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Actinic Cheilosis: Etiology, Epidemiology, Clinical Manifestations, Diagnosis, and Treatment

Michaell A. Huber, DDS; Géza T. Terézhalmy, DDS, MA

Continuing Education Units: 2 hours

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This continuing education course presents the etiology, epidemiology, clinical manifestations, diagnosis, and treatment of actinic cheilosis.

Conflict of Interest Disclosure Statement

- Dr. Huber reports no conflicts of interest associated with this course.
- Dr. Terézhalmy has done consulting work for Procter & Gamble and is a member of the dentalcare.com Advisory Board.

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Overview

Actinic cheilosis is a chronic degenerative disorder primarily of the lower lip caused by long-term exposure to sunlight. It is premalignant and usually occurs in fair-skinned men over 40 years of age. Reducing exposure to sunlight is the single most important measure in preventing actinic cheilosis. Diagnosis is predicated on histological examination of biopsy specimens. Topical chemotherapy may be used in early lesions. Prophylactic ablation or vermilionectomy may be performed in cases where malignant transformation has not yet occurred. The treatment of malignancy is primarily surgical.

Learning Objectives

Upon completion of this course, the dental professional should be able to:

- Discuss the etiology and epidemiology of solar cheilosis.
- Recognize the clinical manifestations of solar cheilosis.
- Diagnose solar cheilosis.
- Develop preventive and treatment management strategies for patients with solar cheilosis.

Course Contents

Introduction

Exposure to sunlight leads to the development of sunburn, premature aging of the skin, cataracts, immune suppression, and skin cancer. Actinic keratosis (AK) of the skin represents an early stage of a continuum that may ultimately progress to squamous cell carcinoma (SCC). Actinic cheilosis is the labial equivalent of AK. The term actinic cheilitis is often used; however, actinic or solar cheilosis (SC) is more accurate because this sun-induced neoplastic disease is primarily non-inflammatory.[1]

The highly developed lip vermilion exists only in man and is bounded by the keratinized skin and mucous membrane of the inner labia.[2] The epidermis is characterized by a highly developed stratum lucidum and a very thin stratum corneum. Hair and sweat glands are absent but dermal papillae are abundant, leading to the rich vascular supply that imparts the characteristic red color (vermilion). In dark-complected individuals, the red hue is camouflaged by increased melanin deposits.[3]

SC is a precancerous neoplasia found primarily on the lower lip of light-skinned individuals. Given the high risk for the progression of SC to SCC of the lip vermilion and the high rate of discordance between clinical and histologic findings, a biopsy is indicated in the presence of clinically discernable degenerative changes.[1] Prevention, early diagnosis, effective therapeutic intervention, and close long-term follow-up are paramount.

Etiology and Epidemiology

The etiologic factors associated with SC are the same as those associated with AK and cutaneous SCC, namely the cumulative effect of exposure to ultraviolet radiation (UVR), skin phenotype, genetic predisposition, increasing age, male gender, outdoor occupation and leisure activities, geographic latitude of residence, failure to use

lip-protective agents, and host immune status.[1,4] The risk associated with smoking, alcohol consumption, and poor oral hygiene is unclear.[1]

Chronic exposure to UVR is the most important cause of SC.[1,5-10] Ultraviolet-B (UV-B) radiation (wavelength 280-320 nm) is principally responsible, but ultraviolet-A (UV-A) radiation (wavelength 320-400 nm) adds to the risk.[7,11,12] AK and SC serve as clinical dose-meters for chronic UVR exposure.[13] UV-B reaches the epidermal cell layer to induce very specific mutational changes which serve to both initiate and promote dysplastic changes in the epidermis.

UV-B damages the DNA at adjacent pyrimidines resulting in double cytosine (CC) to double thymidine transition mutations.[6,14] This mutation is so specific that it is referred to as "UV signature" or "UV fingerprint."[6,14-16] The characteristic UV-B mutations target tumor suppressor genes, the most notable being p53.[10,11,17] Normal p53 acts to allow repair of damaged DNA or induces apoptosis (controlled cell death) when the DNA damage is nonrepairable.[6,11,16]

UVR-induced mutations to the p53 gene lead to impaired tumor suppressor activity. Other UVR-induced molecular alterations affect the normal activity of cyclooxygenases, signal transducer and activator of transcription proteins, fibroblast growth factor, cytokeratin, and cytotoxic killer cells.[1] While these effects contribute to the molecular evolution of SC to SCC, their reliability as clinical markers with predictive or staging value remains unclear.[1,11]

