



Infection Service

Penicillin Allergy Really?

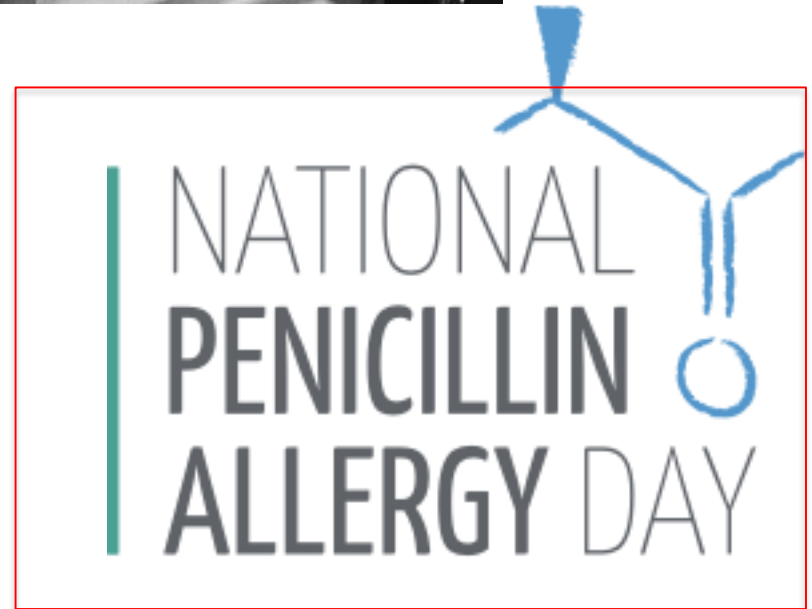
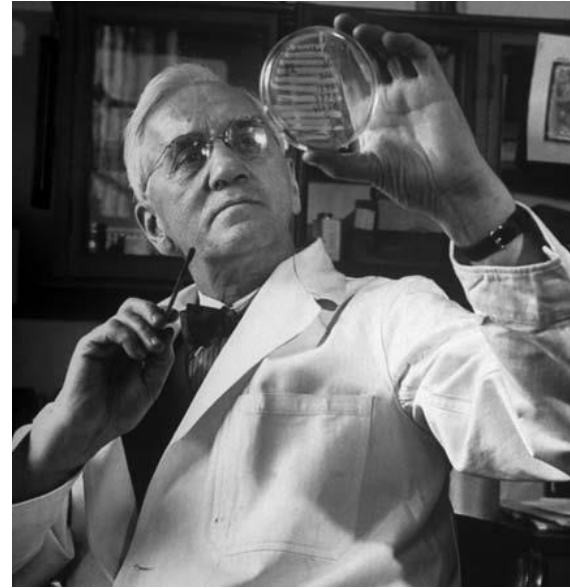
Elham Khatamzas

Consultant Infectious Diseases

14th March 2019



1941: First patient treated with penicillin at Royal Infirmary Hospital Oxford



28th September 1928

Penicillin allergy – background

- 10-20% of patients report penicillin allergy →
 - on testing <1% will have evidence of true hypersensitivity because
 - misdiagnosis – viral exanthem, virus drug interaction
 - misassumption – intolerance (headache, nausea)
 - remote timing – 80% will lose hypersensitivity >10 yrs
 - but also
 - history associated with drug reaction rarely confirmed, reconciled, acted on by health care professionals

