

## eMedicine Specialties > Dermatology > Diseases of the Oral Mucosa

# Cheilitis Glandularis

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Updated: Dec 31, 2008

## Introduction

### Background

Cheilitis glandularis (CG) is a clinically descriptive diagnosis that refers to an uncommon, poorly understood, and fundamentally benign inflammatory disorder of the submucosal glands in the lower lip. Its etiology remains obscure.<sup>1</sup> The condition is characterized by progressive enlargement and eversion of the lower labial mucosa that results in obliteration of the mucosal-vermilion interface. With externalization and chronic exposure, the delicate lower labial mucous membrane is secondarily altered by environmental influences, leading to erosion, ulceration, crusting, and, occasionally, infection. Most significantly, susceptibility to actinic damage is increased. Therefore, cheilitis glandularis can be considered a potential predisposing factor for the development of actinic cheilitis and squamous cell carcinoma.

Historically, the disorder has been subclassified into 3 types: simple, superficial suppurative, and deep suppurative. The deep suppurative type has also been variously referred to as myxadenitis labialis or cheilitis apostematosa, and the superficial suppurative type has been termed Baelz disease. Many believe these subtypes represent a continuum of disease, where the simple type, if not treated, could become secondarily infected and progress to become the superficial or eventually, the deeply suppurative type.

### Pathophysiology

In 1870, von Volkmann introduced the term cheilitis glandularis.<sup>2</sup> He described a clinically distinct, deeply suppurative chronic inflammatory condition of the lower lip characterized by mucopurulent exudates from the ductal orifices of the labial minor salivary glands. In 1914, Sutton proposed that the characteristic lip swelling was attributable to a congenital adenomatous enlargement of the labial salivary glands.<sup>3,4</sup> This remained the prevailing hypothesis until 1984 when Swerlick and Cooper reported 5 new cases and a retrospective analysis of all cases of cheilitis glandularis reported up to that time.<sup>5</sup> Their studies revealed no evidence to support the assertion that submucosal salivary gland acinar hyperplasia is either responsible for or an actual feature of established cheilitis glandularis.

Since then, other authors have corroborated this observation and have variously reported salivary ductal ectasia, hyperplasia, and squamous metaplasia. Stoopler et al reported a papillary cystadenoma-like ductal growth pattern in one patient with cheilitis glandularis.<sup>6</sup> Periductal chronic inflammation (dochitis), scarring, and chronic sclerosing sialadenitis in otherwise unremarkable minor salivary glands have also been noted. Musa and coauthors reported a case with a more generalized presentation of cheilitis glandularis, which they termed suppurative stomatitis

glandularis.<sup>7</sup> In their patient, suppurative labial minor salivary gland involvement extended to also involve the buccal mucosa. Reichart and coauthors reported a retention cyst in the upper lip of an elderly patient with the "simplex" form of the condition; they interpreted the retention cyst as a consequence of cheilitis glandularis. However, this is mere conjecture on the authors' part.<sup>8</sup>

In a case reported by Leao and coauthors, cheilitis glandularis was the presenting clinical finding in a patient later discovered to have undiagnosed HIV-infection.<sup>9</sup> The lip findings could have resulted from (undiagnosed but HIV-related) minor salivary gland dysfunction leading to exfoliative cheilitis, a well-documented and characteristic manifestation of HIV-infection. Butt and coauthors reported a case of cheilitis glandularis that progressed to squamous cell carcinoma in an HIV-infected patient.<sup>10</sup>

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## Pathophysiology

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Although some have speculated that cheilitis glandularis represents a hereditary autosomal dominant condition, composite findings in most cases appear to indicate the condition represents a clinical reaction pattern to chronic irritation of the lip from various highly diverse external causes, which include actinic damage, factitial injury, atopy, infection, and tobacco irritation. Carrington and Horn report a case in which an elderly man developed cheilitis glandularis related to actinic damage following vermilionectomy for squamous cell carcinoma of the lower lip.<sup>11</sup> These authors advocate clinical investigation in cases of cheilitis glandularis to rule out neoplastic, immune suppressive, or inflammatory changes due to local factors. This illustrates the concept that cheilitis glandularis is not a separate and distinct disease. Instead, it appears to be a descriptive phenomenon that could represent any one of a host of diverse clinicopathological entities.

The possibility of a genetic predisposition for cheilitis glandularis has been raised by some authors. Parmar and Muranjan, among others, described a genetic syndrome involving "double lip" of both lips in conjunction with ptosis and other physical abnormalities.<sup>12,13</sup> Dhanapal and coworkers reported a case in which a 14-year-old girl with double lip developed cheilitis glandularis.<sup>14</sup>

## Frequency

### United States

This is an uncommon condition in the United States. However, factitial injury to the lower lip vermilion border and mucosa due to chronic lip biting, lip drying, or habitual lip licking, combined with sun-induced lip damage, are extremely commonplace. Any of the latter influences could result in lip eversion, ulceration, and secondary infection.