Since SC occurs more frequently in light-complected than darker-complected individuals, skin phenotype (Table 1) is an important predisposing factor and it is important in assessing the risk for SC.[4,8,12,13,18,19] The increased melanin in the lip vermilion of dark-complected individuals appears to provide increased protection from the harmful effects of UVR.[4,11] It is of note that SCC of the lower lip occurs 30 times more frequently in white than in black individuals.[4]

Table 1. Skin Phenotypes.[18]

Skin type I: burns easily, never tans
Skin type II: burns easily, tans minimally
Skin type III: burns moderately, tans gradually
Skin type IV: burns minimally, tans well
Skin type V: rarely burns, tans profusely
Skin type VI: deeply pigmented, never burns

Individuals whose sun exposure habits began early in life are at greatest risk for developing SC.[13,20] Persons with SC tend to be over the age of 40 years and men are afflicted more frequently than women by a 12 to 1 ratio.[21,22] This correlates closely with a 10.7 to 1 male to female ratio of SCC of the lip.[23] It has been postulated that women are at lesser risk because they experience less chronic sun exposure and are more likely to use a lip protective agent such as lipstick or sunblock.[1]

While the association between tobacco use and SC is unclear, the habit of leaving a cigarette on the lip has been reported to increase the risk of labial SCC.[10,24] As well, there is a paucity of data on the association between a patient's immune status and SC. However, the association between a patient's immune status and the frequency of developing AK and SCC of the lip is profound.[24-28] Consequently, a patient's immune status is likely to worsen the severity of SC and promote its progression to SCC.

The true incidence of SC is unknown; however, the likelihood that SC will progress to SCC of the lip vermilion is 2.5 times higher than the risk of AK progressing to cutaneous SCC.[29,30] SCC of the lip tends to be more severe in those patients who develop SC at a younger age and in those with severe clinical and histologic evidence of inflammatory infiltrates at the time of diagnosis.[1] The progression of SC to SCC of the lip may take 2 to 3 decades.[31]

It is estimated that in the United States there are 3500 new cases of SCC of the lip diagnosed annually.[32] This represents approximately 50% of all oral cancers. The overall incidence rate of SCC of the lip in Canada is 2.7 per 100,000.[33] The incidence rate of labial SCC in persons with skin types I and II in Canada has been reported to be 12 per 100,000.[34] It is of import that approximately 15% of the patients with SCC of the lower lip will develop a second primary on the lip vermilion.[30,35]

Clinical Manifestations

UVR-induced damage to the lip may be acute, resulting in sunburn, blistering or peeling; chronic exposure leads to SC, primarily of the lower lip.[1,2,12,21,22,36] In its early stages, SC presents as a dry, scaly unobtrusive "chapped lip." Palpation provides a sense of rubbing the fingers over sandpaper.[37] At later stages small nodules; marked parallel fissuring; mottled, opalescent white or gray plaques; erosion or ulceration along with crusting; as well as loss of definition of the lip vermilion are noted.[1,22,38]

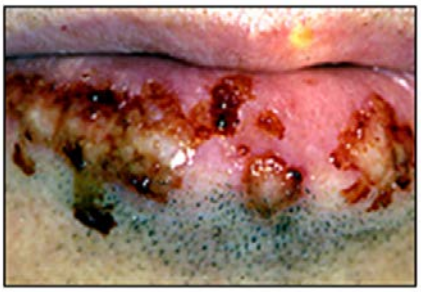

Figure 1. Blistering secondary to acute exposure to UVR.

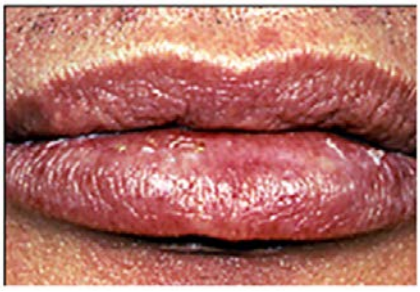

Figure 2. Solar cheilosis presenting as a dry, scaly, unobtrusive "chapped lip."

Figure 3. Solar cheilosis characterized by marked parallel folds and loss of elasticity.

The clinical appearance of SC does not always correlate directly with underlying histological changes and an apparently suspicious lesion may prove to be benign, while a perceived benign lesion may in fact represent severe dysplasia or even SCC.[1] Waxing and waning of erythematous or ulcerative areas with evidence of induration and pain are ominous signs.[21,39] Figures 1-8 document the progression of labial UVR damage from acute sunburn to primary and recurrent invasive SCC.

