FEATURE ARTICLE

CE 1.5 Contact Hours | Rx 0.5 Pharmacology Contact Hour

Skin Cancer, Back to Basics

Actinic Keratosis

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ABSTRACT: Actinic keratoses (AKs) are rough, scaly papules or plaques on sun-exposed areas of the body that may progress to squamous cell carcinoma. AKs are extremely common, with the highest incidence in individuals living close to the equator. Risk factors for AKs include advanced age, fair skin, male gender, baldness in men, immunosuppression, and chronic sun exposure. Many effective therapies for individual AKs exist; however, underlying field cancerization—a mix of clinical and subclinical lesions—must be addressed for treatment to be successful. Nurses can play a pivotal role in empowering and educating their patients to make the right choices to keep their skin healthy and cancer-free for years to come.

Key words: Actinic Keratosis, Nonmelanoma Skin Cancer, Photodynamic Therapy, Squamous Cell Carcinoma

Actinic keratoses (AKs) are rough, scaly papules or plaques on sun-exposed areas of the body that may progress to squamous cell carcinoma (SCC). AKs are extremely common, with the highest incidence in individuals living close to the equator (Rosen & Lebwohl, 2013). Studies in the United States have reported average AK prevalence rates of 25% in older adults; however, in parts of the world with high solar irradiation—such as Australia—prevalence in adults can reach 60% (Vitasa et al., 1990). Risk factors for AKs include advanced age, fair skin, male gender, baldness in men, immunosuppression, and chronic sun exposure (Flohil et al., 2013; Table 1).

PATHOGENESIS

AKs are characterized as precancerous because of the confinement of atypical keratinocytes within the basal cell layer of the epidermis. Once this atypia advances into the deeper layers of the skin and is accompanied by the loss of orderly maturation, changes in immunoreactive cells, and increased DNA damage, the lesion becomes an SCC (Rowert-Huber et al., 2007). Atypical keratinocytes are a direct result of prolonged ultraviolet radiation, which causes alterations in the pathways regulating cell growth and differentiation, inflammation, and immunosuppression (Berman & Cockerell, 2013). Normal-appearing skin surrounding AKs can display molecular changes, including p53 chromosomal mutation, which can lead to the development of more AKs—and subsequently SCC—in the entire field, a process known as "field cancerization" (Figure 1).

Once an AK forms, it has three possible outcomes: regression, persistence, or progression to invasive disease (Rosen & Lebwohl, 2013). Multiple studies have attempted to capture the rate of progression from AK to SCC, with numbers ranging from 0.025% to 20% per year (Quaedvlieg et al., 2006). Conversely, spontaneous regression of AKs is quite common, occurring in 25%–50% of patients (Marks et al., 1986).

CLINICAL FEATURES

A clue to the presence of AKs is background photodamage, consisting of dyspigmentation, telangiectasia, and rhytides (Bolognia et al., 2012; Figure 2). Consequently, AKs typically present on locations with a high degree of sun exposure, including the head, neck, upper trunk, and extremities (Bolognia et al., 2012). The primary AK lesion consists of a rough, scaly, skin-colored or red papule 1–5 millimeters in size (Bolognia et al., 2012; James et al., 2011; Figure 3). The earliest sign of an AK is mild erythema with an almost imperceptible scale, which may be easier to feel than see (James et al., 2011; Figure 4). As lesions progress, they become thicker and well defined with more erythema and hyperkeratosis (Bolognia et al., 2012).

Although the diagnosis of AK is primarily clinical, a biopsy is warranted in individuals with a history of skin cancer, in immunosuppressed patients, and in high-risk anatomical locations—such as the lips and ears (Lebwohl et al., 2018). Other indications for biopsy include tenderness, bleeding, change in size, hyperkeratosis, and treatment failure (Lebwohl et al., 2018). Lesions larger than 6 millimeters should only be

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TABLE 1. Risk Factors for Actinic Keratosis

Risk factors associated with actinic keratosis:

1) Modifiable risk factors:
   Chronic sun exposure;
   geographic location with high UV radiation;
   immunosuppression; and
   HPV infection (Lebwohl et al., 2010).

2) Nonmodifiable risk factors:
   Fitzpatrick Skin Types I and II;
   male gender;
   baldness in men;
   elderly (aged 70 years and older); and
   genetic factors (Jacobs et al., 2015).

Note. Adapted from Bolognia et al. (2012) and Flohil et al. (2013).

considered AKs if they have been histologically confirmed (James et al., 2011; Table 2).

Assessment Tools for AKs

To help clinicians differentiate between mild and severe disease, various grading systems have been proposed (Kato et al., 2019). For example, in the Olsen clinical grading system, Grade I (mild) is used for a slightly palpable AK, Grade II (moderate) consists of a readily visible and palpable AK, and Grade III (severe) corresponds to a very thick and hyperkeratotic AK (Olsen et al., 1991; Table 3). However, most clinical grading systems have not been shown to match histological classifications of the same lesions (Schmitz et al., 2016). A newer screening tool—the Actinic Keratosis Area and Severity Index—showed higher scores in patients with invasive SCC compared with AKs and other noninvasive lesions and may be useful in stratifying risk for development of invasive SCC (Schmitz et al., 2018).

