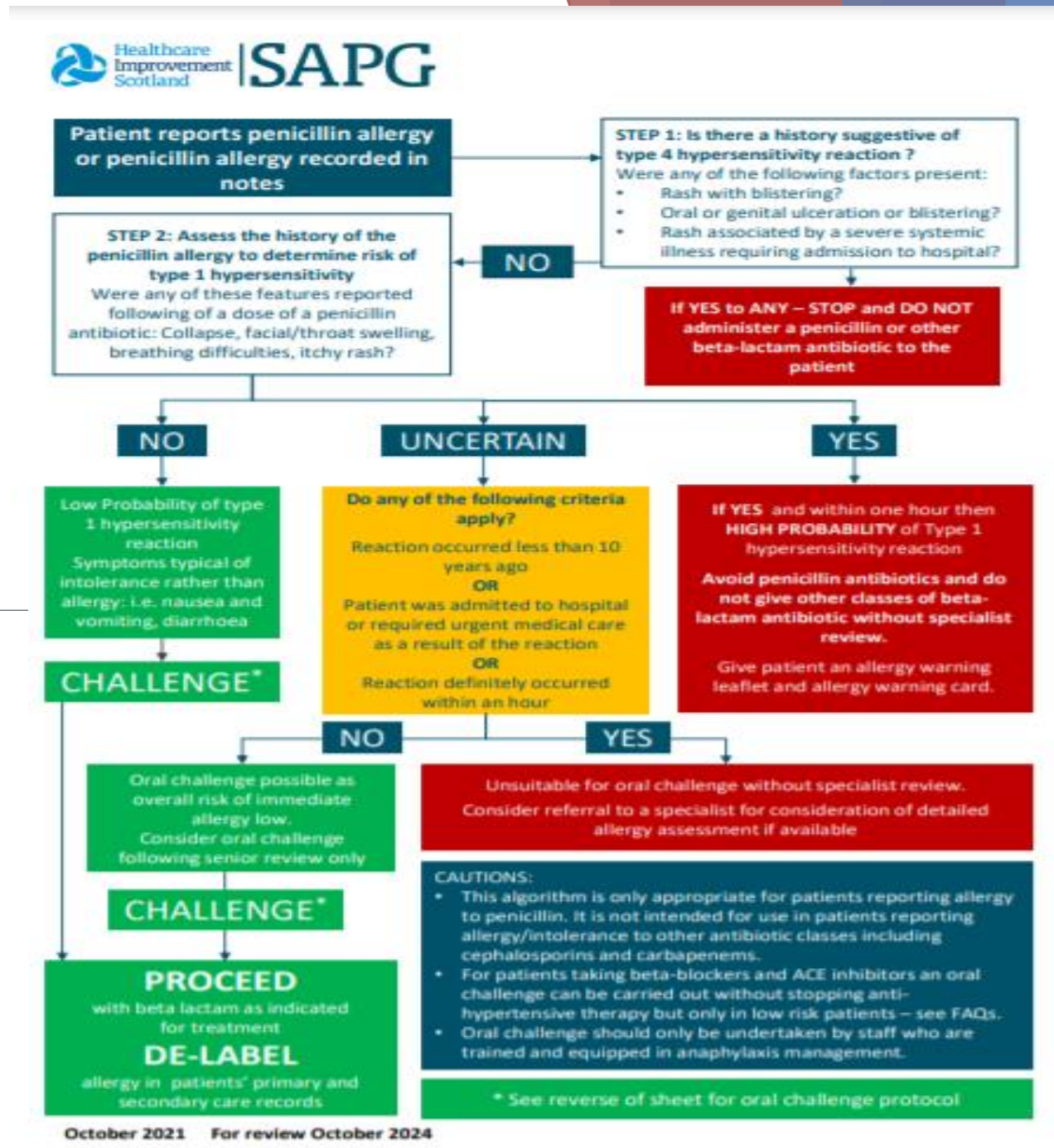
document. All other documents are unchanged.

