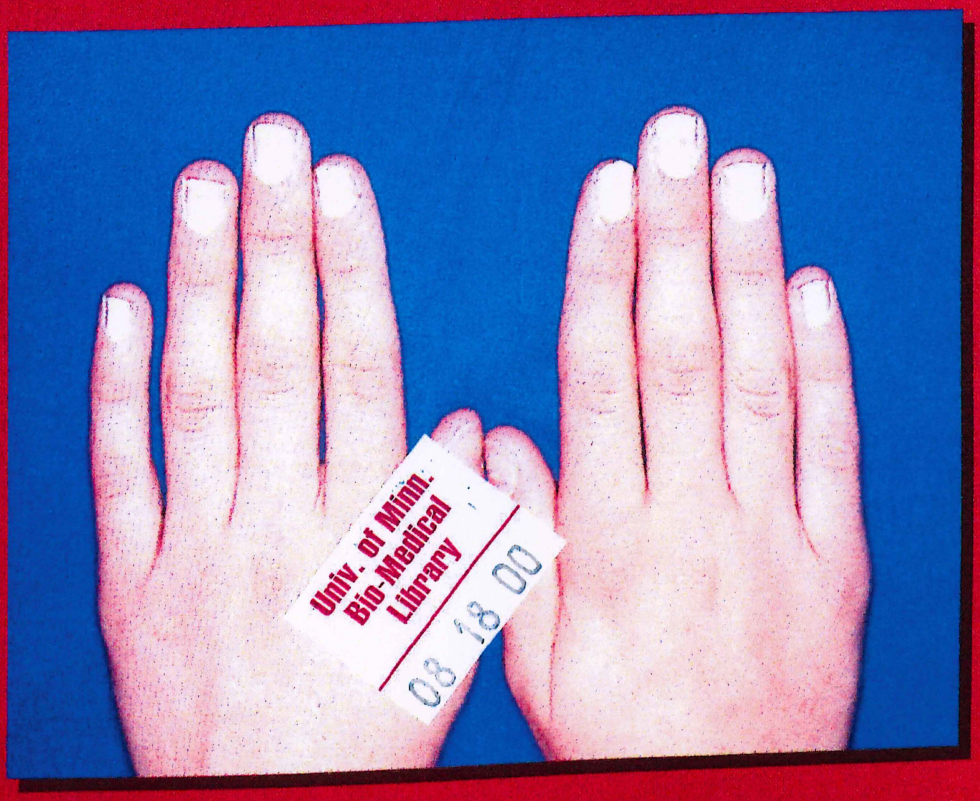
CUTANEOUS MEDICINE
FOR THE PRACTITIONER

VOL. 66 NO. 2
AUGUST 2000

# cutis®



# Treatment of Rosacea With Doxycycline Monohydrate

Joseph B. Bikowski, MD, Pittsburgh, Pennsylvania

*Rosacea is one of the most commonly occurring inflammatory dermatoses treated by dermatologists today. Estimates suggest that at least 13 million Americans have recognized rosacea, and the clinical experience of most practitioners would add considerably more to that number. Rosacea is an inflammatory condition of the skin, classically presenting with a history of flushing and/or blushing along with the clinical findings of erythema, edema, telangiectasia, papules, pustules, and nodules of the face. Severity and distribution vary considerably. A patient may have only a few scattered papules and pustules of the central third of the face or there may be numerous inflammatory, painful, tender, large nodules. In some cases, only the face may be affected. In other cases, there may be lesions of the scalp, neck, and/or torso. Although the exact etiology is unknown, rosacea is thought by most experts to be an inflammatory process incited by vascular instability with subsequent leakage of fluid and inflammatory mediators into the dermis.*

Treatment frequently consists of a topical medication in combination with a systemic antibiotic. The choice of an appropriate therapeutic regimen that fits the lifestyle and desires of the patient is key to patient compliance, which is necessary to obtain and maintain suppression of the disease. Two cases of inflammatory rosacea of the face in patients who desired rapid clearing without the use of topical medication are presented. Oral antibiotics are a well-established treatment for rosacea, however, these patients improved dramatically within 1 to 2 months of beginning treatment, exclusively with doxycycline monohydrate.