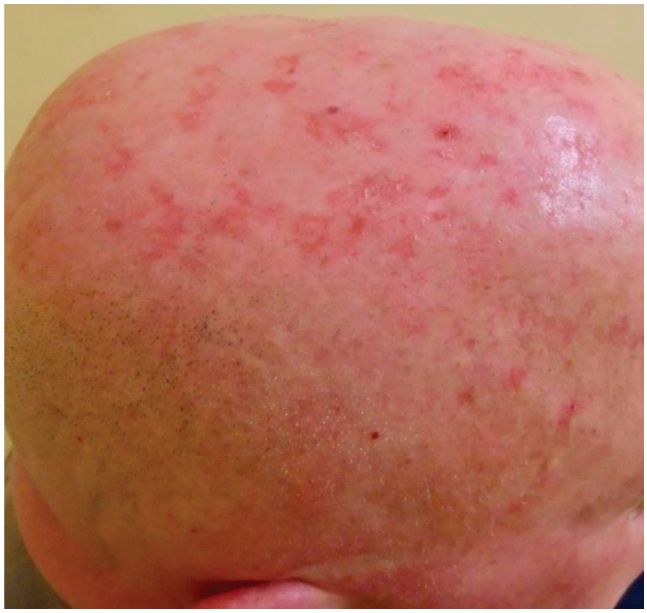

FIGURE 1. Multiple actinic keratoses on the scalp. This photo depicts the phenomenon known as "field cancerization." Photo courtesy of Maral Skelsey, MD, Dermatologic Surgery Center of Washington. Used with permission.

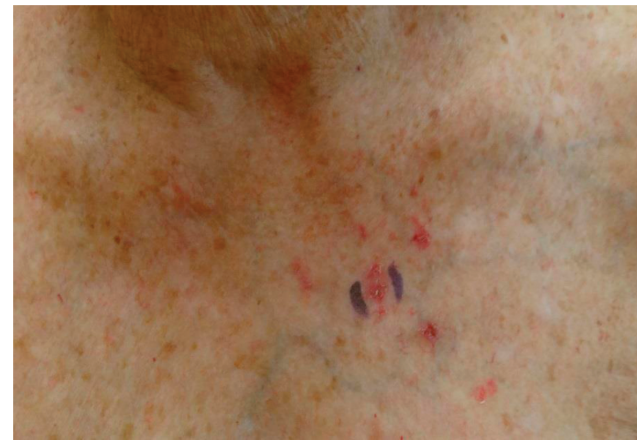

FIGURE 2. Actinic keratoses on the chest of a patient with background photodamage. Photo courtesy of Maral Skelsey, MD, Dermatologic Surgery Center of Washington. Used with permission.

TYPES OF AKS

Hypertrophic (Hyperkeratotic)

Hypertrophic AKs are readily visible upon examination and characterized by a heavy scale or white–yellow thickened crust on an erythematous base (Bolognia et al., 2012; Figure 5). Often, the distinction between hyperkeratotic AK and SCC is a difficult one, necessitating biopsy confirmation. Furthermore, hypertrophic AKs can evolve into cutaneous horns, which manifest as thick cornified material

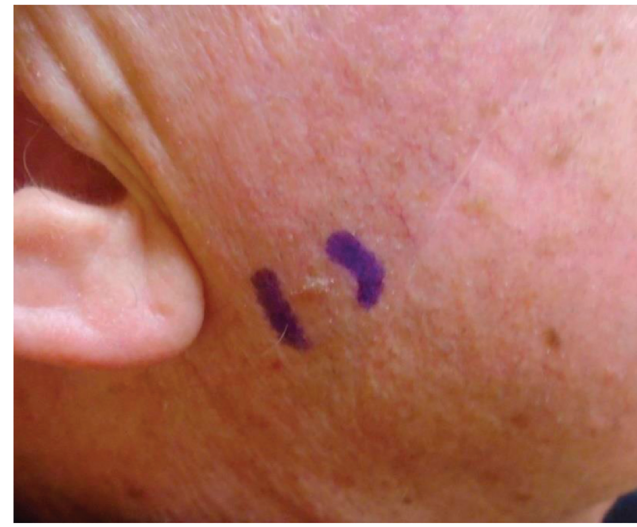

FIGURE 3. Typical presentation of an actinic keratosis as a scaly pink papule on the right lateral cheek. Photo courtesy of Maral Skelsey, MD, Dermatologic Surgery Center of Washington. Used with permission.

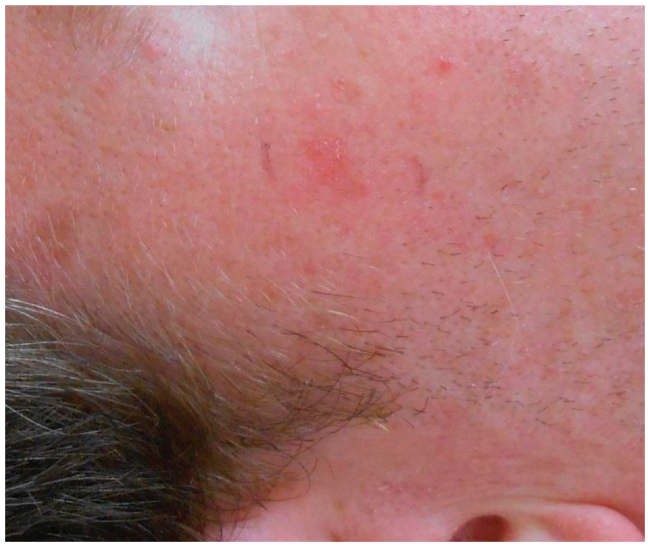

FIGURE 4. Early actinic keratosis on the temple. Note the mild erythema and almost imperceptible scale. Photo courtesy of Maral Skelsey, MD, Dermatologic Surgery Center of Washington. Used with permission.

protruding from the skin (Rossi et al., 2007; Figure 6). Cutaneous horns should always be biopsied as approximately 15% have invasive SCC at their bases (Bolognia et al., 2012).

Atrophic

Atrophic AKs are often difficult to identify given their appearance as light pink, slightly scaly macules or patches with only minimal surface change. They are found to have an atrophic epidermis on histologic examination (Bolognia et al., 2012).

Pigmented

Pigmented AKs often lack erythema and have an associated hyperpigmented or reticulated appearance (Bolognia et al., 2012). A biopsy is usually warranted to distinguish these lesions from lentigo maligna melanoma (Figure 7).