Resources for clinicians

- Protocol for implementation of penicillin allergy de-labelling in adult patients in acute hospitals (pdf)
- Patient risk allergy algorithm (pdf)
- Management of patients experiencing allergic symptoms (pdf)
- Frequently asked questions to support use of the penicillin allergy de-labelling algorithm and oral challenge test (pdf)
- GP de-labelling letter (positive) (docx)
- GP de-labelling letter (negative) (docx)
- Allergy card front (pdf)
- Allergy card back (pdf)

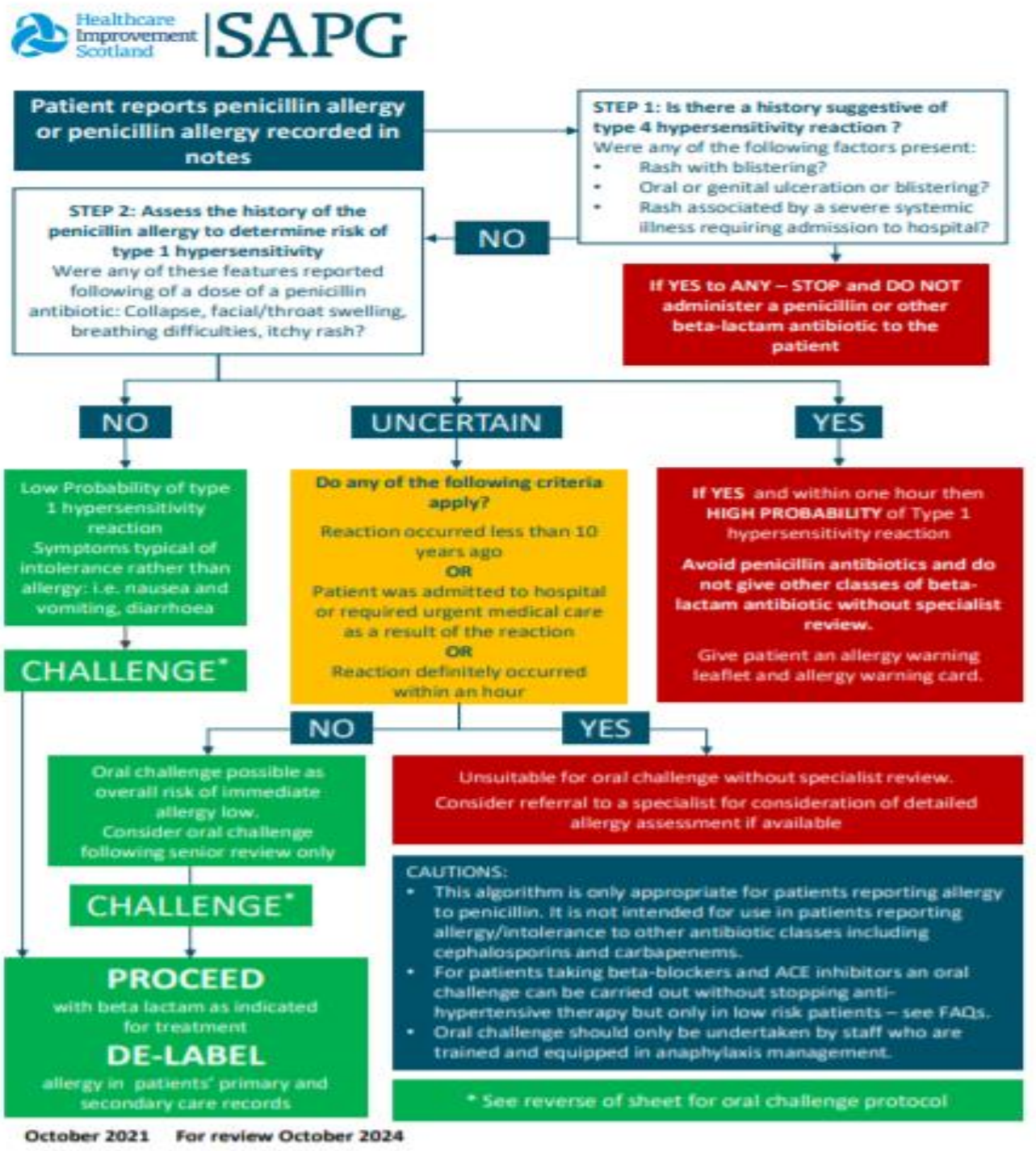
Resources for patients

- Pre test information for patients (pdf)
- Patient permission form to be signed if proceeding with test (docx)
- Patient post test result (positive) (pdf)
- Patient post test results (negative) (pdf)

