Beta-lactam allergy: Benefits of de-labeling can be achieved safely

Far too many patients carry an inaccurate label of beta-lactam allergy and consequently receive alternative antibiotics, often with too broad a spectrum, a higher risk of adverse events, an increased chance of selecting for resistance, and greater cost. Ten percent of patients are labeled with a penicillin allergy and 2% with a cephalosporin allergy. Yet, among patients with a reported penicillin allergy, only 5% to 8% of adults and 2% of children have a positive penicillin skin test.[1-3] This disconnect may result from a poor understanding of allergy by patients and a lack of useful assessment tools in many primary care settings. An episode of gastrointestinal intolerance can be reported as an allergy. A viral rash that shows up after initiation of antibiotics may be mislabeled as an allergy. Some assume that antibiotic allergies are familial and label a relative. Even when the initial label is accurate, we often fail to acknowledge that the risk of repeat IgE-mediated hypersensitivity to similar drugs diminishes with time, falling 80% over 10 years.[4]

In dentistry, substitution to clindamycin makes up 13% of all prescriptions in BC, significantly increasing the risk for adverse events such as *C. difficile* infection. Efforts should be made to investigate the nature of the allergy and determine if patients can safely receive a beta-lactam, even in the setting of a well-documented prior reaction. Avoiding unnecessary substitutions or staying within the beta-lactam

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Beta-lactam Antibiotic Cross-Allergy Chart

Beta-lactams	AMOXICILLIN*	AMPICILLIN	CLOXACILLIN	PENICILLIN	PIPERACILLIN*	CEFADROXIL	CEFAZOLIN	CEPHALEXIN	CEFOXITIN	CEFPROZIL	CEFUROXIME	CEFIXIME	CEFOTAXIME	CEFTAZIDIME	CEFTRIAXONE	CEFEPIME	ERTAPENEM	IMIPENEM	MEROPENEM
AMOXICILLIN*		X[1]	X[5]	X[4]	X[3]	X[1]	✓	X[1]	✓	X[2]	✓	✓	✓	✓	✓	✓	✓	✓	✓
AMPICILLIN	X[1]		X[5]	X[4]	X[3]	X[2]	✓	X[2]	✓	X[2]	✓	✓	✓	✓	✓	✓	✓	✓	✓
CLOXACILLIN	X[5]	X[5]		X[5]	X[5]	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
PENICILLIN	X[4]	X[4]	X[5]		X[5]	✓	✓	✓	X[3]	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
PIPERACILLIN*	X[3]	X[3]	X[5]	X[5]		X[3]	✓	X[3]	✓	X[3]	✓	✓	✓	✓	✓	✓	✓	✓	✓
CEFADROXIL	X[1]	X[2]	✓	✓	X[3]		✓	X[1]	✓	X[2]	✓	✓	✓	✓	✓	✓	✓	✓	✓
CEFAZOLIN	✓	✓	✓	✓	✓	✓		✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
CEPHALEXIN	X[1]	X[2]	✓	✓	X[3]	X[1]	✓		✓	X[2]	✓	✓	✓	✓	✓	✓	✓	✓	✓
CEFOXITIN	✓	✓	✓	X[3]	✓	✓	✓	✓		✓	X[2]	✓	✓	✓	✓	✓	✓	✓	✓
CEFPROZIL	X[2]	X[2]	✓	✓	X[3]	X[2]	✓	X[2]	✓		✓	✓	✓	✓	✓	✓	✓	✓	✓
CEFUROXIME	✓	✓	✓	✓	✓	✓	✓	✓	X[2]	✓		X[3]	X[1]	X[3]	X[1]	X[2]	✓	✓	✓
CEFIXIME	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	X[3]		X[3]	X[3]	X[3]	X[3]	✓	✓	✓
CEFOTAXIME	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	X[1]	X[3]		X[3]	X[1]	X[1]	✓	✓	✓
CEFTAZIDIME	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	X[3]	X[3]	X[3]		X[3]	X[3]	✓	✓	✓
CEFTRIAXONE	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	X[1]	X[3]	X[1]	X[3]		X[1]	✓	✓	✓
CEFEPIME	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	X[2]	X[3]	X[1]	X[3]	X[1]		✓	✓	✓
ERTAPENEM	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓		X[5]	X[5]
IMIPENEM	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	X[5]		X[5]
MEROPENEM	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	X[5]	X[5]	

