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Common Skin Lesions of the Face

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<http://dx.doi.org/10.5772/63426>

Abstract

Skin lesions are common and range from acute inflammatory dermatoses, such as urticaria, to malignant melanoma, which may be life-threatening. When confronting skin diseases, it is important that the maxillofacial surgeon collaborate with both the dermatologist and pathologist. The clinical history, gross appearance, and course of any disease are as important as the microscopic findings. In this chapter, we discuss the more common skin lesions of the face.

Keywords: acute and chronic dermatoses, infectious, auto immune, blistering, skin lesion

1. Introduction

In this chapter, the more common skin lesions of the face are discussed. These include the following:

- **Acute inflammatory dermatoses:** urticaria, acute eczema dermatitis, and erythema multiforme
 - **Chronic inflammatory dermatoses:** psoriasis and lichen planus
 - **Infectious dermatoses:** bacterial infections (impetigo, cat-scratch disease), fungal infections, and viral infections (herpes simplex, chickenpox, herpes zoster)
 - **Autoimmune diseases:** systemic lupus erythematosus, chronic cutaneous (discoid) lupus erythematosus, scleroderma, and angioedema
 - **Blistering (bullous) disorders:** pemphigus, bullous pemphigoid, and dermatitis herpetiformis
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- **Benign and premalignant epithelial lesions and nevi:** melanocytic nevus, dysplastic nevus, actinic keratosis, seborrheic keratosis, and keratoacanthoma
- **Malignant epidermal tumors:** basal cell carcinoma, squamous cell carcinoma, and malignant melanoma
- **Miscellaneous:** Sturge-Weber syndrome, *Paederus* dermatitis, and melasma

2. Acute inflammatory dermatoses

2.1. Urticaria

Urticaria (“hives”) is a common disorder mediated by localized mast cell degranulation, which leads to dermal microvascular hyperpermeability. The resulting erythematous, edematous, and pruritic plaques are termed “wheals”. In most cases, urticaria stems from an immediate (type 1) hypersensitivity reaction in which antigens trigger mast cell degranulation by binding to immunoglobulin E (IgE) antibodies displayed on the mast cell surface. The responsible antigens include pollens, foods, drugs, and insect venom (**Figure 1**) [1].



Figure 1. Urticaria.

2.2. Acute eczematous dermatitis

“Eczema” is a clinical term that embraces a number of conditions with varied underlying etiologies. New lesions take the form of red papules, often with overlying vesicles, that ooze and become crusted. With persistence, these lesions develop into raised, scaling plaques. The

nature and degree of these changes vary among the clinical subtypes, which include the following:

- **allergic contact dermatitis**, which stems from topical exposure to an allergen;
- **atopic dermatitis**, which has traditionally been attributed to allergen exposure but is now thought to stem from defects in keratinocyte barrier function, many with a genetic basis;
- **drug-related eczematous dermatitis**, a hypersensitivity reaction to a drug;
- **photoeczematous dermatitis**, in which eczema appears as an abnormal reaction to UV or visible light;
- **primary irritant dermatitis**, which results from exposure to substances that chemically, physically, or mechanically damage the skin.

In most cases, these skin lesions resolve completely when the offending stimulus is removed or exposure is limited, stressing the importance of investigating the underlying cause. Only contact dermatitis, the most common form, is considered here.

Contact dermatitis is triggered by exposure to an environmental contact sensitizing agent, such as poison ivy, that chemically reacts with self-proteins (**Figure 2**) [2].



Figure 2. Acute eczematous dermatitis.

2.3. Erythema multiforme

Erythema multiforme is a self-limited, sometimes episodic, disease of the skin that may also involve the mucous membranes. It is characterized by a pleomorphic eruption consisting of erythematous macules, papules, urticarial plaques, vesicles, and bullae. Individual lesions may evolve through a papular, vesicular, and target (iris) stage in which bullae surmount an

erythematous maculopapule. Lesions tend to be distributed symmetrically with a predilection for the extremities, particularly the hands.