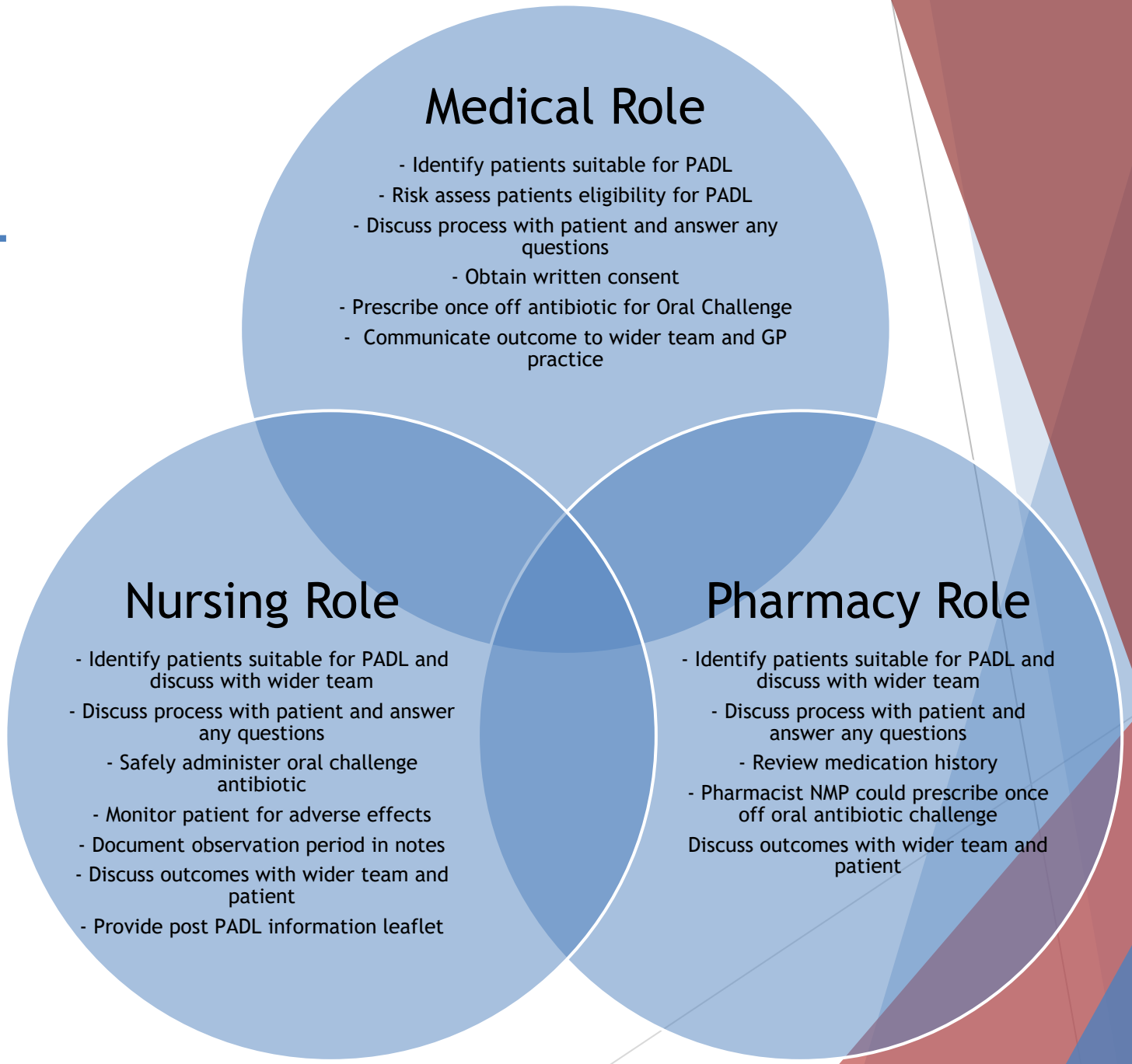


PADL Process

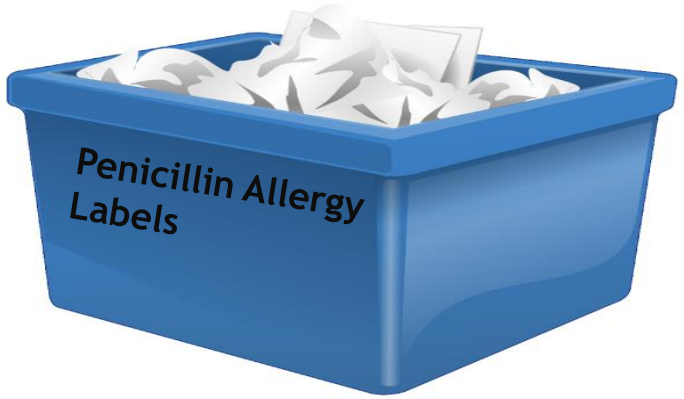
- [PowerPoint Presentation (sapg.scot)]
- PADL SOP and supporting documents accessible on NHS Tayside Antimicrobial website
- Informed written consent must be obtained prior to oral challenge



Multidisciplinary Approach to PADL



Ways to Communicate PADL to Primary Care



Op Comms Form in Clinical Portal

Diagnosis and comments.

Provisional Diagnosis *

Comments/ Recommendations

Follow up by clinic required? * No

Specific Monitoring Required? * No

Recommended treatment Clear Add Row

Medication	Dose	Frequency	Indication	Duration

Medication discontinued.

Is any medication to be discontinued? * No

Further comments.

Any further comment or recommendation? * No

Electronic Discharge Form

Allergies		
Amlodipine	Swollen ankles	27/11/2020

Deleted Allergies		
Received 12/12/00 - Result : NFA - REPEAT 6/12	Prostate specific antigen	Confirmed not allergic
	Adverse reaction to cefaclor	Confirmed not allergic
Received 08/08/2003 - Result : Satisfactory	Prostate specific antigen	Not applicable

Upload letter to Docman

PENICILLIN ALLERGY TEST, NO REACTION - REMOVE PENICILLIN ALLERGY LABEL [insert patient name].

Dear Dr XXXXXXXXXX ,

Your patient **[insert patient name].**underwent assessment of their penicillin allergy label during a recent hospital attendance.
After review of their history, and discussion of the risk and benefits, a supervised oral challenge was performed. A dose of 500mg of **amoxicillin / flucloxacillin** was administered on **[date]** with no evidence of a type 1 hypersensitivity response.
Based on this we can advise you that **there is no evidence to now support a "penicillin allergy" label.** We request that you remove this allergy label from your patient's medical record and record details of the allergy test (antibiotic and date). This information should be shared with other healthcare providers within your Practice and also their regular community pharmacy and general dental practitioner if possible.
The risk of allergic reaction to penicillin in a de-labelled patient is the same as that of the general population and **they can therefore receive penicillin antibiotics**. This is important for management of any future infections as penicillins are often recommended as first line therapy due to their effectiveness and lower risk of driving antimicrobial resistance.
Your patient has also been informed that they can safely take penicillin based antibiotics in future and a copy of the information which they received after the test is included with this letter.
If you have any queries regarding the test process or outcome please do not hesitate to contact me.

