Treatment of actinic keratosis

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Disclosures: **Joseph Jorizzo, MD** Consultant/Advisory Boards: Amgen (psoriasis); Leo (psoriasis). **Robert P Dellavalle, MD, PhD, MSPH** Nothing to disclose. **June K Robinson, MD** Nothing to disclose. **Rosamaria Corona, MD, DSc** Nothing to disclose. Contributor disclosures are reviewed for conflicts of interest by the editorial group. When found, these are addressed by vetting through

All topics are updated as new evidence becomes available and our peer review process is complete.
Literature review current through: May 2015. | **This topic last updated:** May 11, 2015.

INTRODUCTION — Actinic keratoses (AKs or solar keratoses) are keratotic macules, papules, or plaques resulting from the intraepidermal proliferation of atypical keratinocytes in response to prolonged exposure to ultraviolet radiation. Although most AKs do not progress to squamous cell carcinoma (SCC), AKs are a concern because the majority of cutaneous SCCs arise from pre-existing AKs, and AKs that will progress to SCC cannot be distinguished from AKs that will spontaneously resolve or persist [1,2]. Because of these factors, most clinicians routinely treat AKs [3]. Improvement in associated symptoms and cosmetic appearance can be additional benefits of treatment.

The treatment of AKs will be reviewed here. The epidemiology, clinical manifestations, and diagnosis of AKs are discussed separately. (See "Epidemiology, natural history, and diagnosis of actinic keratosis".)

TREATMENT OPTIONS

Overview — Treatment options for actinic keratosis (AK) include destructive therapies (eg, surgery, cryotherapy, dermabrasion), topical medications (eg, 5-fluorouracil [5-FU], imiquimod, ingenol mebutate, diclofenac), chemical peels (eg, trichloroacetic acid), and photodynamic therapy (PDT). In general, lesion-directed treatments, such as cryotherapy and surgical procedures, are the primary approach for isolated lesions [3]. Field-directed therapies, such as topical 5-FU, imiquimod, ingenol mebutate, and diclofenac, are particularly useful for treating areas with multiple AKs. Evidence for efficacy of these therapies is derived from multiple randomized trials and systematic reviews [4-8].

One systematic review and meta-analysis of 83 randomized trials evaluating 24 treatments in over 10,000 patients found sufficient evidence to conclude that 3% diclofenac in 2.5% hyaluronic acid, 0.5% 5-FU, 5% imiquimod, and 0.025% to 0.05% ingenol mebutate are superior to placebo for complete clearance of lesions in the treated field in patients with AKs [4]. In addition, this systematic review and meta-analysis found that PDT performed with aminolevulinic acid (ALA-PDT) with red light or blue light or with methyl aminolevulinate (MAL-PDT) with red light was superior to placebo for the treatment of individual AK lesions [4]. The meta-analysis also found that treatment with imiquimod or PDT generally resulted in better cosmetic outcomes than 5-FU and cryotherapy [4].

A subsequent network meta-analysis of 26 individual or pooled randomized trials evaluated the relative efficacy in inducing complete lesion clearance for eight main interventions for AK [5]. This analysis suggests that topical 5-FU is the most effective treatment followed by: 5-aminolevulinic acid (ALA) PDT; topical imiquimod; ingenol mebutate; 5-methylaminolaevulinate (MAL) PDT; cryotherapy; topical diclofenac with hyaluronic acid; and placebo. However, the ranking of relative efficacies should be interpreted with caution because of the variability in the parameters used to describe the AK severity in the included studies.

Destructive treatments

Liquid nitrogen cryotherapy — Liquid nitrogen cryotherapy is the most widely utilized treatment for AK. This

treatment may be quickly performed in an office-based setting and is well tolerated by patients. (See "Dermatologic procedures", section on 'Cryosurgery'.)

The efficacy of liquid nitrogen was demonstrated in a study of 70 patients with a total of 1018 treated AKs [9]. A cure rate of 99 percent was reported after one year of follow-up. Most of the lesions treated were thin, not on the arms or hands, and aggressive therapy was used (thaw times of 20 to 45 seconds).