In the past, erythema multiforme was classified into erythema multiforme minor and erythema multiforme major, the latter being characterized by a severe and sometimes fatal illness in which fever, systemic symptoms, and severe oral lesions were usually present. Stevens-Johnson syndrome was also diagnosed in these severe cases with oral involvement. Recently, an attempt has been made to distinguish Stevens-Johnson syndrome from erythema multiforme major with mucosal lesions on the basis of their different cutaneous lesions and their etiology; their mucosal lesions are similar. Stevens-Johnson syndrome is said to be characterized by flat atypical target lesions or purpuric macules that are widespread or limited to the trunk. Erythema multiforme major with mucosal lesions has typical or raised atypical target lesions, located on the extremities and/or the face. With these definitions, Stevens-Johnson syndrome is usually related to drugs and erythema multiforme to herpes or other infections.

Erythema multiforme major occurs in younger males, has frequent recurrences, and is marked by mild fever, milder mucosal lesions, and a lack of association with collagen vascular diseases, human immunodeficiency virus (HIV) infection, or cancer. Recent or recurrent herpes simplex infection is the principal risk factor. The criteria used to distinguish the component diseases that form this spectrum have been criticized on fundamental clinical differences between the two related conditions. Stevens-Johnson syndrome is associated with systemic symptoms and the involvement of internal organs, whereas erythema multiforme is not.

Toxic epidermal necrolysis has been widely regarded as a separate entity or as representing the severe end of the spectrum of erythema multiforme major or Stevens-Johnson syndrome. Some clinicians have arbitrarily diagnosed toxic epidermal necrolysis when blisters and



Figure 3. Erythema multiforme.

peeling involved more than 30% of the total body surface area and Stevens-Johnson syndrome when mucosal lesions were present and blistering involved less than 30% of the body surface (**Figure 3**) [3–5].

3. Chronic inflammatory dermatoses

3.1. Psoriasis

Psoriasis is a chronic inflammatory dermatosis that appears to have an autoimmune basis. It is a common disorder, affecting as many as 1% to 2% of people in the United States. Persons of all ages may develop the disease. Approximately 15% of patients with psoriasis have associated arthritis. Psoriatic arthritis may be mild or may produce severe deformities resembling the joint changes seen in rheumatoid arthritis. It can affect any joint in the body and may be symmetrical or unilateral only. In addition, psoriasis may also be associated with myopathy, enteropathy, and AIDS. Psoriasis results from interactions of genetic and environmental factors. As in the case of many autoimmune diseases, it is linked to genes within the HLA locus, most frequently affecting the skin of the elbows, knees, scalp, lumbosacral areas, intergluteal cleft, and glans penis.

The typical lesion is a well-demarcated, pink to salmon-colored plaque covered by loosely adherent silver-white scales (**Figure 4**) [6–8].



Figure 4. Psoriasis (before and after treatment).

3.2. Lichen planus

Lichen planus, a relatively common eruption of unknown etiology, displays violaceous, flat-topped papules that are usually pruritic. A network of fine white lines (Wickham striae) may be seen on the surface of the papules. There is a predilection for the flexor surface of the wrists, the trunk, the thighs, and the genitalia. Oral lesions are common; rarely, the esophagus is also involved. Lesions localized to the vulva and eyelids have been reported. Lichen planus localized to a radiation field may represent an isomorphic response. It has also developed in a healed herpes zoster scar. Nail changes occur, and, as with oral lesions, these may be the only manifestations of the disease. Clinical variants include atrophic, annular, hypertrophic, linear, zosteriform erosive, oral, actinic, follicular, erythematous, and bullous forms. An eruptive variant also occurs. Spontaneous resolution of lichen planus may occur and is usual within 12 months, although postinflammatory pigmentation may persist for some time afterwards. Familial cases are uncommon, and rarely these are associated with HLA-D7. An association with HLA-DR1 has been found in nonfamilial cases (**Figure 5**) [9–14].



Figure 5. Lichen planus.

