

A REVIEW OF NEOMYCIN

This article discusses the history of neomycin, its properties and prevalence as a contact allergen.

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Allergic contact dermatitis (ACD) is an important disease that notably affects 14.5 million Americans each year.¹ The economic impact of this disease is high in terms of both patient morbidity and loss of income, school and work, not to mention significant expenditures for healthcare visits and medicaments. A correct diagnosis of ACD will improve, prevent or “cure” the dermatitis and decrease overall costs to the healthcare system.¹ Once patch testing is performed and a culprit has been identified, education becomes the critical intervention to ensure adherence to an avoidance regimen. With allergen avoidance, remission of the dermatitis ensues. If patients are unable to comply with the avoidance regimen, they become at risk for recurrent or sus-

tained dermatitis or progression to a systematized presentation.^{2,3}

The 2 main types of contact dermatitis are irritant and allergic, with irritant contact dermatitis (ICD) being the most common. ICD may occur in anyone who is exposed to an irritating substance with significant duration or in significant concentrations such as chronic or frequent water exposure, abrasive cleansers, detergents and soaps. It is important to note that ICD can at times precede or be a concomitant diagnosis with ACD.^{4,5} ACD represents a T-helper cell type 1 dependent delayed-type (type IV) hypersensitivity reaction that can occur to a large number of chemicals from poison ivy to metals to fragrances. These instigating exogenous antigens are primarily small lipophilic chemicals (haptens) with

molecular weights of less than 500 Da.⁶ On direct antigen exposure to the skin or mucosa, an immunologic cascade is initiated which includes cytokines (ie, interleukin 2 and interferon gamma), T cells and dendritic cells. This complex interaction is the basis for the clinical expression of ACD.

The evaluation of ACD fits well with theranostic theory, as the epicutaneous patch test diagnostic evaluation dictates the avoidance management in each individual patient. Although ACD is not “curable,” many individuals will achieve complete remission with assiduous avoidance. In this column, we highlight we highlight ACD and explore top relevant allergens, regional-based dermatitis presentations, topic-based dermatitis presentations and clinical tips and pearls for diagnosis and treatment. This article focuses on the antibiotic, neomycin.

HISTORY

The history of wound healing treatments dates back to 2200 BC.⁷ The first wound dressings, referred to as plasters, were composed of mud, clay, plants, oil and herbs. The Egyptians later utilized a mixture of grease, honey and lint as a wound ointment. Similar to oil, grease and honey were believed to prevent infection. The Egyptians would also paint wounds green, the copper in the green paint serving as a bactericidal agent.⁷

Of interest, it was not established until the latter half of the 19th century that a microorganism could be capable of destroying another microbiotic species, when Louis Pasteur observed the antagonistic effect of saprophytic (soil) bacteria on the growth of anthrax bacteria. This spurred the notion that this interaction might be put to therapeutic use and the antimicrobial field was borne. Along this same line, Sir Alexander Fleming, a Scottish bi-

ologist, observed that the common mold *Penicillium notatum* could destroy *Staphylococcus* bacteria in culture (c.1928). Ten years later, penicillin was isolated and proven effective in the treatment of bacterial infections.⁸

The race was on to discover more antibiotics, especially one with gram-negative class bioactivity. In 1943, Selman Waksman, Albert Schatz and Elizabeth Bugie isolated the first aminoglycoside antibiotic, streptomycin, derived from *Streptomyces griseus*.⁹ With its diverse spectrum of action, streptomycin revolutionized the treatment of tuberculosis and other previously untreatable bacterial infections.

A few years later, Waksman discovered a new member of the aminoglycoside class of antibiotics, neomycin, derived from *Streptomyces fradiae*.⁹ Neomycin was rapidly bactericidal and had better bioactivity than streptomycin against gram-negative bacilli. Although its systemic use was limited by ototoxicity, nephrotoxicity and poor absorption from the gastrointestinal tract,¹⁰ it proved efficacious as a topical preparation for skin and mucous membrane infections, wounds and burns.

To this day, the aminoglycosides are among the most commonly used antibiotics worldwide, due to their high efficacy and low cost. Furthermore, neomycin has become a household staple in the prevention and treatment of superficial skin infections.

PROPERTIES, USES AND CROSS-REACTIONS

Neomycin inhibits protein synthesis by binding to the 30s subunit of ribosomal RNA and is bactericidal against gram-negative and gram-positive organisms, especially *S aureus*. It is not effective in the treatment of *Pseudomonas aeruginosa* and anaerobic bacteria, and it is weakly effective against streptococci.¹¹

Neomycin is found in a variety of over-the-counter (OTC) antibacterial products, including “triple antibiotic” — a combination of neomycin, bacitracin and polymyxin B. It is a common contact allergen postoperatively and in patients with leg ulcers,¹¹ as well as in patients with venous stasis dermatitis. In those who present with exacerbations of venous stasis dermatitis, it