In a subsequent prospective study including 90 patients with 421 AKs, the overall complete response rate (defined as 100 percent lesion clearance) to liquid nitrogen cryotherapy was 67 percent [10]. The response rate varied with the freeze time (time lapse from the formation of the ice ball to the beginning of thawing), from 39 percent for five seconds of freezing to 83 percent for 20 seconds of freezing.

Although hypertrophic AKs can be effectively treated with cryotherapy, thick lesions may respond less well than thin lesions [11]. AKs on the dorsum of the hand may also be more resistant to liquid nitrogen [11].

Surgical therapies — Surgical therapies for AKs include surgical excision, shave excision, curettage with or without electrodesiccation, and dermabrasion. None of these therapies has been evaluated in clinical trials and their use is based upon limited evidence from small observational studies and clinical experience [12].

- Surgical excision is not routinely used for the treatment of AKs; it is usually undertaken for lesions that warrant histopathologic examination, such recurrent or infiltrated lesions that are suspicious for invasive squamous cell carcinoma.

- Shave excision and curettage followed by electrodesiccation are frequently used for AKs, particularly for hyperkeratotic lesions. Although these techniques can provide tissue for histopathologic evaluation, the specimens are usually not adequate to determine whether a lesion is invasive or intraepidermal.

- Dermabrasion, or surgical skin planing, may be used for treating large areas such as a sun-damaged bald scalp or forehead when lesions are too large to treat effectively with topical preparations. Dermabrasion is a procedure in which a specialized hand-held instrument is used to "sand" the skin to improve skin contour. The surface of the epidermis of the skin (the stratum corneum) is removed, leaving the skin red and raw-looking. The procedure can be very painful and usually requires procedural sedation and analgesia.

  A retrospective study of 23 patients treated with dermabrasion found that 96 percent remained free of new AKs at one year after treatment. However, the benefits of dermabrasion gradually diminished with 83 percent clear at two years and 54 percent at five years [12].

Photodynamic therapy — PDT is an effective therapy for AK that consists of topical application of a photosensitizer followed by exposure of the treatment area to a light source. The procedure results in cellular destruction. 5-aminolevulinic acid (ALA) and methyl aminolevulinate (MAL) are the two photosensitizing agents utilized in PDT for AK.

Multiple PDT regimens have been used for treatment of AK. The topical photosensitizer, incubation times, light sources, and pretreatment regimens have varied across studies. An effect of the length of the incubation period on treatment efficacy was illustrated in a randomized trial (n = 149) in which patients were treated with a self-adhesive ALA patch. The trial found that a four-hour incubation period was more effective for complete clearance of AKs than shorter incubation times of 0.5, 1, or 2 hours [13].

Multiple trials and two meta-analyses have compared PDT with other therapies for AK [4,14-21]. One meta-analysis of four randomized trials (641 participants with 2170 AKs) comparing PDT with cryotherapy found that PDT had a 14 percent greater likelihood of achieving complete lesion clearance at three months than cryotherapy [21]. Although data are insufficient for definitive conclusions on comparative efficacy, the cosmetic outcome from PDT appears to be superior to 5-FU and cryotherapy [4,21].

Photodynamic therapy has the advantage of allowing the treatment of multiple lesions with a single application. The most common complaint during photodynamic therapy is burning or stinging during light exposure; in addition, there is a small risk of producing pigmentary changes.

Medical treatments

Topical 5-fluorouracil — 5-FU inhibits thymidylate synthetase, a critical enzyme in the synthesis of DNA. The lack of DNA synthesis, particularly in fast-growing dysplastic cells, prevents cell proliferation and causes cell death. 5-FU 5% cream has been used with good success in patients with multiple AKs. It causes inflammation and destruction of the lesions (picture 1). Inflammation typically subsides approximately two weeks after 5-FU is discontinued. It typically takes four to six weeks (two to four weeks of which are active treatment) for the skin to progress through erythema, blistering, necrosis with erosion, and reepithelialization.