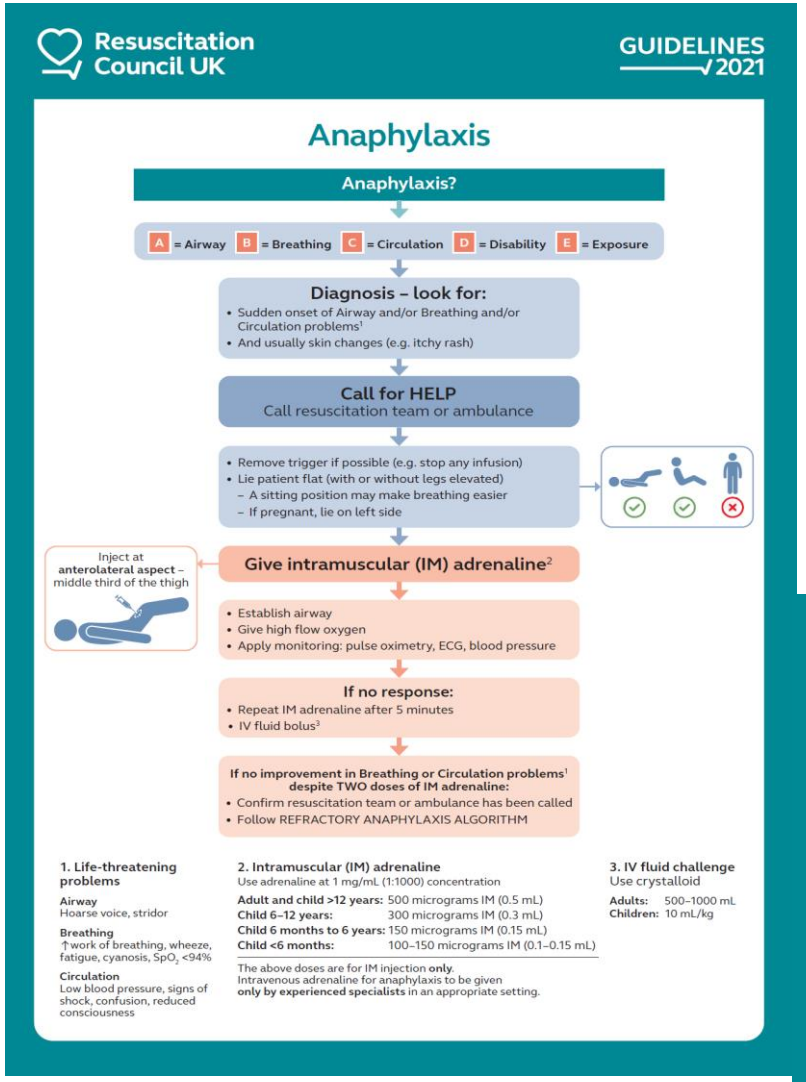
GP must be informed of PADL outcome as electronic records are updated in GP practice which in turn will update hospital record

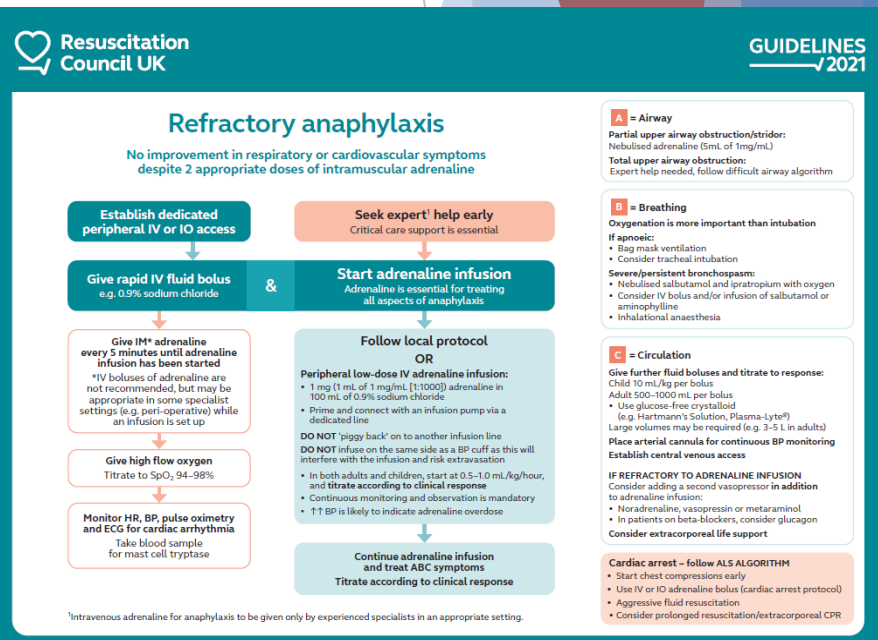
Anaphylaxis

- Anaphylaxis is defined as:

  a severe and potentially life-threatening reaction to a trigger such as an allergy