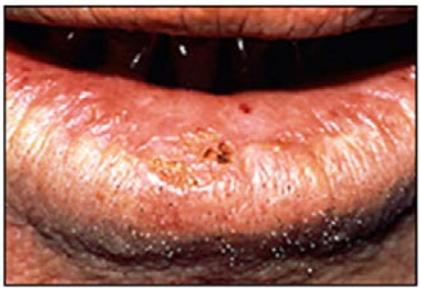

Figure 4. Isolated areas of crusting and loss of definition of the vermilion border - biopsy-proven moderate dysplasia.

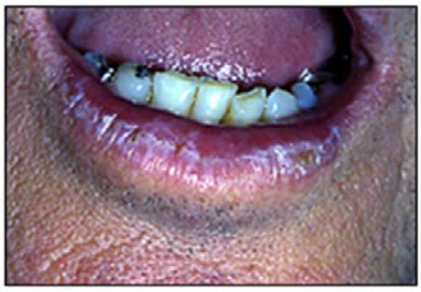

Figure 5. White/gray opalescent plaques of the vermilion - biopsy proven severe dysplasia.

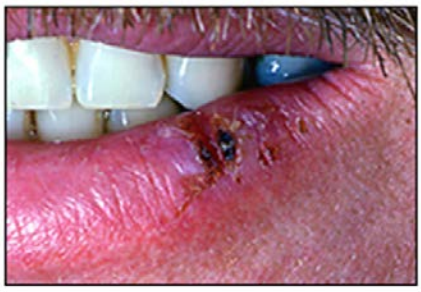

Figure 6. Waxing and waning erythematous ulceration with induration - biopsy-proven carcinoma-in-situ.

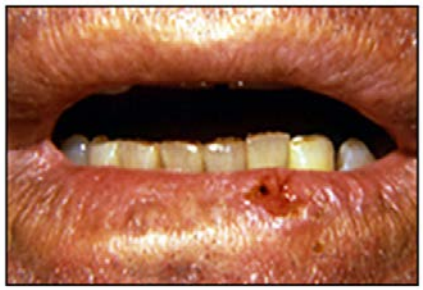

Figure 7. Persistent ulceration with induration and recent onset of pain - biopsy-proven invasive SCC.

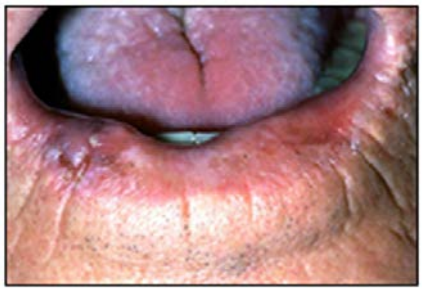

Figure 8. Biopsy-proven recurrent SCC with ulceration and induration 10 years after excision of primary SCC.

Diagnosis

The working diagnosis of SC is usually straightforward. It devolves from correlating a thoroughly discerned history with clinical findings in an at-risk patient. The presence of concurrent AK on sun-exposed areas (face, neck, bald scalp, ears) reinforces the clinical impression. Several other conditions affecting the lip may mimic SC and should be considered in the differential diagnosis. Table 2 provides a comprehensive list of differential diagnoses and associated characteristics.[2,3,39-53]

Because of the progressive nature of SC, the presence of a chronic lesion on the lip vermilion mandates a biopsy.[1] The spectrum of histological findings associated with clinical SC include hyperkeratosis, parakeratosis/orthokeratosis, epithelial atrophy, vasodilation, inflammatory infiltrates, solar elastosis, atypia, dysplasia, SCC-in-situ (SCIS) and invasive SCC.[1,7,21,22,39,54-62] In one study, 10.34% of the patients had mild, 27.57% had moderate, and 62.07% had severe biopsy-proven dysplasia.[22]

Table 2. Differential Diagnoses Associated with Solar Cheilosis.

Condition	Characteristics
Chronic cheek biting/chewing	Factitial shaggy lesions commonly observed on buccal mucosa, lateral tongue, lips. Historical clues and direct observation for habit.
Exfoliative cheilitis[2,3]	Unusual condition, typically affects young women, often attributed to factitial self-induced trauma. Hyperkeratosis and desquamation limited to lip vermilion, possible yellow hyperkeratotic or thick hemorrhagic crusts, no underlying physiologic disorder noted. Proposed psychogenic cause.
Contact dermatitis[2,3]	Any age involved, scaling and erythema may be limited to lip vermilion, both upper and lower lips typically involved. Careful history necessary to elucidate possible causes. **Irritant** – Extremes of dry, cold, windy, hot, humid may lead to sloughing. **Allergic** – Possible causes include toothpaste (flavorings, preservatives), tarter control toothpastes (pyrophosphate compounds) and lipsticks and lip balms (oxybenzone, lanolin, preservatives). **Phototoxic** – Numerous medications (tetracyclines, sulfamethoxazole, chlorthiazide, bupropion, ibuprofen, diuretics, many others). Psoralens in citrus fruits may react with UV light to induce cheilitis.
Lichen planus[40,41]	Common mucocutaneous disorder, female predominance, 4th – 6th decade, may wax and wane, variable discomfort. Characteristic lacy striations, papules, plaques. **Histological:** Dense subepithelial band like infiltrate of T-cells, basal cell layer liquefaction, disruption of the basement membrane.
Lichenoid drug reaction[42]	Clinical appearance indistinguishable from LP. Careful historical analysis necessary to determine inciting agent. Diagnosis validated by lesion resolution after discontinuance of suspected agent (and reappearance on reexposure to inciting agent). **Histological:** Essentially identical to LP.