4. Infectious dermatoses

4.1. Bacterial infection

4.1.1. Impetigo

Impetigo is a superficial infection of the skin that is caused by *Staphylococcus aureus*, alone or in combination with *Streptococcus pyogenes* (group A, β -hemolytic). Two main patterns are seen: Seventy percent of the cases are **nonbullous impetigo**, which typically demonstrates a mixture of *S. aureus* and *S. pyogenes*, whereas **bullous impetigo** is less common and predominantly caused by *S. aureus*. The term “impetigo” is derived from a Latin word meaning “attack” because of its common presentation as a scabbing eruption. Intact epithelium normally is

protective against infection; thus, most cases arise in damaged skin, such as preexisting dermatitis, cuts, abrasions, or insect bites. Secondary involvement of an area of dermatitis has been termed **impetiginized dermatitis**. An increased prevalence is associated with debilitating systemic conditions, such as HIV infection, type 2 diabetes mellitus, and dialysis. **Nonbullous impetigo (impetigo contagiosa)** is the more prevalent pattern and occurs most frequently on the legs, with less common involvement noted on the trunk, scalp, and face. Facial lesions usually develop around the nose and mouth. In an infrequent pattern of impetigo termed **ecthyma**, the central area of the crust becomes necrotic and forms a deep indurated ulceration. Weakness, fever, and diarrhea may be seen. Lymphadenopathy and cellulitis are unusual complications. Meningitis and pneumonia are very rare but may lead to serious complications, even death (**Figure 6**) [15, 16].



Figure 6. Impetigo.

4.1.2. Cat-scratch disease

Cat-scratch disease is an infectious disorder that begins in the skin but classically spreads to the adjacent lymph nodes. This infection is the most common cause of chronic regional lymphadenopathy in children, with an estimated 22,000 cases occurring annually in the United States. The causative organism was initially named *Rochalimaea henselae* but was reclassified as *Bartonella henselae* when the genera *Bartonella* and *Rochalimaea* were combined. Almost all cases arise after contact with a cat. The spread of the infection between cats appears to occur through cat fleas. The organism becomes an intraerythrocytic parasite and may be transmitted to humans via saliva or from a scratch. Infection from other sources is highly unlikely, but the disease rarely has been described in dogs, monkeys, porcupine quills, and thorns. Person-to-person transmission has not been documented. Eighty percent of the cases occur in patients younger than 21 years. Cat-scratch disease begins as a papule that develops in 3 to 14 days along the initial scratch line. The lesion typically progresses through erythematous, vesicular, and papular-crust stages, with resolution usually occurring within 1 to 3 weeks. About the time the skin lesion heals, lymph node changes arise and may be accompanied by fever or malaise. In about half of the cases, a single node is involved. Multiple regional nodes are affected in about 20%, and nodal enlargement is discovered in multiple sites in about 33%. Suppuration is noted in approximately 10% of affected patients. The most frequently affected nodes are those in the head and neck, axillary, epitrochlear, and groin regions. Although the

vast majority of affected patients present with typical cat-scratch disease as described above, a variety of systemic manifestations may be seen. Of these, prolonged fever of unknown origin and hepatosplenic disease are the most common. Less common problems include cardiac, hematologic, neurological, ocular, orthopedic, and pulmonary manifestations (**Figure 7**) [17].



Figure 7. Cat-scratch disease.

4.1.3. Cutaneous leishmaniasis

Cutaneous leishmaniasis is a chronic self-limited granulomatous disease of the skin usually caused by *Leishmania tropica*. It is common in children. It is endemic in the Middle East, around the Eastern Mediterranean, in North Africa, and in areas of Asia. The term "Old World" leishmaniasis has been used for such cases (**Figure 8**) [18, 19].



Figure 8. Cutaneous leishmaniasis.

4.2. Fungal infections

4.2.1. Mucormycosis

Mucormycosis is an opportunistic, frequently fulminant fungal infection that is caused by normally saprobic organisms of the subphylum Mucoromycotina, including such genera as

Absidia, *Mucor*, *Rhizomucor*, and *Rhizopus*. The presenting symptoms of rhinocerebral mucormycosis may be exhibited in several ways. Patients may experience nasal obstruction, bloody nasal discharge, facial pain or headache, facial swelling or cellulitis, and visual disturbances with concurrent proptosis. Symptoms related to cranial nerve involvement (e.g., facial paralysis) are often present. With progression of the disease into the cranial vault, blindness, lethargy, and seizures may develop, followed by death (**Figure 9**) [20].



Figure 9. Mucormycosis.

