Blair Lonsberry, MS, OD, MEd., FAAO
Professor of Optometry
Pacific University College of Optometry
blonsberry@pacificu.edu

Disclosures:

- Maculogix: advisory board
- Sun Pharmaceuticals: speakers bureau,
- Avellino: advisory board,
- Dompe: advisory board,
- RVL Pharmaceuticals: advisory board

Agenda

- Benign vs. Malignant lesions
- Benign Eyelid Lesions
  - Various types
  - Diagnostic criteria and differentials
  - Treatment and management options
- Malignant Eyelid Lesions
  - Various types
  - Diagnostic criteria and differentials
  - Treatment and management options

Lesion Distribution and Morphology

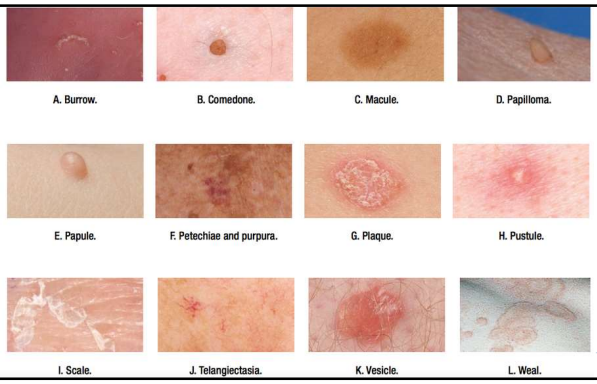
- Two of the most useful characteristics that aid in forming a differential diagnosis are the morphology of individual lesions (type of lesion) and distribution of lesions.
- The arrangement of lesions in relationship to each other, the color of lesions, and the consistency and feel of lesions also add important information.

Lesion Descriptor Terms

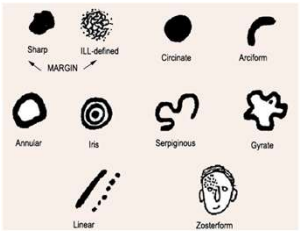
- **Primary lesions** — Primary lesions represent the initial pathologic change. The terms used to describe primary skin lesions include the following:
  - **Macules and Patches:**
    - Macules are nonpalpable lesions <1 cm that vary in pigmentation from the surrounding skin.
    - Patches are nonpalpable lesions >1 cm.
    - These lesions are flush with the surrounding skin.
  - **Papules** – Papules are palpable, discrete lesions measuring <1 cm in diameter. They may be isolated or grouped.
  - **Plaques** – Plaques are elevated lesions that are >1 cm in diameter. Plaques may be formed by a confluence of papules
  - **Nodules and Tumors:**
    - Nodules are palpable, solid or cystic, discrete lesions measuring between 1 and 2 cm in diameter.
    - Tumors are solid or cystic, discrete lesions measuring >2 cm in diameter.
    - These lesions may be isolated or grouped and may or may not have surface changes
  - **Telangiectasia** – Telangiectasia is a dilated, superficial blood vessel.
  - **Purpura** – Purpura are red-purple lesions that do not blanch under pressure, resulting from the extravasation of blood from cutaneous vessels into the skin. Purpuric lesions can be macular or raised (palpable purpura)

Lesion Descriptor Terms

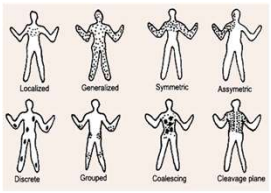
- **Pustules** – Pustules are small, circumscribed skin papules containing purulent material
- **Vesicles** – Vesicles are small (<1 cm in diameter), circumscribed skin papules containing clear serous or hemorrhagic fluid. Bullae are large (>1 cm in diameter) vesicles.
- **Wheals** – Wheals are irregularly shaped, elevated, edematous skin areas that may be erythematous or paler than surrounding skin. The borders of a wheal are well demarcated but not stable; they may move to adjacent, uninvolved areas over periods of hours.
- **Scale** – Scale is flakes on the skin surface formed by desiccated, thin plates of cornified epidermal cells.
- **Atrophy** – Atrophy is a depression from the surface of the skin caused by underlying loss of epidermal or dermal substance.
- **Pigmentary changes** – Hyperpigmentation is increased skin pigment; hypopigmentation is decreased skin pigment. Depigmentation is total loss of skin pigment.
- **Comedone** - small, flesh-colored, white, or dark bumps that give skin a rough texture. The bumps are caused by acne.
- **Burrow** - These raised lines are usually grayish-white or skin-colored and secondary to scabies tunneling underneath the skin.
- **Papilloma** - a benign epithelial tumor growing outwardly, projecting in nipple-like and often finger-like fronds.



- Configuration
  - Refers to the shape or outline of lesions
    - Annular - round or circular with central clearing
    - Circinate - round, circular > arciform: partial circle
    - Iris or target -also known as target lesions and are a series of concentric rings. These have a dark or blistered center.
    - Gyrate - connecting arcs
    - Linear - straight
    - Serpiginous – meandering; wander as though following the track of a snake.
    - Margination – sharp, ill-defined?
    - Satellite Lesions - commonly used to describe a portion of the rash of cutaneous candidiasis in which a beefy red plaque may be found surrounded by numerous, smaller red macules located adjacent to the body of the main lesions
    - Zosteriform - dermatomal



- **Lesion distribution** — The location of one or multiple skin lesions and the arrangement of multiple lesions in relation to each other can suggest a particular diagnosis.
- Common arrangements of lesions are:
  - Localized - grouped into specific areas
  - Generalized - dispersed all over
  - Symmetric - no pattern
  - Asymmetric - pattern lacking randomness
  - Discrete - separate
  - Grouped - clustered (as seen in herpes simplex infections)
  - Confluent (coalescing) - smaller into larger
  - Cleavage plane - arranged along lines of skin tension



Eyelid Lumps and Bumps

- 15-20% of periocular skin lesions are malignant
- Benign vs malignant:
  - Benign lesions are:
    - Well circumscribed and possibly multiple
    - Slow growing
    - Less inflamed
    - Look "stuck on" instead of invasive and deep

Is it Benign?