### International

Similar to its prevalence in the United States, the condition is uncommon worldwide

## Mortality/Morbidity

Cheilitis glandularis has been associated with a heightened risk for the development of squamous cell carcinoma. In many cases, dysplastic (pre-malignant) surface epithelial change is evident histopathologically, and frank carcinomas have been reported in 18-35% of cases. Rarely, cases of chronic persistent or recurrent suppurative infection may result from inappropriate antibiotic treatment.

A case of persistent suppurative cheilitis glandularis, confirmed by punch biopsy, in a 52-year-old African American woman with a 15-pack year smoking history responded to a 4-week course of oral penicillin at 1 g/d combined with oral fluoroquinolone at 1 g/d. Two weeks into the therapy, the swelling was significantly reduced. The antibiotic regimen was continued for 2 additional weeks, with resolution of the lip lesions and continued normality at 1-year follow-up.<sup>18</sup>

## Race

Cheilitis glandularis has no apparent racial predilection. However, actinic damage is more common in whites than in darker-skinned individuals.

## Sex

The disorder appears to favor adult males; however, cases have been reported in women and in children. One possibility is that some purported childhood cases actually represent exfoliative cheilitis, frequently attributable to factitial injury. Actinic cheilitis favors adults in midlife or older, and a male predilection is reported for the latter condition.

## Age

The condition most frequently occurs between the fourth and seventh decades of life; however, the age range is wide. One report exists of cheilitis glandularis in a child, and several cases have arisen in teenagers and young adults.

The risk of dysplasia and carcinoma increases with age, especially in fair-skinned individuals with sun-damaged skin. This is because the characteristic eversion of the lower lip results in long-term chronic exposure of the thinner, more vulnerable labial mucosa to actinic influence.

## Clinical

### History

Cheilitis glandularis is a chronic progressive condition. Patients typically present for diagnostic consultation within 3-12 months of onset. Complaints vary according to the nature and the degree of pain, the enlargement and the loss of elasticity of the lip, and the extent of evident surface change.

- Asymptomatic lip swelling initially occurs with clear viscous secretion expressible from dilated ductal openings on the mucosal surface.
- Some patients report periods of relative quiescence interrupted by transient or persistent painful episodes associated with suppurative discharge.
- A burning discomfort or a sensation of rawness referable to the vermilion border may be reported. This is associated with atrophy, speckled leukoplakic change, erosion, or frank ulceration with crusting.

### Physical

- Cheilitis glandularis affects the lower lip almost exclusively. It manifests as progressive, often multinodular enlargement, eversion, and induration.
- Salivary gland duct orifices may be dilated and appear as red or black puncta.

- Viscous clear secretions may initially exit the duct openings spontaneously.
- In more suppurative cases, application of gentle pressure can elicit mucopurulent exudates.
- With advancing lip prominence and mucosal eversion, the mucosal-vermilion junction is obfuscated.
- Prolonged exposure to the external environment results in desiccation and disruption of the labial mucous membrane, predisposing it to inflammatory, infectious, and actinic influences.
- Cheilitis glandularis had historically been subclassified into 3 types, now believed to represent evolving stages in severity of a single progressive disorder.
  - In the simple type, multiple, painless, papular surface lesions with central depressions and dilated canals are seen.
  - The superficial suppurative type (also referred to as Baelz disease) consists of painless, indurated swelling of the lip with shallow ulceration and crusting.
  - Cheilitis glandularis of the deep suppurative type (cheilitis glandularis apostematosa, cheilitis glandularis suppurativa profunda, myxadenitis labialis) comprises a deep-seated infection with formation of abscesses, sinus tracts and fistulas, and potential for scarring.
  - The latter 2 types of cheilitis glandularis have the highest association with dysplasia and carcinoma, respectively.

## Causes

Cheilitis glandularis is an unusual clinical manifestation of cheilitis that evolves in response to one or more diverse sources of chronic irritation.

- Lip enlargement is attributable to inflammation, hyperemia, edema, and fibrosis.
- Surface keratosis, erosion, and crusting develop consequent to longstanding actinic exposure or unusual repeated manipulations that include self-inflicted biting or other factitial trauma, excessive wetting from compulsive licking, drying (sometimes associated with mouth breathing, atopy, eczema, and asthma), and any other repeated stimulus that could serve as a chronic aggravating factor.

## Differential Diagnoses

Candidiasis (angular cheilitis)

Cheilitis Granulomatosa (Miescher-Melkersson-Rosenthal Syndrome)

Hyperhidrosis

Premalignant Conditions of the Oral Cavity

Squamous cell carcinoma of lip

## Other Problems to Be Considered

- Granulomatous conditions - Cheilitis granulomatosa, orofacial granulomatosis, Crohn disease, sarcoidosis
- Angioedema
- Lymphangioma and other vascular proliferations
- Mucus extravasation or retention phenomena
- Minor salivary gland neoplasms
- Chronic actinic injury
- Actinic cheilitis
- Bacterial infection - Elephantiasis nostras (after repeated streptococcal lymphangitis) of the lips
- Atopic (eczematous) cheilitis
- Chronic factitial injury (eg, habitual licking [ie, excessive moisture], biting, chewing, or sucking on the lip), excessive drying (from mouth breathing, exposure to wind, medication-induced xerostomia, or salivary dysfunction from autoimmunity, eg, Sjögren syndrome or HIV-infection)
- Tobacco irritation or carcinogenic influence