4.3. Viral infections

4.3.1. *Herpes simplex virus*

The two herpes simplex viruses (type 1 and type 2) are similar in structure and disease mechanisms but differ in antigenicity, anatomical site predilection, and epidemiology. Differences in envelope glycoproteins account for their distinct antigenicity. Nevertheless, there is potential for antibody cross-reactivity and antibodies directed against one type may decrease the likelihood or severity of infection with the other type. HSV-1 is spread predominantly through infected saliva or active perioral lesions of the oral, facial, and ocular areas. The pharynx, intraoral mucosa, lips, eyes, and skin above the waist are involved most frequently. Genital HSV-1 infection is uncommon, although recent studies have shown an increase in the proportion of genital herpes caused by HSV-1 in developed nations. This trend has been attributed to an increase in oral-genital sexual behavior and lower rates of nonsexual HSV-1 acquisition in childhood. **Primary infection** refers to initial exposure of an individual without antibodies to the virus. Primary infection with HSV-1 typically occurs at a young age, often is asymptomatic, and usually does not cause significant morbidity. For symptomatic cases, the usual incubation period is 3 to 9 days. After primary infection is established, the virus is taken up by sensory nerves and transported to the associated sensory or, less frequently, autonomic ganglia where the virus remains in a latent state. The most common site of latency for HSV-1 is the trigeminal ganglion. The virus uses the axons of the sensory neurons to travel back to the skin or mucosa. **Recurrent (secondary or recrudescient) infection** occurs with reactivation of the virus. Old age, ultraviolet light, physical or emotional stress, fatigue, heat, cold, pregnancy, allergy, trauma, dental treatment, respiratory illnesses, fever, menstru-

ation, systemic diseases, and malignancy have been associated with reactivation. Symptomatic recurrences are fairly common and affect the epithelium supplied by the sensory ganglion; however, reactivation with asymptomatic viral shedding greatly exceeds clinically evident recurrences. Spread to an uninfected host can occur from symptomatic active lesions or asymptomatic viral shedding. In addition, the virus may spread to other sites in the same host to establish residency at the sensory ganglion of the new location (**Figure 10**) [21, 22].

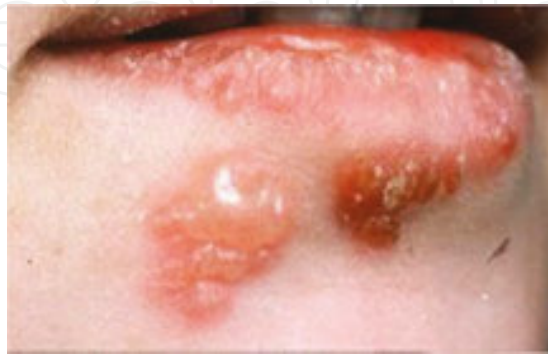


Figure 10. Herpes simplex virus.

4.3.2. *Herpes zoster (shingles)*

After primary infection with varicella virus (chickenpox), the virus is transported up the sensory nerves and establishes latency in the dorsal root ganglia. Clinically evident herpes zoster develops after reactivation of the virus, with involvement of the distribution of the affected sensory nerve.

Immunosuppression, HIV infection, treatment with cytotoxic or immunosuppressive drugs, radiation, malignancy, old age, alcohol abuse, stress (emotional or physical), and dental manipulation are additional predisposing factors for reactivation. The long-term impact of varicella virus vaccination on herpes zoster prevalence is controversial and presently under evaluation. Interestingly, it is possible to develop herpes zoster by reactivation of either the wild type or the vaccine strain virus, although the risk for vaccine strain zoster seems to be much lower than that for wild-type zoster. The clinical features of herpes zoster can be grouped into three phases: prodromal, acute, and chronic. During initial viral replication, ganglionitis develops with resultant neuronal necrosis and severe neuralgia. This inflammatory reaction is responsible for the prodromal pain present in more than 90% of cases. The virus travels down the nerve (dermatome) and may be accompanied by fever, malaise, and headache. Typically, one dermatome is affected, but involvement of two or more can occur. The thoracic dermatomes are affected in about two thirds of the cases. This prodromal pain normally precedes the acute phase rash by 1 to 4 days and, depending on which dermatome is affected, may masquerade as sensitive teeth, otitis media, migraine headache, myocardial infarction, or appendicitis.

The acute phase begins as the involved skin develops clusters of vesicles set on an erythematous base. The lesions tend to follow the path of the affected nerve and terminate at the midline.