Dr. Bikowski is a Clinical Assistant Professor, University of Pittsburgh, Department of Dermatology, Pittsburgh, Pennsylvania. REPRINT REQUESTS to Sewickley Dermatological Associates

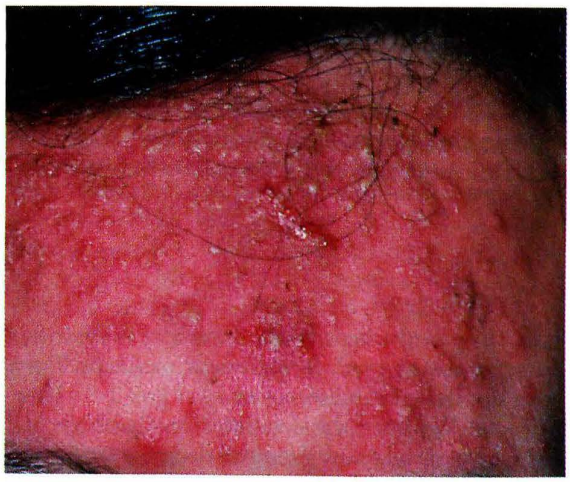


**FIGURE 1.** A 45-year-old man presented with an erythematous papulo-pustular eruption on the forehead, nose, medial cheeks, and chin. Forehead lesions were most impressive.

## Case Reports

*Patient 1*—A 45-year-old attorney initially presented with a 3- to 4-day history of a pruritic, erythematous, linear vesicular eruption of the posterior right thigh. A diagnosis of allergic contact dermatitis secondary to poison ivy was made, and the patient was treated with prednisone 40 mg/day for 10 days. The patient was also noted to have an inflammatory eruption of the face and related a 3-year history of intermittent "break outs" that had become constant over the preceding 6 months. In addition, he recalled episodes of flushing, which occurred after drinking alcohol or hot beverages. An erythematous papulo-pustular eruption was present on the forehead, nose, medial cheeks, and chin. The forehead lesions were most impressive (Figure 1). There were no lesions of the neck, scalp, chest, or back. Because of the initial consideration of a primary pyoderma, a bacterial culture was obtained from a pustule of the forehead, and a 5-

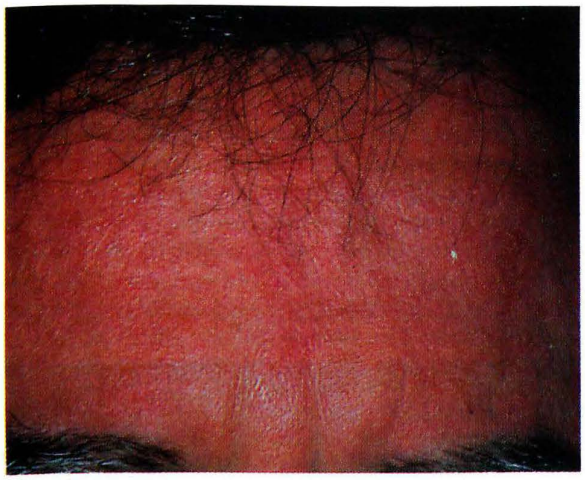


**FIGURE 2.** Nine weeks of therapy with doxycycline monohydrate 100 mg daily produced near-complete clearance.

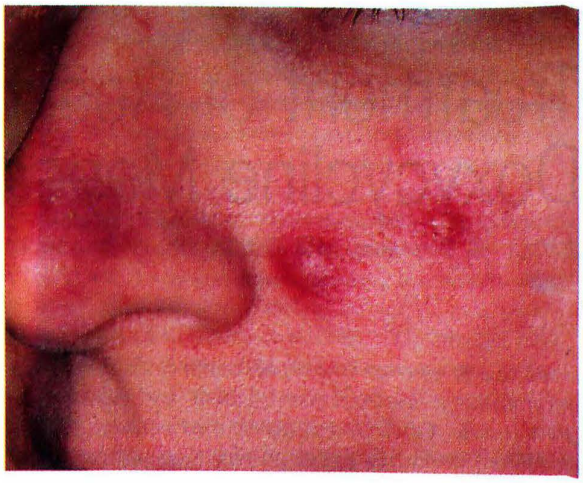


**FIGURE 3.** A 49-year-old female with a history of rosacea presented with tender, painful, erythematous swelling of the left side of the nasal tip and symptomatic inflammatory nodules of the left malar area. She was diagnosed with moderately severe stage III plaque rosacea.

ture was positive for a heavy growth of normal skin flora and a rare growth of *Staphylococcus aureus*. These were not thought to be causative.

Eight days later, the dermatitis on the thigh had resolved and there was a marked decrease in the erythema of the inflammatory lesions on the face. A diagnosis of severe inflammatory stage III rosacea was made. Treatment with doxycycline monohydrate 100 mg/day was initiated. The patient refused topical medications in combination with the systemic antibiotic because of his full-face beard. He did not feel that he would be compliant with daily application of medication to his entire face. Nine weeks later, the eruption had essentially cleared (Figure 2). The cheeks, chin, and nose were also free of erythema, papules, and pustules. The patient had tolerated doxycycline monohydrate well and denied headache, gastrointestinal upset, or photosensitivity. The same dose of doxycycline monohydrate (100 mg/day) was continued as maintenance therapy and the patient remained clear of all inflammatory lesions at follow-up 6 months after initiation of therapy.