Lichenoid

Lichenoid AKs have a similar presentation to a classic AK, but with more erythema surrounding the base (Bolognia et al., 2012). In addition, patients may report pruritus or mild tenderness coinciding with the onset of lichenoid infiltrate in the preexisting AK (Bolognia et al., 2012).

TABLE 2. Indications for Biopsy of Actinic Keratosis

Indications for Biopsy	
Subjective:	Objective:
• History of skin cancer	• Lesion is in a high-risk anatomic location
• History of immunosuppression	• Hyperkeratosis or cutaneous horn
• Symptoms:	• Lip involvement (actinic chelitis)
○ Pain	• Pigmented AK
○ Bleeding	• Lesion is >6 mm
○ Change in size	

Note. AK = actinic keratosis.

TABLE 3. The Olsen Clinical Classification Scale for AKs

Clinical Classification of AKs	
Grade 1 = mild	Slight palpability, with AKs felt better than seen
Grade 2 = moderate	Moderately thick AKs that are easily seen and felt
Grade 3 = severe	Very thick and/or obvious AKs

Note. Adapted from Olsen et al., 1991. AKs = actinic keratoses.

Actinic Chelitis

Actinic chelitis is a term used to describe moderate-to-severe photodamage of the lip (Bolognia et al., 2012). It typically presents with well-demarcated erythematous papules or plaques with scale. In some cases, areas of leukoplakia—white or gray patches on the mucous membranes—are present (Bolognia et al., 2012; Figure 8). A clinical diagnosis of actinic chelitis should always be supported by histologic evidence, as the appearances of early actinic chelitis, SCC in situ, and invasive SCC can be very similar (Wood et al., 2011).

HISTOPATHOLOGY

Histologically, AKs are characterized by the presence of atypical cells in the basal epidermis and the loss of orderly keratinocyte maturation (Rosen & Lebwohl, 2013). As lesions progress, these changes may involve the full thickness of the epidermis (Rosen & Lebwohl, 2013). The cytologic features of AKs—atypical keratinocytes, nuclear pleomorphism, and increased numbers of mitotic figures—are virtually indistinguishable from SCCs, leading some researchers

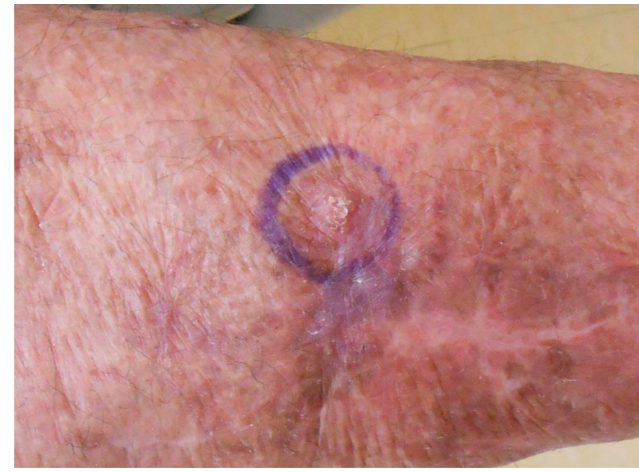

FIGURE 5. Hypertrophic (hyperkeratotic) actinic keratosis on the left pretibia. Photo courtesy of Maral Skelsey, MD, Dermatologic Surgery Center of Washington. Used with permission.

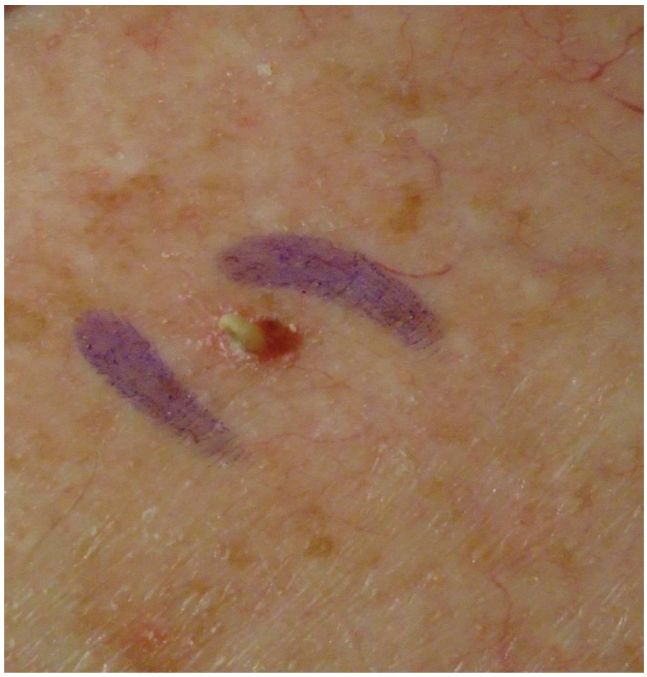

FIGURE 6. Actinic keratosis with cutaneous horn on the left upper back. Photo courtesy of Maral Skelsey, MD, Dermatologic Surgery Center of Washington. Used with permission.

to propose that these two conditions are really one and the same (Rossi et al., 2007).

DERMOSCOPY

Dermoscopy has been shown to improve diagnostic accuracy, sensitivity, and specificity in skin cancer detection (Marghoob et al., 2013). In mild, Grade I AKs, dermoscopy shows light scale and red pseudonetwork patterns. Moderate, Grade II AKs show the characteristic "strawberry pattern," which results from background erythema punctuated by adnexal openings and accentuated by a white halo (Kato et al., 2019; Wolner et al., 2017). More severe, Grade III AKs show marked hyperkeratosis or enlarged follicles filled with hyperkeratotic plugs over a white-to-yellow background (Kato et al., 2019). Distinguishing pigmented AKs from lentigo maligna can be challenging because of the common findings of a superficial brown network and an annular-granular-like pattern (Lallas et al., 2016). However, a study comparing the two lesions showed that the preservation of follicle integrity is 12.45 times more likely in a pigmented AK than a lentigo maligna (Lallas et al., 2016). The presence of rosettes—which consists of four bright white dots arranged in a two-by-two pattern—is another common dermoscopic finding in AKs; however, this phenomenon may also exist in SCCs, limiting its diagnostic value (Kato et al., 2019; Wolner et al., 2017; Figure 9).

