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Perspective

The economic implications of penicillin allergy

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The incidence of penicillin allergy has been widely exaggerated. Although up to 10% of patients report penicillin allergies to their physicians, more than 90% of these individuals can, in fact, tolerate penicillins when challenged.¹ Despite this reality, many physicians are reluctant to refer patients with self-reported penicillin allergy for testing, often out of concern for the cost-effectiveness of allergy testing relative to simple avoidance. Similarly, many allergists do not offer allergy testing to penicillin because of the high cost of testing materials and low reimbursement from the insurance companies. The cost of the major determinant far outpaces the reimbursement at approximately \$140 per single-use ampule, whereas reimbursement may be less than 10% of that. Furthermore, obtaining the minor determinant, penicillin G, is difficult, necessitating oral graded challenges in which only double-dose challenges are compensated. Compensation for these procedures is \$121, according to the Center for Medicare and Medicaid Services 2020 fee schedule. Much has been written about the benefits of penicillin allergy testing from the perspective of antibiotic stewardship.¹ Many with low-risk histories can be unlabeled penicillin-allergic with a single-dose challenge and follow-up. However, for high-risk patients, there is also clear evidence that from a financial standpoint, allergy testing represents the most cost-effective option for the system. The Infectious Disease

Society of America has included penicillin testing as part of its guidelines for antibiotic stewardship.

The economic impact of penicillin allergy is not insignificant. Unverified penicillin allergies result in the widespread use of broad-spectrum antibiotics such as cephalosporins, macrolides, quinolones, and lincosamides (eg, clindamycin), which are believed to contribute to a growing problem of antibiotic resistance.^{1,2} Moreover, avoidance of beta-lactam antibiotics frequently results in the use of alternative antibiotics with increased toxicity, decreased efficacy, and considerably higher costs.^{1,2} Although oral penicillin typically costs between \$0.78 and \$2.02 per 500-mg tablet, and parenteral penicillin typically costs between \$33 and \$42 per 5 million units, alternative antibiotics used in cases of penicillin allergy range in cost (Table 1). However, direct drug costs are only 1 component of the increased health care spending associated with penicillin allergy.

In a 2018 systematic review, researchers found that health care costs for patients with reported penicillin allergy are significantly higher than for those without penicillin allergy.¹ In the outpatient setting, prescription costs were estimated to be between \$14 and \$193 higher per patient with penicillin allergy. The effect in the inpatient setting is even greater; although direct drug costs during inpatient admissions ranged from no difference to up to \$609 higher for patients with penicillin allergy, the total inpatient costs were between \$1145 and \$4254 higher per patient for patients with penicillin allergy when compared with controls with no penicillin allergy, largely owing to an increased length of stay.¹ Researchers also found that 86% of patients who received negative test results for penicillin allergy went on to receive beta-lactam antibiotics on subsequent admissions, suggesting the potential for immediate and lifelong cost-savings.^{1,3}

Many professional bodies, including the Centers for Disease Control and Prevention and the Infectious Disease Society of America, currently recommend penicillin allergy testing as a method to

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Table 1Frequently Used Penicillins, Alternative Antibiotics, and Cost (Lexicomp Clinical Drug Information⁵)

