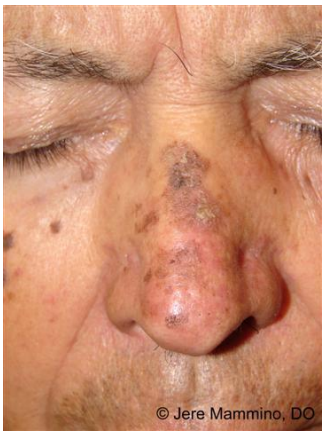
Cancer Association of South Africa (CANSA)

Fact Sheet
on
Actinic Keratosis

Introduction

Actinic keratosis (AK) forms on the face, lips, back of neck, hands, and bald scalp following sun exposure over a period of time. It appears as a rough, dry, scaly patch or growth on the exposed skin. The blemishes are often elevated, rough in texture and resemble warts. Individuals with Actinic Keratosis usually have more than one blemish.



[Picture Credit: Actinic Keratosis]

If it is left untreated, AKs may turn into squamous cell carcinoma. In some cases it may turn into basal cell carcinomas, the most common form of skin cancer, it is, therefore important that a dermatologist is consulted before any cancerous changes occur.

Hashim, P.W., Chen, T., Rigel, D., Bhatia, N. & Kircik, L.H. 2019.
"Actinic keratosis (AK) develops on chronically sun-exposed skin and constitutes one of the most common diseases managed by dermatologists. The incidence of AKs continues to rise among aging as well as younger sun damaged populations worldwide, underscoring the importance of effective therapy options. Various treatments are available, including light-based therapies, topical therapies, and destructive therapies."

Siegel, J.A., Korgavkar, K. & Weinstock, M.A. 2017.
"Actinic keratoses (AKs) are common, with prevalence in the U.S.A. estimated at almost 40 million in 2004 and annual costs of > $1 billion (U.S.D.). However, there is no universally accepted definition of AK and thus it is difficult to identify reliably. AKs are lesions of epidermal keratinocytic dysplasia that result from chronic sun exposure and have the ability to progress to invasive squamous cell carcinoma (SCC), but clinicians disagree about whether AKs are premalignant lesions, superficial SCCin situ or epiphenomena of chronically sun-damaged skin. Yearly AK to SCC progression rates of 0·6% were reported in an elderly population with multiple prior keratinocyte carcinomas (KCs); and rates of spontaneous AK regression have been reported to be > 50%, but regressed lesions often reappear. As AKs have both cosmetic consequences and potential for malignant transformation, there are multiple reasons for treatment. There is no current agreement on the most efficacious

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treatment, but 5-fluorouracil has been shown to both prevent and treat AKs, and imiquimod and photodynamic therapy may have the best cosmetic outcomes. AKs may be treated to improve appearance and relieve symptoms, but the keratinocytic dysplasia that gives rise to malignancy, and sometimes appears as an AK, may be what actually threatens patient health. Thus, treatments should aim to decrease the risk of KC or facilitate KC diagnosis by reducing the potential for misidentification created when a KC appears in a field of AKs. Improved agreement among clinicians on AK definition may improve management."

Incidence of Actinic Keratosis (AK) in South Africa.

The outdated National Cancer Registry (2016) does not provide any information regarding the incidence of Actinic Keratosis (AK) as it is a pre-cancerous condition.

Causes and Risk Factors of Actinic Keratosis (AK)

longterm sun exposure is the major cause of actinic keratosis. Sun damage to the skin is cumulative, so every period of sun exposure adds to the lifetime total.

Another important cause of actinic keratosis is exposure to the ultraviolet radiation given off by tanning beds.

[Picture Credit: Tanning Bed]

A further possible cause of actinic keratoses is extensive exposure to X-rays or certain industrial chemicals, like arsenic, coal tar, soot, pitch, creosote, shale oils, and petroleum products, such as mineral oil or motor oil.

[Picture Credit: Albinism]

The following individuals are also more vulnerable to actinic keratosis:

- Individuals whose immune defences are weakened by cancer chemotherapy, Aids, or organ transplantation
- People with fair skin, blonde or red hair, and blue, green, or grey eyes
- People with certain rare conditions that make the skin very sensitive to the sun's UV rays, such as albinism and xeroderma pigmentosum (XP), are also at higher risk.