Table 2. Differential Diagnoses Associated with Solar Cheilosis. (continued)

Candidiasis (angular cheilitis)	Most typically noted at commissures, mixed red/white lesions with ulceration or crusts. White curds or plaques that wipe off leaving an erythematous base. **Histological:** Evidence of candidal hyphae and spores noted on specimen (smears, tissue biopsy).
Cheilitis glandularis[43,44]	Rare, chronic inflammatory conditions manifesting minor salivary gland hypersecretion and ductal ectasia. Lips are swollen, nodular, and everted and associated minor salivary gland secretion is thick and sticky. Cause is unknown. **Histological:** Nonspecific with possible glandular hyperplasia and ductal ectasia.
Erythema multiforme[45,46]	Characteristic abrupt onset with pain. Most common in adolescents/young adults and frequently associated with prior HSV outbreak. Variable oral presentation with intraoral bullae and erosions, often with crusting lesions on lips and cutaneous target lesions. **Histological:** Nonspecific evidence of inflammation; immunofluorescent staining for perivascular IgM, IgG, C3 may be noted, but are nonspecific.
Pemphigus vulgaris[47,48]	Median age of onset 50+ with slight female predominance. Oral lesions (blisters, erosions, and ulcers) occur in over 85% of cases and often precede occurrence of cutaneous lesions. Typical sites affected are buccal mucosa, tongue, floor of mouth, and palate. **Histological:** Suprabasilar splitting and clefting. Characteristic immunofluorescent staining of intercellular deposits of IgG and C3 throughout the epithelium.
Discoid lupus erythematosus[49]	**Five** – 20% of cases progress to SLE. Positive ANA titers unusual. Typical oral lesions presents as a red atrophic center with peripheral border of radiating hyperkeratotic striae. **Histological:** Granular or homogenous bands of immunoglobin (IgG and IgA) in the BMZ
Graft Versus Host Disease[50]	History of allogeneic stem cell transplantation. Clinical appearance similar to LP. Frequent involvement of salivary gland tissues leads to xerostomia. **Histological:** Virtually identical to LP
Systemic lupus erythematosus[49]	Oral lesions are often painless and occur in about 19% of cases. Positive ANA titers in 95% - 100% of cases. Variable oral presentation (discoid, plaques, ulcers, lichen planus-like lesions). **Histological:** Granular or homogenous bands of immunoglobin (IgG and IgA) in the BMZ
Plasma cell cheilitis[51]	Rare inflammatory disorder manifesting glistening red lower lip, fissuring, ulceration, tenderness. **Histological:** Band-like infiltrate of plasma cells in upper dermis
Cheilitis granulomatosa (Miescher's cheilitis)[52,53]	Rare idiopathic condition manifesting episodic nontender enlargement of one or both lips. Lips may feel soft, firm or nodular. Onset typical in young adults with no racial or gender predilection. Many consider a monosymptomatic form of Melkerson-Rosenthal syndrome. **Histological:** Lymphedema and noncaseating granulomas noted in lamina propria.

Prevention

Given the strong etiologic link between UVR and SC, reducing exposure to sunlight or other forms of UVR is the single most important measure in preventing SC.[63] General protection guidelines published by the American Cancer Society include avoiding sun exposure when UV rays are strongest (between 10 AM and 4 PM); covering up exposed skin; wearing a hat that shades the neck, face and ears; wearing sunglasses; and using a sunscreen with a sun protection factor (SPF) of 30 or higher.[64]

The SPF of a sunscreen product is determined using a calibrated artificial UV radiation source to

induce minimal erythema on skin protected by the application of 2 mg/cm^2 of the test sunscreen.[65] SPF is the ratio of UV radiation dose required to induce minimal erythema on protected skin versus the dose required to induce the same degree of erythema on unprotected skin.[65,66] It is of note that UV-B radiation is 1,000 times more erythemogenic than UV-A radiation.[67,68]

Sunscreens are divided into two types: inorganic and organic. Inorganic sunscreens contain zinc or titanium dioxide and act to physically block, reflect, or scatter UV radiation.[69] Organic agents have variable absorptive spectra and sunscreen manufacturers typically combine several agents to produce a broad spectrum product capable of blocking both UV-A and UV-B.[67,70,71] Table 3 lists selected FDA-accepted sunscreen formulations, the concentration of active ingredients, and their UVR spectrum.