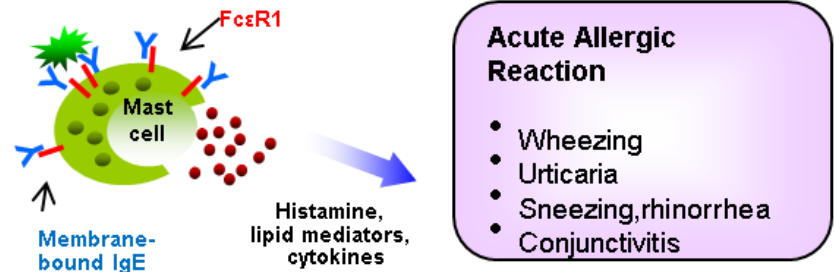
Types of reaction

IgE mediated - acute

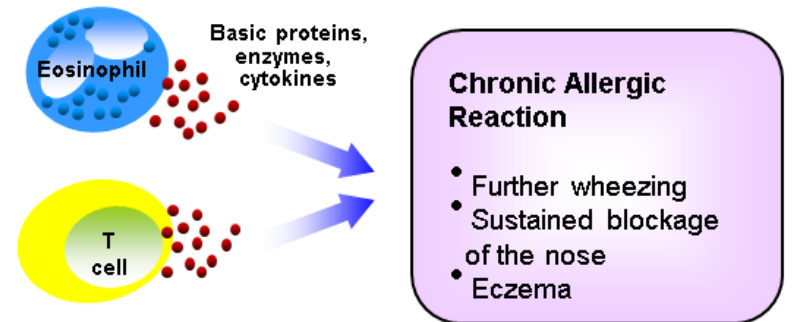
- Immediate <1h (6h)
- Severe, anaphylaxis