*Patient 2*—A 49-year-old female patient presented after 18 months without therapy and complained that her rosacea was flaring. She had previously been treated with a systemic antibiotic and topical metronidazole, but decided to stop treatment when her face cleared. In the 2 months before this visit, she had noted increased total face flushing and renewed "break-outs" on the nose and cheek. On examination swelling of the left side of the nasal tip and two similarly symptomatic inflammatory nodules of the left malar area measuring 1.1 and 0.6 cm in diameter. There were no lesions on the remainder of the face, scalp, neck, or torso. The patient was diagnosed with moderately severe stage III plaque rosacea (Figure 3). Because of the severity of her condition, she elected to pursue systemic antibiotic therapy, but declined the concomitant use of a topical agent because she did not feel that she would comply with daily applications. Therapy with doxycycline monohydrate 50 mg/day was initiated.

The patient was seen in follow-up 1 month later. At that time, there was a marked decrease in the edema and erythema of the nasal and cheek lesions (Figure 4). She had experienced no ill side effects from the doxycycline monohydrate. She was instructed to continue the same dose—50 mg/day—and return in 1 month. At follow-up she was essentially clear. There was minimal postinflammatory erythema of the nasal tip and left cheek (Figure 5). She had no complaints of headache, gastrointestinal upset, or increased sun sensitivity. The doxycycline monohydrate was decreased to 50 mg every other day for long-term maintenance therapy.

## Comments

The efficacy of systemic antibiotics alone or in combination with a topical agent for the treatment of rosacea is well documented.[1] Initial therapy usually

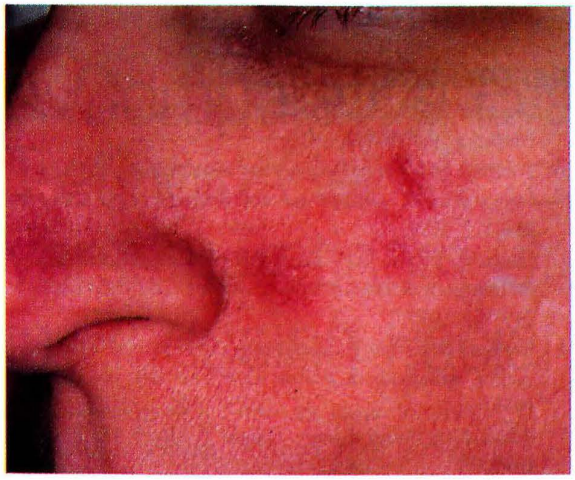


**FIGURE 4.** After 1 month of therapy with doxycycline monohydrate, the patient demonstrated a marked decrease in the edema and erythema of the nasal and cheek lesions.

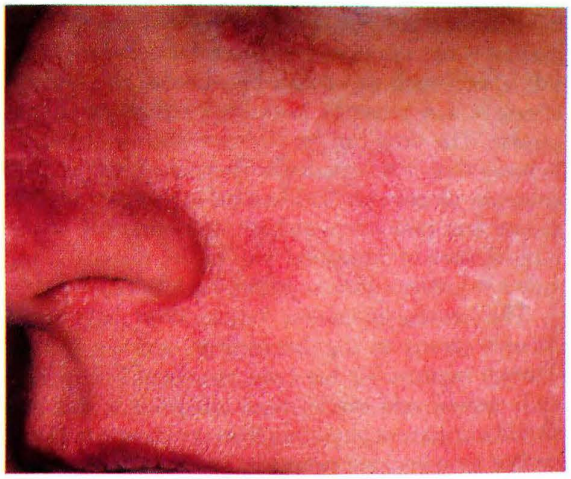


**FIGURE 5.** Two months after the initiation of therapy, the patient was essentially clear with minimal postinflammatory erythema of the nasal tip and left cheek.

cin, doxycycline, minocycline) in combination with a topical preparation (metronidazole, clindamycin, sodium sulfacetamide, and/or sulfur). The clinician's goal is to achieve rapid remission with the oral agent and to maintain remission with the topical medication if at all possible. Any of the commonly used systemic antibiotics will usually clear the inflammatory lesions of moderately severe stage II or III rosacea in 2 to 6 weeks. The topical agents will demonstrate clinical improvement in 4 to 12 weeks, although complete clearing may not be obtainable in that period of time with topical medications alone. Though the ultimate goal is to taper down and/or discontinue oral therapy, intermittent low-dose systemic antibiotics in addition to daily topical treatment may be necessary to maintain complete remission in the majority of patients.