- H: loss of hair bearing structures?
  - Loss of hair bearing structures more common with malignancy
- A: asymmetrical?
  - Benign lesions tend to be symmetrical
- A: abnormal blood vessels?
  - Abnormal "feeder" vessels sign of malignancy
- B: borders irregular?
  - Benign lesions typically have smooth regular borders
- B: bleeding reported?
  - Bleeding often a sign of malignancy
- C: multicolored?
  - Benign lesions generally uniform in color
- C: change in the size or color of the lesion?
  - Increasing size or changes in color can indicate malignancy
- D: overall diameter > 5 mm?
  - Larger lesions more likely to be malignant

Benign Skin Lesions

Benign Eyelid Lesions

- Most common types of benign eyelid lesions include:
  - Squamous papillomas (skin tags)-most common
  - Hordeola/chalazia
  - Epidermal inclusion cysts
  - Seborrheic keratosis
  - Capillary hemangioma (common vascular lesion of childhood)

Acrochordon (skin tag)

- Acrochordons, commonly known as skin tags, are an outgrowth of normal skin.
- They appear as pedunculated lesions on narrow stalks.
- Skin tags occur in approximately 50 percent of adults; the risk increases with age.
- Skin tags also appear with increased frequency during the second trimester of pregnancy and may regress postpartum.
- Skin tags are frequently seen in obese patients and in patients with diabetes mellitus

Acrochordon (skin tag)

- Acrochordons usually occur in sites of friction, particularly the axilla, neck, inframammary, and inguinal regions.
  - They become symptomatic when caught on jewelry or rubbed by clothing.
- The diagnosis of acrochordons is usually based upon clinical appearance
- Treatment is indicated if lesions are irritating or the patient desires removal for cosmetic reasons
  - Cryosurgery with liquid nitrogen
  - Electrodesiccation
  - Radiosurgery
  - Chemical e.g. TCA

Radiofrequency (RF) Surgery

- Radiosurgery is the passage of high frequency radiowaves through soft tissue to cut, coagulate, and/or remove the target tissue
- Cuts and coagulates at the same time
- Nearly bloodless field
- Minimal biopsy artifact damage
- Quick and easy (to do and to learn)
  - Pressureless & bacteria-free incisions
- Minimal lateral heat
- Minimal Post-op pain
- Rapid healing
- Fine control with variety of tips

Milia

- Milia are minute subepidermal keratin cysts that arise from the pilosebaceous units or eccrine sweat ducts.
- They present as firm, white papules, 1 to 2 mm in diameter, most frequently located on the face.
- Milia are common lesions; they occur at all ages and are a common finding in newborns.
  - In adults, when milia are small, they may at times be confused with other common lesions, such as flat warts or syringoma

Milia

- may develop spontaneously or as secondary lesions during the healing process of second-degree burns, blistering diseases, dermabrasion, and ablative laser resurfacing
- Milia can be treated for cosmetic reasons with:
  - topical retinoids applied daily for several weeks
  - incision of the overlying epidermis and expression of the content
  - CO2 laser ablation
- Recurrence is uncommon

CO2 ablation of milia before and after https://www.shensaesthetics.com/treatments/skin/others/milia-removal/

Syringoma

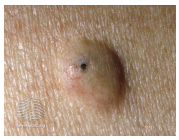
- A syringoma is a skin colored or yellowish firm rounded bump, 1-3 mm in diameter.
- They start to appear in adolescence and are more common in women than men. There is sometimes another affected member of the family.
- Eruptive syringomas appear abruptly in adult life, as a crop of multiple lesions typically on the chest or lower abdomen.
- Multiple or eruptive syringomas may be associated with Down's syndrome, anti-epileptic medications, and hyperthyroidism.
- Syringoma may be confused with xanthelasma
- Syringomas are often treated by electrosurgery or laser. This may or may not prove successful and can result in small scars. If they recur, they can be treated again the same way.

Xanthelasma

- Xanthelasma are soft, yellow plaques that usually appear symmetrically on the medial aspects of the eyelids.
- They occur most often in middle-aged and older adults, tend to be painless, and build gradually over time.
- Larger xanthelasma may cause discomfort.
- Cholesterol-filled xanthelasma are often associated with hypercholesterolemia, and thus it is recommended obtaining a lipid profile if the patient has not already undergone screening.
  - Dyslipidemia is present in approximately 50% of adult patients with xanthelasma
  - In patients with a normal lipid profile, the association between xanthelasma and atherosclerosis is not clear
- Xanthelasma lesions themselves generally do not require treatment.
  - Lipid-lowering drug therapy may induce regression of xanthelasma in some patients, but the effect is not consistent
  - Surgical excision, carbon dioxide laser therapy, or topical trichloroacetic acid (TCA) can be performed for cosmetic reasons, but recurrence is common

Epidermoid cyst

- Epidermoid cysts, also called epidermal cysts, epidermal inclusion cysts, or, improperly, "sebaceous cysts," are the most common cutaneous cysts.
- They can occur anywhere on the body and typically present as skin-colored dermal nodules, often with a clinically visible central punctum.
- The size ranges from a few millimeters to several centimeters in diameter.
- The diagnosis of epidermoid cyst is usually clinical, based upon the clinical appearance of a discrete cyst or nodule, often with a central punctum, that is freely movable on palpation
- Treatment is by excision




Pyogenic Granuloma

- Most common acquired vascular lesion to involve the eyelids
- Usually occurs after trauma or surgery as a fast growing, fleshy, red-to-pink mass which readily bleeds with minor contact
- Treatment can include use of steroid to reduce the inflammation or surgical excision at the base of the lesion.

Lipoma

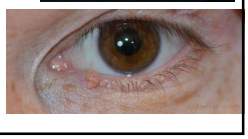
- Superficial subcutaneous lipomas are the most common benign soft-tissue neoplasms. They consist of mature fat cells enclosed by thin fibrous capsules. Lipomas can occur on any part of the body and usually develop superficially in the subcutaneous tissue.
- Lipomas present as soft, painless subcutaneous nodules ranging in size from 1 to >10 cm. They occur most frequently on the trunk and upper extremities and can be round, oval, or multilobulated
- The diagnosis of lipoma is usually made clinically.
- The treatment of lipomas, if needed because of pain, cosmesis, or concerns over diagnosis, is surgical removal of the fat cells and fibrous capsule. Recurrence of an excised lipoma is not common.

Molluscum Contagiosum

- Common viral skin disease caused by a large DNA pox virus
- Infection usually from direct contact in children and sexually transmitted in adults
- Typical lesion appears as a raised, shiny, white-to-pink nodule with a central umbilication filled with cheesy material
- Eyelid lesions may produce a follicular conjunctival reaction
- Patients with AIDS may have a disseminated presentation (30-40 each eyelid or a confluent mass)
- Usually spontaneously resolves 3-12 months but may be treated to prevent spread by excision, incision and curettage, cryosurgery, RF and electrodesiccation.

Verruca Vulgaris

- Common cutaneous wart caused by the epidermal infection of the human papillomavirus
- More common in children and young adults and may occur anywhere on the skin
- Lesions appear elevated with an irregular, hyperkeratotic papillomatous surface
- Lesions along lid margin may cause papillary conjunctivitis
- Tend to be self limiting but if treatment required cryotherapy, RF or surgical excision.