Two systematic reviews found an approximately 50 percent overall efficacy rate of 5-FU for 100 percent clearance of AKs [8,22]. However, in patients who do not have hyperkeratotic AKs (which generally require destructive modalities of treatment), topical 5-FU is effective in more than 90 percent of patients who can tolerate it, and has the advantage of treating clinically undetectable AKs [23].

Treatment with topical 5-FU may be effective for the long-term control of AKs. In a randomized trial, 932 participants with a mean total count of 11 AKs on the face and ears were treated with 5% 5-FU cream or vehicle twice daily for four weeks and followed-up for an average time of 2.6 years [24]. At six months, the number of AKs on the face or ears was reduced to 3.0 (73 percent reduction) and 8.1 (24 percent reduction) per participant in the treatment and control group, respectively. The complete clearance rate at six months was 38 percent in the 5-FU group and 17 in the control group. Compared with the control group, the 5-FU group was less likely than the control group to receive any spot treatment for AKs during the follow-up period and had fewer AKs at 42 months (4.3 versus 5.7).

A 0.5% preparation of 5-FU for daily application is available in the United States, but not in Europe. Once daily application is associated with minimal systemic absorption and is better tolerated than higher-strength preparations [25]. Treatment courses of one, two, and four weeks have demonstrated superiority over placebo for the clearance of AKs, with the four-week course demonstrating the greatest benefit [26].

In Europe, a cutaneus solution of 0.5% of 5-FU in 10% salicylic acid (SA) is available for the treatment of slightly palpable or moderately thick hyperkeratotic actinic keratosis (grade I/II). In a small randomized study, treatment with 0.5% 5-FU/SA once daily for six weeks achieved a higher rate of histologic clearance than two cryotherapy treatments three weeks apart (62 versus 42 percent) [27]. The recurrence rates of cleared lesions at 14 weeks were 39 percent in the 0.5% 5-FU/SA group and 85 percent in the cryotherapy group. Adverse events, including local erythema, scabbing, and crusting were more common in the 5-FU/SA group than in the cryotherapy group (24 versus 6 percent).

Imiquimod — Imiquimod cream, a topical immune response modifier that stimulates local cytokine induction, is an effective therapy for AKs [4,22,28].

- Imiquimod **5% cream** – A meta-analysis of five randomized trials including approximately 1300 patients found that treatment with imiquimod 5% cream (two to three times per week for 12 to 16 weeks) resulted in complete resolution of AKs in 50 percent of patients compared with 5 percent with the control vehicle [28].

  Adverse event information was reported on 1200 patients. The proportion of patients with treatment-related adverse events was higher with imiquimod than with the control vehicle (42 versus 12 percent). Patients most frequently experienced local adverse events that included erythema, scabbing, and flaking. All-cause withdrawals occurred more frequently with imiquimod than with vehicle (12 versus 7 percent). Withdrawals due to adverse events were not significantly different between imiquimod and vehicle (4 versus 3 percent).

  The manufacturer's prescribing information for imiquimod 5% cream states that patients should be treated twice weekly for 16 weeks and that treatment should be applied to a single contiguous treatment area of approximately 25 cm^2 (forehead, scalp, or one cheek) [29]. Shorter-course therapy with a treatment-free interval and retreatment if needed may also be effective for non-hypertrophic AKs, and would be less expensive [30-32].

- Imiquimod **3.75% cream** – A cream containing a 3.75% concentration of imiquimod is also available and has been shown in randomized trials to be superior to placebo for the treatment of AK [33,34]. When applied to the entire face or scalp daily for two two-week treatment cycles, imiquimod 3.75% cream led to a higher complete clearance rate than a 2.5% formulation of imiquimod or placebo (36, 31, and 6 percent, respectively) [33].

  Treatment-related adverse effects (most commonly discomfort at the site of application) occurred in 19 percent

of patients treated with 3.75% imiquimod cream, an incidence lower than reported in randomized trials of twice weekly application of imiquimod 5% cream for 16 weeks (34 percent) [35]. Similar to the 16-week trials of imiquimod 5% cream [35], severe local skin reactions occurred in approximately one-third of patients.