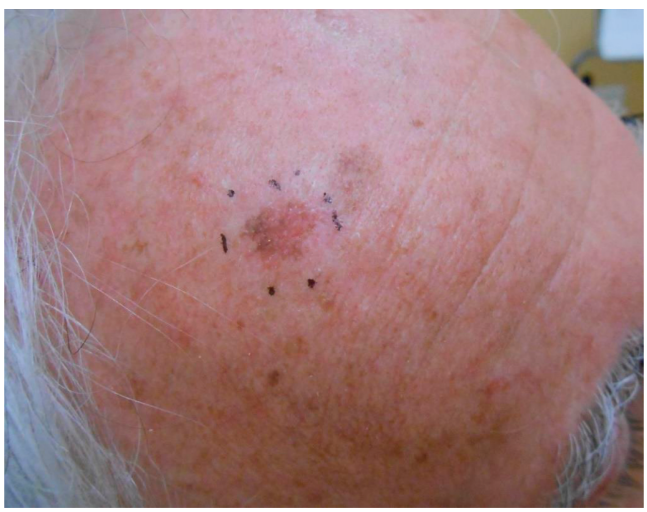

FIGURE 7. Pigmented actinic keratosis of the right forehead. Photo courtesy of Maral Skelsey, MD, Dermatologic Surgery Center of Washington. Used with permission.

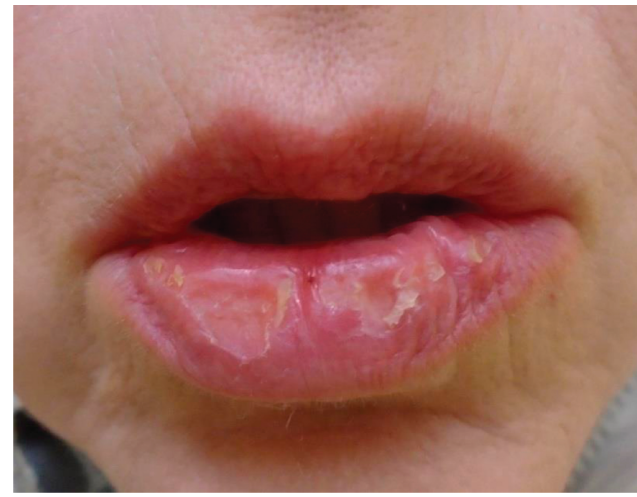

FIGURE 8. Actinic chelitis of the lip. Photo courtesy of Maral Skelsey, MD, Dermatologic Surgery Center of Washington. Used with permission.

DIFFERENTIAL DIAGNOSIS OF AK

AKs can be readily confused with SCCs; therefore, a biopsy is frequently necessary to differentiate between the two diseases. Similarly, superficial BCCs share common clinical features with AKs; however, BCCs typically have a more translucent quality with a slightly elevated border (Bolognia et al., 2012). Patients with psoriasis or eczema may have concurrent diffuse actinic damage, making the distinction between the two conditions difficult in sun-exposed areas (Bolognia et al., 2012). In addition, patients with pigmented AKs pose a diagnostic challenge when differentiating these lesions from SKs, lentigo maligna, and lentigines (Rossi et al., 2007). Finally, verruca can appear clinically similar to hyperkeratotic AKs (Rossi et al., 2007; Table 4).

TREATMENT OF AK

Although many therapeutic modalities exist for AKs, some are better than others at treating underlying field cancerization and preventing SCC (Jansen et al., 2019). Selection of

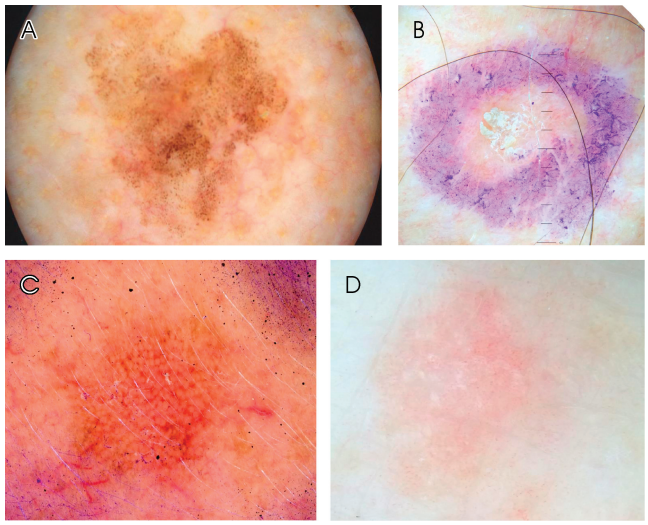

FIGURE 9. (a) Dermoscopy of actinic keratosis (AK): pigmented AK. (b) Dermoscopy of AK: hyperkeratotic AK. (c) Dermoscopy of AK: strawberry pattern. (d) Dermoscopy of AK: rosettes. Photo courtesy of Maral Skelsey, MD, Dermatologic Surgery Center of Washington. Used with permission.

treatment must take into account the presence of background photodamage and number of AKs present. The patient's preference and treatment side effects should also be considered.