* Also applies to beta-lactamase inhibitor combinations (amoxicillin-clavulanate and piperacillin-tazobactam)

AVOID ALL beta-lactam antibiotics if:

- ICU admission related to allergy
- Delayed beta-lactam antibiotic allergy causing:
  - interstitial nephritis
  - hepatitis
  - hemolytic anemia
- Delayed severe skin allergic reactions:
  - Stevens-Johnson syndrome
  - toxic epidermal necrolysis
  - exfoliative dermatitis
  - acute generalized exanthematous pustulosis (AGEP)
  - drug reaction with eosinophilia and systemic symptoms (DRESS)

LEGEND:	
Penicillins	
1st Generation Cephalosporins	
2nd Generation Cephalosporins	
3rd Generation Cephalosporins	
4th Generation Cephalosporins	
Carbapenems	
✓	Different structure. CONSIDERED SAFE TO PRESCRIBE
Reaction likely based on side chain:	
X[1]	Same side chain - clinical evidence of cross reaction. DO NOT PRESCRIBE
X[2]	Same side chain - Theoretical risk of cross reaction, no clinical studies. DO NOT PRESCRIBE
X[3]	Similar side chain - Potential for cross reaction. DO NOT PRESCRIBE
Reaction likely based on Beta-lactam ring	
X[4]	Clinical evidence of cross reaction. DO NOT PRESCRIBE
X[5]	Theoretical risk of cross reaction, no clinical studies. DO NOT PRESCRIBE

FIGURE 1. Beta-lactam cross-allergy chart.

Source: Interior Health Authority.

class, when safe, can bring both clinical and public health benefits.

Traditional teaching attributes beta-lactam allergy to the commonality of the beta-lactam ring implying broad cross-reactivity between beta-lactams. This probably applies mostly to penicillins but not cephalosporins. Recently, it has been recognized that cross-reactivity is predominantly due to side chain similarity when it comes to cephalosporins. Those with only minor and delayed allergic symptoms such as a rash do not have an absolute contraindication to beta lactam use and can be safely retreated using guidance around cross reactivity. **Figure 1** is a chart from the Interior Health Authority that illustrates when this risk is present or absent. Keeping a graphic like this as an office wall chart can aid decisions on subsequent antibiotic therapy. Many people with minor reactions who receive the same agent years later do not have a repeat reaction.

The goal of an allergy assessment strategy is to allow use of the most optimal antibiotic and make sure that any ongoing documentation of allergy is accurate. An effective assessment should employ a short, logical series of questions possibly aided by a flowchart (e.g., **Figure 2**). What were the symptoms that led to the diagnosis of allergy? How soon after first receiving the drug were they experienced? Was there severe wheezing or swelling of the mouth or throat consistent with anaphylaxis? Were there any very severe manifestations such as Stevens-Johnson syndrome or interstitial nephritis, and did the reaction take your patient to an ICU?

Following such questions, patients who merely had GI intolerance, an unpleasant taste in the mouth, a headache, or other nonallergic symptoms might have their allergy label removed. This can be documented on their chart, by handing them information, and ideally should prompt a revision to the Pharmacare record. The BC Provincial Antimicrobial Clinical Experts are developing a standardized practice guideline and tools for hospital stewardship programs for de-labeling beta-lactam allergies.

Anaphylaxis history rightly deserves more caution and can benefit from further assessment by an allergist, but cross-reactions to agents with a different R1 side chain are rare. Some more severe reactions such as Stevens-Johnson syndrome, interstitial nephritis, and hemolytic anemia [**Figure 1**] represent an ongoing contraindication to beta-lactam use.

All professions involved in prescribing and administering antibiotics play a role in accurate labeling of allergies. We need to engage pharmacists, dentists, nurses, and others in the effort. Allergy specialists do not have the capacity to evaluate every case, but consultation may be wise if there is a history of anaphylaxis or other severe outcome or a high likelihood of needing to treat with an agent to which there has been a true allergic reaction. If we focus on accurately charting beta-lactam allergy status, we can increase the efficacy and safety of treatment while decreasing costs and risk. ■

