Penicillin Allergy De-Labelling in Elective Surgical Patients

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**PADLES**

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- Study hosted by Leeds Teaching Hospitals Trust
- Establishes the feasibility of an abbreviated pathway to de-label pre-op patients
- Collaboration between Anaesthetics, Immunology, Microbiology, Pharmacy and Surgery
- Ethics approval confirmed May 2017 – currently recruiting
Benefits of De-Labelling Surgical Patients

• Patients receive first-line antimicrobial prophylaxis at the time of surgery (and beyond)

• Clear evidence that the PenA label is associated with:
  - Increased Clostridium Difficile, VRE and MRSA infection (Macy et al)
  - Increased length of stay (Charneski et al)
  - Increased critical care admission (Picard et al)
  - Increased readmission to hospital (Knezevic et al)

• Applied to this cohort, potential cost benefits are significant, and immediate
How do we typically investigate penicillin allergy?
History is Everything!!

............Is This Likely To Be Type 1 Hypersensitivity?

Suggestive of type I hypersensitivity

- Wheeze/SOB
- Hypotension
- Angioedema/swelling
- Urticaria
- Collapse/anaphylaxis
- Strong temporal relation
- Treatment required (eg adrenaline)

Suggestive of delayed and/or non-immune mediated reactions (side effects)

- Maculo-papular rash
- Nausea/vomiting/diarrhoea
- Thrush
- Symptoms delayed
- No treatment required

*Patients with reactions suggestive of SJS/DRESS must also be excluded from testing
Next Stage

• Skin testing
  - Demonstrates presence of IgE to penicillin
  - Risk stratifies patients for challenge test
  - Superficial test (SPT) initially – if negative → intradermal injections (IDT)
  - Wheal +/- flare caused by localised histamine release due to specific IgE

• Challenge tests
  - ‘gold standard’ to establish tolerance to penicillin
  - ideally, index penicillin given via the index route
  - Supervised, incremental 1st dose (prolonged course to pick up delayed reactions)
Is It All Necessary?

- Skin testing is expensive, time consuming, and has poor positive predictive value

- Skin tests become less sensitive (less useful) over time
  - Up to 100% of positive skin tests to amoxicillin become –ve at 5 years
  - Study in Leeds demonstrated that after 15 years, skin tests are invariably negative

- In historic and ‘low risk’/unknown reactions - **direct oral challenge** shown to be safe and appropriate

- Quicker, cheaper and less invasive

- Now standard care in Australia, New Zealand, Denmark
Other Barriers to De-Labelling

• Significant **human factor barriers** still exist:
  
  ➢ **Patient anxiety:** “Mum told me I must **never** have penicillin”

  ➢ **Clinician anxiety:** “Why **take the risk when there are alternatives?**”
PADLES asks: ‘Is it feasible to de-label ‘low risk’ patients prior to surgery?  

- Aims to develop a rapid access, abbreviated de-labelling pathway in ‘low risk’ patients 

- ‘Low risk’ defined as: 
  - Historic reaction, and not suggestive of type 1 hypersensitivity 
  - *ie* a cohort in whom skin testing is uninformative and direct challenge is safe 

- Other eligibility criteria include: 
  - *Require penicillin for surgical prophylaxis* 
  - *Sufficient time to undergo testing*
Why Focus on Pre-Operative Patients?

- Demonstrable, immediate benefit from de-labelling
- Large and accessible population: >400 patients/week attend pre-op clinic in LTHT
- Study of >1200* LTHT patients found:
  - 17% have an historic ‘penicillin allergy’ label
  - 85% had history NOT suggestive of type 1 hypersensitivity
  - Half required penicillin for surgery

*(Presented at BSACI ASM 2016)*
• LTHT performs 68,000 elective surgical procedures/year

  ➢ Cost of the *single dose* alternative surgical antimicrobial prophylaxis alone

    estimated at £45-50K

  ➢ **Potential costs** of increased infections, length of stay, and critical care admission

• Surgical patients are looked after by anaesthetists!