Although the complete clearance rate reported with imiquimod 3.75% cream is lower than the 50 percent clearance rate reported with longer courses of imiquimod 5% cream [28], differences in study methodology (eg, size of area of application) preclude a conclusion on relative efficacy. The shorter duration of therapy may be preferable for some patients.

Ingenol mebutate — Ingenol mebutate, a substance derived from the sap of the *Euphorbia peplus* plant, is a newer topical treatment for AK available in the United States and Europe [36-39]. The mechanism of action involves two stages: initial disruption of cell plasma membranes and mitochondria leading to cell necrosis (chemoablation) followed by the induction of neutrophil-mediated antibody dependent cellular cytotoxicity that eliminates remaining tumor cells [38,40]. Ingenol mebutate is available in two gel formulations: 0.015%, indicated for a three-day treatment course on the face or scalp; and 0.05%, indicated for a two-day treatment course on the trunk or extremities.

An advantage of ingenol mebutate over other topical treatments is the short duration of therapy. A combined analysis of the findings of two randomized trials with 547 patients revealed that ingenol mebutate 0.015% gel applied once daily for three days to a 25 cm^2 area on the face or scalp with multiple AKs was superior to placebo for lesion resolution [41]. At study day 57, complete clearance of AK was detected in 42 versus 4 percent of patients. Similar results were obtained in two randomized trials with a total of 458 patients in which ingenol mebutate 0.05% gel was applied once daily for two days to a 25 cm^2 area on the trunk or extremities [41]. By day 57, 34 versus 5 percent of patients had complete lesion clearance.

Treatment with ingenol mebutate appears to have a lasting effect. Although slightly more than half of the patients who achieved complete clearance in the above trials had recurrence of one or more AKs in the treatment area during an additional year of follow-up (54 percent in the face and scalp trials and 56 percent in the trunk and extremity trials), the number of AKs remained dramatically reduced in this population [42]. At the end of the follow-up period, the number of AKs was reduced by 87 percent in both trial groups.

Local skin reactions are an expected event during ingenol mebutate therapy [39]. Erythema, scale, crusting, edema, vesiculation, pustulation, or ulceration may occur. Patients may complain of symptoms of pain, pruritus, or irritation.

Topical diclofenac — Diclofenac is a nonsteroidal antiinflammatory drug that inhibits both cyclooxygenase and upregulation of the arachidonic acid cascade. Because the production of prostaglandins from arachidonic acid may play a role in ultraviolet B-induced skin cancer (eg, basal cell carcinoma and squamous cell carcinoma), inhibition of this cascade by diclofenac may explain its efficacy in the treatment of AKs.

Topical diclofenac 3% in 2.5% hyaluronan gel is effective for the treatment of AKs [4,43,44]. A meta-analysis of three randomized trials (n = 364) found that treatment with diclofenac gel resulted in complete resolution of AKs in approximately 40 percent of patients versus 12 percent with placebo [45]. The efficacy of diclofenac may be lessened for AKs on sites other than the face [4].

Diclofenac is applied twice daily for 60 to 90 days. The most common adverse effects of diclofenac gel are dry skin, pruritus, erythema, and rash at the application site. Twice daily treatment with diclofenac gel appears to be better tolerated than twice daily application of 5-FU [46], although it may be somewhat less effective.

Retinoids — Topical retinoids have been studied for the treatment of AKs. In a nine-month randomized trial of 90 patients with multiple AKs, adapalene gel (0.1 or 0.3%) applied daily as field therapy for four weeks and twice daily thereafter significantly but modestly decreased the number of AKs compared with placebo, and also appeared to improve the appearance of photodamaged skin [47]. In contrast, a randomized trial including 1131 patients found that long-term use of topical tretinoin 0.1% cream was ineffective in reducing the number of AKs [48]. Additional studies are necessary to determine the role of topical retinoids in the management of these lesions.