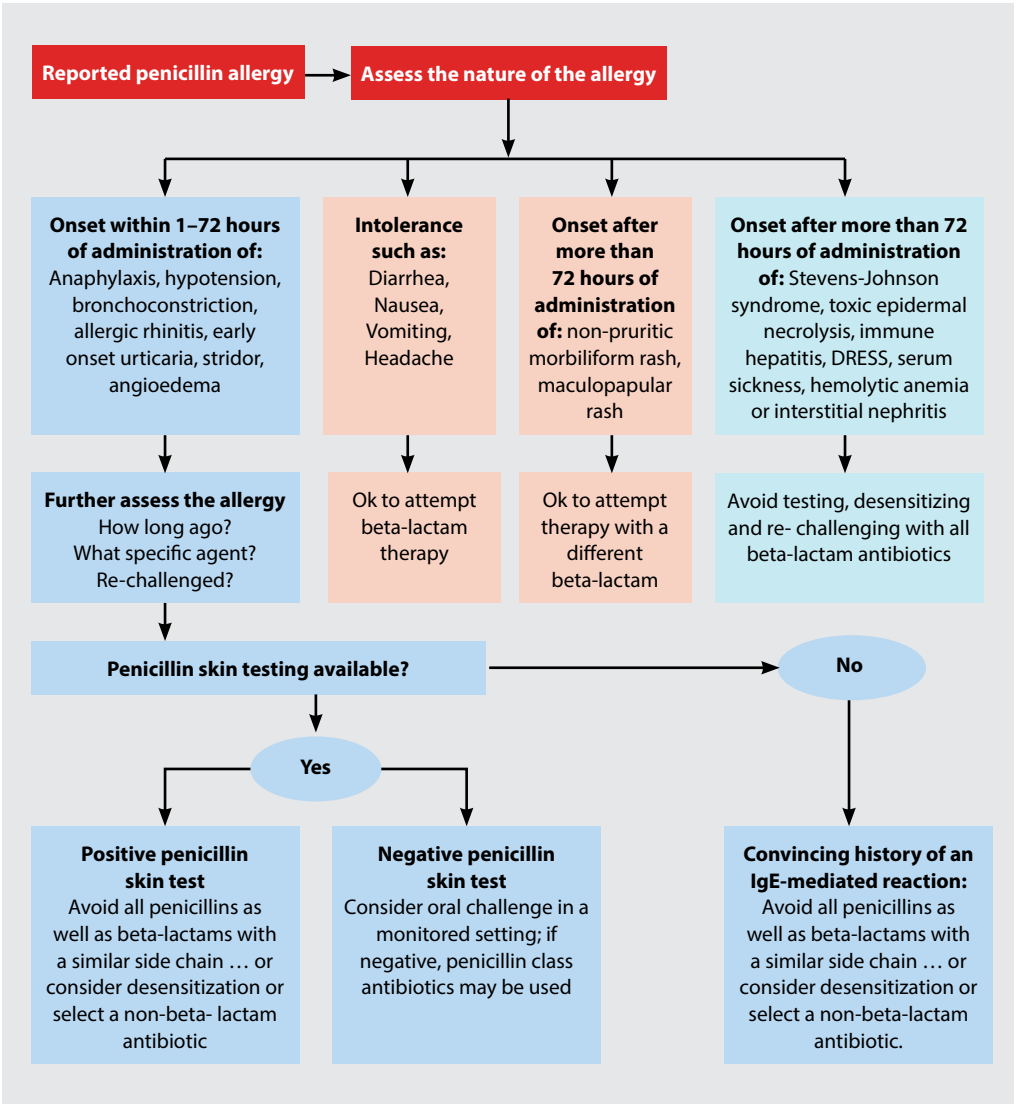

FIGURE 2. **Flowchart from New Brunswick for assessing penicillin allergy.**
Source: New Brunswick Provincial Health Authorities Anti-infective Stewardship Committee (https://en.horizonnb.ca/media/951180/antimicrobial_treatment_guidelines_for_common_infections_en.pdf)

—David M. Patrick, MD, MHSc, FRCPC
BCCDC
University of British Columbia, School of Population and Public Health

—Abdullah Al Mamun, MBBS, MPH
BCCDC

—Nick Smith, MPH
BCCDC

—Emily Rempel, PhD
BCCDC

—Piera Calissi, PharmD
Interior Health Authority

—Edith Blondel-Hill, MD, FRCPC
Interior Health Authority

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CME calendar

Rates: $75 for up to 1000 characters (maximum), plus GST per month; there is no partial rate. If the course or event is over before an issue of the *BCMJ* comes out, there is no discount. **Deadlines:** ONLINE: Every Thursday (listings are posted every Friday). PRINT: The first of the month 1 month prior to the issue in which you want your notice to appear, e.g., 1 February for the March issue. The *BCMJ* is distributed by second-class mail in the second week of each month except January and August. **Planning your CME listing:** Advertising your CME event several months in advance can help improve attendance; we suggest that your ad be posted 2 to 4 months prior to the event. **Ordering:** Place your ad at www.bcmj.org/cme-advertising. You will be invoiced upon publication. Payment is accepted by Visa or MasterCard on our secure online payment site.