  ➢ > 14,000 anaesthetists in the UK

  ➢ useful resource within any de-labelling service
The pathway

• PAC nurse identifies PenA patients when they attend for pre-op assessment

• All PenA patients complete screening questionnaire

• Eligibility determined by PAC nurse using proforma

• Eligible patients booked into de-labelling clinic and given information leaflet
De-Labelling Clinic

- Incremental oral challenge with amoxicillin (or index penicillin if known)
  - 10%, 50%, 100% full dose (500mg);
  - 20min intervals, and 1 hour observation after last dose

- Performed by specialist nurse, anaesthetist immediately available

- 3-day course to take home, with follow-up phone call when completed

- Patient, surgeon & GP receive written advice. Hospital electronic record updated.
Long Term Follow-Up

• Notes review to determine antibiotic used for surgical prophylaxis

• Telephone follow-up with GP to ensure records updated

• Telephone follow-up with patient at 1 year
Interim results (to November ’17)

• 128 patients PenA patients screened
  ➢ 27 eligible
  ➢ 101 ineligible

• All eligible patients offered direct challenge testing
  ➢ So far 22 de-labelled uneventfully
  ➢ 1 advised to avoid penicillins after minor delayed reaction

• All de-labelled patients received appropriate first line penicillin during surgery
Ineligible patients

• Often >1 reason for ineligibility

• 53 had ‘high risk’ symptoms
  ➢ 15/53 high risk patients excluded because of *itchy rash* alone

• 48 had ‘low risk’ symptoms (but other reasons for ineligibility)

• 19/101 excluded **only** because penicillin not required or operation too soon
What do patients say?

• 77% of all patients with the label would like to be tested
  
  ➢ 78% ‘low risk’ group
  
  ➢ 75% ‘high risk’ group (incl 65% of patients reporting life-threatening symptoms)

• One patient denied her high risk symptoms in order to be tested

• Greater public awareness?..........or good advertising in pre-assessment?
• Few patients know the index penicillin
  ➢ 14/128 remember
  ➢ 12 of these – amoxicillin

• Majority of reactions are historic (>15 years ago/in childhood)

• Almost 1/4 cannot recollect what happened.
Why do people decline testing?

• 30/128 declined

• Usually NOT because of genuine high risk symptoms!

  ➢ 5 ‘would never take penicillin whatever the result of testing’ *(unreachable group)*

  ➢ 7 ‘do not want to take part in research’

  ➢ 5 ‘do not have time’ for additional clinic visit

  ➢ 13 – reason not given
Feedback from de-labelled patients

• Universally positive about the concept of de-labelling

• Low levels of anxiety about receiving penicillin (100% described none/mild)

• Most patients would prefer to undergo testing at time of original PAC visit

• Minor complaints about the tea/coffee/bathroom facilities – now improved!
Modifications to eligibility criteria

• ‘Penicillin not required for surgery’
  - Patients now offered testing regardless of surgical prophylaxis required

• ‘Operation too soon’
  - Patients now offered testing post-operatively

• ‘Reaction > 15 years ago’
  - All patients with clear ‘low risk’ history offered testing

- Single dose oral challenge?

- Prospective identification of PenA patients to allow same-day testing in PAC?
In Summary

• We have demonstrated it is possible to:
  
  ➢ Use a proforma-based screening tool for identifying ‘low risk’ surgical patients
  ➢ De-label selected patients using direct oral challenge
  ➢ Integrate a de-labelling pathway into the pre-op patient journey

• Patient demand for testing higher than anticipated
• Testing must be **rapid and simple** to maximise uptake
• Clinicians appear to follow the advice (in short term)
To be determined......

• Can the pathway be shortened even further?

• Do GPs follow the advice given?

• Is there a cohort of patients who might accept de-labelling without any testing?
Exploring Knowledge And Attitudes

DALES - Drug Allergy de-Labelling in Elective Surgical patients

• UK-wide study to determine:
  ➢ Prevalence of all drug allergy labels in the elective population (est. 18,000 pts)
  ➢ Likelihood of these labels representing true allergy
  ➢ Patient attitudes towards their PenA label

• Includes survey of 2500 anaesthetists
  ➢ Explores understanding of drug allergy
  ➢ Determine attitudes towards penicillin allergy labels/de-labelling
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**De-Labelling Team**

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Any Questions?