

POEMs

Patient-Oriented Evidence That Matters

Amoxicillin Oral Challenge Is Safe and Accessible for Removing Erroneous Penicillin Allergy Label

Clinical Question

Is an amoxicillin oral provocation challenge safe and accessible for distinguishing an erroneous penicillin allergy from a true one in adults and children?

Bottom Line

The study reported that the outcome of an amoxicillin oral provocation challenge—conducted in 99 adults and children who were initially labeled as having a penicillin allergy—subsequently identified the participants by history to be at low risk of having a true allergy. A total of 96 patients (97%) completed an amoxicillin oral provocation challenge with no reaction, which resulted in the removal of an erroneous penicillin allergy label. The three patients who had an allergic reaction had mild symptoms and required minimal intervention (i.e., no epinephrine). Use of this method to identify the millions of adults and children who have been incorrectly labeled as having a penicillin allergy may result in significant health care savings by eliminating the use of alternative antibiotics that are less effective and safe and more expensive. (Level of Evidence = 2b)

Synopsis

Although approximately 10% of adults and children are labeled as having an allergy to penicillin, less than 20% of those are truly allergic. It is not practical to refer the millions of adults who are labeled allergic to penicillin for testing. However, an easy rule is available that can identify adults at low risk of a true penicillin allergy (the adult version is reliably accurate; this is not true when using the same decision

rule for children 12 years or younger). The investigators, using similar criteria as those in the PEN-FAST decision tool, identified 99 adults and children, 18 months or older, who were considered low risk (less than 5%) for having a true penicillin allergy. Clinical settings were equipped with oral diphenhydramine elixir to manage mild reactions and epinephrine to manage anaphylactic reactions. Amoxicillin was given as an oral suspension (250 mg per 5 mL). The first 10% of the challenge dose (50 mg, or 4.5 mg per kg if the patient weighed less than 10 kg [22 lb]) was given, and the patients were observed for 20 minutes. If no reaction occurred, patients received the remaining 90% of the calculated dose (450 mg, or 40.5 mg per kg) and were observed for one hour. A positive reaction was the development of objective findings, including urticaria, wheezing, or swelling, and did not include subjective symptoms such as pruritus without skin changes or dizziness. Patients were instructed to report any delayed symptoms of rash, hives, wheezing, or swelling up to a week later.

Of the 99 eligible patients who completed the protocol, a mild reaction occurred in three patients (3%) and required the administration of oral diphenhydramine only. The remaining 96 patients (97%) had the penicillin allergy label removed from their medical record. No delayed reactions were reported.

Study design: Cohort (retrospective)

Funding source: Self-funded or unfunded

Setting: Outpatient (any)

Reference: *Gateman DP, Rumble JE, Protudjer JLP, et al. Amoxicillin oral provocation challenge in a primary care clinic: a descriptive analysis. CMAJ Open. 2021;9(2):E394-E399.*

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No Increased Risk of Esophageal Cancer With Nonerosive Gastroesophageal Reflux

Clinical Question

Are patients with nonerosive gastroesophageal reflux disease (GERD) at an increased risk of esophageal cancer compared with the average population?

Bottom Line

Nonerosive GERD does not increase the likelihood of esophageal cancer. However, erosive GERD is associated with a doubled, but still low, risk of developing cancer, with the likelihood increasing over time. (Level of Evidence = 1b)

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This series is coordinated by Natasha J. Pyzocha, DO, contributing editor.

A collection of POEMs published in *AFP* is available at <https://www.aafp.org/afp/poems>.

Synopsis

The Scandinavian researchers followed up on 486,556 adults who underwent endoscopy in Denmark, Finland, and Sweden. These countries have national registries, which allows follow-up of patients over time; the study took place over a 32-year period that ended in 2019. Among the 285,811 patients with nonerosive GERD, 228 (0.08%) developed esophageal cancer during 2,081,051 person-years of follow-up (median follow-up was 6.3 years, although some patients were followed for up to 31 years). This rate is similar to the rate of developing esophageal cancer in the general population. In contrast, 542 patients (0.27%) with erosive GERD subsequently developed cancer. These results may not apply to Eastern Asia, where the overall incidence of esophageal cancer is higher than other countries.

Study design: Cohort (prospective)

Funding source: Foundation

Setting: Population-based

Reference: Holmberg D, Santoni G, von Euler-Chelpin M, et al. Non-erosive gastro-oesophageal reflux disease and incidence of oesophageal adenocarcinoma in three Nordic countries: population based cohort study. *BMJ*. 2023;382:e076017.

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Network Analysis Finds Oral Isotretinoin Most Effective for Acne Vulgaris

Clinical Question

What are the most effective therapies for acne vulgaris?