## Workup

## Laboratory Studies

- To rule out systemic granulomatous diseases (eg, sarcoidosis, Crohn disease) - ACE levels, erythrocyte sedimentation rate, CBC count and differential

## Other Tests

- Microbial culture and sensitivity testing: In cases with acute or chronic suppuration, bacterial culture and sensitivity testing is indicated for selection of appropriate antibiotic therapy.
- Fungal culture or smear: Chronic angular cheilitis or erosive surface changes may be indicative of chronic candidal infection. Confirmation is an indication for appropriate antifungal therapy.

## Procedures

- Lip biopsy is indicated to rule out specific granulomatous diseases that predispose to lip enlargement and to aid in establishing a definitive diagnosis. A representative incisional biopsy specimen should consist of a wedge (or punch) of lip tissue that includes surface epithelium and is of adequate depth to ensure inclusion of several submucosal salivary glands.

## Histologic Findings

The term cheilitis glandularis is a provisional descriptive designation rather than a definitive diagnosis. It refers to a constellation of clinical findings that can reflect a broad scope of possible histologic changes; therefore, no consistent or pathognomonic features of this disorder are seen at the microscopic level. Instead, a diverse array of possible alterations can be seen in both the surface epithelium and the submucosal tissues. These findings best enable the clinician to presumptively determine the etiology and the nature of individual cases.

The maturational profile of the epithelium can be essentially normal or show evidence of disturbance that ranges from varying degrees of atypia or dysplasia to frank carcinoma. Epithelial alterations attended by basophilic collagen degeneration (solar elastosis) constitute a diagnosis of actinic cheilitis. The severity of epithelial maturational disturbance tends to correspond with the degree of risk for progression to carcinoma.

The minor salivary glands may appear normal under the microscope, or they may exhibit various changes indicative of nonspecific sialadenitis. These changes can include atrophy or distention of acini, ductal ectasia with or without squamous metaplasia, chronic inflammatory infiltration and replacement of glandular parenchyma, and interstitial fibrosis. Suppuration and sinus tracts may be present in cases that involve bacterial infection.

Other possible histologic findings include stromal edema, hyperemia, surface hyperkeratosis, erosion, or ulceration.

## Treatment

### Medical Care

The approach to treatment is based on diagnostic information obtained from histopathologic analysis, the identification of likely etiologic factors responsible for the condition, and attempts to alleviate or eradicate those causes. Given the relatively small number of reported cases of cheilitis glandularis, neither sufficient nor reliable data exist with regard to medical approaches to the condition. Therefore, treatment varies accordingly for each patient.

- For cases attributable to angioedema, administration of an antihistamine may effect temporary reduction in acute nonpurulent swelling.
- Suppurative cases of cheilitis glandularis require management with appropriate antimicrobial treatment as determined by culture and sensitivity testing. Concomitant intralesional or oral corticosteroid treatment may potentiate the effectiveness of antimicrobial

therapy in cases with nodularity; however, the potential systemic adverse effects of long-term corticosteroid treatment, plus its propensity for promoting local fibrosis and scarring, limit its potential use either as an adjunct to antibiotic treatment or as a single therapeutic modality for cheilitis glandularis.

- Topical 5-fluorouracil is useful for treatment of dysplastic actinic cheilitis and to curtail its progression. In conjunction with clinical supervision, it can be prescribed as an alternative to vermilionectomy or as a prophylactic measure following vermilionectomy.

## Surgical Care

In cases in which a history of chronic sun exposure exists (especially if the patient is fair skinned or the everted lip surface is chronically eroded, ulcerated, or crusted), biopsy is strongly recommended to rule out actinic cheilitis or carcinoma.

- Surgical excision is not necessary when the diagnosis is actinic cheilitis with atypia or only mild dysplasia; however, patients require ongoing clinical vigilance at regular intervals and instruction in measures to protect the lips from further sun damage.
- Treatment options for cases of actinic cheilitis with moderate-to-severe dysplasia include surgical stripping or vermilionectomy, cryosurgery or laser surgery, or topical chemotherapy with 5-fluorouracil. Given the potential for recurrence and the risk for development of carcinoma, sun protective measures and regular clinical monitoring must be instituted.
- Carcinoma of the vermilion is treated with surgical wedge resection with adequate margins or vermilionectomy. A palpatory examination of the submental lymph nodes is indicated to rule out regional metastasis.
- In cases in which eversion, extensive fibrosis, and induration have resulted in lip incompetence with functional and cosmetic compromise, chronic pain, and surface disruption, debulking with surgical cheiloplasty is indicated to restore normal lip architecture and function. Cheiloplasty is also a prophylactic measure for reducing the risk of actinic injury.

