A ctinic keratoses (AKs) and acne are common skin disorders in dermatology. The previous articles provided an overview of the pathogenesis and treatment of acne and AKs. The following four case studies provide examples of how to put this information into practice.

CASE STUDY 1: ACTINIC KERATOSIS

Presentation
A 78-year-old man with a history of squamous cell carcinoma (SCC) and numerous AKs returns for his routine follow-up examination (See Figure 1). He wears a hat and long sleeves when outdoors, but refuses to apply sunscreen. He is not interested in home therapy and prefers to have lesions “burned off” while in the office.

Treatment Options
There are a variety of options for treating patients with AKs. In this case, choices include cryotherapy alone, photodynamic therapy (PDT), or a combination of 0.5% 5-fluorouracil (FU) for 1 week followed by cryotherapy. Each treatment is discussed briefly below, and additional information can be found in the previous article by Joseph L. Jorizzo, M.D.

Cryotherapy. Liquid nitrogen or cryotherapy is the most commonly used treatment for AK. It is a simple and convenient method, which can be done quickly during an office visit. However, there is a significant risk of hypopigmentation, which can be minimized by using a single freeze-saw cycle and reducing the duration of cryotherapy.

PDT. This innovative treatment modality for AK has received FDA approval for lesional therapy; however, “field” therapy remains off-label. Topical 5-aminolevulinic acid (ALA) is converted to protoporphyrin IX, which is a potent photosensitizer. When it is exposed to light, protoporphyrin IX generates oxygen-free radicals, which results in destruction of AKs. There are several potential light sources available, including blue light, intense pulsed light and laser. The efficacy of PDT is comparable to that of 5-FU, and the cosmetic results are good. Side effects include photosensitivity, stinging and burning. Also, the incubation period for 5-ALA and the cost can be inconvenient for patients.

0.5%-FU for 1 week followed by cryotherapy. Often, combination therapy is found to be an effective method for treatment of AKs. With this method, the patient is treated with 0.5%-FU for 1 week. Then, at the 4-week follow-up visit, any residual lesions are treated with cryotherapy. Evaluations were determined at 4 weeks and 6 months. This method was studied in a prospective, multicentered, randomized, double-blind, vehicle-controlled clinical trial, discussed in further detail in Dr. Jorizzo’s article. The study showed those treated with 0.5%-FU had better improvement in lesion counts compared to placebo. This brief 1-week treatment course may be an acceptable alternative for patients who are not interested in a traditional 2- to 4-week course of 5-FU.

Treatment Plan
With this patient, the idea of a 1-week treatment with the topical 0.5%-FU followed by cryotherapy was a practical approach. The use of 0.5%-FU as a “blanket” or “field” treatment would decrease the number of AKs that need to be “frozen off” with cryotherapy. This is a good option for patients who come in every 2 to 3 months with more than 15 lesions.
CASE STUDY 2: ACNE

Presentation
You are asked to evaluate a 17-year-old boy with moderate acne who tells you he uses “whatever soap is in the shower.” He has been taking 100-mg minocycline twice a day, which was prescribed by his pediatrician, for 6 weeks with minimal improvement. Examination reveals a healthy adolescent with oily skin, comedones and inflammatory papules and pustules on the forehead, cheeks, chin, back and shoulders (See Figure 2).8

Treatment Plan
A treatment regimen should be designed based on the severity of the disease and the patient’s ability to comply with treatment. It is important to target the four factors that trigger acne (see Susan C. Taylor, M.D.’s article): (1) follicular epidermal hyperproliferation; (2) Propionibacterium acnes; (3) inflammation; and (4) excess sebum.

For this patient, a topical retinoid was added to his current regimen to reverse follicular hyperkeratinization, prevent future comedones and provide an anti-inflammatory effect. He was continued on minocycline for the anti-inflammatory effect and to suppress P. acnes. A benzoyl peroxide-containing product was added to minimize the emergence of antibiotic-resistant strains of P. acnes and suppress comedone formation.9 Excess sebum was addressed by vehicle selection (ie, gel) and by discussing appropriate skin care, such as the use of a benzoyl peroxide cleanser or salicylic acid wash.

At the initial visit, it is important to counsel the patient on the proper use of all medications and discuss potential adverse effects. Setting reasonable expectations of when improvement will be achieved (eg, the patient will see 40% to 50% improvement in 6 to 8 weeks) and discussion of skincare methods to minimize potential irritation is a vital part of patient education. A 6-week follow-up appointment should be scheduled to evaluate the patient’s progress.