Bottom Line

Oral isotretinoin was the most effective therapy for decreasing the number of lesions in patients with acne. However, oral isotretinoin is not considered first-line therapy. Topical retinoids and benzoyl peroxide combined with oral or topical antibiotics were comparably effective in achieving the assessment of treatment success. Another analysis suggested starting treatment with adapalene (Differin) plus benzoyl peroxide, clindamycin plus benzoyl peroxide, or adapalene alone. (Level of Evidence = 1a-)

Synopsis

The ambitious, data-laden network meta-analysis sought to identify the most effective therapies for a condition that many think of as trivial or a rite of passage for adolescents. However, the psychological and cosmetic impacts make acne vulgaris an important condition for primary care physicians to properly manage. The authors searched PubMed and Embase to identify randomized trials that assessed the effectiveness of therapies for acne. They included 210

papers with 65,601 patients. The median duration of the studies was 12 weeks (range = 2 to 48 weeks). The studies evaluated six oral antibiotics, five topical antibiotics, oral isotretinoin, five topical retinoids, six combined oral contraceptives, topical clascoterone (Winlevi), 10 combination therapies, benzoyl peroxide, azelaic acid, and placebo. The most common outcomes were disease-oriented inflammatory and noninflammatory lesion counts, but 69 studies reported the investigators' global assessment of success. No study reported patients' self-assessments. Overall, the studies were of decent quality. Oral isotretinoin was the most effective agent at decreasing the number of lesions (relative reduction = 48.4%), followed by combination therapy (i.e., oral antibiotic, topical retinoid, and benzoyl peroxide; relative reduction = 38.2%). For patients with inflammatory lesions, oral isotretinoin was also the most effective (relative reduction = 54.2%), followed by a combination of topical antibiotics plus azelaic acid (relative reduction = 43.6%). The effectiveness of combined oral contraceptives was inconsistent, possibly due to studies that included patients without hormonally sensitive acne. Using the investigators' assessment of treatment success, topical retinoids and benzoyl peroxide combined with oral or topical antibiotics were comparable (odds ratio = 6.04 and 6.76, respectively). Patients taking topical trifarotene (Aklief) had the greatest odds of discontinuing treatment due to adverse events (odds ratio = 11.4). There were moderate to high degrees of heterogeneity among the data (I^2 range = 61% to 79%). There was no strong evidence of publication bias.

Study design: Meta-analysis (randomized controlled trials)

Funding source: Unknown/not stated

Setting: Outpatient (any)

Reference: Huang CY, Chang IJ, Bolick N, et al. Comparative efficacy of pharmacological treatments for acne vulgaris: a network meta-analysis of 221 randomized controlled trials. *Ann Fam Med*. 2023;21(4):358-369.

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Nicotine Replacement With e-Cigarettes Might Help Smokers Quit

Clinical Question

Is switching to e-cigarettes effective for helping smokers who want to quit?

Bottom Line

For adults who want to quit smoking, nicotine delivery via e-cigarettes plus counseling may be more effective than other means of nicotine replacement for long-term smoking cessation. There was no report of the percentage of patients

who maintained e-cigarette use while remaining abstinent from smoking. (Level of Evidence = 1a)

Synopsis

The investigators searched three databases, including Cochrane CENTRAL, and identified five randomized controlled trials that studied a total of 3,253 people who smoked and wanted to quit. The studies were limited to those published in English or French. Two authors independently selected articles for inclusion and extracted the data. Two studies compared nicotine replacement with e-cigarettes plus counseling, nicotine-free e-cigarettes plus counseling, and counseling alone. Three studies compared nicotine replacement with e-cigarettes plus counseling with nicotine-free e-cigarettes and any conventional smoking cessation therapy (e.g., a patch). There were no studies of any comparison with varenicline (Chantix) or bupropion. Biochemically confirmed abstinence (via expired carbon monoxide levels) at six months (four studies) or one year (one study) was more likely with nicotine replacement with e-cigarettes than

conventional therapy (relative risk = 1.77; 95% CI, 1.29 to 2.44), with a number needed to treat of 19 (95% CI, 10 to 51). e-Cigarettes with nicotine were also more effective than nicotine-free e-cigarettes (relative risk = 1.56; 95% CI, 1.13 to 2.15). There was no heterogeneity for these results among the studies. Study quality was generally high.

Study design: Meta-analysis (randomized controlled trials)

Funding source: Foundation

Setting: Various (meta-analysis)

Reference: Levett JY, Filion KB, Reynier P, et al. Efficacy and safety of e-cigarette use for smoking cessation: a systematic review and meta-analysis of randomized controlled trials. *Am J Med.* 2023;136(8):804-813.e4.

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