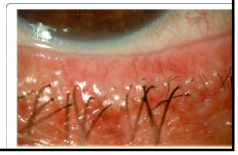


Acne Rosacea

- Rosacea is a common, chronic disorder that can present with a variety of cutaneous or ocular manifestations.
- Skin involvement primarily affects the central face, with findings such as persistent centrofacial redness, papules, pustules, flushing, telangiectasia, and phymatous skin changes (eg, rhinophyma).
- Ocular involvement may also occur, manifesting with lid margin telangiectasia, conjunctival injection, ocular irritation, or other signs and symptoms.

Acne Rosacea

- affects females>males (although males are more disfigured) of Celtic/Northern European descent after age 30 with peak incidence 4-7th decade
  - Prevalence thought to be between 1-10% of fair skinned individuals
- Pathogenesis:
  - Proposed contributing factors include abnormalities in innate immunity, inflammatory reactions to cutaneous microorganisms, ultraviolet damage, and vascular dysfunction.



Acne Rosacea and Demodex

- Demodex is a natural part of human microbiome
- *Demodex folliculorum* live in hair follicles, primarily on the face, as well as in the meibomian glands of the eyelids;
- *Demodex brevis* live in the sebaceous glands of the skin.
- *Demodex folliculorum* frequently occur in greater numbers in those with rosacea and this overabundance is thought to trigger an immune response.
  - increased density of *Demodex* mites in patients with rosacea has been reported in multiple studies
  - the immune response may also be triggered by bacteria that is associated with Demodex.
    - *Bacillus oleronius* has been found to be associated with Demodex mites and may also trigger an immune response

Acne Rosacea Management

- Traditionally, treatment for acne/ocular rosacea has focused on symptom suppression to improve patient quality of life and to help manage the disease.
- Treatment should be initiated even in patients with mild disease, as early intervention can be key in minimizing both the progression of rosacea and its effects on symptoms and visual function.
- Nonpharmacologic interventions may be useful for the management of the cutaneous manifestations of rosacea.
  - avoidance of triggers including gentle skin care, sun-protection and avoiding the use of cosmetic products known to cause flushing.
  - Treatment options for ocular rosacea include omega- 3 fatty acids (FAs) and gamma linolenic acid (GLA), lipid-based artificial tears, lid hygiene with a mild cleanser, hypochlorous acid, and warm compresses.
    - Omega-3 FAs and GLA supplements have been shown to reduce symptoms, lid margin inflammation, and meibomian gland dysfunction (MGD).
    - Hypochlorous acid products contain antiinflammatory and antibacterial properties that decrease the signs and symptoms of ocular irritation that occur when there is an excessive quantity of bacteria on the lids
    - use a tea tree oil–based soap to wash the entire face in order to get the Demodex under control.

Acne Rosacea Management

- Tetracycline, doxycycline, and minocycline have been used for many years for the management of rosacea. These agents are most useful for improving inflammatory papules and pustules, and may also reduce erythema
  - Since no definitive microbial cause of rosacea has been identified, the efficacy of oral antibiotics in rosacea is often attributed to their anti-inflammatory properties
  - Support for the efficacy of subantimicrobial doses of doxycycline (20 mg taken twice daily or a combination pill containing 30 mg of immediate release doxycycline and 10 mg of delayed release doxycycline taken once daily) come from both randomized trials and an open label study of almost 1200 patients

Acne Rosacea Management

- The pharmacologic agent with the strongest evidence for efficacy for persistent facial erythema in rosacea is topical brimonidine (brimonidine tartrate gel 0.33% (Brand name: Mirvaso)
  - Effects can be seen as quickly as 30 minutes after application
  - MIRVASO topical gel is for topical use only and not for oral, ophthalmic, or intravaginal use.
- Topical metronidazole, azelaic acid, and topical ivermectin are also considered first-line therapies in mild to moderate facial disease
- Laser and light-based therapies, which have been used extensively for the treatment of a variety of vascular lesions, have also been used for the vascular features of rosacea, especially telangiectasias.
  - The mechanism of actions are well known and include immunomodulation of the inflammatory burden, destruction of Demodex, decrease of the bacterial load, photomodulation of mitochondrial activity and rejuvenation of collagen production.

Benign Eyelid Lesions: Capillary Hemangioma

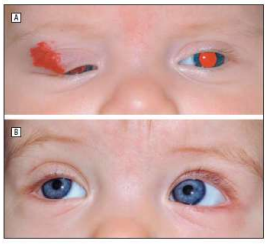
- Most common vascular lesion in childhood (5-10% of infants)
- Females 3:2
- Periorbital may appear as a superficial cutaneous lesion, subcutaneous, deep orbital or combination
- 1/3 visible at birth, remainder manifest by 6 months
- 75% regress to some extent by 7 years

Benign Eyelid Lesions: Capillary Hemangioma

- Classic superficial lesion
  - strawberry lesion, appears as a red, raised, nodular mass which blanches with pressure
- Most common ocular complication is amblyopia
- regression is common, treatment is reserved for patients who have specific ocular, dermatologic or systemic indications for intervention.

Benign Eyelid Lesions: Capillary Hemangioma

- Mainstay treatment includes the use of oral propanolol
- Recent protocols include use of topical timolol 0.25 or 0.50% Gel Forming Solution (GFS) BID for 3-4 months for superficial hemangiomas
- The exact mechanism of action of β-blockers for the treatment is not yet completely understood, however, it is postulated to inhibit growth by at least four distinct mechanisms: vasoconstriction, inhibition of angiogenesis or vasculogenesis, induction of apoptosis, and recruitment of endothelial progenitor cells (EPCs) to the site of the hemangioma



ARCH OPHTHALMOL/VOL 129 (NO. 3), MAR 2011

Allergic Contact Dermatitis (ACD)

- Allergic contact dermatitis (ACD) is the classic presentation of a T cell-mediated, delayed-type hypersensitivity response to exogenous agents
- The agents most frequently implicated included latex materials, protective equipment, soap and cleansers, resins, and acrylics.
- The location will often suggest the cause:
  - Allergens applied to the scalp, including hair dyes and shampoos, may elicit dermatitis in adjacent skin.
  - Facial lesions may result from direct contact with cosmetic products or tools or from involuntary transfer of allergens to the face (eg, eyelid ACD from nail polish)
  - A pendant-like distribution of lesions (berloque dermatitis) in the neck and chest suggests a reaction to fragrances in perfumes and lotions
  - A diffuse or patchy dermatitis of the trunk, often with accentuation in the axillary folds, may be caused by cloth dyes or textiles.
- Reactions may not develop for 48–72 hours after exposure.

- The acute phase is characterized by intense pruritus, tiny vesicles and weepy and crusted lesions.
- The lesions, distributed on exposed parts or in bizarre asymmetric patterns, consist of erythematous macules, papules, and vesicles and may occur beyond the contact area, distinguishing it from irritant dermatitis.
- The affected area may also be edematous and warm, simulating—and at times complicated by—infection.