Follow-up
At a 6-week follow-up visit, the patient demonstrates 40% to 50% improvement. He is tolerating oral and topical medications well, and the current regimen is continued. The patient schedules a follow-up visit. Eight weeks later, an approximate 80% improvement has been obtained. The current regimen is continued and he schedules a follow-up visit in 2 months. At this visit, continued improvement is noted and has been sustained, thus it is necessary to plan maintenance therapy for this patient.

Maintenance Therapy
There are several options for maintenance therapy in this patient, including continuing the topical retinoid as monotherapy, continuing the benzoyl peroxide-containing product as monotherapy, continuing with combination topical retinoid and benzoyl peroxide-containing product therapy or tapering to a lower dose of minocycline and continuing with the topical retinoid. In this case, the patient continued with a combination topical retinoid and benzoyl peroxide-containing product therapy, and he continued taking 100-mg minocycline twice a day. Limiting the duration of systemic antibiotics.

TABLE 1: Tips to Lessen Antibiotic Resistance During Acne Treatment

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FIGURE 2. A 17-Year-Old Male with Moderate Inflammatory Acne

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while adding a benzoyl peroxide-containing product, can prevent and reduce resistant strains of *P. acnes*. Topical retinoids can be continued because they do not promote antibiotic resistance and have the ability to prevent future comedones, follicular hyperproliferation and inflammation.

**Antibiotic Resistance**

It is important to consider the potential for antibiotic resistance when establishing a maintenance therapy routine for patients with acne. Dermatologists are increasingly aware of this problem.9-11 Resistance occurs when the bacteria genes for resistance are exposed to chronic antibiotic therapy. This exposure eradicates the susceptible bacteria (target pathogen) and the resistant bacteria (nonpathogenic bacteria) proliferate, thus the number of bacteria can increase. The nonpathogenic bacteria that are resistant to the antibiotic now act as a reservoir of resistant genes that can be transferred to other potentially pathogenic bacteria.10

**Combating resistance.** Dermatologists can help limit antibiotic resistance of *P. acnes* simply by re-evaluating their individual prescribing practices used for acne and following the suggestions provided in Table 1.9,11 If a non-antibiotic topical preparation will suffice, do not prescribe antibiotics. Try to use medications that do not promote resistance (eg, topical retinoids). When an antibiotic is necessary, the duration of use should be brief. If further treatment is required, reuse the same antibiotic whenever possible to avoid resistance to both products. Adding a benzoyl peroxide-containing product to the regimen, as done with this patient, will help prevent and reduce resistant strains of *P. acnes*. Benzoyl peroxide is a broad-spectrum antibacterial agent, which contains oxidized intermediates that interact with and kill microbes. To date, no resistance to benzoyl peroxide has been reported. When used in combination with an antibiotic, benzoyl peroxide prevents the selection of the antibiotic-resistant organisms.13 Finally, try to avoid concomitant use of chemically dissimilar systemic and topical antibiotics.9,11 If a topical antibiotic is necessary, be sure to include a benzoyl peroxide-containing product to minimize resistance.

**CASE STUDY 3: ACNE**

**Presentation**

You are asked to examine a 23-year-old woman who presents with acne. She has already tried “everything” and...
is now using a topical retinoid once daily and has been taking doxycycline 100 mg twice daily for 8 weeks. She is still breaking out, particularly on the lower face, jawline and neck. Physical examination reveals oily skin, a few comedones on her cheeks and nose, two inflamed nodules on her jawline and several inflammatory papules and erythema on her chin, neck and cheeks (See Figure 3).13

**Treatment Plan**

As with the previous patient, the treatment plan should target factors that promote the development of acne. Follicular epidermal hyperproliferation and inflammation are addressed with the continued use of the topical retinoid. She continued to take doxycycline 100 mg twice daily to provide an adjunctive anti-inflammatory effect. Also, by avoiding rotation of the antibiotic, the risk of \textit{P. acnes} resistance was minimized. A benzoyl peroxide-containing product was added to her regimen to further reduce the threat of antibiotic-resistant strains, as well as an oral contraceptive to target the sebaceous gland activity and sebum production.

**Oral contraceptives for acne control**. Oral contraceptives have been shown to be effective in targeting sebaceous gland activity and excess sebum production. However, improvement in acne is not expected until the oral contraceptive has been taken for 3 months or longer. Combination oral contraceptive pills decrease androgen production in the ovaries and the amount of circulating androgen by increasing sex hormone-binding globulin. Excess androgen results in the production of excess sebum. It is important to remember that oral contraceptives need to be used as supplemental therapy, because they do not target all four causes of acne.