For the prevention of SC, the product chosen should be formulated for use on the lip and provide broad-spectrum protection against both UV-B and UV-A radiation.[69] Table 4 lists some commercially available broad spectrum lip sunscreens/sunblocks. As product lines and formulations are subject to change, clinicians and consumers should always check the product label. If a lip balm is not available, a broad-spectrum liquid or gel sunscreen applied to the lips may prove effective.[72]

Table 3. Some FDA Accepted Sunscreen Agents.[72]

Agent	Allowable Concentration	Spectrum Blocked (nm)
Inorganic agents		
Titanium dioxide	25%	290 - 350
Zinc oxide	25%	290 - 400
Organic agents		
Avobenzone	3%	310 - 400
Cinoxate	3%	270 - 328
Dioxybenzone	3%	206 - 380
Ecamsule	10%	295 - 390
Homosalate	15%	290 - 315
Menthyl anthranilate	5%	200 - 380
Octocrylene	10%	287 - 323
Octyl methoxycinnamate	7.5%	280 - 310
Octyl salicylate	5%	260 - 310
Oxybenzone	6%	270 - 350
Padimate O	8%	290 - 315
Para aminobenzoic acid	15%	260 - 313
Phenylbenzimidazole sulfonic acid	4%	290 - 340
Sulisobenzone	10%	250 - 380
Trolamine salicylate	12%	269 - 320

Table 4. Some Commercially Available Lip Balms.

Product	Manufacturer
Aloe Gator SPF 30 Medicated Lip Balm	Aloe Gator Suncare Co. (Irving, TX)
Aloe Gator SPF 30 Tropical Lip Balm (various flavors)	Aloe Gator Suncare Co. (Irving, TX)
Banana Boat Sport Performance Lip Balm SPF 50	Sun Pharmaceuticals, LLC
Banana Boat Aloe Vera with Vitamin E Lip Balm SPF 45	Sun Pharmaceuticals, LLC
Chaptstick Ultra 30	Pfizer Consumer Healthcare (King Mountain, NC)
Chapstick LipShield 365	Pfizer Consumer Healthcare (King Mountain, NC)
Eco Lip Sport	Eco Lips, Inc. (Cedar Rapids, IA)
Five Star Lip Protection	Blistex, Inc. (Oak Brook, IL)
Herpacin L	Chattem, Inc. (Chattanooga, TN)
Lipcotz Lip Balm SPF 45	Fallen, Inc. (West Nirriton, PA)
RPM for Men	Blistex, Inc. (Oak Brook, IL)
Sport Lip Balm SPF 30	Kiss My Face, LLC (Gardiner, NY)
SPF 30 Luxe Sport Lip Balm	S&G Hampton Sun, LLC, (New York, NY)

Regardless of the product chosen, sunscreens should be applied liberally 15-30 minutes prior to exposure to UVR.[69] They should be reapplied liberally after any vigorous activity that may wash or rub away the product.[69,73] Finally, and perhaps more importantly, the patient should be educated that the purpose of sunscreens is to provide protection against UV radiation when one needs to be outside, but that the ultimate goal of prevention is to reduce elective sun exposure.

Therapeutic Strategies

The progressive nature of SC emphasizes the need for (1) prevention (2) early diagnosis, (3) effective therapeutic intervention, and (4) close long-term follow-up. Measures to reduce UVR exposure and the consistent use of a sunscreen may occasionally result in spontaneous resolution of SC.[15,74] Available therapeutic options include the application of topical chemicals and the use of ablative or surgical methods.[39] Importantly, clinicians must avoid treating SC on the basis of clinical findings alone.

When SC presents as a well-circumscribed nodule or papule < 5 mm in diameter it is amenable to an excisional biopsy.[39] Serial sections of the surgical specimen must be prepared and evaluated histologically. Alternatively, Mohs micrographic surgery (MMS), because of its excellent cosmetic yield, may be considered. If the histologic diagnosis confirms mild to moderate dysplasia no further treatment is indicated, but the patient should be placed in a closely monitored follow-up program.