Management

- The identification of the offending allergen is a key step in the management of ACD. Although the offending allergen is often identified through a detailed history, patch testing may be necessary to identify specific antigens.
- Prompt and thorough removal of the causative oil by washing with liquid soap may be effective if done within 30 minutes after exposure to poison oak or ivy.
- Local Measures:
  - Gentle cleansing and drying compresses
  - Topical corticosteroids are the first line treatment for localized ACD
    - High-potency topical corticosteroids in gel or cream form (eg, fluocinonide, clobetasol, or halobetasol)
    - This should be followed by a taper and use of milder steroids
  - Topical tacrolimus or pimecrolimus (calcineurin inhibitor) may be an alternative to topical corticosteroids in the management of chronic, localized ACD; localized ACD resistant to topical corticosteroids; ACD involving the face or intertriginous areas (where two skin areas rub together); and ACD induced by topical corticosteroids

Management

- Oral corticosteroids are the first line treatment for ACD involving >20 percent of the body surface area or for acute ACD involving the face, hands, feet or genitalia if quick relief is desired (eg, involvement of the eyelids). Oral corticosteroids for ACD have not been studied in randomized trials. However, in clinical experience they are frequently beneficial in the treatment of poison ivy dermatitis, a common form of ACD.
- Severe Weeping:
  - For acute severe cases, prednisone may be given orally for 12–21 days.
  - Prednisone, 60 mg for 4–7 days, 40 mg for 4–7 days, and 20 mg for 4–7 days without a further taper is one useful regimen.
  - The key is to use enough corticosteroid (and as early as possible) to achieve a clinical effect and to taper slowly over 2–3 weeks to avoid rebound.

Atopic Dermatitis (Eczema)

- Atopic dermatitis is a chronic pruritic inflammatory skin disease that occurs most frequently in children, but also affects adults.
- Atopic dermatitis is often associated with elevated serum level of immunoglobulin E (IgE) and a personal or family history of atopy, which describes a group of disorders that includes eczema, asthma, and allergic rhinitis
- affects approximately 5 – 20% of children worldwide
- Approximately 70% of patients have a positive family history of atopic diseases

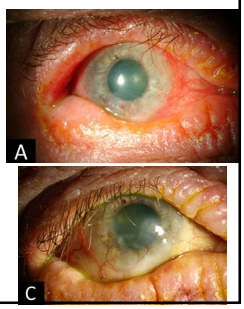
- Signs and Symptoms:
  - Atopic dermatitis occurs in the first year of life in 60 percent of cases and by the age of five years in nearly 85 percent of cases.
  - Dry skin and severe pruritus are the cardinal signs of atopic dermatitis.
  - Itching is a key clinical feature and may be severe and prolonged.
  - Ill-defined, scaly, red plaques affect the face, neck, and upper trunk.
  - The flexural surfaces of elbows and knees are often involved
  - Up to 80 percent of patients with atopic dermatitis have increased serum IgE levels, often with eosinophilia.

Management

- Atopic patients have hyperirritable skin and anything that dries the skin can trigger dermatitis
- Warm soaking baths or showers using mild or soap-free cleansers should be part of the routine skin care for patients with atopic dermatitis.
- Skin should be patted dry (not rubbed) and immediately after covered with emollient or corticosteroid
  - Topical anti-inflammatory therapy with topical corticosteroids or topical calcineurin inhibitors (e.g. tacrolimus) is effective in controlling pruritus.
- In patients with diffuse pruritus that is not controlled with topical therapy alone, narrowband ultraviolet B (NBUVB) or ultraviolet A1 (UVA1) phototherapy are therapeutic options
- Oral H1 antihistamines are widely used as a therapeutic adjunct in patients with atopic dermatitis to alleviate pruritus

Ocular Comorbidities

- Ocular comorbidities occurring in patients with atopic dermatitis include atopic keratoconjunctivitis (AKC) and vernal keratoconjunctivitis (VKC).
- AKC is a chronic allergic ocular disease that occurs most often in adults with a history of atopic dermatitis .
- VKC most commonly occurs in children living in warm, dry subtropical climates.
- Ocular itching, burning, tearing, and mucus discharge are common symptoms.
- Complications include keratoconus, infectious keratitis, and blepharitis.
  - Keratoconus presents as bilateral ectasia and has an incidence rate of approximately 1 per 2,000 in the general population. However, for patients with AD, the incidence rate ranges from 0.5% to 39%.
  - A number of studies have demonstrated a link between eye rubbing and keratoconus. Itching is a symptom of AD, which elicits eye rubbing.
  - In unilateral cases of keratoconus, 13 out of 17 patients developed KC on the side of the dominant hand.



Ocular Comorbidities

- more prevalent is children and young adults
- ~20-40% of atopic dermatitis patients will have ocular involvement
- AKC patients have high rates of atopic dermatitis (95%), asthma (87%) and periocular eczema is almost always present
- Treatment aimed at minimizing inflammation: antihistamines, mast cell stabilizers, steroids, cyclosporin and tacrolimus ointment to the lids

Acne Vulgaris: Essentials of Diagnosis

- The most common skin condition.
- Almost universal in puberty, though may begin in premenarchal girls and present or persist into the fourth or fifth decade.
- Comedones (white/blackheads) are the hallmark.
- Severity varies from purely comedonal to papular or pustular inflammatory acne to cysts or nodules.
- Face, neck, and upper trunk may be affected.
- Scarring may be a sequela of the disease or picking by the patient.

Management

- Lesions take 4-6 weeks to improve, clinical improvement should be measured by the number of new lesions that form after 6-8 weeks of therapy
- Additional time (3–4 months) will be required to see improvement on the back and chest, as these areas are slowest to respond.
- Topical retinoids: tretinoin, adapalene, tazarotene, trifarotene
  - applied once daily and traditionally at night due to photolability reported with tretinoin
- Benzoyl peroxide: topical agent with antibacterial and comedolytic properties
- Topical or oral antibiotics
- Isotretinoin (oral) is used for the treatment of severe acne

Psoriasis

- Psoriasis is a common chronic inflammatory disease of the skin, scalp, nails, and joints that may exhibit a variety of clinical manifestations.
  - It is a scaly rash that occurs most frequently on the elbows, knees and scalp, but can cover much of the body.
  - Chronic plaque psoriasis is the most common subtype
- psoriasis can begin at any age, though it is less common in children than adults. Peak ages for the onset of psoriasis are between 30 and 39 years and between 50 and 69 years
- typical clinical findings of scaling, induration, and erythema are the result of hyperproliferation and abnormal differentiation of the epidermis, inflammatory cell infiltrates, and vascular dilatation.
  - A normal skin cell matures and falls off the body's surface in 28 to 30 days, but a psoriatic skin cell takes only three to four days to mature and gathers at the surface, thus forming lesions.