Cryotherapy

Cryotherapy with liquid nitrogen is the most common treatment strategy for AKs as it is effective and can be performed promptly in the office setting (Lebwohl et al., 2018). A prospective multicenter study evaluating the efficacy of cryotherapy in the treatment of AKs showed a 67.2% complete response rate, with clearance of lesions ranging from 39% to 83%, depending on the length of the freeze time (Thai et al., 2004). A common side effect with cryotherapy is hypopigmentation, which was found in 29% of lesions treated in one study (Thai et al., 2004). Cryotherapy is limited to the treatment of one solitary lesion at a time.

5-Fluorouracil

Topical 5% fluorouracil has been used with great success in the management of individual AKs while also benefiting the field. A randomized controlled trial of 624 patients showed superiority of 5% fluorouracil over multiple other treatment modalities for AKs, with clinical cure rates of 96% after 1 year (Gupta & Paquet, 2013; Jansen et al., 2019; Krawtchenko et al., 2007). Common side effects to topical 5% fluorouracil include localized skin reactions and allergic contact dermatitis (Kishi & Price, 2018; Figure 10). Rarely, there have been reports of life-threatening reactions in patients receiving topical 5% fluorouracil therapy with an underlying dihydropyrimidine dehydrogenase deficiency (Kishi & Price, 2018).

Imiquimod

Studies have shown complete clearance rates of 45%–73% with topical 5% imiquimod for the treatment of AKs (Krawtchenko et al., 2007; Lebwohl et al., 1904). Application site reactions were the most commonly noted side effect, with up to 34.4% experiencing skin eruptions compared with vehicle. Erythema, edema, erosion, or scaling was most commonly reported (Lebwohl et al., 1904; Figure 11).

Ingenol Mebutate

Ingenol mebutate is a topical therapy for AKs provided in a concentration of 0.015% once daily for 2 consecutive days on the face and scalp and 0.05% once daily for 3 consecutive days on the trunk and extremities. A multicenter, randomized, double-blind report evaluating ingenol mebutate in the treatment of AKs revealed complete clearance rates of 42% on the face and scalp and 34% on the trunk and extremities (Lebwohl et al., 2012). Other studies have shown similar efficacy; however, hypertrophic AKs have traditionally been excluded from these trials (Anderson et al., 2009; Lebwohl et al., 2012). Erythema, flaking, scaling, and crusting were reported in most patients using this medication (Anderson et al., 2009).

Diclofenac Sodium

Diclofenac is a nonsteroidal anti-inflammatory drug that has been shown to treat AKs by blocking cyclo-oxygenase-2, thereby reducing angiogenesis and cellular proliferation (Nelson, 2011). Diclofenac sodium 3% gel used twice daily resulted in clearance rates of 33% of patients when used for 60 days and 50% when used for 90 days (Wolf et al., 2001). However, other head-to-head studies showed inferior treatment outcomes. For example, a study comparing ingenol mebutate to diclofenac sodium resulted in higher clearance rates with ingenol mebutate (34%) compared with diclofenac sodium (23%; Stockfleth et al., 2018). Notably, diclofenac sodium was associated with greater patient satisfaction and lower rates of skin inflammation compared with other topical treatments (Nelson, 2011).

TABLE 4. Differential Diagnosis of Actinic Keratosis (AK)

Differential Diagnosis of AKs	
Benign:	Malignant or premalignant:
• Psoriasis	• Squamous cell carcinoma
• Eczema	• Basal cell carcinoma
• Seborrheic keratosis	• Lentigo maligna melanoma
• Lentigines	• Paget's disease
• Verruca vulgaris	
• Allergic contact or irritant dermatitis	

Note. Adapted from Bolognia et al., 2012.

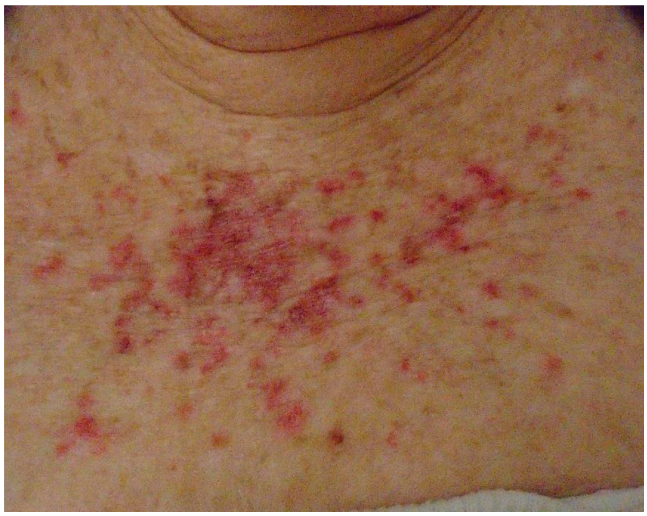

FIGURE 10. Localized skin reactions after a 2-week treatment course of topical 5% fluorouracil. Photos courtesy of Maral Skelsey, MD, Dermatologic Surgery Center of Washington. Used with permission.

Photodynamic Therapy

Photodynamic therapy (PDT) utilizes a topical photosensitizing agent that is applied to the tumor and followed by exposure to a specific wavelength of light. Light activation induces an oxidation reaction in the tumor, resulting in local cell destruction (PDQ Adult Treatment Editorial Board, 2018). A comprehensive evidence-based review for the use of PDT in treating nonmelanoma skin cancers, including AKs, concluded that PDT is highly effective, offers excellent cosmetic results, and should be considered as first-line therapy (Braathen et al., 2007; Figure 12). Pain and burning were the most frequently reported side effects with PDT, but only resulted in discontinuation of therapy in 3.2% of patients (Jansen et al., 2019).