After early claims in the French and Belgian literature touted the success of chloramphenicol in the treatment of rosacea, Sneddon[1] became one of the first to detail the success of tetracycline for this indication. In studies conducted from 1964 to 1965, he noted an 80% success rate treating rosacea patients with 250 mg tetracycline twice daily.[1] Maibach's[2] review of the second-generation tetracyclines was extremely thorough and is worthy reading. The highlights of that study and another recent study[5] will be detailed later.

The second-generation tetracyclines include minocycline, doxycycline hyclate (hydrochloric

pared to tetracycline, all three have increased bioavailability, improved absorption when taken with food, and broader antibacterial activity.

Minocycline is not photosensitizing, nor is it commonly associated with pseudotumor cerebri. However, many other adverse effects have been associated to some degree with minocycline therapy. Two long-known side effects are vertigo—which is more common in women than in men—and blue staining of the legs, feet, face, or gums. Bluish staining may also present in acne scars. Frequently termed "minocycline hyperpigmentation," this blue-gray staining may appear within 3 to 6 months of the start of therapy. Staining of the teeth may also occur, usually after more than 5 years of continuous minocycline use. Other side effects have more recently been identified with minocycline therapy. Some young women experience a lupus-like syndrome characterized by pain, swelling, and stiffness of the joints as well as by fever, pleuritic chest pain, malaise, and fatigue. A hypersensitivity syndrome has also been identified, characterized by fever, lymphadenopathy, eosinophilia, lymphocytosis, or rash, occuring about 24 days after the start of therapy. Finally, a serum sickness-like reaction has also been identified with onset about 2 weeks after the start of minocycline therapy. Symptoms include fever, lymphadenopathy, arthralgias/arthritis, or rash. With a pH of 2, doxycycline hyclate has been associated with a high rate of esophageal irritation and gastrointestinal upset. How-

drate is not associated with esophageal irritation and has a lower incidence of gastrointestinal upset. Doxycycline is not associated with central nervous system side effects such as vertigo, but, like all the tetracyclines, it may rarely be associated with pseudotumor cerebri. The drug can be photosensitizing—typically in fewer than 1% of patients. Photosensitivity is most common in patients with excessive summer sun exposure and presents as redness and blistering of the nose, dorsum of the hands, and fingers. Sunscreen use may not prevent photosensitivity reactions.

The second-generation tetracyclines have contributed greatly to the dermatologic armamentarium. Though minocycline has been associated with potentially serious side effects, their incidence is rare and should not prevent physicians from prescribing it. Doxycycline monohydrate represents an effective therapeutic option with advantages over doxycycline hyclate.

Doxycycline monohydrate was selected for the patients presented because it is associated with decreased risk of gastrointestinal upset and esophageal ulceration as compared to doxycycline hyclate. Once-daily dosing promotes patient compliance. Doxycycline monohydrate also carries decreased risk of the central nervous system side effects associated with minocycline therapy.

**Product Information**—Monodox®, doxycycline monohydrate, Oclassen Dermatologics.

## REFERENCES


1. Sneddon IB: A clinical trial of tetracycline in rosacea. *Br J Dermatol* 78: 649-652, 1966.
2. Maibach H: Second-generation tetracyclines, a dermatologic overview: clinical uses and pharmacology. *Cutis* 48: 411-417, 1991.
3. Green R, Brown JR, Calvert RT: The disposition of four tetracyclines in normal subjects. *Eur J Clin Pharmacol* 10: 245-250, 1976.
4. Carlborg B, Farmer J: Esophageal corrosion tests with doxycycline monohydrate tablets. *Curr Ther Res* 34: 110-116, 1983.
5. White GM: Acne therapy. *Disease A Month* 45: 301-332, 1999.
6. Rebora A, Drago F, Parodi A: May *Helicobacter pylori* be important for dermatologists? *Dermatology* 191: 6-8, 1995.
7. Bonnar E, Eustace P, Powell FC: The Demodex mite population in rosacea. *J Am Acad Dermatol* 28: 443-448, 1993.
8. Lloyd KM: Surgical correction of rhinophyma. *Arch Dermatol* 126: 721-723, 1990.
9. Plewig G, Nikolowski J, Wolff HH: Action of isotretinoin in acne, rosacea, and gram-negative folliculitis. *J Am Acad Dermatol* 6: 766-785, 1982.