Oral contraceptives are used most safely in women younger than 35 years who do not smoke, do not have migraine headaches and who are normotensive. Although oral contraceptives decrease androgen production, the patient’s androgen levels do not need to be abnormal for oral contraceptives to be effective.14 Any female patient with acne who is not responding appropriately to traditional combination therapy and does not have contraindications to oral contraceptives is a candidate. Oral contraceptives also can be considered in female patients planning to take isotretinoin or in those who are unable or unwilling to take systemic antibiotics. They may be used early in the treatment of acne, particularly when they are also being used for another indication (eg, desire to prevent pregnancy or premenstrual dysphoric disorder). In addition, women with signs of hyperandrogenism (eg, hirsutism or abnormal/irregular menstrual periods) may benefit from the antiandrogen effects of oral contraceptives.

An appropriate laboratory evaluation should be performed before beginning treatment with an oral contraceptive only if there are signs of hyperandrogenism. Make sure the patient has not taken oral contraceptive pills for at least 6 weeks before laboratory analysis for an endocrine disorder. Also avoid testing near ovulation; advise laboratory tests be taken during menses or 1 week before.13 Tests should include serum dehydroepiandrosterone sulfate (DHEAS), free and total testosterone, luteinizing hormone/follicle-stimulating hormone ratio (>3 indicates polycystic ovarian disease) and 17-hydroxyprogesterone (helps determine androgen etiology [adrenal or ovarian]).14 A list of contraindications is provided in Table 2,15 and three methods for beginning oral contraceptive treatment in acne are listed in Table 3.16

**Spironolactone for acne control**. Another option for reducing sebum production is oral spironolactone.14,17 Spironolactone is an aldosterone antagonist that binds the androgen receptor. It inhibits androgen biosynthesis in the gonads and adrenal gland and suppresses 5\(\alpha\)-reductase activity in the sebaceous gland. Adverse effects, which are typically dose related, include polyuria, menstrual disturbances, gynecomastia, dizziness, headache and weight gain. Guidelines for the use of spironolactone are provided in Table 4.14,18,19

A survey study with comparison chart review evaluated the long-term safety and tolerance of spironolactone in women with acne.20 The women, followed for up to 8 years, had favorable results. Ninety-one surveys were analyzed, comprising 506 person-years of follow-up and 200 person-years of spironolactone exposure. The mean length of treatment was 28.5 months. During the 8-year follow-up period, there were no cases of serious illness as a result of the use of spironolactone. The most common side effects experienced were diuresis and menstrual irregularities. Of those, 15% resulted in discontinuation of the drug. Long-term use of this agent appeared to be safe.
In a separate open-labeled prospective study, the side effects of spironolactone and how it affected serum blood levels were examined. In the study, 35 women were given spironolactone 100 mg/day for 16 days each month for 3 months. DHEAS and total testosterone levels were measured before and after treatment. Clinically significant improvement was noted in 85.7% of patients who had corresponding decreased DHEAS levels after treatment. There was no change in the total testosterone levels. The most common side effect reported was menstrual irregularities. The authors reported safety and efficacy, while suggesting spironolactone be offered as an alternative choice for women with acne vulgaris.

CASE STUDY 4: ACTINIC KERATOSIS

Presentation
A 62-year-old woman with a fair complexion is evaluated for numerous AKs on her lower extremities (See Figure 4). Two skin biopsies were performed and both showed AKs. She has never had skin cancer and denies a history of arsenic exposure. She does have a long history of sun exposure.

Treatment Plan
Skin cancer is the most common form of human cancer. AKs and SCC have common features (see previous article by Dr. Jorizzo), and if left untreated, AKs can progress to SCC.

You decide the optimal treatment for this patient is a topical retinoid in combination with topical 5-FU. A topical retinoid accelerates the penetration of this antimitotic agent. The synergistic effect of these two topical agents has been demonstrated in a randomized, double-blind trial (n=19). In this study, 5-FU cream was applied twice daily, followed by 0.05% tretinoin cream nightly to one arm, and a control cream was applied to the opposite arm until discomfort curtailed further applications. It was concluded that the daily application of 0.05% tretinoin cream appeared to enhance the efficacy of topical 5-FU in destruction of AK of the arms.

CONCLUSIONS
There are many factors to consider when deciding how to treat patients with AK or acne. When managing patients with AKs, it is important to identify, treat and prevent the lesions, because 0.1% to 10% progress to SCC. Individualized education and surveillance is essential to prevent morbidity. For patients with acne, it is important to create a treatment plan that targets the factors that cause acne. Using combination therapy is an effective way to accomplish this. Adding a benzoyle peroxide-containing product to topical antibiotics reduces the risk of selecting resistant P. acnes. The addition of oral contraceptive pills for women can result in further improvement. Negotiating with patients about vehicles, general skin care and frequency of application of topical agents and administration of oral agents can improve patient comfort and enhance compliance.

References