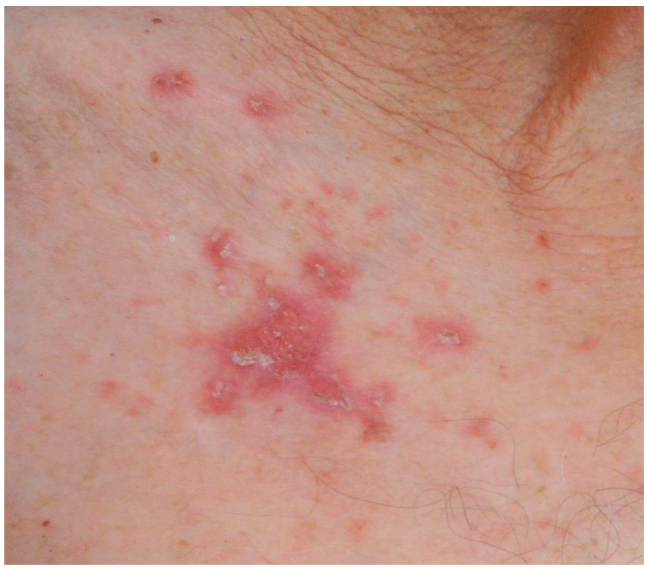

FIGURE 11. Localized skin reactions after application of imiquimod 5% cream twice a week for 4 weeks. Photos courtesy of Maral Skelsey, MD, Dermatologic Surgery Center of Washington. Used with permission.

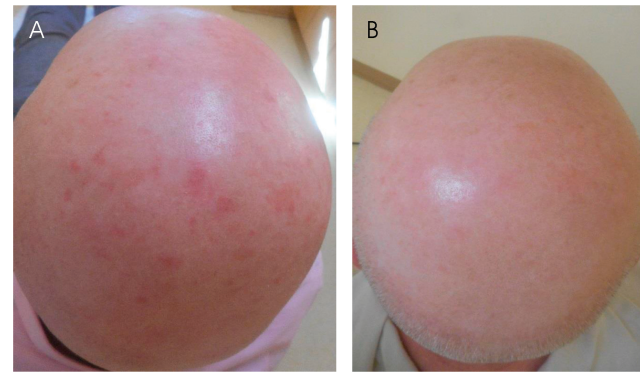

FIGURE 12. (a) "Before" picture: actinic keratoses (AKs) on scalp before photodynamic therapy (PDT) treatment. b) "After" picture: significant improvement noted in AKs on scalp after PDT. Photo courtesy of Maral Skelsey, MD, Dermatologic Surgery Center of Washington. Used with permission.

Chemical Peels

Limited studies have shown beneficial effects in the treatment of field AKs with medium-depth chemical peels, such as 35%–70% trichloroacetic acid, alpha-hydroxy acids 70%, and phenol 88% (Witheiler et al., 1997). One small prospective study showed a similar reduction in AKs when comparing chemical peels with 5% fluorouracil cream. However, recurrences were common in the peels group after 12 months (Witheiler et al., 1997).

Laser

Laser resurfacing with full-face ultrapulse CO_2 laser or erbium:YAG showed benefit in treating AKs and the surrounding field, with cure rates up to 44% (Iyer et al., 2004). Nonablative types of laser resurfacing, however, were shown to be inadequate in the management of AKs (Katz et al., 2011). A major disadvantage to ablative laser resurfacing is the significant postoperative healing time and meticulous skin care that is necessary after treatment (Iyer et al., 2004).

Sunscreen

Studies have indicated that the regular use of sunscreens as low as SPF 17 applied at least once daily is beneficial in preventing the development of AKs and hastening the remission of existing lesions (Thompson et al., 1993). New novel sunscreens containing DNA-photolyase—a DNA-repair enzyme—have been shown in small studies to reduce AKs by up to 76.6% (Navarrete-Dechent & Molgo, 2017). Given the known relationship between AKs and solar irradiation, sunscreens are an essential component in the management strategy for all patients with AKs.

Nicotinamide

Nicotinamide (Vitamin B3) has been shown to decrease nonmelanoma skin cancer rates by 23% when taken at

doses of 500 mg twice daily for 12 months (Chen et al., 2015). Unfortunately, this chemopreventive effect was lost after discontinuation of the supplement (Chen et al., 2015). As an adjunct to traditional AK therapies, nicotinamide can be beneficial in preventing SCC in individuals with multiple AKs.

Surgery

Surgical treatment options are not traditionally used for AKs, as they are considered too invasive. Given the precancerous nature of AKs, the risks of surgery almost always outweigh the benefits. However, for recalcitrant or hyperkeratotic lesions, curettage or excision may be considered (Lebwohl et al., 2018).

IMPLICATIONS FOR NURSES

In summary, AKs are an extremely common dermatologic disease that will be frequently encountered by dermatology nurses. Therefore, it is crucial for nurses to be knowledgeable in the assessment and management of this precancerous condition. Given their propensity to advance to SCC, AKs should be treated promptly. In addition, follow-up skin examinations are necessary once to twice per year to monitor for the progression to SCC (American Academy of Dermatology, 2020). As discussed in this review, many effective treatments exist for AKs, but treatment choice must be tailored to each individual patient with consideration made to patient preference and potential side effects. Patients should understand that the management of AKs remains a long-term undertaking and an emphasis on prevention and progression of new AKs is essential for successful outcomes (Kircik, 2019). Nurses can play a pivotal role in empowering and educating their patients about AK prevention and treatment so that they can make the choices necessary to keep their skin healthy and cancer-free for years to come. ■

REFERENCES

American Academy of Dermatology. (2020). Actinic keratosis: Diagnosis and treatment. Retrieved April 7, 2020, from https://www.aad.org/public/diseases/skin-cancer/actinic-keratosis-treatment

Anderson, L., Schmieder, G. J., Werschler, W. P., Tschen, E. H., Ling, M. R., Stough, D. B., & Katsamas, J. (2009). Randomized, double-blind, double-dummy, vehicle-controlled study of ingenol mebutate gel 0.025% and 0.05% for actinic keratosis. *Journal of the American Academy of Dermatology*, *60*(6), 934–943.