Systemic retinoids have been used in the secondary prevention of AKs in renal transplant recipients. A 12-month study found that low-dose acitretin therapy (20 mg daily) is safe, well tolerated, and partially effective in chemoprophylaxis of nonmelanoma skin cancer [49].

Combination therapy — Newer approaches to the treatment of AK use lesion-directed therapies in combination with field-directed therapies to optimize the clearance of visible, discrete lesions as well as subclinical lesions in photodamaged skin [3,4,50,51]. Applying a topical treatment after a lesion-directed approach may reduce the potential of subclinical lesions for progression to visible AKs. Conversely, pretreating areas of AK involvement with topical agents may reveal subclinical lesions that can be treated with destructive methods, such as cryotherapy.

Examples of combined or sequential treatments that have been evaluated in randomized trials with variable results include:

- Cryotherapy before or after topical 5-FU [52,53]
- Cryotherapy before or after topical imiquimod [54]
- PDT before or after topical imiquimod [14]

One randomized, vehicle-controlled clinical trial compared the efficacy of cryotherapy alone with cryotherapy following 5-fluorouracil applications for the treatment of AKs in 144 patients with five or more visible or palpable AKs on the face. After six months, 30 percent of patients treated with combination therapy remained clear of AKs versus 8 percent of those treated with cryotherapy alone [52].

The value of sequential treatment with methyl aminolevulinate (MAL)-PDT and imiquimod was investigated in a randomized trial completed by 105 patients [14]. Better response rates were seen for combination treatment than for either monotherapy; however, the difference in response was statistically significant only for the comparison between combination therapy and MAL-PDT monotherapy.

Other interventions

Chemical peels — A chemical peel is a procedure in which a topically applied wounding agent creates smooth, rejuvenated skin by way of an organized repair process and exfoliation. Usually, this procedure is performed on the face.

A medium-depth chemical peel with 35 to 50% trichloroacetic acid (TCA) alone or at 35% in combination with Jessner's solution, 70% glycolic acid, or solid CO_2 may effectively treat multiple non-hypertrophic AKs [55]. In a nonrandomized split-face study, Jessner's solution plus 35% TCA demonstrated similar efficacy and decreased rates of morbidity when compared with 5-FU [56].

Medium-depth peels cause injury at the level or through the papillary dermis and should be applied by a clinician in a controlled setting. Prior to treatment, patients should be educated about possible complications of stinging or burning sensation, visible peeling (which usually lasts five to seven days), pigmentary changes, infections, and rarely scarring.

Patients with a history of herpes simplex virus (HSV) infection, previous radiation exposure, immunosuppression, postinflammatory hyperpigmentation, keloids, recent facial surgery, or taking photosensitizing medications may experience higher rates of complications from chemical peels. Patients likely to be noncompliant with post-treatment sunscreen use or who are unable to avoid sun exposure because of occupation are unsuitable candidates for a chemical peel.

Laser therapy — Additional therapies that have been utilized for AKs include ablative laser resurfacing with carbon dioxide (CO_2) [57] and erbium:yttrium aluminum garnet (Er:YAG) lasers [58]. A few uncontrolled studies have reported reductions in AKs following treatment with nonablative fractional lasers [59-61]; however, a six-month follow-up with histologic evaluation performed in one of the studies revealed persistence of AKs after treatment [60].

APPROACH TO MANAGEMENT — Given the multiple effective treatment options for actinic keratoses (AKs), the choice of therapy is influenced by factors such as the number and distribution of lesions; lesion characteristics; patient preference for the mode of treatment (eg, office-based versus home administered, duration of therapy); patient tolerance for side effects (eg, pain, inflammation, hypopigmentation, scarring); and treatment availability and cost.

In general, lesion-directed treatments, such as cryotherapy and surgical interventions such as shave excision or curettage followed by electrodesiccation, are the primary approach for isolated lesions. Cryotherapy is most

frequently used because it is rapid, inexpensive, and does not require local anesthesia.