Psoriasis

- There are often no symptoms, but itching may occur and be severe
- The lesions are red, sharply defined plaques covered with silvery scale
- The combination of red plaques with silvery scales on elbows and knees, with scaliness in the scalp or nail findings, is diagnostic
- The psychosocial impact of psoriasis is a major factor in determining the treatment of the patient.

Psoriasis: Treatment

- Systemic corticosteroids should never be used to treat psoriasis flare ups.
  - Even tiny doses of systemic corticosteroids given to patients with psoriasis may lead to severe rebound flares of their disease when they are tapered
- High- to ultra–high-potency topical corticosteroids are the mainstay for limited disease (less than 10% BSA).
- For patients with numerous small plaques, phototherapy is the best therapy.
- Methotrexate is very effective for severe psoriasis in doses up to 25 mg once weekly
- Cyclosporine (oral) dramatically improves psoriasis and may be used to control severe cases.
- The tumor necrosis factor (TNF) inhibitors etanercept (Enbrel), infliximab (Remicade), and adalimumab (Humira) are effective in pustular and chronic plaque psoriasis and are also effective for the associated arthritis
  - These medications are referred to as Biologics and their expense may be prohibitive for treatment
  - Biosimilars are now being approved for treatment
    - Biosimilars or follow-on biologics, which are less costly versions of biologics but, unlike generic versions of chemically derived drugs, may have a different structure than the reference biologic

Fungal Infections

- Dermatophyte infections are common worldwide, and dermatophytes are the prevailing causes of fungal infection of the skin, hair, and nails
- The diagnosis of fungal infections of the skin is usually based on the location and characteristics of the lesions and on the following laboratory examinations:
  - (1) Direct demonstration of fungi in 10% KOH evaluation of suspected lesions. "if it's scaly, scrape it"
  - (2) Cultures of organisms from skin scrapings.
  - (3) Histologic sections of biopsies stained with periodic acid-Schiff technique may be diagnostic if scrapings and cultures are falsely negative

- The major clinical subtypes of dermatophyte infections are:
  - **Tinea corporis** – Infection of body surfaces other than the feet, groin, face, scalp hair, or beard hair
  - **Tinea pedis** – Infection of the foot (also known as athlete's foot) is the most common dermatophyte infection.
  - **Tinea cruris** – Infection of the groin
  - **Tinea capitis** – Infection of scalp hair
  - **Tinea unguium (dermatophyte onychomycosis)** – Infection of the nail

- Tinea Corporis:
  - Classic appearance: ring-shaped lesions with an advancing scaly border and central clearing or scaly patches with a distinct border.
  - Microscopic examination of scrapings or culture confirms the diagnosis.
  - The lesions are often on exposed areas of the body such as the face and arms.
  - Itching may be present.

- Tinea Corporis Management:
  - Tinea corporis responds to most topical antifungals, including terbinafine, butenafine, econazole, miconazole, and clotrimazole, most of which are available over the counter.
  - Treatment should be continued for 1-2 weeks after clinical clearing.
  - Systemic treatment is an alternative for patients with extensive skin involvement and patients who fail topical therapy. Terbinafine and itraconazole are common treatments.
  - Tinea corporis usually responds promptly to conservative topical therapy or to an oral agent within 4 weeks.

Herpes Simplex

- Herpes Simplex Virus type 1
- Over 85% of adults have serologic evidence of herpes simplex type 1 (HSV-1) infections, most often acquired asymptomatically in childhood
- HSV-1 is typically transmitted from person to person via infected oral secretions during close contact.
  - After initial infection, HSV-1 establishes chronic infection in neural ganglia and reactivates on mucosa and skin.
  - Although infections are frequently asymptomatic, they can produce a variety of signs and symptoms
  - Primary outbreak is typically mild or subclinical
    - Many patients with primary HSV-1 infections are asymptomatic. Retrospective studies demonstrate that only 20-25 percent of patients with HSV-1 antibodies have a clinical history of oral-labial or genital infections

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- Herpes simplex virus type 2
- Both HSV-1 and HSV-2 can cause genital herpes, and infection of the same anatomic site by both HSV-1 and HSV-2 has been documented
- About 25% of the US population has serologic evidence of infection with herpes simplex type 2 (HSV-2).
  - HSV-2 causes lesions whose morphology and natural history are similar to those caused by HSV-1 but are typically located on the genitalia of both sexes
  - Most cases of recurrent genital herpes are caused by HSV-2
  - The infection is acquired by sexual contact
    - It is estimated that the majority of genital herpes infections are transmitted by persons unaware that they have the infection, or are asymptomatic when transmission occurs

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- HSV-1 reactivation:
- After primary infection, the virus becomes latent in the trigeminal ganglion and potentially the cornea (controversial but may be important in cornea transplantation surgery)
- Stress, UV radiation, and hormonal changes can reactivate the virus
  - Recurrent HSV-1 infections of the lips and perioral area are estimated to occur in 20 to 40 percent of the infected population
- Lesions are common in the immunocompromised (i.e. recent organ transplant or HIV patients)

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Herpes Simplex: Signs and Symptoms

- Most patients (>85 percent) develop prodromal symptoms about 24 hours before the appearance of painful lesions at the lip borders.
- The principal symptoms are burning and stinging, but can also include pain, tingling, and pruritus and may last from 6 to 53 hours prior to the appearance of the first vesicles
- Neuralgia may precede or accompany attacks.
- The lesions consist of small, grouped vesicles on an erythematous base that can occur anywhere but which most often occur on the vermilion border of the lips (the line just above the colored portion that connects the lip tissue to the rest of face), the penile shaft, the labia, the perianal skin, and the buttocks
- Recurrent HSV-1 lesions progress from vesicle to crust in five to eight days in the absence of antiviral therapy, with significant diminution of pain after the first 24 hours

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- **Epithelial Keratitis:**
  - Recurrent HSV-1 keratitis continues to be a leading cause of corneal blindness in high-income countries
  - Symptoms:
    - Ocular irritation, redness, photophobia, watering, blurred vision
  - Signs:
    - Swollen opaque epithelial cells arranged in a course punctate or stellate pattern
    - Central desquamation results in a dendrite***
      1. Central ulceration
      2. Terminal end bulbs
    - ***Corneal sensation is reduced***

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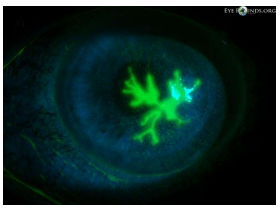

Pediatric HSV Keratitis

- children with HSV infection of the cornea are at high risk for recurrence, corneal scarring, and vision loss
  - pediatric herpes simplex keratitis has an 80% risk of recurrence, a 75% risk of stromal disease, and a 30% rate of misdiagnosis
  - 80% of children with herpes simplex keratitis develop scarring, mostly in the central cornea
    - results in the development of astigmatism
    - 25% of children have more than 2 D of astigmatism, most of which is irregular
  - consider pediatric HSV when a patient has unilateral recurrent anterior segment disease
- Recommend oral acyclovir treatment
  - Although its use in children is off label, acyclovir has a wide safety margin, with a maximum daily dosage in children of 40 to 80 mg/kg daily
  - There are age dependent dosing tables for infants and toddlers, though dosing should be individualized for the child
- The dosage of acyclovir must be adjusted as the child grows to maintain adequate suppressive levels.
- Refractive correction and amblyopia management are essential to optimize visual outcomes in children with HSV infection.