## Consultations

- Consultation with the patient's other providers regarding the possibility of prescribing alternative, less desiccating medications is indicated in cases where medication-induced xerostomia is believed to be contributory to or causative of lip dryness.
- Patients with angioedema or atopic dermatitis (cheilitis) with or without a personal or family history of allergic rhinitis, asthma, or urticaria could benefit from consultation with an allergist-immunologist.
- Psychiatric consultation is recommended in cases where psychogenic factors appear to be contributory. Clinical and historical evidence or suspicion of deliberate, self-inflicted injury to the lip (Munchausen syndrome) should prompt referral for a psychiatric evaluation, particularly if a surgical treatment approach is being considered.<sup>18</sup>

## Medication

For cases attributable to angioedema, administration of an antihistamine may effect temporary reduction in acute nonpurulent swelling.

Suppurative cases of cheilitis glandularis require management with appropriate antimicrobial treatment as determined by culture and sensitivity testing. Concomitant intralesional or oral corticosteroid treatment may potentiate the effectiveness of antimicrobial therapy in cases with significant nodularity; however, potential systemic adverse effects of long-term corticosteroid treatment, plus propensity for promoting local fibrosis and scarring, limit its potential use either as an adjunct to antibiotic treatment or as a single therapeutic modality for cheilitis glandularis.

Topical 5-fluorouracil is useful for the treatment of dysplastic actinic cheilitis and to curtail its progression. In conjunction with clinical supervision, it can be prescribed as an alternative to vermilionectomy or as a prophylactic measure following vermilionectomy.

## Antihistamines

These agents are used to treat angioedema or suspected allergic reaction.

## Diphenhydramine (Benadryl)

For symptomatic relief of symptoms caused by release of histamine in allergic reactions.

### Dosing

#### Adult

25-50 mg PO q6-8h prn for 48 h; not to exceed 300 mg/d

Alternatively, 10-50 mg IM/IV q2-3h; not to exceed 400 mg/d

#### Pediatric

<6 years: 6.25-12.5 mg PO q4-6h

6-12 years: 12.5-25 mg PO q4-6h; not to exceed 150 mg/d

>12 years: Administer as in adults

### Interactions

Potentiates effect of CNS depressants; because of alcohol content, do not give syr dosage form to patient taking medications that can cause disulfiramlike reactions; concomitant alkaloids present in belladonna, antidepressants with strong anticholinergic effects (eg, amitriptyline, trimipramine, amoxapine, doxepin, imipramine, nortriptyline, maprotiline), or phenothiazines with strong anticholinergic effects (eg, chlorpromazine, triflupromazine, thioridazine) and antihistamines may increase possibility of adynamic ileus, urinary retention, or chronic glaucoma (more prominent in elderly patients)

### Contraindications

Documented hypersensitivity; acute asthma; newborns; breastfeeding

### Precautions

#### Pregnancy

B - Fetal risk not confirmed in studies in humans but has been shown in some studies in animals

#### Precautions

May exacerbate angle-closure glaucoma, hyperthyroidism, peptic ulcer, and urinary tract obstruction; elderly persons more susceptible to adverse effects; caution in history of bronchial asthma, cardiovascular disease or hypertension; may cause excitation in young children

## Pyrimidine antagonists

These agents are used to treat actinic cheilitis (dysplastic).

## Fluorouracil (Efudex, Fluoroplex, Carac)



Interferes with DNA synthesis by blocking methylation of deoxyuridylic acid, inhibiting thymidylate synthetase and subsequently cell proliferation.  
Topical forms approved for actinic keratoses; only 5% (Efudex) form approved for superficial basal cell carcinoma.

## Dosing

### Adult

Apply 0.5-5% strength thinly to affected area qd/bid for 2-4 wk

### Pediatric

Not established

## Interactions

None reported

## Contraindications

Documented hypersensitivity; potentially serious infections

## Precautions

### Pregnancy

X - Contraindicated; benefit does not outweigh risk

### Precautions

Inflammatory reactions may occur with use of occlusive dressings; porous gauze dressing may be applied for cosmetic reasons without increase in reaction; patients should expect inflammatory reaction with crusting; because contraindicated for use on mucous membranes, cream rather than liquid form is preferable for use on vermillion surface; duration of application to lip may be shorter than on skin because of its propensity to induce intense inflammatory responses

## Corticosteroids

These agents have anti-inflammatory properties and cause profound and varied metabolic effects. They modify the body's immune response to diverse stimuli.

## Prednisone (Deltasone, Orasone)

Immunosuppressant for treatment of autoimmune disorders; may decrease inflammation by reversing increased capillary permeability and suppressing PMN activity. Stabilizes lysosomal membranes and also suppresses lymphocyte and antibody production. Single morning dose is safer for long-term use, but divided doses have more anti-inflammatory effect.

