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The Death of Desensitization—Delabeling the Destroyer

To the Editor—Penicillin allergy is clinically burdensome to infectious diseases (ID) practice, substantially impacting antimicrobial choice and leading to use of suboptimal second-line agents [1]. Penicillin allergy desensitization induces a temporary tolerance through incrementally administering increasing amounts of the drug. It is used historically in clinical ID practice to manage patients with an immediate allergic reaction deemed too high risk for allergy testing or where testing is not available [2]. With the increased implementation of penicillin allergy inpatient and ambulatory testing programs, we question if this has brought about the death of desensitization.

In a single-center retrospective cohort study, we examined patients who underwent penicillin desensitization, to any oral or intravenous penicillin, before and after introducing an inpatient and ambulatory penicillin allergy program at a tertiary care hospital in Melbourne, Australia. Our outpatient antibiotic allergy testing program was implemented in 2015 [3] and inpatient service in 2017 [4, 5], as previously described. Six patients (3 female; median age, 77.5 [interquartile range, 75.5–81] years) underwent a total of 7 penicillin desensitizations from 2012 to 2017 (3 benzylpenicillin, 2 amoxicillin, 1 flucloxacillin, 1 ampicillin; Table 1). No desensitizations were undertaken after the penicillin allergy testing program was initiated, 2017 to the present. Indications for desensitization included methicillin-susceptible *Staphylococcus aureus* endocarditis, recurrent *Enterococcus faecalis* sepsis, and refractory group B *Streptococcus* (GBS) bacteremia (Table 1). Five patients (84%) were of advanced age with multiple comorbidities, and 1 patient (16%) had a terminal metastatic disease. All patients tolerated desensitization; however, 6 (100%) experienced treatment delays, 1 for 7 days while waiting for a critical care bed.

When applying the clinically validated PEN-FAST clinical decision rule [6], 5 patients (84%) who were desensitized would have met criteria for a single-step penicillin direct oral challenge (DOC) and 1 patient (16%) would have been considered appropriate for traditional skin prick and intradermal testing.

The first reported penicillin desensitization case series described 15 pregnant syphilis-infected women being delivered in 1985 [7]. Using today's knowledge and applying PEN-FAST, 10 (67%) would be deemed low risk and candidates for a penicillin DOC in the modern era. Current data demonstrate that penicillin allergy testing is safe even in pregnancy, a common setting for which desensitization is deployed (eg, in the management of syphilis infection and GBS) [8]. Of the same original cohort, 7 (47%) later

Table 1. Demographics, Indication for Penicillin Therapy, Index Reaction, and Retrospective Risk Stratification of Patients Who Underwent Penicillin Desensitization, 2012–2017

Patient Age (y)/Sex	Indication for Penicillin	Index Penicillin Reaction	Desensitization	PEN-FAST[a]	Proposed Penicillin Testing Strategy
82/F	MSSA bacteremia, mitral valve endocarditis	Amoxicillin: Historic label, reaction unknown. Flucloxacillin: During admission, reported sensation of tongue swelling after the first dose. No respiratory compromise, no treatment.	Flucloxacillin: IV desensitization, completed course.	1, treatment unknown. 4, swelling, recent.	Skin testing
75/M	Recurrent *Enterococcus faecalis* urosepsis	Penicillin: "Shakes," time interval not documented. No treatment.	Amoxicillin: PO desensitization, completed course.	NA	DOC
78/M	GBS bacteremia	Penicillin: Childhood lip tingling and swelling. Treatment unknown.	Benzylpenicillin: IV desensitization, completed course. Later switched to amoxicillin.	1, treatment unknown.	DOC
77/F	Recurrent *E faecalis* bacteremia	Penicillin: Rash described as "blisters," >10 y ago. Treatment unknown.	Benzylpenicillin: IV desensitization, treatment ceased due to acute renal failure. Ampicillin: IV desensitization 2 mo later, completed course.	1, treatment unknown.	DOC
84/F	*E faecalis* endocarditis with aortic root abscess	Flucloxacillin: Historic label, reaction unknown.	Benzylpenicillin: IV desensitization, died before completion.	1, treatment unknown.	DOC
67/M	*Finegoldia magna* osteomyelitis of left great toe	Penicillin: Childhood swelling. Treatment unknown.	Amoxicillin: PO desensitization, completed course.	1, treatment unknown.	DOC

Abbreviations: DOC, direct oral challenge; F, female; GBS, group B *Streptococcus*; IV, intravenous, M, male; MSSA, methicillin-susceptible *Staphylococcus aureus*; NA, not applicable; PO, oral administration.

[a]PEN-FAST (Penicillin Allergy Clinical Decision Rule) uses 3 clinical criteria of time from penicillin allergy episode, phenotype, and treatment required to assess likelihood of positive penicillin challenge: 0, very low risk (<1% positive); 1–2, low risk (5% positive); 3, moderate risk (20% positive); 4–5, high risk (50% positive) [6].

tolerated penicillin without desensitization within the study timeframe, confirming tolerance [7].

The increasing deployment of antibiotic allergy programs, in particular penicillin allergy DOC in the inpatient setting, has drastically diminished the need for the art of inducing temporary immune tolerance via desensitization. Our experience reflects this and shows that by using validated risk-stratification tools and proactive point-of-care delabeling, especially with DOC, the role of resource-intensive and temporizing desensitization is being demolished. The birth of delabeling has induced the death of penicillin desensitization.

Notes

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Ethics. Ethically approved research project.

Data availability. Further information on the data can be acquired from the corresponding author at coxff@tcd.ie.

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References

1. Trubiano JA, Chen C, Cheng AC, et al. Antimicrobial allergy "labels" drive inappropriate antimicrobial prescribing: lessons for stewardship. J Antimicrob Chemother **2016**; 71:1715–22.
2. Shenoy ES, Macy E, Rowe T, Blumenthal KG. Evaluation and management of penicillin allergy: a review. JAMA **2019**; 321:188–99.
3. Trubiano JA, Thursky KA, Stewardson AJ, et al. Impact of an integrated antibiotic allergy testing program on antimicrobial stewardship: a multicenter evaluation. Clin Infect Dis **2017**; 65:166–74.
4. Trubiano JA, Smibert O, Douglas A, et al. The safety and efficacy of an oral penicillin challenge program in cancer patients: a multicenter pilot study. Open Forum Infect Dis **2018**; 5:ofy306.
5. Chua KYL, Vogrin S, Bury S, et al. The penicillin allergy delabeling program: a multicenter whole-of-hospital health services intervention and comparative effectiveness study. Clin Infect Dis **2020**; 73:487–96.
6. Copaescu AM, Vogrin S, James F, et al. Efficacy of a clinical decision rule to enable direct oral challenge in patients with low-risk penicillin allergy: the PALACE randomized clinical trial. JAMA Intern Med **2023**; 83:944–52.
7. Wendel GD Jr, Stark BJ, Jamison RB, Molina RD, Sullivan TJ. Penicillin allergy and desensitization in serious infections during pregnancy. N Engl J Med **1985**; 312:1229–32.
8. Macy E. Penicillin skin testing in pregnant women with a history of penicillin allergy and group B *Streptococcus* colonization. Ann Allergy Asthma Immunol **2006**; 97:164–8.

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