IgG mediated – chronic

- >24hrs
- Urticaria, fever, arthralgia

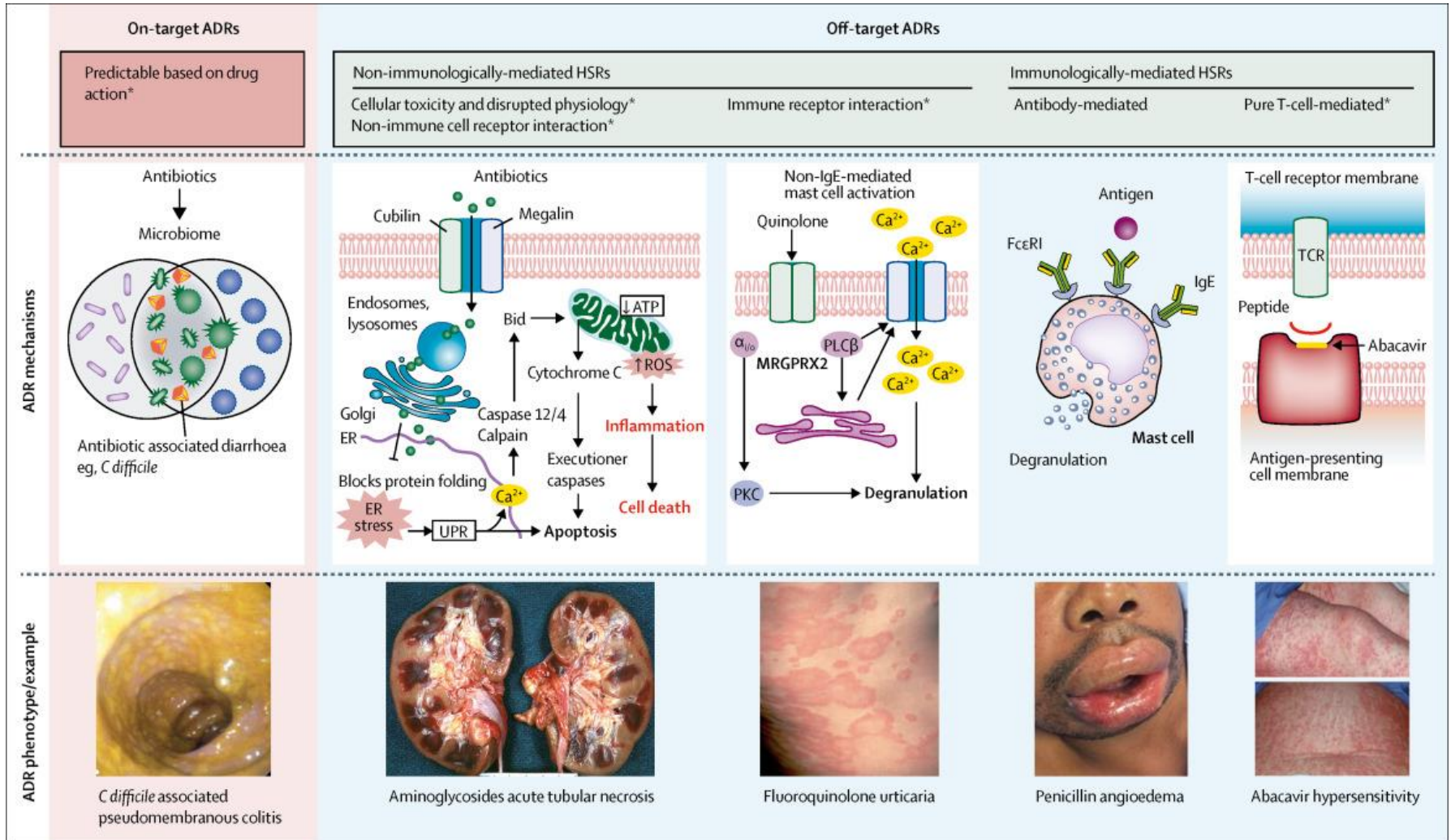


Acute: Allergen Specific IgE is pre-bound to the FcεR1 receptor on mast cells. Circulating allergen binds the IgE causing receptor cross linking and mast cell degranulation.



Chronic: Recruitment and activation of allergen specific T cells and other cells by mast cell derived mediators

Adverse drug reactions – hypersensitivity reactions



Penicillin allergy label results in

- Suboptimal clinical outcomes
- More frequent hospital admissions
- Increase in healthcare associated infections
- Increased rate of surgical site infections
- Increased toxicity
- Increased antibiotic costs
- Increased lengths of stay
- Increased anxiety to patients
- Risk of mislabel and anaphylaxis



Risk of meticillin resistant *Staphylococcus aureus* and *Clostridium difficile* in patients with a documented penicillin allergy: population based matched cohort study

Setting – UK general practice 1995-2015

- Participants – 301 399 adults with previous MRSA or *C difficile* enrolled in Health Improvement Network database
- Results: 64 141 adults with penicillin allergy – 237 258 matched comparators
- Mean follow-up for 6 yrs

Outcomes	Penicillin allergy	No penicillin allergy
MRSA:		
No of patients	64 141	237 258
No of MRSA cases	442	923
Person years	383 199	1 446 753
Hazard ratio (95% CI)*	1.84 (1.64 to 2.06)	1.0 (reference)
Multivariable adjusted hazard ratio (95% CI)†	1.69 (1.51 to 1.90)	1.0 (reference)
<i>C difficile</i>:		
No of patients	64 141	237 258
No of <i>C difficile</i> cases	442	1246
Person years	383 469	1 446 658
Hazard ratio (95% CI)*	1.37 (1.23 to 1.53)	1.0 (reference)
Multivariable adjusted hazard ratio (95% CI)†	1.26 (1.12 to 1.40)	1.0 (reference)

70% risk

26% risk

Health care use and serious infection prevalence associated with penicillin “allergy” in hospitalized patients: A cohort study

Eric Macy, MD, MS,^a and Richard Contreras, MS^b *San Diego and Pasadena, Calif*

- Retrospective matched cohort study Kaiser Foundation Hospital California
- 51,582 hospitalized subjects with penicillin allergy matched with 103,164 control subjects
- Follow-up 20.1 \pm 10.5mo
- Results:
 - Penicillin “allergic” patients
 - 0.59 (0.47-0.71) more hospital days
 - Received more clindamycin, quinolones, vancomycin (p<0.0001)
 - 23.4% (15.6-31.7%) more *C difficile*, 14.1% (7.1-21.6%) more MRSA, 30.1% (12.5-50.4%) more VRE infection

Health care use and serious infection prevalence associated with penicillin “allergy” in hospitalized patients: A cohort study