Risk Factors Include individuals:

- Usually of the male gender
- A fair skin
- Light eye colour
- Who spend lots of time outdoors in the sun
- Who are organ transplant recipients
- High alcohol consumption

- β human papillomaviruses (HPVs)

Donà, M.G., Chiantore, M.V., Gheit, T., Fiorucci, G., Vescio, M.F., La Rosa, G., Accardi, L., Costanzo, G., Giuliani, M., Romeo, G., Rezza, G., Tommasino, M., Luzi, F. & Di Bonito, P. 2019.
"Many findings support the role of β human papillomaviruses (HPVs) in cutaneous squamous cell carcinoma (cSCC) and its precursor Actinic Keratosis (AK), in cooperation with UV radiation [1]. Differently from the mucosal high-risk types, which are required throughout the entire carcinogenic process, β-HPVs appear to play a role only at an early stage of skin carcinogenesis. Indeed, β-HPV DNA is not present in all cancer cells and cutaneous HPV prevalence and/or viral load is higher in AK than in cSCC [2, 3, 4]."

Signs and Symptoms of Actinic Keratosis (AK)
The signs and symptoms of an actinic keratosis include:

- Rough, dry or scaly patch of skin
- Blemishes may range in size from a tiny spot to as much as an 2,5cm
- Flat to slightly raised patch or bump on the top layer of skin
- In some cases it may have a hard, wart-like surface
- Colour varies between pink, red or brown, or flesh-coloured patches
- There may also be itching or burning of the affected areas

Diagnosis of Actinic Keratosis (AK)
A medical practitioner (preferably a dermatologist) should be consulted when blemishes on the skin are noticed. He/she will:

- Conduct a full physical examination
- Obtain a biopsy to confirm the diagnosis

Mir-Bonafé, J.F., Rozas-Muñoz, E., Dalmau, J., Mir-Bonafé, M., Iznardo, H., García-Melendo, C. & Puig, L. 2019.
"Diagnosis of actinic keratosis (AK) is mainly clinical, but dermoscopy has proven useful in improving diagnostic accuracy. The patterns, structures and colors of AK can vary widely.[1] Lesions may appear as white scales on a pseudo-network pattern, as keratotic plugs on a scaly white to yellow background, or as a strawberry pattern with white to yellow areas and keratotic follicular openings on an erythematous background."

Reducing the Risk of Actinic Keratosis (AK)
The following will assist in reducing the risk for actinic keratosis:

- Avoiding the midday sun.
- Apply an effective sunscreen (SPF30 or higher) regularly at least 20 minutes before going out into the sun
- Pay special attention to the lips. Apply a lip balm that contains sunscreen (if available)

- Protect the skin with clothing, preferably with a good UPF value. Whenever possible wear:
    - A wide-brimmed hat
    - Long sleeves
    - Long pants
- Avoid tanning beds or other indoor tanning devices
- Check the skin as often as recommended by a dermatologist
- One should contact a dermatologist right away if patches:
    - Starts to itch or bleed
    - Become noticeably thicker
    - Remain after treatment
    - Change in size, shape, or colour.
- Avoid alcohol or, at least, reduce alcohol consumption

Treatment of Actinic Keratosis (AK)

Treatment may include:

- Application of liquid nitrogen
- Regular use of prescribed topical creams, gels and solutions

Sharma, M., Sharma, G., Singh, B. & Katare, P.O. 2019.

INTRODUCTION: Actinic keratosis is one of the most common disorder characterized by erythematic and generally attached scaly lesions which are present either alone or in clusters. World Health Organization defines actinic keratosis as a common intraepidermal neoplasm of sun-damaged skin, characterized by variable atypia of keratinocytes.

AREAS COVERED: At the beginning of the 20th century, a new immunomodulator molecule, imiquimod, appears in the market for the treatment of actinic keratosis but suffers from the pitfalls of the conventional approach of dosage form preparation including high dose, poor stability and more side effects. The present article attempts to compile the scatter information related to actinic keratosis and imiquimod at one place. The special emphasis will be made on the information available in various research articles and patents with respect to the efforts made for overcoming shortcomings associated with imiquimod by novel drug delivery or other approaches.