## Dosing

## Adult

0.5-2 mg/kg/d (around 1 mg/kg/d) PO; taper as condition improves

## Pediatric

Administer as in adults but dose more around 1-2 mg/kg/d range

## Interactions

Coadministration with estrogens may decrease clearance; when used with digoxin, digitalis toxicity secondary to hypokalemia may increase; phenobarbital, phenytoin, and rifampin may increase the metabolism of glucocorticoids (consider increasing maintenance dose); monitor for hypokalemia with coadministration of diuretics; coadministration with ritonavir may significantly increase serum concentrations of prednisone; concomitant therapy with montelukast may result in severe peripheral edema; clarithromycin may increase risk of psychotic symptoms

## Contraindications

Documented hypersensitivity; viral, fungal, tubercular skin, or connective tissue infections; peptic ulcer disease; hepatic dysfunction; GI disease

## Precautions

### Pregnancy

B - Fetal risk not confirmed in studies in humans but has been shown in some studies in animals

### Precautions

May unmask hypertension or diabetes or exacerbate peptic ulcer disease and tuberculosis; long-term sequelae associated with long-term steroid use include osteoporosis, cataracts, and pituitary-hypothalamic axis suppression; with high doses, patients may develop a steroid psychosis and are at increased risk of infections, particularly when oral steroids are used in conjunction with other immunosuppressants; frequently monitor patient's blood glucose level, blood pressure, and weight; monitor for Cushing syndrome  
In cheilitis glandularis, persistent swelling or increasing nodularity are indications for ceasing intralesional or PO use

## Follow-up

### Further Outpatient Care

- Monitor patients with documented actinic cheilitis with clinical observation once or twice a year for an indefinite period. This is because, in some cases, the condition has the potential for the development of lip carcinoma. Also, some patients with cheilitis glandularis may be at risk for the development of suppurative episodes if trauma to the lip surface is continuous. This can result in chronic ulceration or erosion, leading to portals of entry for bacterial invasion and inflammatory sequelae.
- Clinical evidence of disease progression mandates biopsy and an appropriate treatment plan (topical chemotherapy with 5-fluorouracil or vermilionectomy, or in cases of squamous cell carcinoma, lip wedge resection).
- Decisions concerning the advisability and timing of surgical cheiloplasty or vermilionectomy can be challenging in patients who exhibit clinical evidence of persistent habitual or deliberate factitial injury.
  - Undertaking surgery is ill advised if the source of irritation or trauma is perpetuated.
  - Patients who are highly symptomatic and/or functionally compromised by lip enlargement and its complications should be offered the option of surgical debulking, regardless of the cause.
  - Whether or not the surgical approach is ultimately successful depends on factors unique to the patient.

## **Deterrence/Prevention**

- Where relevant, patients who habitually lick their lips should be advised to avoid this behavior.
- Sun-protective measures (eg, wearing a hat with a visor, lip balm with sun-blocking agents, avoidance of direct and protracted sun exposure) must also be instituted.

## **Prognosis**

- Cheilitis glandularis has been associated with a heightened risk for the development of squamous cell carcinoma.
- In many cases, dysplastic (pre-malignant) surface epithelial change is evident, and frank carcinomas have been reported in 18-35% of cases.