When the nodules, papules, areas of atrophy, erosions or prolonged ulcerations are > 5 mm in diameter, an incisional biopsy is indicated.[39] Serial sections of the specimen must be evaluated histologically. If the histologic diagnosis is mild to moderate dysplasia the area may be treated with 5% topical 5-fluorouracil or imiquimod. Despite excellent clinical remission of SC, neither of these two drugs has been shown to completely eradicate dysplasia at the microscopic level.[39]

Alternatively, ablation with cryotherapy (liquid nitrogen applied with a cryoprobe) or electrosurgery can be useful for the treatment of focal SC. Cryotherapy requires no local anesthesia and five-year cure rates as high as 99% have been reported.[39] Electrosurgery requires local anesthesia and may lead to damage to adjacent tissues and scar formation. A major disadvantage of both of these techniques is that they do not yield specimens for histologic evaluation of serial sections.

SC characterized by diffuse leukoplakia or atrophy of the lip vermilion should have a single incisional biopsy of the most suspicious area, which has generally been shown to correspond to a greater degree of dysplasia. If the histologic diagnosis is mild to moderate dysplasia, field therapy with 5% topical 5-fluorouracil or imiquimod may be an option. However, CO_2 laser ablation has been shown to more predictably resolve both the clinical and histological manifestations of SC.[39]

SC with severe dysplasia is considered equivalent to or indistinguishable from SCIS. Patients with SCIS of the lower lip tend to have late cervical lymph node metastasis and poor 5-year survival rates.[62] When there are marked dysplastic changes histologically, serial sections have shown actual invasive SCC in 12 to 13% of the cases.[74] Patients with histologic evidence of severe dysplasia and those with lesions clinically suspected to be malignant must be referred to a maxillofacial surgeon.

Surgical excision is the most prudent and effective approach to the treatment of diffuse SC, as it allows for the physical removal of part or all of the lip vermilion.[39] The most common surgical technique is vermilionectomy or lip-shave. Unlike CO_2 ablation, it has the advantage of providing specimens for histologic evaluation of serial sections. The advantage of CO_2 laser ablation when compared to scalpel vermilionectomy is that it results in fewer esthetic side effects.

When scalpel vermilionectomy is performed, the orbicularis oris muscle is conserved and closure is obtained by advancing and suturing the labial mucosa to the skin to create a new lip line. The technique can also be combined with a wedge procedure to simultaneously eliminate SCIS or a small SCC. Side effects are common and may include the presence of hairs near the newly established lip line, paresthesia, and scarring, which may result in restriction of labial motion.[39]

Clinically highly suspicious lesions thought to be SCIS or SCC must promptly be referred to a head-and-neck surgeon to maximize prognostic outcome.[8,56] The risk of local metastasis increases in direct proportion to tumor size.[56-60] The risk of local metastasis for T_1 tumors is up to 15%, for T_2 tumors the risk may be as high as 35%.[64] The most commonly involved nodes are the submandibular, followed by the submental, jugular chain, and the intraparotid groups.[61]

Conclusion

SC represents the early clinical manifestations of a continuum that may ultimately develop into SCC of the lip. It shares the same etiology with AK and cutaneous SCC of the skin. Thus, labial SCC differs from other forms of intraoral SCCs. The only proven method of reducing the risk of developing SC is to reduce exposure to the harmful effects of UV radiation. Patients should be advised to avoid unnecessary sun exposure and to consistently use a broad-spectrum sunscreen when outdoors.

The issue of how to effectively diagnose SC is a major clinical challenge. A combined diagnostic-therapeutic approach may offer the best solution to this dilemma. Complete surgical excision is the favored treatment modality. Lesions that are not amenable to surgical excision must have a random biopsy followed by the most effective treatment to eradicate the disease. Surgical specimens must undergo serial sectioning and histologic evaluation.

Course Test Preview

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1. Which of the following statements is correct relative to solar cheilosis (SC)?

a. The major etiologic factor associated with SC is ultraviolet radiation, principally UV-B.
b. Factors predisposing to SC include skin phenotype, age, male sex, outdoor occupation, rural living, and host immune status.
c. AK and SC serve as clinical dose-meters for chronic UVR exposure.
d. All of the above.

2. Which of the following statements is correct relative to the carcinogenic effects of UV-B?

a. UV-B damages DNA at adjacent pyrimidines resulting in double cytosine to double thymidine transition mutations.
b. UV-B induced mutations are so specific that they are frequently referred to as the "UV signature" or "UV fingerprint."
c. UV-B mutations target tumor suppressor genes (impair tumor suppressor activity), the most notable being p53.
d. All of the above.