EXPERT OPINION: The conventional drug delivery systems are unsuccessful to improve the actinic keratosis. The patient acceptance and compliance with these treatments are generally poor due to associated side effects, poor cosmetic outcomes and high costs. Therefore, several available and reported novel therapeutic approaches are being developed in order to provide better action.

de Oliveira, E.C.V., da Motta, V.R.V., Pantoja, P.C., Ilha, C.S.O., Magalhães, R.F., Galadari, H. & Leonardi, G.R. 2019.

"Actinic keratosis (AK) is a lesion that arises as a result of excessive exposure to solar radiation and appearing predominantly on Fitzpatrick phototype I and II skin. Given that some AKs evolve into squamous cell carcinoma, these lesions are considered premalignant in nature, occurring mostly in elderly men and immunosuppressed individuals chronically exposed to ultraviolet (UV) radiation. There are several mechanisms for the formation of AKs; among them are oxidative stress, immunosuppression, inflammation, altered proliferation and dysregulation of cell growth, impaired apoptosis, mutagenesis, and human papillomavirus (HPV). Through the understanding of these mechanisms, several treatments have emerged. Among the options for AK treatment, the most

commonly used include 5-fluorouracil (5-FU), cryotherapy, diclofenac, photodynamic therapy (PDT), imiquimod (IQ), retinoids, and ingenol mebutate (IM). There have been recent advances in the treatment options that have seen the emergent use of newer agents such as resiquimod, betulinic acid, piroxicam, and dobesilate. The combination between therapies has presented relevant results with intention to reduce duration of therapy and side effects. All AK cases must be treated because of their propensity to transform into malignancy and further complicate treatment. In addition to medical or surgical care, education about sun exposure prevention remains the best and most cost-effective method for AK prevention."

About Clinical Trials

Clinical trials are research studies that involve people. They are conducted under controlled conditions. Only about 10% of all drugs started in human clinical trials become an approved drug.

Clinical trials include:

- Trials to test effectiveness of new treatments
- Trials to test new ways of using current treatments
- Tests new interventions that may lower the risk of developing certain types of cancers
- Tests to find new ways of screening for cancer

The South African National Clinical Trials Register provides the public with updated information on clinical trials on human participants being conducted in South Africa. The Register provides information on the purpose of the clinical trial; who can participate, where the trial is located, and contact details.

For additional information, please visit: www.sanctr.gov.za/

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BACKGROUND: Actinic keratosis is the most frequent premalignant skin disease in the white population. In current guidelines, no clear recommendations are made about which treatment is preferred.

METHODS: We investigated the effectiveness of four frequently used field-directed treatments (for multiple lesions in a continuous area). Patients with a clinical diagnosis of five or more actinic keratosis lesions on the head, involving one continuous area of 25 to 100 cm^2, were enrolled at four Dutch hospitals. Patients were randomly assigned to treatment with 5% fluorouracil cream, 5% imiquimod cream, methyl aminolevulinate photodynamic therapy (MAL-PDT), or 0.015% ingenol mebutate gel. The primary outcome was the proportion of patients with a reduction of 75% or more in the number of actinic keratosis lesions from baseline to 12 months after the end of treatment. Both a modified intention-to-treat analysis and a per-protocol analysis were performed.

RESULTS: A total of 624 patients were included from November 2014 through March 2017. At 12 months after the end of treatment, the cumulative probability of remaining free from treatment failure was significantly higher among patients who received fluorouracil (74.7%; 95% confidence interval [CI], 66.8 to 81.0) than among those who received imiquimod (53.9%; 95% CI, 45.4 to 61.6), MAL-PDT (37.7%; 95% CI, 30.0 to 45.3), or ingenol mebutate (28.9%; 95% CI, 21.8 to 36.3). As compared with fluorouracil, the hazard ratio for treatment failure was 2.03 (95% CI, 1.36 to 3.04)

with imiquimod, 2.73 (95% CI, 1.87 to 3.99) with MAL-PDT, and 3.33 (95% CI, 2.29 to 4.85) with ingenol mebutate (P≤0.001 for all comparisons). No unexpected toxic effects were documented.
CONCLUSIONS: At 12 months after the end of treatment in patients with multiple actinic keratosis lesions on the head, 5% fluorouracil cream was the most effective of four field-directed treatments.

Medical Disclaimer

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