Eric Macy, MD, MS,^a and Richard Contreras, MS^b *San Diego and Pasadena, Calif*

- Retrospective matched cohort study Kaiser Foundation Hospital California
- 51,582 hospitalized subjects with penicillin allergy matched with 103,164 control subjects
- Follow-up 20.1_±10.5mo
- Results:

were presented. It was estimated that the cost of performing penicillin skin testing on the 51,582 subjects with penicillin “allergy” would be approximately \$6.8 million, whereas \$64.6 million would be saved by virtue of shortening the hospital stay by 0.59 days per patient. This analysis assumes that 95% or more of the

The Impact of Reported Beta-Lactam Allergy in Hospitalized Patients With Hematologic Malignancies Requiring Antibiotics

Kuan-Hsiang Gary Huang,^{1,2} Valerie Cluzet,³ Keith Hamilton,³ and Olajumoke Fadugba¹

- Retrospective cohort study 2010-2015
- N=4671 35.1% antibiotic allergy, 14.1% beta-lactam (9.3% penicillin)
- Results allergic vs non-allergic:
 - Longer length of stay
 - Higher 30 day re-admission rate
 - Higher mortality rate at 30 days and 180 days
 - Higher *C. difficile* rates
 - Higher hospital charges
 - Increased antibiotic classes used and antibiotic duration

Anaesthesia, Surgery and Life-Threatening Allergic Reactions

Report and findings of the
Royal College of Anaesthetists'
6th National Audit Project:
Perioperative Anaphylaxis

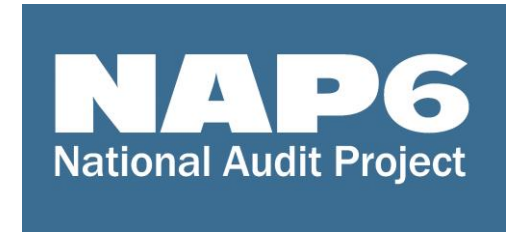
MAY 2018



Relevant findings

- 266 cases: 40 patients cardiac arrests, 10 deaths
- Culprit agents: 47% antibiotics
- Teicoplanin 12% of antibiotic exposures but 38% antibiotic-induced anaphylaxis

→ Teicoplanin is 17-fold more likely to cause anaphylaxis than alternatives



Strategies to remove penicillin allergy label

- Awareness

- Do not
- fail
- pa
- ris

NICE

National Institute for
Health and Care Excellence

New York Times

to check for over fears being put at

By [DAILY MAIL REPORTER](#)



Solensky, J Allergy Clin Immunol 2014

NYT 22 Jan 2019

Daily Mail 25 Sep 2018

Original Investigation

Assessing the Diagnostic Properties of a Graded Oral Provocation Challenge for the Diagnosis of Immediate and Nonimmediate Reactions to Amoxicillin in Children

Cohort study 2012-2015, allergy clinic Montreal

818 children, median age 1.7 yrs (1.0-3.9)

770 (94.1%) tolerated penicillin challenge

17 (2.1%) mild immediate, 31 (3.8%) non-immediate reactions

Graded PC

specificity 100%

negative predictive value 89.1%

positive predictive value 100%

Penicillin allergy – SAPG

Scottish
Antimicrobial
Prescribing
Group

- Started autumn 2017

Develop a national approach and algorithm for assessing and confirming or de-labelling penicillin allergy

Pilot Survey on prevalence of penicillin allergy completed March 2018



Penicillin allergy NHS Lothian

- Point Prevalence Survey as part of national SAPG led data collection
February 2018
WGH ARU and colorectal (Wd 23, 24, 57), also RHSC but numbers very low
Results:
Prevalence of penicillin allergy label 10%
 - Avg age 69y
 - 56% female
 - 63% had antibiotic prescribed
 - including 30% vancomycin, 5% ciprofloxacin
 - 69% reaction >10yrs ago