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Skin HSV 1-2 Treatment

- For first clinical episodes of herpes simplex in adults:
  - Dosing of antiviral therapy — Oral treatment options for adolescents and adults with primary infection include:
    - Acyclovir:
      - has modest oral bioavailability, about 15-30%, which decreases with higher doses
      - Acyclovir is remarkably well tolerated in most patients (caution in patients with acute renal failure and IV administration
      - 400 mg orally three times daily or 200 mg five times daily
    - Valacyclovir:
      - Acting as an oral prodrug, valacyclovir is converted in vivo to acyclovir.
      - three to fivefold greater oral bioavailability (about 55%) than acyclovir
      - 1000 mg twice daily
    - Famciclovir:
      - oral prodrug that is converted by first-pass metabolism to the antiviral drug penciclovir
      - well absorbed, featuring an oral bioavailability of 77%
      - 250 mg three times daily or 500 mg twice daily
  - HSV isolates resistant to acyclovir are also resistant to valacyclovir, famciclovir, and penciclovir.
- The duration of treatment is from 7 to 10 days depending on the severity of the outbreak.

Skin HSV 1-2 Treatment of Recurrences

- Suppressive therapy may be effective in controlling disease.
- Suppressive treatment will reduce outbreaks by 85% and reduces viral shedding by more than 90%.
- Results in about a 50% reduced risk of transmission. The recommended suppressive doses, taken continuously, are:
  - acyclovir, 400 mg orally twice daily;
  - valacyclovir, 500 mg orally once daily (most studied).
  - famciclovir, 125–250 mg orally twice daily;

Herpes Simplex Keratitis Management

- Topical antiviral therapy and oral antivirals are both effective for treatment of dendritic and geographic herpes simplex keratitis.
- The choice between oral and topical treatment can be made based on patient preference.
- Oral treatments are often preferred because of their convenience and potential to avoid corneal epithelial toxicity
- Topical:
  - Viroptic (trifluridine) every 2 hours until epithelium healed then taper down for 10-14 days.
    - Viroptic is toxic to the cornea.
  - Zirgan (ganciclovir) available, use 5 times a day until epithelium healed then 3 times for a week (US only)

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- Oral treatments:
  - Oral antiviral agents appear to be safe and effective for the treatment of HSV epithelial keratitis, but are not specifically FDA approved for the condition.
  - Three oral antiviral agents (acyclovir, valacyclovir, and famciclovir) demonstrate acceptable safety and proven effectiveness for HSV infections.
  - The efficacy of oral antiviral agents for the treatment of HSV epithelial keratitis, when compared to topical acyclovir ointment, was demonstrated in two double blind placebo controlled randomized clinical trials. Both studies compared acyclovir 400 mg five times daily to topical acyclovir ointment five times daily, and concluded that oral acyclovir performed at least as well as topical acyclovir in the treatment of HSV epithelial keratitis.
    - Acyclovir 400 mg five times per day
    - Valacyclovir 500 mg three times per day
    - Famciclovir 250 mg three times per day
  - Treatment should be 7-10 days

Herpes Simplex Keratitis

- Prophylactic Treatment:
  - Long-term acyclovir therapy is well tolerated but has not been studied for ocular HSV.
  - Limiting suppressive treatment to those with more frequent episodes and the threat of vision loss may be a cost-effective approach to management
    - Frequent debilitating recurrences, bilateral involvement, or HSV infection in a monocular patient or post corneal graft patient
  - Suppressive acyclovir has been successful and well tolerated in children and may prevent amblyopia from vision-threatening keratitis
  - there is evidence that long-term oral prophylaxis may predispose to antiviral resistance
  - Herpes Eye Disease Study Group (HEDS) determined that acyclovir reduces the rate of recurrence of epithelial and stromal keratitis by ≈ 50% (19% controls, 32% in treatment group)
    - However, this requires that the patient be treated continuously
- Prophylactic dosing:
  - Acyclovir 400 mg twice a day
  - Valacyclovir 500 mg once a day
  - Famciclovir 250 mg once a day

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Herpes Zoster

Varicella-zoster virus (VZV) infection causes two clinically distinct diseases.

Primary infection with VZV results in varicella (chickenpox), which is characterized by vesicular lesions on an erythematous base in different stages of development; lesions are most concentrated on the face and trunk.

Herpes zoster, also known as shingles, results from reactivation of latent VZV that gained access to sensory ganglia during varicella. Herpes zoster is characterized by a painful, unilateral vesicular eruption, which usually occurs in a restricted dermatomal distribution

Primary infection – Chicken pox (Varicella)

- Usually in children
- Highly contagious
- Very itchy maculopapular rash with vesicles that crust over after ≈ 5 days
- 96% of people develop by 20 years of age
- Vaccine now available

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Reactivation – Shingles (Herpes Zoster)

- More often in the elderly and immunosuppressed (AIDS)
  - Age is considered one of the most important risk factors for developing zoster
  - Dramatic increase in patients 50 and older
  - The severity of disease and the likelihood of complications, including postherpetic neuralgia (PHN), also increase with age
  - Systemic work-up if Zoster in someone < 40
  - Can get shingles anywhere on the body
  - Pain along a dermatome usually precedes the eruption by 48 hours or more and may persist after the lesions have disappeared.
  - Herpes Zoster Ophthalmicus (HZO)
    - Shingles involving the dermatome supplied by the ophthalmic division of the cranial nerve V (trigeminal)
      - 15% of zoster cases

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- Signs and Symptoms:
  - The presenting clinical manifestations of herpes zoster are usually rash and acute neuritis.
  - Fewer than 20 percent of patients who develop a rash have significant systemic symptoms, such as headache, fever, malaise, or fatigue
  - The rash starts as erythematous papules, typically in a single dermatome or several contiguous dermatomes.
    - The dermatomal distribution of the vesicular rash of herpes zoster corresponds to the sensory fields of the ganglion (or neighboring ganglia) involved.
  - Within three to four days, the rash becomes pustular.
  - the lesions crust by 7 to 10 days and are no longer considered infectious
  - the rash can occur in any dermatome, the thoracic and lumbar dermatomes are most commonly involved
  - Pain is the most common symptom of herpes zoster. Most patients describe a deep "burning," "throbbing," or "stabbing" sensation
  - Postherpetic neuralgia (PHN) is frequently defined as significant pain persisting for 90 days after the onset of rash. Approximately 10-15% develop PHN with majority in patients over age of 60.