Drug	Dose unit	Price	Cost relative to amoxicillin
Penicillin V	500 mg	\$0.78–\$2.02	>\$0.65
Penicillin G	5,000,000 unit	\$33.00–\$42.18	>\$32.87
Benzathine	600,000 units	\$109.03	>\$108.90
Nafcillin	1 g	\$17	>\$16.87
Oxacillin	1 g	\$17	>\$16.87
Amoxicillin	250 mg	\$0.13–\$0.25	>\$0
Ampicillin	1 g	\$4.20–\$9.00	>\$4.07
Amoxicillin-clavulanate	875–125 mg	\$5.05	>\$4.92
Piperacillin-tazobactam	2.25 (2–0.25) g	\$6.60–\$14.50	>\$6.47
Ampicillin-sulbactam	1.5 (1–0.5) g	\$4.20–\$9.54	>\$4.07
Cephalexin	250 mg capsule	\$0.19–\$0.87	>\$0.06
Cefdinir	1 capsule	\$5.11	>\$4.98
Cefpodoxime	100 mg	\$6.74	>\$6.61
Azithromycin	250 mg capsule	\$7.77	>\$7.64
Doxycycline	50 g capsule	\$1.50	>\$1.37
Clindamycin	7 5mg capsule	\$0.60	>\$0.47
Ciprofloxacin	250 mg capsule	\$5.88	>\$5.75
Levofloxacin	250 mg tablet	\$0.12–\$17.53	<\$0.01
Moxifloxacin	400 mg tablet	\$9.26–\$27.23	>\$9.13
Ceftriaxone	1 g	\$1.80–\$47.05	>\$1.67
Cefepime	1 g	\$6–\$20	>\$5.87
Vancomycin	1 g	\$0.14	>\$0.01
Meropenem	1 g	\$35	>\$34.87
Imipenem	250 mg	\$5.99–\$15.00	>\$5.86
Ertapenem	1 g	\$145	>\$144.87
Aztreonam	1 g	\$33	>\$32.87
Metronidazole	500 mg	\$0.03	<\$0.10

encourage antibiotic stewardship.⁴ According to the professional guidelines, the recommended method for the evaluation of a true immunoglobulin E-mediated penicillin allergy is skin testing for moderate-to-high-risk patients. A 2018 study estimated that penicillin allergy evaluation (consisting of skin testing followed by a 1-step amoxicillin 500 mg oral challenge if negative) cost \$220 in 2016 US dollars, including \$98 for personnel costs, \$119 for consumables, and \$3 for space, with only modest increases in expected costs of testing (\$214–\$246) taking into account the probability of anaphylaxis.⁴ However, this evaluation vastly underestimates the actual cost today, because the list price of Pre-Pen (Alk Laboratories, Round Rock, Texas) is now close to \$700, and the rent of a room to perform the oral challenge often exceeds the total payment. In reality, most allergists cannot afford to do this testing because they are reimbursed only \$30 for the test administration and \$8 for the Pre-Pen.

The allergy community should continue to advocate for the continued availability of penicillin testing materials, given that frequent Food and Drug Administration oversight threatens to make

testing materials completely unavailable. As physicians and other health care providers strive to achieve high-value care, it is imperative that providers who perform the test also receive a fair payment for the service rendered. Clearly, from a macroeconomic point of view, establishing most people labeled as penicillin-allergic as able to tolerate penicillins would save the health care system significant costs. Unfortunately, the microeconomics makes this determination an almost insurmountable financial and time burden in the outpatient setting on both providers and patients.

One option to solve this problem would be to advocate to the Relative Values Update Committee to create a separate code for penicillin allergy. This has not been pursued in the past because of the high cost to our specialty societies and very low chance of success. Alternatively, doctors could request a higher payment for the existing code—again, a high-cost low-yield proposition. In view of the prohibitive cost and high false-negative rate, a third option is for clinicians to skip skin testing altogether and move straight to a graded oral challenge for low-risk patients, given that data have not indicated an increased risk of anaphylaxis but rather may be susceptible to false-positive results on testing. Beginning with an oral challenge will decrease the cost to both providers and patients.

Too often, in the American health care system, it is economically prohibitive to provide preventive services like penicillin testing that will benefit society as a whole. Certainly, the expansion of hospital systems that work in collaboration with allergists to test most admitted patients would save the system money. Although the cost of penicillin allergy testing is significantly less than the overall burden of providing unnecessary and expensive alternative antibiotics, the individual who performs the test is penalized with a payment that, in most cases, does not come close to the actual cost of providing the service. Moreover, morbidity from multidrug resistance may occur owing to the use of unnecessary antibiotics. Bridging this gap could undoubtedly have widespread economic benefits within the health care system overall.

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