Field-directed therapies are indicated for the treatment of areas with multiple AKs, subclinical lesions that are not detected by visual inspection or palpation, and field cancerization. They include topical agents (eg, 5-fluorouracil [5-FU], imiquimod, ingenol mebutate, diclofenac), photodynamic therapy (PDT), or field ablation with dermabrasion, chemical peels, and carbon dioxide laser resurfacing [3].

Topical therapies have many advantages (noninvasive, effective against subclinical lesions, self-administered). However, patient adherence to these treatments is generally low, due to the high frequency of adverse events (eg, skin irritation, erosions, ulcerations) and the long duration of treatment.

Patients with few, isolated lesions — Lesion-directed treatments, such as cryotherapy and surgical interventions such as shave excision or curettage followed by electrodesiccation are the primary approach for isolated lesions. Cryotherapy is most frequently used because it is rapid, inexpensive, and does not require local anesthesia.

We suggest liquid nitrogen cryotherapy for patients with few, isolated AKs. The treatment is delivered by either spray or contact with a cryoprobe. The contact technique is particularly useful for treating small lesions in sensitive areas of the face (eg, periocular, perioral). The freezing time varies from 5 to 10 sec or more, depending upon lesion size and thickness. (See "Dermatologic procedures", section on 'Cryosurgery'.)

Since liquid nitrogen cryotherapy does not produce a specimen for histologic confirmation, the procedure should only be performed when the clinical diagnosis of AK is relatively certain. If there is doubt about the diagnosis, a biopsy for histologic confirmation is warranted.

Patients with hyperkeratotic/hypertrophic lesions — We suggest liquid nitrogen cryotherapy as the initial treatment for hyperkeratotic/hypertrophic lesions (picture 2). Because thick lesions are more resistant to liquid nitrogen, freezing times >10 sec or repeat applications may be necessary. (See "Dermatologic procedures", section on 'Cryosurgery'.)

Shave removal or curettage followed by electrodesiccation to ensure hemostasis may be used as alternative treatment modalities for thick lesions that do not respond to liquid nitrogen cryotherapy. Lesion specimens should be sent for histopathologic examination to exclude invasive squamous cell carcinoma (SCC), as discussed below. (See 'When to biopsy' below.)

When to biopsy — A skin biopsy for histopathologic examination to exclude or confirm the presence of invasive SCC should be performed in the following circumstances [62]:

- Lesions that appear indurated (a finding that suggests the possibility of SCC).
- Painful, ulcerated, or bleeding lesions.
- Hyperkeratotic/hypertrophic AKs that failed to resolve after standard therapies or recurred rapidly (<3 months).

A low threshold for considering the possibility of SCC is particularly important in immunocompromised patients, since these patients are more likely to have biologically aggressive lesions.

Patients with multiple lesions — For patients with multiple thin lesions on the face and/or scalp, we suggest field treatment with topical 5-FU. 5-FU 5% cream is applied once or twice daily for two to three weeks, until superficial erosion occurs.

For the treatment of facial lesions, a 0.5% preparation applied once daily for up to four weeks may be used. To improve patient's adherence to treatment, some clinicians utilize topical corticosteroids (eg, desonide ointment 0.025%) in combination with 5-FU to reduce the inflammatory response associated with treatment.

Alternative therapies for patients with multiple AKs include topical imiquimod, ingenol mebutate, or photodynamic therapy. The choice depends upon patient's preference and ability to tolerate adverse effects, treatment duration, costs, and availability.

- Imiquimod 5% cream is applied to the involved area twice weekly for 16 weeks.
- Ingenol mebutate 0.015% gel is applied to involved areas of face and scalp once daily for three days. Involved

areas of trunk or extremities are treated with the 0.05% gel once daily for two days.

- Photodynamic therapy is usually administered as a single treatment.

Patients with multiple AKs who also have hyperkeratotic lesions may benefit from the sequential use of lesion-directed and field-directed therapies. For these patients, we suggest cryotherapy for the treatment of individual lesions followed by the application of 5-FU cream to the involved area.