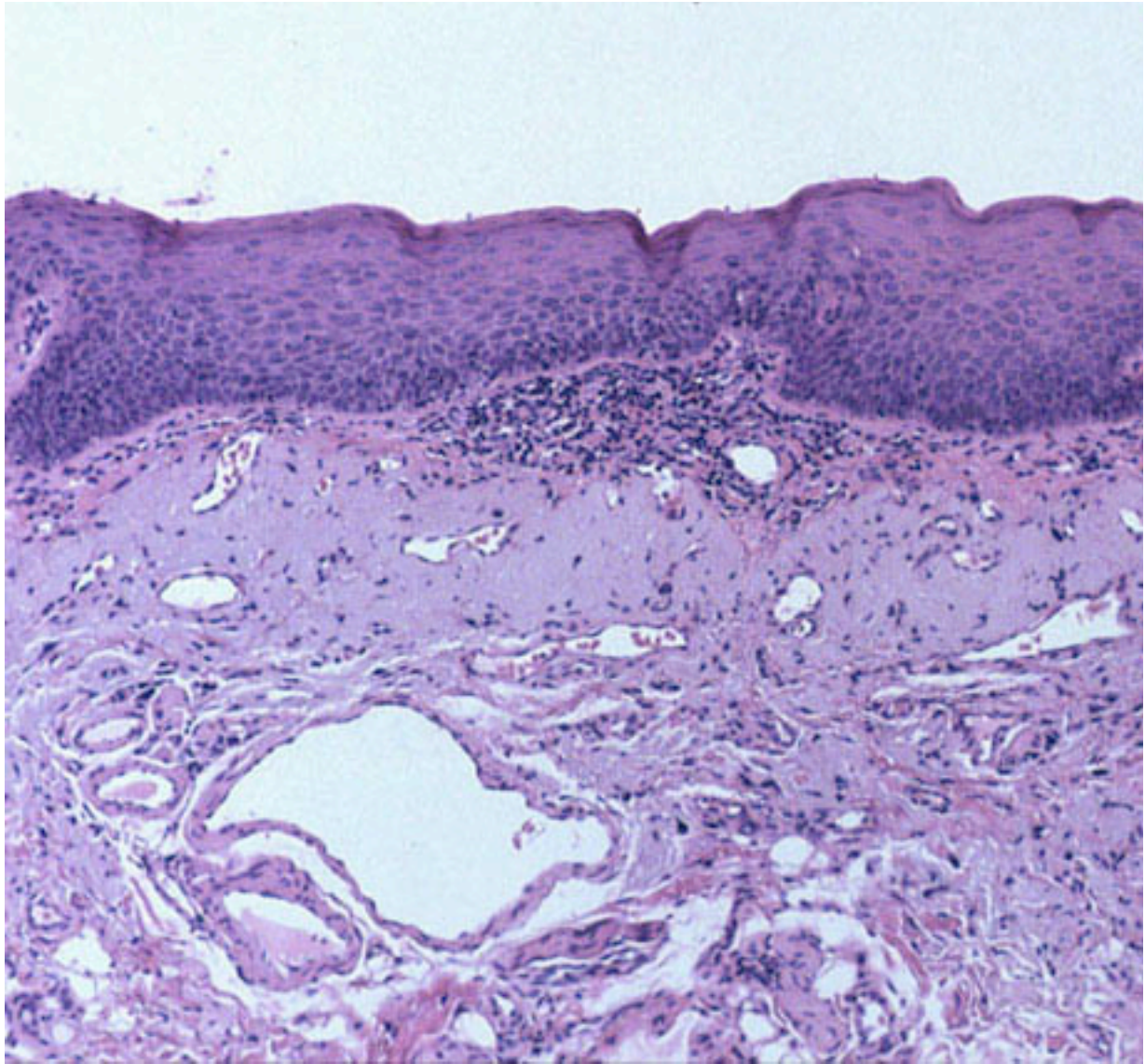
## **Patient Education**

- Reinforce instruction in measures for sun protection.