CME ON THE RUN

VGH and various videoconference locations, 22 Nov–5 Jun (Fri)

CME on the Run sessions are held at the Paetzold Lecture Theatre, Vancouver General Hospital and there are opportunities to participate via videoconference from various hospital sites. Each program runs on Friday afternoons from 1 p.m. to 5 p.m. and includes great speakers and learning materials. Dates and topics: 22 Nov (dermatology and allergy). Topics include: Hair loss and thinning in middle age; Chronic leg ulcers: The best office approach; Psoriasis: Multimodal treatment—topical and beyond; "Is this lesion cancer?": What's new, what not to miss; Rosacea: What's old, what's new, and what's best?; Acne: A stepwise approach for office practice; Early allergen exposure: Can we reduce incidence of food and environmental allergies?; Do they really have a penicillin allergy? The office challenge. The next sessions are: 31 Jan (psychiatry); 3 Apr (infectious disease and travel); 1 May (prenatal, pediatric, and adolescents); 5 Jun (internal medicine). To register and for more information visit ubccpd.ca, call 604 675-3777; or email cpd.info@ubc.ca.

GP IN ONCOLOGY CASE STUDY DAY & FAMILY PRACTICE ONCOLOGY CME DAY

Vancouver, 22–23 Nov (Fri–Sat)

BC Cancer's Family Practice Oncology Network is presenting two practice-ready CME events for family physicians at BC Cancer's Annual Summit, 22–23 November, at the Sheraton Vancouver Wall Centre. 22 Nov: GPO (General Practitioner in Oncology) Case Study Day, and 23 Nov: Family Practice Oncology CME Day. GPO Case Study Day (up to 5.5 Mainpro+ credits) provides in-depth exploration of prevalent and emerging challenges in cancer care through case-based discussion, while Family Practice Oncology CME Day (up to 5.75 Mainpro+ credits) provides insight into new developments and practice changing guidelines in cancer care. Both offer opportunity to build helpful cancer care connections. Full details at fpon.ca or via dilraj.mahil@bccancer.bc.ca.

MINDFULNESS IN MEDICINE WORKSHOPS AND RETREATS

Various locations, 29 Nov–24 May

Join Dr Mark Sherman and your community of colleagues for a transformative workshop or retreat! Foundations of Theory and Practice Workshop for Health Professionals, 29 Nov–1 Dec, Kingfisher Resort, Royston, and A Physician Meditation Retreat, 24–29 May, Hollyhock, Cortes Island. Physician Heal Thyself workshops focus on the theory and practice of mindfulness and meditation—reviewing definitions, clinical evidence, and neuroscience, and introducing key practices of self-compassion, breath work, and sitting meditation to nurture resilience and healing. This annual meditation retreat is an opportunity to delve deeply into meditation practice in order to recharge, heal, and build a practice for life. Each workshop is accredited for 16 Mainpro+ group learning credits and has a 30-person limit, so please register today! Contact us at hello@livingthismoment.ca, or check out www.livingthismoment.ca/event for more information.

GP IN ONCOLOGY TRAINING

Vancouver, 3–14 Feb (Mon–Fri)

The BC Cancer's Family Practice Oncology Network offers an 8-week General Practitioner in Oncology training program beginning with a 2-week introductory session every spring and fall at the Vancouver Centre. This program provides an opportunity for rural family physicians, with the support of their community, to strengthen their oncology skills so that they may provide enhanced care for local cancer patients and their families. Following the introductory session, participants complete a further 30 days of customized clinic experience at the cancer centre where their patients are referred. These can be scheduled flexibly over 6 months. Participants who complete the program are eligible for credits from the College of Family Physicians of Canada. Those who are REAP-eligible receive a stipend and expense coverage through UBC's Enhanced Skills Program. For more information or to apply, visit www.fpon.ca, or contact Jennifer Wolfe at 604 219-9579.

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