- **Anaphylaxis is considered a very rare event**
- Anaphylaxis can be managed by following the Resuscitation Council UK guideline
- Anaphylaxis is a medical emergency – escalate as per local policy and call 2222 if required
- All staff who are involved in PADL, must complete the NHS Tayside anaphylaxis LearnPro





In summary……

- Key Points:
- Penicillin allergy is often over reported.
- Incidence of true anaphylactic reaction is 0.05% of the population and hypersensitivity occurs in 1 -10% of population
- Approximately 90% of reported penicillin allergies likely to be penicillin intolerance such as GI upset
- Obtaining clinical history can assist in determining nature of allergy and whether penicillin use is safe
- Avoid cephalosporins and other Beta-lactams in the treatment of mild-moderate infection in Type 1 allergy when alternative agents are available

Clinical Scenarios

Scenario 1
What symptoms would be present in anaphylaxis, massive pulmonary embolism and septic shock?

- Sudden drop in blood pressure
- Tongue swelling
- Tachycardia
- Reduced capillary refill
- Chest clear on auscultation
- Wheeze on auscultation
- Altered consciousness
- Stomach cramps

Scenario 1 Answer:

- **Sudden drop in blood pressure** – **Correct.**
- **Tongue swelling** – This is a feature which is specific to anaphylaxis
- **Tachycardia** – **Correct.** A fall in blood pressure would trigger tachycardia in all cases
- **Reduced capillary refill** – Correct.
- **Chest clear on auscultation** – correct.
- **Wheezy on auscultation** – correct. Bronchospasm may happen in anaphylaxis, Acute Respiratory Distress Syndrome (ARDS) could lead to wheeze and (although much less common) infarcted lung change cause wheeze
- **Altered consciousness** – Correct. This may occur as a result of cerebral hypoperfusion
- **Stomach cramps** – incorrect. This is specific to anaphylaxis and results from local histamine release

All these 3 types of shock can lead to reduced end tissue prefusion. In sepsis and anaphylaxis this is due to vasodilation and capillary leak and massive PE is reduced cardiac output and ventilation/perfusion mismatch. Clinical evaluation can be challenging but anaphylaxis often has exposure and onset minutes after. 80% of patients will have skin or mucosal changes in anaphylaxis so it is important to look for them. A video explaining the pathophysiology of anaphylaxis can be seen here

Scenario 2:

Alisa is a 75 years old lady with PMH asthma - she has bronchiectasis and requires a course of antibiotics. Unfortunately she reports penicillin allergy. An allergy focused history identified she had a rash 2 days after starting pen V for a sore throat - she was 18 at the time. She has not had penicillin since. She is otherwise well and her only regular medication is a fostair (folmetrol/beclometasone) inhaler. You consider de-labelling and consult the SAPG algorithm.

Using this protocol for penicillin challenge , you concluded that:

- It would be useful to find out if she is truly penicillin allergic but not safe to challenge
- It would be both useful and safe to proceed
- It would be neither useful nor safe to proceed
- It would be safe but not of clinical benefit to proceed

Scenario 2 Answer:

- Using the SAPG protocol for penicillin challenge , you concluded that…..
- **It would be useful to find out if she is penicillin allergic but not safe to challenge:** Incorrect. She has a low probability of penicillin allergy and is currently well so it would be safe to give a penicillin challenge.
- **It would be both useful and safe to proceed:** Correct**.** She is is currently well and has a low probability of penicillin allergy so it would be safe to challenge. She requires antibiotics so it would beneficial is she could have penicillin base antibiotics
- **It would be neither useful nor safe to proceed:** Incorrect. She is is currently well and has a low probability of penicillin allergy so it would be safe to challenge. She requires antibiotics so it would be beneficial if she could have penicillin base antibiotics
- **It would be safe but not of clinical benefit to proceed:** Incorrect. She requires antibiotics so it would be beneficial if she could have penicillin base antibiotics

Scenario 3:
You perform an oral penicillin challenge with 500mg amoxicillin according to the SAPG protocol. 1 hour later she reports no symptoms and her observations are unchanged.