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Shingles (Skin) Treatment

- Antiviral treatment within 72 hours of rash decreases the duration and severity of acute herpes zoster
  - antiviral therapy after 72 hours if new lesions are appearing at the time of presentation, as this indicates ongoing viral replication.
- Since such treatment also reduces postherpetic neuralgia, those with a risk of developing this complication should be treated
- The doses used to treat herpes zoster are as follows:
  - Acyclovir: 800 mg five times daily for seven days
  - Valacyclovir: 1000 mg three times daily for seven days
  - Famciclovir: 500 mg three times daily for seven days

- For those with moderate to severe pain that disturbs sleep, management can be more difficult, and additional agents may be needed. The choice of treatment is based upon the patient's comorbidities, concurrent medications, pain intensity, and preferences. Options include:
  - The use of agents such as short-acting narcotics or a 10- to 14-day tapering course of oral prednisone (starting at 60 mg/day and administered in combination with antiviral therapy).
  - If short-acting narcotics or prednisone are unsuccessful, treatments that are used for management of postherpetic neuralgia (eg, gabapentin or tricyclic antidepressants, anesthetic nerve blocks) may be reasonable.

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Herpes Zoster Vaccine

- There are two types of zoster vaccine:
  - A recombinant glycoprotein E vaccine (designated recombinant zoster vaccine [RZV]; sold as Shingrix).
  - A live attenuated vaccine (designated zoster vaccine live [ZVL]; sold as Zostavax).
- As of July 2020, ZVL is no longer sold in the United States

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Shingrix Vaccine

- Approved in US/Canada as of October 2017
- non-live antigen, to trigger a targeted immune response, with a specifically designed adjuvant to enhance this response and help address the natural age-related decline of the immune system
- Shingrix is 97% effective against shingles for people between the ages of 50 and 69 and 91% effective for people 70 or older.
- It is 91% effective against postherpetic neuralgia for people 50 and older.
- These rates are based on evidence presented to the committee from clinical trials with over 38,000 total participants.

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- recommended for healthy adults aged 50 years and older to prevent shingles and related complications
- recommended for adults who previously received the live attenuated shingles vaccine (Zostavax®) to prevent shingles and related complications
- Shingrix is the preferred vaccine for preventing shingles and related complications

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Pigmented Skin Lesions

- Pigmented skin lesions are extremely common, with almost all patients having a number of pigmented lesions on their skin.

Seborrheic Keratosis

- Seborrheic keratoses are common epidermal tumors consisting of a benign proliferation of immature keratinocytes
- They usually develop after the age of 50, but they can also appear in young adulthood.
- There is a genetic predisposition to develop a high number of seborrheic keratoses, although the precise inheritance pattern is unknown.
- The pathogenesis is incompletely understood. Evidence for a role of cumulative UV radiation exposure or human papillomavirus (HPV) infection is inconsistent
- Common and may occur on the face, trunk and extremities
- Usually affect middle-aged and older adults, occurring singly or multiple, greasy, stuck-on plaques

Seborrheic Keratosis

- present as well-demarcated, round or oval lesions with a dull, verrucous surface and a typical stuck-on appearance.
- They are generally asymptomatic, but chronic irritation due to friction trauma may occasionally cause pruritus, pain, or bleeding.
- Color varies from tan to brown and these are not considered pre-malignant lesions
- Differentials include skin tags, nevus, verruca vulgaris, actinic keratosis and pigmented basal cell carcinoma
  - Biopsy may be necessary if the diagnosis is uncertain and there is concern for malignancy.
- Simple excision for biopsy or cosmesis or to prevent irritation.

Freckles

- Freckles are also extremely common.
- Childhood freckles are induced by sun exposure and are more common in fair-skinned people, especially those with red hair.
- The color of freckles is due to extra pigment induced by sun exposure, and not due to an increase in the number of melanocytes.
- Freckles often slowly reduce with age and sun protection.
- They tend to fade in the winter

Moles (melanocytic nevi)

- Moles (melanocytic nevi) are also extremely common.
- Congenital melanocytic nevi occur in approximately 1 in every 100 babies.
- The risk of developing melanoma is very low, even in very large nevi.
- Most melanocytic nevi appear within the first few years of life, but new nevi may continue to appear throughout life.
- More nevi will develop if there is increased sun exposure, especially excessive exposure in the first 10 years of life.
- Excessive sun exposure in this time significantly increases the risk of melanoma later in life.
- Melanocytic nevi are usually classified by their size in an adult. There are several different classifications.
  - small melanocytic nevus is < 1.5 cm in diameter.
  - medium melanocytic nevus is 1.5–19.9 cm.
  - large or giant melanocytic nevus is ≥ 20 cm in diameter.

- The risk of melanoma developing in any particular nevus is in the order of 1 in 10,000.
- Dysplastic nevi are difficult to accurately define, and a number of attempts have been made using clinical, histological and genetic criteria.
- However, a useful practical definition for general practice is an unusual-looking mole that is stable.
- Dysplastic nevi are not particularly more susceptible to malignant change, but they are a potentially important clue to overall melanoma risk.
- There is a significant correlation between having five or more dysplastic nevi and the lifetime risk of melanoma.

Dysplastic nevus

Lid Nevi

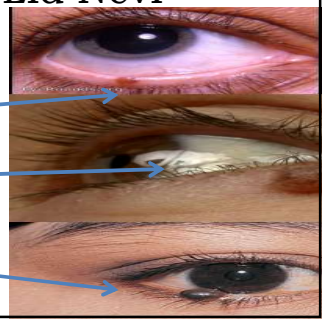
- The **congenital eyelid nevus** is a special category with implications for malignant transformation.
  - With time, slow increased pigmentation and slight enlargement can occur.
- An **acquired nevus** generally becomes apparent between the ages of 5 and 10 years as a small, flat, lightly pigmented lesion

Congenital Nevus

- The nevus is generally well circumscribed and not associated with ulceration.
- The congenital nevus of the eyelids may present as a "kissing nevus" or "split nevus" in which the melanocytes are present symmetrically on the upper and lower eyelids.
  - suggesting their development between the 9th and 20th week of gestation when the eyelids are fused
- most nevi of the skin are not considered to be at increased risk of malignancy.
  - However, the large congenital melanocytic nevus appears to have an increased risk of malignant transformation of 4.6% during a 30 year period