Similar results found on 2017 PPS at SJH

SAPG nation wide de-labelling

Aim: To exclude or confirm hypersensitivity to penicillin

LOW PROBABILITY OF TRUE ALLERGY

De-labelling at front door

PILOT beginning March/April 2019

WGH ARU RIDU MOE

Patients with Penicillin allergy label screened based on history

Patient information leaflet

Oral Amoxicillin challenge

No reaction → patient de-labelled
GP and patient informed

Collection of data and feedback with plan for wider roll out





SAPG nationwide de-labelling

LOW probability of hypersensitivity

- Symptoms typical of intolerance – nausea, vomiting, headache, diarrhoea
- Reaction occurred more than 10yrs ago
- Reaction did not lead to hospital admission
- Reaction did not happen within 60 mins

ORAL CHALLENGE AT BEDSIDE

Penicillin allergy testing

doi: 10.1111/cea.12468

Clinical & Experimental Allergy, 45, 300–327

BSACI GUIDELINE

© 2015 John Wiley & Sons Ltd

History

Skin testing:

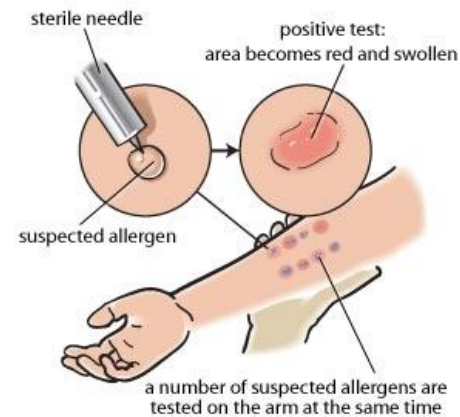
- Prick testing
- Intradermal testing

Drug provocation test

Management of allergy to penicillins and other beta-lactams

R. Mirakian¹, S. C. Leech², M. T. Krishna³, A. G. Richter³, P. A. J. Huber⁴, S. Farooque⁵, N. Khan⁶, M. Pirmohamed⁷, A. T. Clark¹ and S. M. Nasser¹

¹Cambridge University Hospitals NHS Foundation Trust, Cambridge, UK, ²Department of Child Health, King's College Hospital, London, UK, ³Birmingham Heartlands Hospital, Birmingham, UK, ⁴British Society for Allergy and Clinical Immunology, London, UK, ⁵Imperial College NHS Trust, St Mary's Hospital, London, UK, ⁶University Hospitals of Leicester NHS Trust, Glenfield Hospital, Leicester, UK and ⁷The Wolfson Centre for Personalised Medicine, Department of Molecular and Clinical Pharmacology, Institute of Translational Medicine, University of Liverpool, Liverpool, UK



RIDU Outpatient Penicillin allergy Service

- **Purpose:** To exclude or confirm hypersensitivity to penicillin aiming to de-label patients without a true allergy
- **Patients:**
 - Identified and referred by RIDU/NIS/other specialists
 - e.g. recurrent cellulitis, UTI, chronic infections
 - clear exclusion criteria
 - outpatients only
 - spend min 4 hrs in clinic
 - 3 patients per clinic
- **Staff:** EK, nurse – all trained and competent
- **Frequency:** One day/week
- **Safety:** Information leaflet, Anaphylaxis protocol in place



Penicillin allergy testing in RIDU

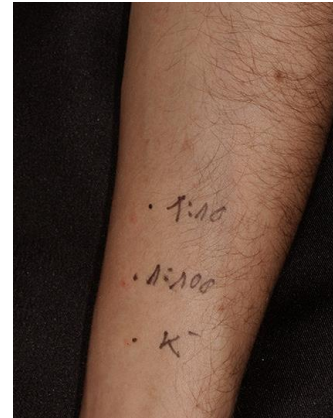
History

Observations

Informed signed consent

Skin testing with penicillin
allergenic determinants
(PPL, MDM), amoxicillin, benzyl
penicillin in 1:100-neat dilutions

1. Skin prick with 15min interval
2. intra-dermal test with 15min interval
3. Oral graded amoxicillin challenge



Who needs assessment of their penicillin allergy label?

Almost everybody

Thank you