From this information you conclude that

- She does not have a type 1 hypersensitivity to penicillin and can use penicillin safely in the future
- If is unclear if she had a type 1 hypersensitivity as not enough time has passed
- She needs specific IgE testing to be sure if there is a type 1 hypersensitivity to penicillin
- She needs skin prick testing to be sure if there is a type 1 hypersensitivity to penicillin

Scenario 3 Answer:

- **She does not have a type 1 hypersensitivity to penicillin and can use penicillin safely in the future** - Correct this lady had the most sensitive test for a penicillin allergy and not had a reaction. She can safely use penicillin in the future.
- **If is unclear if she had a type 1 hypersensitivity as not enough time has passed :** Incorrect
- **She needs specific IgE testing to be sure if there is a type 1 hypersensitivity to penicillin:** Incorrect
- **She needs skin prick testing to be sure if there is a type 1 hypersensitivity to penicillin:** Incorrect

Scenario 4.
Mrs Jones, a 35 years old lady with recurrent urine infections, attends the day case unit for a penicillin challenge after being identified as low risk penicillin allergy. Following oral challenge, what features would suggest a type 1 hypersensitivity?

From this information provided, please select the correct answer/s

- 20 minutes following challenge, develops stomach cramps and rash. Blood pressure changed 130/60 to 100/50.
- 5 hours later feels clammy hot and light headed. She notes she has missed dinner and was getting hungry. Symptoms resolved after sugary drink.
- 30 minutes after challenge she feels the sensation of unease, develops a rash on her trunk and has cardiovascular instability with a pulse of 110 and blood pressure 100/40.
- 50 minutes following challenge she is tight chested with a wheeze and reports tongue swelling. Her hands are cold and you notice a rash developing on her back.
- 45minutes following challenge, felt light headed and nauseous. Pulse reduced to 46bpm, blood pressure was 90/60. She looked pale. Chest was clear and no rash was evident on examination.

Scenario 4 Answer:

- **20 minutes following challenge, develops stomach cramps and rash. Blood pressure changed 130/60 to 100/50.** Correct. This is a short time after exposure of potential allergen. Blood pressure changed and she developed additional features consistent with type 1 hypersensitivity reaction.
- **5 hours later feels clammy hot and light headed. She nots she has missed dinner and was getting hungry. symptoms resolved after sugary drink.** Incorrect. These symptoms developed 5 hours after exposure meaning type 1 hypersensitivity is less likely.
- **30 minutes after challenge she feels the sensation of unease, develops a rash on her trunk and has cardiovascular instability with a pulse of 110 and blood pressure 100/40**. Correct These symptoms are consistent with anaphylaxis and occur in the expected time frame. Anaphylaxis is the most likely diagnosis.
- **50 minutes following challenge she is tight chested with a wheeze and reports tongue swelling. Her hands are cold and you notice a rash developing on her back.** Correct. These symptoms are consistent with anaphylaxis and occur in the expected time frame. Anaphylaxis is the most likely diagnosis.
- **45 minutes following challenge, felt light headed and nauseous. Pulse reduced to 46bpm, bloop pressure was90/60. She looked pale. Chest was clear and no rash was evident on examination.** Incorrect. Although there are blood pressure changes within the expected time frame the lack of other features and bradycardia make type 1 hypersensitivity less likely.

Key resources

- https://www.sapg.scot/quality-improvement/hospital-prescribing/penicillin-allergy-de-labelling/
  - The Scottish antimicrobial group's resources on penicillin de-labelling. The practicalities and protocols that can be used across Scotland. Everything you need to do a quality improvement project
- https://www.resus.org.uk/library/additional-guidance/guidance-anaphylaxis
  - The resus guidelines for anaphylaxis including the (draft) 2021 version.
- https://www.youtube.com/watch?v=dJeUPKDTSAU
  - A lecture from Dr Lee about Type1 hypersensitivity reactions, allergy and anaphylaxis
- https://www.bsaci.org/wp-content/uploads/2020/01/DrugAllergyGuideline2009.pdf
  - This is an in depth exploration of drug allergy including the types and the pathophysiology of it all

Developed by PADL SLWG