3. Which of the following statements is correct relative to the relationship between actinic cheilosis, gender, and skin phenotype?

a. SC occurs more frequently in light-complected than dark-complected individuals.
b. Susceptible individuals whose sun exposure habits began early in life are at increased risk of developing SC.
c. It has been postulated that women are at lesser risk of developing SC because they experience less chronic exposure to sun than men and they are more likely to use some form of lip protection.
d. All of the above.

4. Which of the following statements related to SC is correct?

a. While the association between tobacco use and SC is unclear, the habit of leaving a cigarette on the lip has been reported to increase the risk of labial SCC.
b. The likelihood that SC will progress to SCC of the lip vermilion is 2.5 times higher than the risk of AK progressing to cutaneous SCC.
c. It is estimated that in the United States there are 3500 new cases of SCC of the lip diagnosed annually.
d. All of the above are correct.

5. All of the following statements are correct relative to the various stages of SC associated with chronic exposure to UVR EXCEPT which one?

a. Chronic exposure to UVR results in sunburn, blistering, and peeling of the lip vermilion.
b. Chronic exposure to UVR initially leads to SC characterized by dry, scaly unobtrusive "chapped lips."
c. Palpation provides a sense of rubbing the fingers over sandpaper.
d. At later stages, chronic exposure to UVR progressively leads to small nodules, marked parallel fissuring.
e. SC may appear mottled, opalescent, with white or gray slightly elevated plaques.

6. **Which of the following statements is correct relative to the relationship between actinic cheilosis and squamous cell carcinoma?**
   a. The clinical appearance of actinic cheilosis does not correlate directly with the underlying histological changes and is not predictive when a given actinic cheilosis evolves into squamous cell carcinoma.
   b. Waxing and waning of erythematous or hemorrhagic area and ulcerations of relatively long duration are ominous signs.
   c. Induration, redness, ulcerations, and the onset of pain are generally suggestive of malignant transformation.
   d. All of the above.

7. **Which of the following statements is correct relative to the diagnosis of SC?**
   a. The working diagnosis of actinic cheilosis is usually derived by correlating history with clinical findings.
   b. The presence of concurrent AK on sun-exposed areas (face, neck, bald scalp, ears) reinforces the clinical impressions.
   c. The progressive nature of SC to squamous cell carcinoma emphasizes the importance of biopsy to establish a definitive diagnosis.
   d. All of the above.

8. **General protection guidelines published by the American Cancer Society to minimize actinic damage include all of the following EXCEPT which one?**
   a. Avoid sun-exposure when UV rays are the strongest, i.e., before 10 AM and after 4 PM.
   b. Covering-up exposed skin.
   c. Wearing a hat that shades the neck, face, and ears; wearing sunglasses.
   d. Using a sunscreen with a sun protection factor (SPF) of 30 or higher.

9. **Which of the following statements is correct with respect to sunscreens?**
   a. Sunscreens can be divided into two types based on their ingredients, i.e., inorganic or organic.
   b. Sunscreens that contain zinc or titanium oxide act to physically block, reflect, or scatter UVR.
   c. Organic agents have variable absorptive spectra and sunscreen manufacturers typically combine several agents to produce a broad spectrum product capable of blocking both UV-A and UV-B.
   d. All of the above are correct.

10. **All of the following statements are correct relative to lip balms EXCEPT which one?**
   a. For the prevention of SC, the product should be formulated for use on the lip
   b. The lip balm should provide broad-spectrum protection against both UV-A and UV-B.
   c. If a lip balm is not available, a board-spectrum crème-formulation sunscreen is preferred.
   d. Regardless of the sunscreen chosen, it should be applied 15-30 minutes prior to exposure UVR and reapplied after any activity that may wash or rub it away.

11. **All of the following statements are correct with respect to SC, which presents as a well-circumscribed nodule or papule <5 mm in diameter EXCEPT which one?**
   a. It is amenable to an excisional biopsy.
   b. Serial sections of the surgical specimen and histologic evaluation are not necessary.
   c. Mohs micrographic surgery (MMS), because of its excellent cosmetic yield, may be considered.
   d. If the histologic diagnosis confirms mild to moderate dysplasia no further treatment is indicated, but the patient should be placed in a closely monitored follow-up program.

12. All of the following statements are correct with respect to SC, which presents as a nodule, papule, area of atrophy, erosion or prolonged ulceration >5 mm in diameter EXCEPT which one?

a. An incisional biopsy is indicated.
b. Serial sections of the specimen must be evaluated histologically.
c. If the histologic diagnosis is mild to moderate dysplasia the area may be treated with 5% topical 5-fluorouracil or imiquimod.
d. Treatment with topical agents has been shown to result in excellent clinical remission of SC and to completely eradicate dysplasia at the microscopic level.