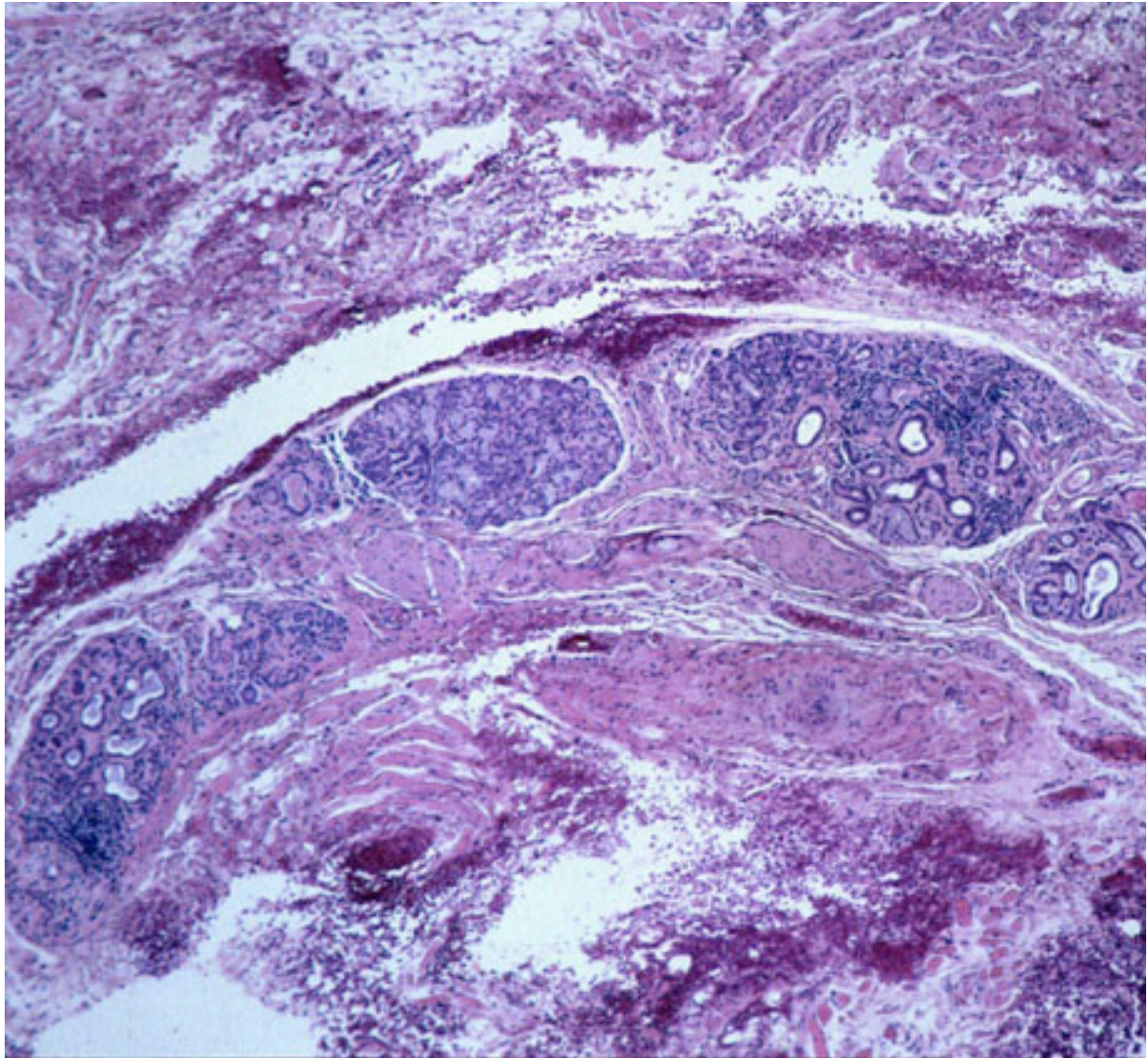
## **Multimedia**



**Media file 1: A 56-year-old woman with an 18-month history of chronic swelling and a dry, burning sensation in her lower lip. She reports intermittent increases and decreases in size of the lip with painful episodes of erosion, crusting, and rare instances of drainage. History reveals medication-induced xerostomia plus a tendency to compulsively lick the lip to maintain hydration. Note eversion of the mucosal surface, which appears erythematous and dry, and narrowing of the vermilion border. The lower labial mucosa appears nodular; however, on palpation, it is diffusely soft. The composite features are consistent with a clinical impression of cheilitis glandularis. A lip biopsy sample was obtained.**



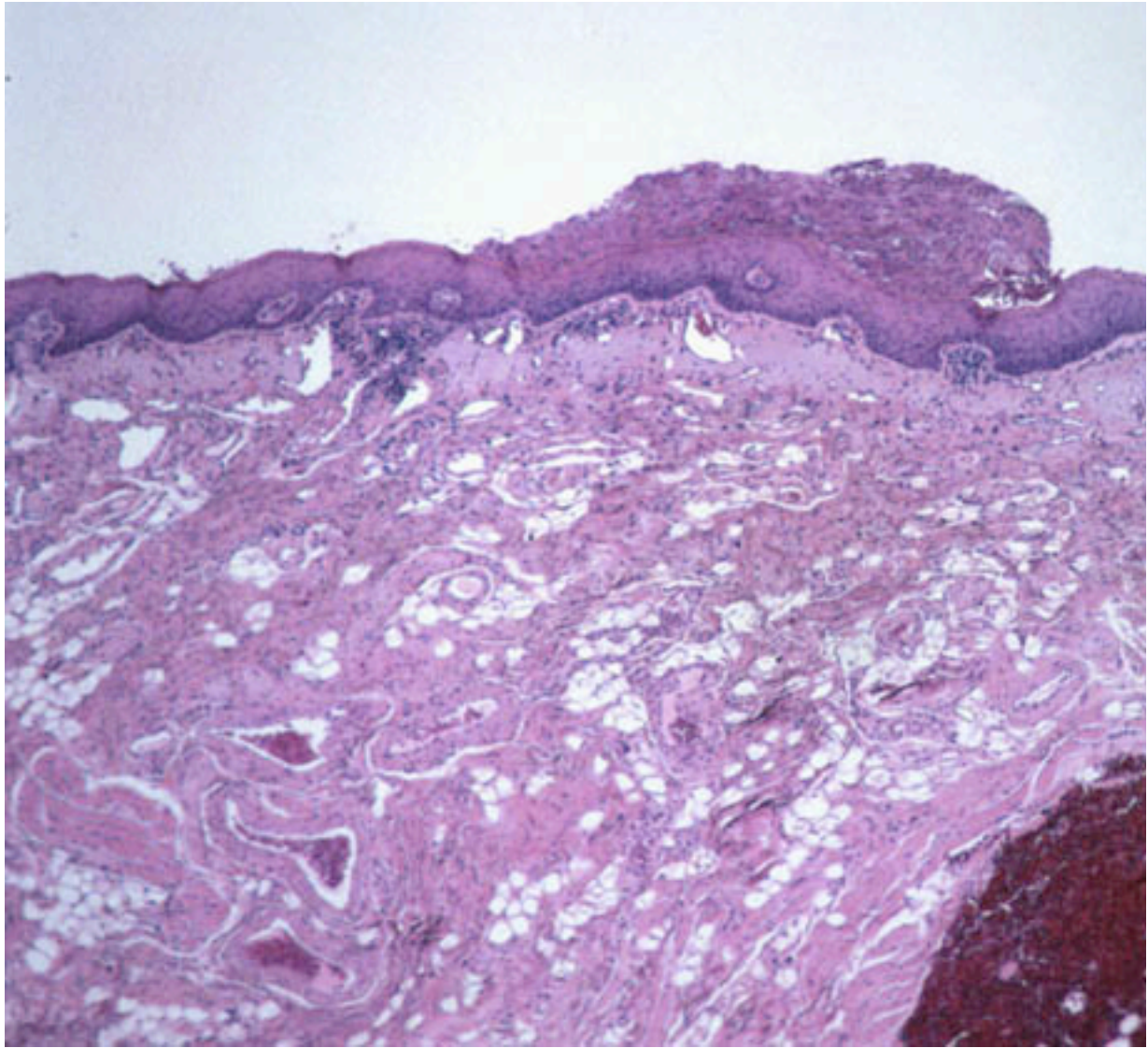
**Media file 2: Medium-power photomicrograph. Note mildly atypical epithelial maturation, modest lymphocytic infiltrate within the lamina propria region, and the striking basophilic collagen degeneration within the superficial stroma plus telangiectasias. The composite features are consistent with a diagnosis of actinic cheilitis (hematoxylin and eosin, original magnification, X100).**