Berman, B., & Cockerell, C. J. (2013). Pathobiology of actinic keratosis: Ultraviolet-dependent keratinocyte proliferation. *Journal of the American Academy of Dermatology*, *68*(1, Suppl. 1), S10–S19.

Bolognia, J. L., Jorizzo, J. L., & Schaffer, J. V. (Eds.) (2012). *Dermatology* (3rd ed.). Elsevier Saunders.

Braathen, L., Szeimies, R., Basset-Seguin, N., Bissonnette, R., Foley, P., Pariser, D., Roelandts, R., Wennberg, A., & Morton, C., International Society for Photodynamic Therapy in Dermatology (2007). Guidelines on the use of photodynamic therapy for nonmelanoma skin cancer: An international consensus: International Society for Photodynamic Therapy in Dermatology, 2005. *Journal of the American Academy of Dermatology*, *56*(1), 125–143.

Chen, A. C., Martin, A. J., Choy, B., Fernandez-Penas, P., Dalziell, R. A., McKenzie, C. A., Scolyer, R. A., Dhillon, H. M., Vardy, J. L., Kricker, A., St George, G., Chinniah, N., Halliday, G. M., & Damian, D. L. (2015). A phase 3 randomized trial of nicotinamide for skin-cancer chemoprevention. *The New England Journal of Medicine*, *373*, 1618–1626.

Flohil, S. C., van der Leest, R. J. T., Dowlatshahi, E. A., Hofman, A., de Vries, E., & Nijsten, T. (2013). Prevalence of actinic keratosis and its risk factors in the general population: The Rotterdam Study. *Journal of Investigative Dermatology*, *133*(8), 1971–1978.

Gupta, A. K., & Paquet, M. (2013). Network meta-analysis of the outcome 'participant complete clearance' in nonimmunosuppressed participants of eight interventions for actinic keratosis: A follow-up on a Cochrane review. *British Journal of Dermatology*, *169*(2), 250–259.

Iyer, S., Friedli, A., Bowes, L., Kricorian, G., & Fitzpatrick, R. E. (2004). Full face laser resurfacing: Therapy and prophylaxis for actinic keratoses and non-melanoma skin cancer. *Lasers in Surgery and Medicine*, *34*(2), 114–119.

Jacobs, L. C., Liu, F., Pardo, L. M., Hofman, A., Uitterlinden, A. G., Kayser, M., & Nijsten, T. (2015). IRF4, MC1R and TYR genes are risk factors for actinic keratosis independent of skin color. *Human Molecular Genetics*, *24*(11), 3296–3303.

James, W. D., Berger, T. G., & Elston, D. M. (2011). *Andrews' diseases of the skin: clinical dermatology* (7th ed.). Elsevier Saunders.

Jansen, M. H. E., Kessels, J. P. H. M., Nelemans, P. J., Kouloubis, N., Arits, A. H. M. M., van Pelt, H. P. A., Quaedvlieg, P. J. F., Essers, B. A. B., Steijlen, P. M., Kelleners-Smeets, N. W. J., & Mosterd, K. (2019). Randomized trial of four treatment approaches for actinic keratosis. *The New England Journal of Medicine*, *380*, 933–946.

Kato, J., Horimoto, K., Sato, S., Minowa, T., & Uhara, H. (2019). Dermoscopy of melanoma and non-melanoma skin cancers. *Frontiers in Medicine*, *6*, 180. 10.3389/fmed.2019.00180

Katz, T. M., Goldberg, L. H., Marquez, D., Kimyai-Asadi, A., Polder, K. D., Landau, J. M., & Friedman, P. M. (2011). Nonablative fractional photothermolysis for facial actinic keratoses: 6-month follow-up with histologic evaluation. *Journal of the American Academy of Dermatology*, *65*(2), 349–356.

Kircik, L. H. (2019). Addressing the challenges of treating actinic keratosis. *Journal of Drugs in Dermatology*, *18*(5), S160.

Kishi, P., & Price, C. J. (2018). Life-threatening reaction with topical 5-fluorouracil. *Drug Safety Case Reports*, *5*(1), 4.

Krawtchenko, N., Roewert-Huber, J., Ulrich, M., Mann, I., Sterry, W., & Stockfleth, E. (2007). A randomised study of topical 5% imiquimod vs. topical 5-fluorouracil vs. cryosurgery in immunocompetent patients with actinic keratoses: A comparison of clinical and histological outcomes including 1-year follow-up. *British Journal of Dermatology*, *157*(Suppl. 2), 34–40.

Lallas, A., Tschandl, P., Kyrgidis, A., Stolz, W., Rabinovitz, H., Cameron, A., Gourhant, J. Y., Giacomel, J., Kittler, H., Muir, J., Argenziano, G., Hofmann-Wellenhof, R., & Zalaudek, I. (2016). Dermoscopic clues to differentiate facial lentigo maligna from pigmented actinic keratosis. *British Journal of Dermatology*, *174*(5), 1079–1085.

Lebwohl, M., Dinehart, S., Whiting, D., Lee, P. K., Tawfik, N., Jorizzo, J., Lee, J. H., & Fox, T. L. (2004). Imiquimod 5% cream for the treatment of actinic keratosis: Results from two phase III, randomized, double-blind, parallel group, vehicle-controlled trials. *Journal of the American Academy of Dermatology*, *50*(5), 714–721.

Lebwohl, M., Swanson, N., Anderson, L. L., Melgaard, A., Xu, Z., & Berman, B. (2012). Ingenol mebutate gel for actinic keratosis. *New England Journal of Medicine*, *366*(11), 1010–1019.