13. All of the following statements are correct with respect to cryotherapy (liquid nitrogen applied with a cryoprobe) or electrosurgery in the treatment of SC EXCEPT which one?

a. Ablation with cryotherapy (liquid nitrogen applied with a cryoprobe) or electrosurgery can be useful for the treatment of focal SC.
b. A major advantage of both of these techniques is that they yield specimens for histologic evaluation of serial sections.
c. Cryotherapy requires no local anesthesia and five-year cure rates as high as 99% have been reported.
d. Electrosurgery requires local anesthesia and may lead to damage to adjacent tissues and scar formation.

14. Which of the following statements is correct with respect to SC characterized by diffuse leukoplakia or atrophy of the lip vermilion EXCEPT which one?

a. Such lesions should have a single incisional biopsy of the most suspicious area, which has generally been shown to correspond to a greater degree of dysplasia.
b. If the histologic diagnosis is mild to moderate dysplasia, field therapy with 5% topical 5-fluorouracil or imiquimod may be an option.
c. CO_2 laser ablation has been shown to more predictably resolve both the clinical and histological manifestations of SC than topical chemotherapy.
d. All of the above are correct.

15. Which of the following statements is correct with respect to SC associated with severe dysplasia?

a. SC with severe dysplasia is considered equivalent to or indistinguishable from squamous cell carcinoma-in-situ (SCIS).
b. Vermilionectomy or lip-shave is the most prudent and effective approach to the treatment of diffuse SC, as it provides specimens for histologic evaluation of serial sections.
c. Scalpel vermilionectomy can be combined with a wedge procedure to simultaneously eliminate SCIS or a small SCC.
d. All of the above are correct.

16. Which of the following statements is correct with respect to clinically highly suspicious lesions thought to be SCIS or SCC?

a. Clinically highly suspicious lesions thought to be SCIS or SCC must promptly be referred to a head-and-neck surgeon to maximize prognostic outcome.
b. The risk of local metastasis increases in direct proportion to tumor size.
c. The most commonly involved nodes associated with SCIS or SCC are the submandibular, followed by the submental groups.
d. All of the above are correct.

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About the Authors

Michaell A. Huber, DDS

Professor
Department of Comprehensive Dentistry
The University of Texas Health Science Center at San Antonio, School of Dentistry, San Antonio, Texas

Dr. Huber received his DDS from the University of Texas Health Science Center at San Antonio Dental School, San Antonio, Texas in 1980 and a Certificate in Oral Medicine from the National Naval Dental Center, Bethesda, Maryland in 1988. He is certified by the American Board of Oral Medicine. As an officer of the Dental Corps, United States Navy, Dr. Huber's assignments included numerous ships and shore stations and served as Chairman, Department of Oral Medicine and Maxillofacial Radiology and Director, Graduate Program in Oral Medicine, National Naval Dental Center, Bethesda, Maryland. In addition he served as Specialty Leader for Oral Medicine to the Surgeon General of the United States Navy, Washington, DC; and Force Dental Officer, Naval Air Force Atlantic, Norfolk, Virginia. He has many professional affiliations and over the past 24 years, he has held a variety of positions in professional organizations.

Since joining the faculty in 2002, Dr. Huber has been teaching both pre-doctoral and graduate dental students at the University of Texas Health Science Center Dental School, San Antonio, Texas, and is the Director of the school's Oral Medicine Tertiary Care Clinic. He is currently serving as the Public Affairs Chairman for the American Academy of Oral Medicine. Dr. Huber has accepted invitations to lecture before many local, state, and national professional organizations. He has been published in numerous journals including: *Medical Clinics of North America*, *Oral Surgery*, *Oral Medicine*, *Oral Pathology*, *Oral Radiology and Endodontology*; *Dental Clinics of North America*, *Journal of the American Dental Association*, and *Quintessence International*.

Email: huberm@uthscsa.edu

Géza T. Terézhalmy, DDS, MA

Professor and Dean Emeritus, School of Dental Medicine, Case Western Reserve University, Cleveland, Ohio; and Consultant, Naval Postgraduate Dental School, Walter Reed National Military Medical Center, Bethesda, Maryland.

Dr. Terézhalmy earned a BS degree from John Carroll University; a DDS degree from Case Western Reserve University; an MA in Higher Education and Human Development from The George Washington University; and a Certificate in Oral Medicine from the National Naval Dental Center.

Dr. Terézhalmy held more than 30 positions in professional societies, served as editor or contributing editor for several publications, co-authored or contributed chapters for several books, published over 225 papers and abstracts, and accepted invitations to lecture before many local, state, national, and international professional societies.

Email: gtt2@case.edu