Organ transplant recipients — Local destructive therapies such as cryotherapy, electrocautery, curettage, or carbon dioxide laser can be used for the management of individual AKs in solid organ transplant recipients [63]. Field-directed therapies such as topical 5-FU and/or imiquimod are often preferred treatment options for patients with numerous lesions. (See "Management of skin cancer in solid organ transplant recipients".)

The efficacy of 5-FU 5% cream for the treatment of AKs in renal transplant recipients has been evaluated in one small, uncontrolled study [64]. In this study, eight patients with an average of 15 AKs on the face were treated with 5-FU 5% cream twice daily for three weeks and followed up for 12 months. The AK clearance rates were 98 and 79 percent at 2 and 12 months, respectively.

Initial theoretical concerns over the induction of immune activation and subsequent organ rejection with topical imiquimod have not been substantiated with any laboratory or clinical evidence in the transplant population. The results of small randomized trials suggest that this agent can be used safely when applied to limited areas (60 or 100 cm^2) three times per week for up to 16 weeks [65,66].

In one study including 43 renal, heart, and liver transplant patients, the application of imiquimod 5% cream three times per week to a 100 cm^2 area led to complete clearance of AKs in 62 percent of subjects [65]. No signs of graft rejection or deterioration of graft function were observed. Another trial of 21 renal transplant patients reported similar safety data; there was no evidence that imiquimod therapy worsened renal function [66].

PREVENTION — Sun avoidance, especially during the peak hours in spring and summer, use of protective clothing, and regular use of broad-spectrum sunscreens are of key importance for the prevention of actinic keratoses (AKs). (See "Selection of sunscreen and sun-protective measures".)

The efficacy of sunscreens in reducing the development of AKs has been demonstrated by several randomized trials [67-69]. Daily sunscreen use may also decrease the risk of AK and squamous cell carcinoma in immunosuppressed organ transplant recipients [70].

Ongoing monitoring for lesion recurrence and cutaneous malignancies are required in all patients with a history of AKs. (See "Epidemiology and risk factors for cutaneous squamous cell carcinoma", section on 'Prevention' and "Management of skin cancer in solid organ transplant recipients", section on 'Follow-up and prevention'.)

INFORMATION FOR PATIENTS — UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5^{th} to 6^{th} grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10^{th} to 12^{th} grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Basics topics (see "Patient information: Actinic keratosis (The Basics)")

SUMMARY AND RECOMMENDATIONS

- Treatment options for actinic keratosis (AK) include lesion-directed, destructive, therapies (eg, surgery, cryotherapy, dermabrasion) and field-directed therapies with topical medications (eg, 5-fluorouracil [5-FU], imiquimod, ingenol mebutate) or photodynamic therapy (PDT). Field-directed therapies are indicated for the treatment of areas with multiple AKs, subclinical lesions that are not detected by visual inspection or palpation,

and field cancerization. (See 'Treatment options' above.)

- We suggest that patients with isolated AKs be treated with liquid nitrogen cryotherapy (**Grade 2B**). Liquid nitrogen cryotherapy can be used as the initial treatment for hyperkeratotic or hypertrophic lesions (picture 2). Shave removal or curettage may be used as alternative treatment modalities, particularly for suspicious lesions requiring histopathologic examination. (See 'Patients with few, isolated lesions' above and 'Patients with hyperkeratotic/hypertrophic lesions' above and 'When to biopsy' above.)

- For patients with multiple thin lesions on the face and/or scalp, we suggest field treatment with topical 5-FU, topical imiquimod, ingenol mebutate, or photodynamic therapy (**Grade 2B**). The choice of therapy depends upon patient preference, cost of treatment, and availability. (See 'Patients with multiple lesions' above.)

- Patients with multiple AKs who also have hyperkeratotic or hypertrophic lesions may benefit of the sequential use of lesion-directed and field-directed therapies. For these patients, we suggest liquid nitrogen cryotherapy for the treatment of hyperkeratotic or hypertrophic lesions followed by the application of 5-FU cream on the involved area (**Grade 2C**). (See 'Patients with multiple lesions' above and 'Patients with hyperkeratotic/hypertrophic lesions' above.)

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