Acquired Lid Nevi

- Acquired nevi are classified as:
  - **junctional** (involving the basal epidermis/dermis junction), typically flat in appearance
  - **intradermal** (involving only the dermis), tend to be dome shaped or pedunculated
  - **compound** (involving both dermis and epidermis) tend to be dome shaped



Pre-Malignant/Malignant Lesions

Keratoacanthoma

- Appears as a solitary, rapidly growing nodule on sun exposed areas of middle-aged and older individuals
- Nodule is usually umbilicated with a distinctive crater filled with keratin
- Lesion develops over weeks and undergoes spontaneous involution within 6 months to leave an atrophic scar
- Lesion on the eyelids may produce mechanical problems such as ectropion or ptosis.
- Differential diagnosis include: squamous cell carcinoma (SCC), basal cell carcinoma (BCC), verruca vulgaris and molluscum
- Many pathologists consider it a type of low-grade SCC
- Complete excision is recommended as there are invasive variants

Actinic Keratosis

- Also known as solar or senile keratosis
- Most common pre-malignant skin lesion
- Develops on sun-exposed areas and commonly effect the face, hands and scalp, tops of ears (less commonly the eyelids)
  - Predominately white males
- Appear as multiple, flat-topped papules with an adherent white scale.
- Development of SCC in untreated lesions as high as 20%
- Management is surgical excision or cryotherapy (following biopsy)

Squamous Cell Carcinoma (SCC)

- Much less common than BCC on the eyelid but has much higher potential for metastatic spread
- Typically affects elderly, fair-skinned and usually found on the lower lid
- Environmental and intrinsic factors initiate cell growth
  - Many SCC arise from actinic lesions

Squamous Cell Carcinoma (SCC)

- Presents as a erythematous, indurated, hyperkeratotic plaque or nodule with irregular margins
- Lesions have a high tendency towards ulceration and tend to affect lid margin and medial canthus
- Diagnosis requires biopsy
- Surgical excision is recommended
  - Mohs' technique

Basal Cell Carcinoma (BCC)

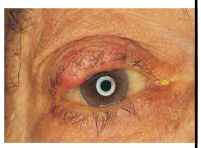
- Most common malignant lesion of the lids (85-90% of all malignant epithelial eyelid tumors)
- 50-60% of BCC affect the lower lid followed by medial canthus 25-30% and upper lid 15%
- Etiology is linked to excessive UV exposure in fair-skinned individuals, ionizing radiation, arsenic exposure and scars
- Metastasis is rare but local invasion is common and can be very destructive

Basal Cell Carcinoma

- Diagnosis is initially made from its clinical appearance, especially with the noduloulcerative type with its raised pearly borders and central ulcerated crater
  - categorized into two basic types: noduloulcerative and morpheaform
  - The morpheaform variant is typically diffuse, relatively flat with indistinct borders. This variant is more aggressive and can be invasive despite showing less obvious features.
- Definitive diagnosis made on histopathological examination of biopsy specimens
  - loss of adjacent cilia is strongly suggestive of malignancy and occurs commonly with basal cell carcinoma of the eyelid
- Surgery is generally accepted as treatment of choice
  - Mohs' surgery technique

Sebaceous Gland Carcinoma

- Highly malignant neoplasm that arises from the meibomian glands, Zeis and the sebaceous glands of the caruncle and eyebrow
- Aggressive tumor with a high recurrence rate, significant metastatic potential and notable mortality rate
  - **rates of misdiagnosis have been reported as high as 50%**
- Relatively rare, 1/3 most common eyelid malignancy
- Uncommon in the Caucasian population and represents only 3% of eyelid malignancies
  - most common eyelid malignancy in Asian Indian population, where it represents approximately 40% or more of eyelid malignancies



Sebaceous Gland Carcinoma

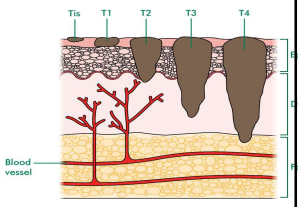
- Upper lid origin in about 2/3 of all cases
- Typically affects older individuals, women more so than men
- has also been reported in younger individuals who are immunosuppressed or who have received radiation treatment.
- Presents as a firm, yellow nodule that resembles a chalazion.
- May mimic:
  - chronic blepharoconjunctivitis,
  - meibomianitis or
  - chalazion that does not respond to standard therapies
- Diagnosis is by biopsy
- Treatment is surgical excision with microscopic monitoring of the margins

Malignant Melanoma (MM)

- MM of the eyelid accounts for about 1% of all eyelid malignancies (leading cause of death due to skin disease)
- Incidence been increasing and it causes about 2/3 of all tumor related deaths from cutaneous cancers
- Incidence increases with age
- Eyelid cutaneous melanoma arises most frequently in the lower eyelid and can appear de novo or grow from a preexisting pigmented lesion that increases in size and changes in shape and color.
- Eyelid melanoma can often involve the eyelid margins.

Malignant Melanoma

- Tumor thickness is the single most important prognostic factor.
- Ten-year survival rates—related to thickness in millimeters—are as follows:
  - less than 1 mm, 95%;
  - 1–2 mm, 80%;
  - 2–4 mm, 55%; and
  - greater than 4 mm, 30%.
- With lymph node involvement, the 5-year survival rate is 62%; with distant metastases, it is 16%.



Melanoma

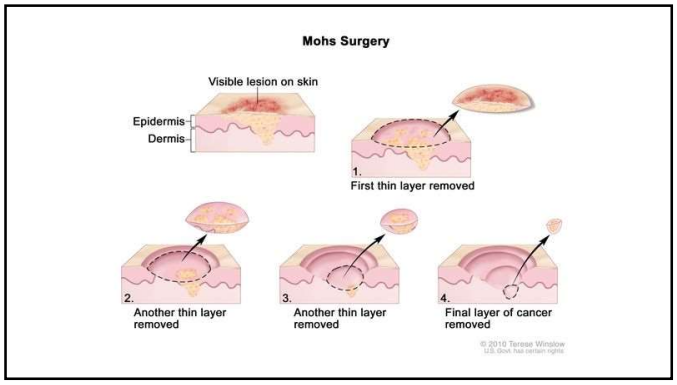
- Risk factors include congenital and dysplastic nevi, changing cutaneous moles, excessive sun exposure and sun sensitivity, family history, age greater than 2 and fair skinned.
- History of a changing mole is the single most important historical reason for a closer inspection or referral
- History of severe sunburns rather than cumulative actinic exposure thought to be a major risk factor

Melanoma

- Flat lesion with irregular borders and variable pigmentation typically occurring in sun exposed areas
- Confirmed diagnosis by biopsy

Melanoma

- Prognosis and metastatic potential are linked to the depth of invasion and thickness of the tumor
- Treatment is wide surgical excision confirmed with histological monitoring



Malignant Eyelid Lesions: Malignant Melanoma