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Antibiotic stewardship in dermatology: reducing the risk of prolonged antimicrobial resistance in skin

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Antibiotics are highly effective treatment options for different dermatologic conditions. However, antibiotic overprescribing contributes to the emergence of antibiotic resistance and places patients at risk for resistant infections and treatment failures. The Centers for Disease Control and Prevention has called upon prescribers to re-evaluate the frequency, dosing, and duration of antibiotic prescriptions and to eliminate unnecessary use. Despite an overall decrease in antibiotic prescribing in dermatology over the past decade, US dermatologists continue to prescribe antibiotics at higher rates than providers of other specialties.[1] Thus, dermatologists are critical stakeholders in antibiotic stewardship efforts and play essential roles in optimizing antibiotic use. This Viewpoint outlines antibiotic prescribing practices of US dermatologists and summarizes the latest evidence on resistance development following exposure to systemic antibiotics routinely prescribed in dermatology. We discuss clinical consequences of antimicrobial resistance and highlight strategies to promote antibiotic stewardship in dermatologic practice. These strategies include: considering alternative therapies to antibiotics, avoiding oral antibiotic monotherapies, prescribing the shortest effective treatment duration, and considering narrow spectrum antibiotics.

Oral antibiotics are commonly prescribed by dermatologists for skin and soft tissue infections, cutaneous surgeries, and chronic inflammatory skin conditions. In a cross-sectional analysis of prescribing trends among US dermatologists from 2008 to 2016, tetracyclines were the most commonly prescribed antibiotics, followed by cephalexin and trimethoprim/sulfamethoxazole (TMP/SMX).[1] Infections and surgical visits were generally associated with short antibiotic courses (median 7–14 days), whereas inflammatory skin diseases, such as acne and rosacea, were commonly associated with extended regimens (>28 days). An analysis of prescription trends revealed a decrease in the use of extended antibiotic courses for acne and rosacea in recent years but a concerning increase in short antibiotic courses after surgical visits.[1] These data support the need for further optimization of antibiotic use in the surgical setting.

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Research efforts are now aimed at understanding how antibiotic prescribing in dermatology leads to the development of antimicrobial resistance. Evidence from human microbiome studies suggests that antibiotic regimens typically used in dermatology can trigger expansion of antibiotic-resistant skin bacteria. A recent prospective, longitudinal study examined resistance development in healthy adults receiving dermatology-relevant antibiotic regimens.[2] Antibiotic-resistant staphylococci were recovered from skin following, but not prior to, receipt of doxycycline or TMP/SMX. Doxycycline-resistant bacteria were isolated from all subjects receiving therapeutic doxycycline dosing (100mg) and from half of the subjects receiving subtherapeutic dosing (20mg). This suggests that subinhibitory (non-lethal) antibiotic concentrations may exert weaker selective pressure on skin bacteria but still lead to the development of antibiotic resistance. Genomic sequencing of resistant *Staphylococcus epidermidis* skin isolates demonstrated specific bacterial genes that confer resistance to doxycycline (*tetk/tetL*) and TMP (*dfrA/dfrG*). Remarkably, antibiotic-resistant bacterial strains were isolated from skin up to 336 days after starting antibiotics.

Antibiotics also alter skin microbial communities. Sequencing-based studies have demonstrated shifts in composition and diversity of the human skin microbiome after systemic antibiotics. In one study, four female acne patients were treated with minocycline for four weeks, and their facial skin microbiomes were profiled before and after antibiotics.[3] Oral minocycline was associated with significant shifts in the relative abundances of select skin bacteria, including decreases in *Cutibacterium* and *Corynebacterium* species and increases in *Pseudomonas* and *Streptococcus* species. Using metagenomic sequencing, Jo et al. analyzed alterations in the composition of skin microbial communities in healthy volunteers at various timepoints after oral antibiotic use, and significant changes were observed in subjects who received doxycycline or TMP-SMX but not in untreated individuals.[2] While skin microbiome changes persisted for >200 days in doxycycline-treated subjects, a return to the baseline composition occurred earlier in some TMP-SMX-treated subjects, suggesting that skin microbiome resilience varies with antibiotic treatment type and duration.

Antimicrobial resistance leads to clinically significant consequences, including antibiotic treatment failures. In acne patients, the presence of antibiotic-resistant *Cutibacterium acnes* on skin may be associated with suboptimal patient outcomes from inadequate responses to both topical and oral antibiotics.[4] Given that human skin can harbor antibiotic-resistant bacteria for extended periods, the skin may represent an underappreciated reservoir for antibiotic-resistant microbes. Routine keratinocyte shedding has the potential to transfer resistant skin bacteria or antimicrobial resistance genes to the environment or possibly other individuals. This is particularly concerning in the context of multidrug-resistant *S. epidermidis* strains persisting on skin.