Lebwohl, M. G., Heymann, W. R., Berth-Jones, J., & Coulson, I. H. (2018). *Treatment of skin disease: Comprehensive therapeutic strategies* (5th ed.). Elsevier Saunders.

Lebwohl, M. G., Rosen, T., & Stockfleth, E. (2010). The role of human papillomavirus in common skin conditions: Current viewpoints and therapeutic options. *Cutis*, *86*(5), suppl 1.

Marghoob, A., Usatine, R., & Jaimes, N. (2013). Dermoscopy for the family physician. *American Family Physician*, *88*(7), 441–450.

Marks, R., Foley, P., Goodman, G., Hage, B. H., & Selwood, T. S. (1986). Spontaneous remission of solar keratoses: The case for conservative management. *British Journal of Dermatology*, *115*(6), 649–655.

Navarrete-Dechent, C., & Molgo, M. (2017). The use of a sunscreen containing DNA-photolyase in the treatment of patients with field cancerization and multiple actinic keratoses: A case-series. *Dermatology Online Journal*, *23*(1), 13030/qt5zc6085s.

Nelson, C. G. (2011). Diclofenac gel in the treatment of actinic keratoses. *Therapeutics and Clinical Risk Management*, *7*, 207–211.

Olsen, E. A., Abernethy, M. L., Kulp-Shorten, C., Callen, J. P., Glazer, S. D., Huntley, A., McCray, M., Monroe, A. B., Tschen, E., & Wolf, J. E. Jr. (1991). A double-blind, vehicle-controlled study evaluating masoprocol cream in the treatment of actinic keratoses on the head and neck. *Journal of the American Academy of Dermatology*, *24*(5, Pt. 1), 738–743.

PDQ Adult Treatment Editorial Board. (2018). *Skin cancer treatment (PDQ)-Health Professional Version*. National Cancer Institute. Retrieved from October 30, 2019, https://www.cancer.gov/types/skin/hp/skin-treatment-pdq

Quaedvlieg, P., Tirsi, E., Thissen, M., & Krekels, G. (2006). Actinic keratosis: How to differentiate the good from the bad ones? *European Journal of Dermatology*, *16*(4), 335–339.

Rosen, T., & Lebwohl, M. G. (2013). Prevalence and awareness of actinic keratosis: Barriers and opportunities. *Journal of the American Academy of Dermatology*, *68*(1, Suppl. 1), S2–S9.

Rossi, R., Mori, M., & Lotti, T. (2007). Actinic keratosis. *International Journal of Dermatology*, *46*(9), 895–904.

Rowert-Huber, J., Patel, M. J., Forschner, T., Ulrich, C., Eberle, J., Kerl, H., Sterry, W., & Stockfleth, E. (2007). Actinic keratosis is an early in situ squamous cell carcinoma: A proposal for reclassification. *British Journal of Dermatology*, *156*(Suppl. 3), 8–12.

Schmitz, L., Gambichler, T., Gupta, G., Stucker, M., & Dirschka, T. (2018). Actinic Keratosis Area and Severity Index (AKASI) is associated with the incidence of squamous cell carcinoma. *Journal of the European Academy of Dermatology and Venereology*, *32*(5), 752–756.

Schmitz, L., Kahl, P., Majores, M., Bierhoff, E., Stockfleth, E., & Dirschka, T. (2016). Actinic keratosis: Correlation between clinical and histological classification systems. *Journal of the European Academy of Dermatology and Venereology*, *30*(8), 1303–1307.

Stockfleth, E., Harwood, C. A., Serra-Guillen, C., Larsson, T., Osterdal, M. L., & Skov, T. (2018). Phase IV head-to-head randomized controlled trial comparing ingenol mebutate 0.015% gel with diclofenac sodium 3% gel for the treatment of actinic keratosis on the face or scalp. *British Journal of Dermatology*, *178*(2), 433–442.

Thai, K. E., Fergin, P., Freeman, M., Vinciullo, C., Francis, D., Spelman, L., Murrell, D., Anderson, C., Weightman, W., Reid, C., Watson, A., & Foley, P. (2004). A prospective study of the use of cryosurgery for the treatment of actinic keratoses. *International Journal of Dermatology*, *43*(9), 687–692.

Thompson, S. C., Jolley, D., & Marks, R. (1993). Reduction of solar keratoses by regular sunscreen use. *The New England Journal of Medicine*, *329*, 1147–1151.

Vitasa, B. C., Taylor, H. R., Strickland, P. T., Rosenthal, F. S., West, S., Abbey, H., Ng, S. K., Munoz, B., & Emmett, E. A. (1990). Association of nonmelanoma skin cancer and actinic keratosis with cumulative solar ultraviolet exposure in Maryland watermen. *Cancer*, *65*(12), 2811–2817.

Witheiler, D. D., Lawrence, N., Cox, S. E., Cruz, C., Cockerell, C. J., & Freemen, R. G. (1997). Long-term efficacy and safety of Jessner's solution and 35% trichloroacetic acid vs 5% fluorouracil in the treatment of widespread facial actinic keratoses. *Dermatologic Surgery*, *23*(3), 191–196.

Wolf, J. E. Jr., Taylor, J. R., Tschen, E., & Kang, S. (2001). Topical 3.0% diclofenac in 2.5% hyaluronan gel in the treatment of actinic keratoses. *International Journal of Dermatology*, *40*(11), 709–713.

Wolner, Z. J., Yelamos, O., Liopyris, K., Rogers, T., Marchetti, M. A., & Marghoob, A. A. (2017). Enhancing skin cancer diagnosis with dermoscopy. *Dermatologic Clinics*, *35*(4), 417–437.

Wood, N. H., Khammissa, R., Meyerov, R., Lemmer, J., & Feller, L. (2011). Actinic cheilitis: A case report and a review of the literature. *European Journal of Dentistry*, *5*(1), 101–106.

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