**Media file 3: Low-power photomicrograph. Deep submucosa of the lip. Several minor salivary glands demonstrate ductal ectasia, interstitial inflammation, atrophy, and fibrosis. No evidence of salivary gland hypertrophy is seen (hematoxylin and eosin, original magnification X40).**

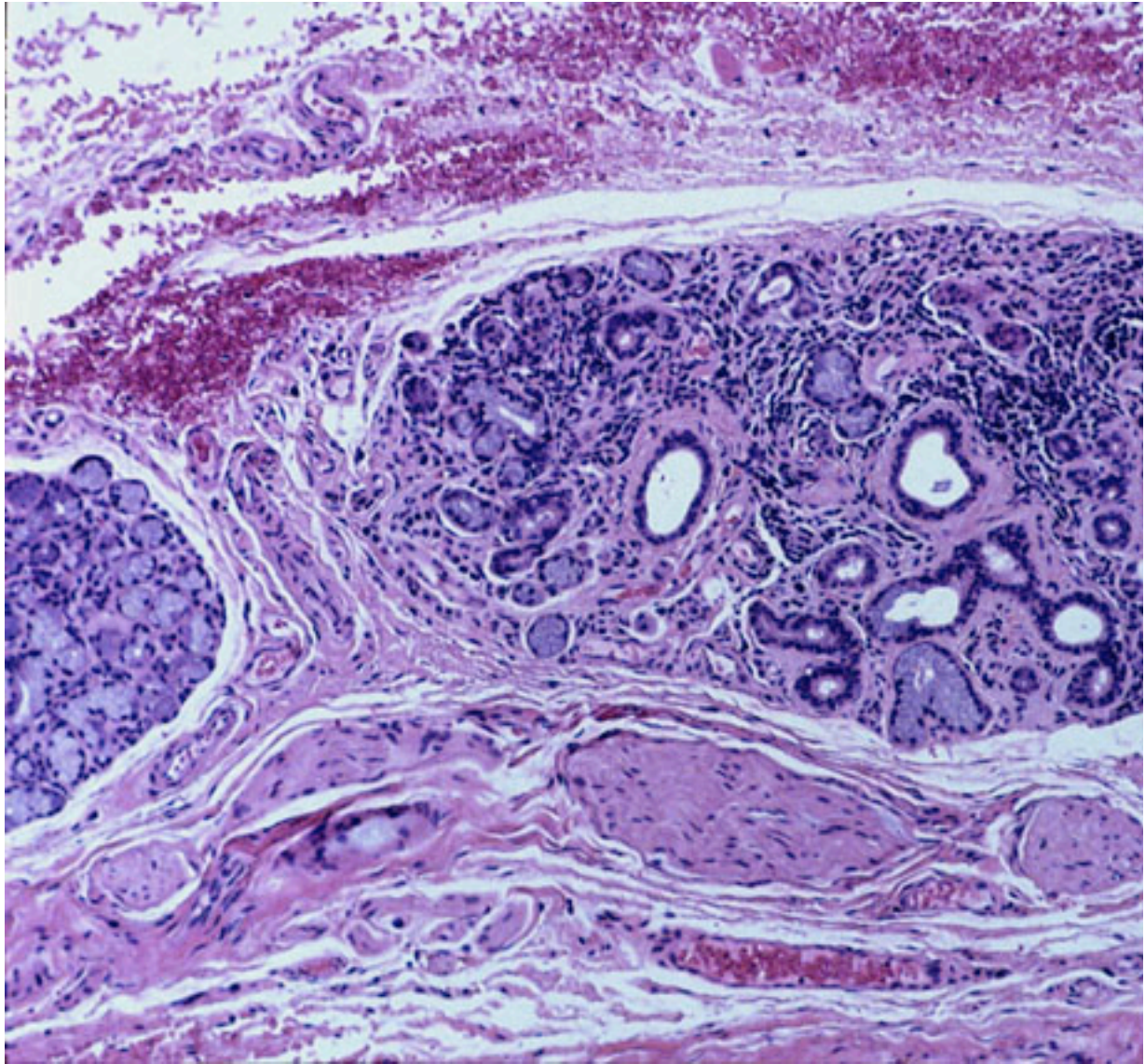


**Media file 4: Note the fullness of the lower portion of the lip and the indistinct junction between the vermilion border and the skin.**



**Media file 5: Lip biopsy specimen. Low-power photomicrograph reveals focal surface hyperkeratosis accompanied by vascular congestion and fibrosis of the underlying stroma (hematoxylin and eosin, original magnification X40).**





**Media file 6: High-power photomicrograph of the minor salivary glands. Note ductal ectasia, acinar atrophy, interstitial fibrosis, and inflammation (hematoxylin and eosin, original magnification X100).**

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