As drug-resistant microbes continue to emerge from antibiotic overuse, it is critically important that dermatologists incorporate principles of antibiotic stewardship into prescribing practices. The CDC calls on outpatient specialists to focus on potential alternative treatment options for high priority conditions. For dermatologists, these conditions include acne[4,5], rosacea[5], hidradenitis suppurativa[6] and surgical site infection prophylaxis[7] (Table 1). Suggested strategies for acne include: considering spironolactone,

oral contraceptives, or systemic retinoids; adding topical retinoids and/or benzoyl peroxide; and using narrow-spectrum antibiotics.[4,5] Published strategies for rosacea include avoiding triggers, considering physical modalities, and adding topical agents.[5] For hidradenitis suppurativa, consider intralesional steroids (for acute lesions), procedural-based interventions, hormone-based therapies, or biologics.[6] For surgical site infection prophylaxis consider topical decolonization, intralesional antibiotics, and one-time preoperative antibiotic dosing.[7] The strategy of using the shortest effective oral antibiotic regimen duration has led to recommended limits of 3–4 months for acne[4] and hidradenitis suppurativa and 1–2 months for rosacea[5]. However, antibiotic resistance to doxycycline can be detected as early as 14 days of treatment.[2]

While practitioners should aim to eliminate unnecessary antibiotic use, it is important to acknowledge the potential limitations of non-antibiotic therapies (e.g. inability to avoid triggers, medication side effects, insurance denials). Evidence-based guidelines for non-antibiotic therapies are currently limited by a paucity of prospective randomized controlled trials comparing the effectiveness of systemic antibiotics versus alternative treatments for dermatologic conditions. Additionally, investigations into long-term antibiotic resistance risks of topical antibiotics and of approaches that combine antibiotic and non-antibiotic therapies are needed to further guide clinical practice.

In summary, the optimal approach to antibiotic prescribing in dermatology involves a risk-benefit analysis. To achieve the most effective outcomes, dermatologists should consider all therapeutic options. By incorporating antibiotic stewardship principles into prescribing practices, dermatologists can optimize appropriate antibiotic use while limiting the development and spread of antimicrobial resistance and minimizing antibiotic-associated complications.

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Table 1:

Current Suggestions to Promote Antibiotic Stewardship in Dermatology Based on Available Evidence

General CDC-based recommendations	Acne vulgaris[4]	Rosacea (with papulopustular lesions)[5]	Hidradenitis Suppurativa[6]	Surgical Site Infection prophylaxis[7]
Utilize alternatives to systemic antibiotics	Consider spironolactone, oral contraceptives, or isotretinoin when indicated	Encourage proper skin care, sun protection and trigger avoidance Consider topical ivermectin, topical metronidazole, topical azelaic acid, physical modalities (e.g. laser and light devices) or oral isotretinoin for refractory cases	Consider intralesional corticosteroids (acute lesions)[%], procedure-based interventions (e.g. laser hair removal, deroofing, excision), or biologics.	Consider no prophylactic antibiotics in low risk groups[ǂ] Consider topical decolonization with antiseptic (e.g. chlorhexidine) Consider intraincisional antibiotics
Avoid oral antibiotics as monotherapies	Consider concurrent use of antibiotics AND topical retinoids +/− benzoyl peroxide	Consider concurrent use of antibiotics AND topical metronidazole, topical azelaic acid or topical oxymetazoline (if persistent centrofacial erythema is present)	–	–
Prescribe optimal dose and shortest effective duration of antibiotic treatment	Limit antibiotic treatment period[*] followed by topical retinoid +/− benzoyl peroxide for maintenance	Consider subantimicrobial tetracycline dosing[#]	Limit antibiotic treatment period[*]	Consider a single preoperative oral antibiotic dose[ǂ]
Consider narrow spectrum antibiotics	Consider narrow spectrum tetracyclines	–	–	Consider primary coverage for gram positive species of *Staphylococcus* and *Streptococcus* (e.g. cefalexin)

[*] Consensus statements suggest 3–4 months for tetracyclines; recent data indicate antibiotic resistance develops within 14 days[2]

[ǂ] May not be appropriate for high-risk patients (e.g. immunocompromised, high risk cardiac conditions, joint prostheses) or high-risk anatomic sites (e.g. lower limb, groin)

[#] May exert weaker selective pressure but can still lead to resistance development

[%] May not be beneficial based on results of recent randomized controlled trial

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