Table 1. PRODUCTS CONTAINING NEOMYCIN

Neosporin Antibiotic Ointment	Generic Neomycin Antibiotic Ointment
Neosporin + Pain Relief Ointment and Cream	Bactine Pain Relieving Protective Antibiotic
Cortisporin Cream	Bacimycin
Band-Aid Plus Ointment	Gold Bond Triple Action Ointment
Tobradex Ointment and Solution	Cortisporin-TC Otic Suspension
Tobrex Ointment and Solution	Cortisporin Ophthalmic Suspension

Table 2. PRODUCTS WITHOUT NEOMYCIN

Mupirocin 2% Ointment	Biofine Cream
Silvadene Cream	Ciprodex Otic Suspension
Bactine Liquid	Floxin Otic
Petroleum Jelly	Vigamox Ophthalmic Solution
Aquaphor Ointment	Diloxan Ophthalmic Solution
Bacitracin Ointment	Betadine Ointment

is important to inquire as to the use of topical neomycin.

Although not as commonly recognized, neomycin is also found in dental paste, creams, eye drops, pet food, veterinary products, deodorants, soaps, cosmetics and vaccines.¹² The amount of neomycin in vaccines is quite low and unlikely to cause a systemic reaction in patients who exhibit a delayed-type hypersensitivity reaction to it. In those patients with a history of anaphylaxis after exposure to neomycin, neomycin-containing vaccines should be avoided. Vaccines containing neomycin include Varivax (varicella), Attenuvax (measles), Fluvirin (influenza) and Imovax (rabies).¹⁰

Allergy to neomycin may cause cross-sensitivity to other related antibiotics, such as gentamicin, kanamycin, paromomycin and streptomycin. Products containing any of these substances should be avoided in neomycin-allergic patients. Bacitracin, which is not an aminoglycoside, co-reacts, but does not cross react, with neomycin. This phenomenon occurs due to the simultaneous use of bacitracin and neomycin, which are found together in a variety of OTC products.¹¹

NEOMYCIN AND PREVALENCE OF ACD

Neomycin is one of the most common contact allergens in the United States and was named the American

Contact Dermatitis Society (ACDS) Allergen of the Year in 2010.¹⁰ The North American Contact Dermatitis Group patch test results from 2009 to 2010 found neomycin to be the second most frequent allergen, with a prevalence of 8.7%, as well as the most common topical antibiotic to cause a contact allergy.¹³ The overall prevalence for neomycin contact sensitivity has dropped significantly from prior years, when its prevalence was 10.1% to 11.4%.¹³

Notably, and not unexpectedly, neomycin is also one of the most common contact allergens in children. Recent data showed a prevalence of 6.6%, following nickel and cobalt.¹⁴ Due to its popularity as a childhood contact allergen, neomycin has been included in a basic screening panel of 20 contact allergens for preliminary pediatric patch testing.¹⁵

PRACTICALS OF PATCH TESTING

Patch testing is often necessary to confirm the diagnosis of ACD and to identify the relevant allergen(s) responsible. Screening patch test trays are available, which isolate the most common chemicals and offer the provider clues for potential sources. Neomycin (20% pet.) is included in the ACDS Standard 80 Core Allergen Series and neomycin sulfate, 230 mcg/cm² is on the Thin-Layer Rapid

Use Epicutaneous Patch Test (position 3).^{16,17} Neomycin patch-test reactions may be late delayed and may persist for a few weeks.¹⁰

PEARLS OF TREATMENT: EVERY DOSE COUNTS

A person may be exposed to and subsequently sensitized to a contact allergen for days to years before demonstrating the clinical picture of ACD. With each exposure, there is an increased risk of reaching a point at which the immune system meets its metaphorical “threshold” and subsequent exposures at this point can lead to elicitation of a cutaneous response.¹⁸ Just as repeated contact over time led to this immune response, repeated avoidance of the majority of exposures over time will be required to induce remission. **Table 1** highlights products that contain neomycin,¹⁹ while **Table 2** lists products that can be substituted for neomycin in allergic patients.²⁰ ■

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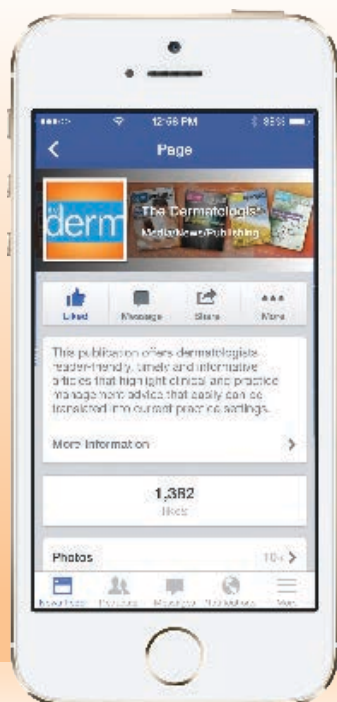
Disclosure: Dr. Jacob has served as an independent investigator on the safety and efficacy of T.R.U.E. Test™ (SmartPractice; Phoenix, AZ) panels 1.1, 2.1 and 3.1 in children and adolescents, Pediatric Research Equity Act (PREA-1) trial and now serves as an investigator on PREA-2. She has served as a consultant for Johnson & Johnson.

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