Within 3 to 4 days, the vesicles become pustular and ulcerate, with crusts developing after 7 to 10 days. The lesions are contagious until they crust, although the rate of varicella zoster virus (VZV) transmission from herpes zoster lesions is lower than that from varicella lesions. The exanthema typically resolves within 2 to 3 weeks in otherwise healthy individuals. On healing, scarring with hypopigmentation or hyperpigmentation is not unusual. Infrequently, there is dermatomal pain without development of a rash; this pattern is called **zoster sine herpete** (zoster without rash). Ocular involvement is present in approximately 10% to 25% of cases and can cause significant morbidity, including permanent blindness. The ocular manifestations are highly variable and may arise from direct virus-mediated epithelial damage, neuropathy, immune-mediated damage, or secondary vasculopathy. Lesions on the tip of the nose (Hutchinson sign) indicate involvement of the nasociliary branch of the trigeminal nerve and an increased risk for severe ocular infection. In these cases, referral to an ophthalmologist is mandatory. Reactivation of VZV in the geniculate ganglion may cause **Ramsay Hunt syndrome**, which is characterized by cutaneous lesions of the external auditory canal and involvement of the ipsilateral facial and auditory nerves. Affected individuals may exhibit facial paralysis as well as hearing deficits, vertigo, and other auditory and vestibular symptoms. In addition, some patients may develop loss of taste in the anterior two thirds of the tongue. By using PCR or serology, investigators have detected active VZV infections in approximately 30% of patients thought to have Bell's palsy. Similar associations also have been demonstrated with HSV and EBV. These findings suggest an underlying viral cause for many cases of "idiopathic" facial paralysis. Approximately 15% of patients progress to the chronic phase of herpes zoster (termed **postherpetic neuralgia**), which is characterized by persistent pain after resolution of the rash. In defining postherpetic neuralgia, there is a lack of consensus regarding the duration of pain persistence following the rash, although many investigators consider a minimum period of 1 to 3 months. Risk factors include female sex, older age, history of prodromal pain, moderate to severe rash and/or pain during the acute phase, and ophthalmic involvement (**Figures 11 and 12**) [23–27].



Figure 11. Chickenpox.



Figure 12. Herpes zoster.

5. Autoimmune disease

5.1. Systemic lupus erythematosus (SLE)

SLE is an autoimmune disease involving multiple organs that is characterized by a vast array of autoantibodies, particularly antinuclear antibodies (ANAs), in which injury is caused mainly by deposition of immune complexes and binding of antibodies to various cells and tissues. The disease may be acute or insidious in its onset and is typically a chronic, remitting, relapsing, and often febrile illness. Injury to the skin, joints, kidney, and serosal membranes is prominent. SLE predominantly affects women, with the female-to-male ratio being 9:1 (**Figure 13**) [28–30].



Figure 13. Systemic lupus erythematosus.

5.2. Chronic cutaneous lupus erythematosus (CCLE)

Patients with CCLE usually have few or no systemic signs or symptoms, with lesions being limited to skin or mucosal surfaces. The skin lesions of CCLE most commonly present as **discoid lupus erythematosus**. They begin as scaly, erythematous patches that are frequently distributed on sun-exposed skin, especially in the head and neck areas. Patients may indicate that the lesions are exacerbated by sun exposure. With time, the lesions may heal spontaneously in one area but only to appear in another area. The healing process usually results in cutaneous atrophy with scarring and hypopigmentation or hyperpigmentation of the resolving lesion (**Figure 14**) [31, 32].



Figure 14. Chronic cutaneous lupus erythematosus.

5.3. Systemic sclerosis (scleroderma)

Systemic sclerosis is autoimmunity of chronic inflammation with damage to small blood vessels and perivascular fibrosis in the skin and multiple organs. The skin is most commonly affected, but the gastrointestinal tract, kidneys, heart, muscles, and lungs also are frequently involved. In some patients, the disease seems to remain confined to the skin for many years, but in the majority, it progresses to visceral involvement with death from renal failure, cardiac failure, pulmonary insufficiency, or intestinal malabsorption, in which the skin involvement is often confined to the fingers, forearms, and face. Visceral involvement occurs late; hence,

the clinical course is relatively benign. Some patients with the limited disease also develop a combination of calcinosis, Raynaud's phenomenon, esophageal dysmotility, sclerodactyly, and telangiectasia, collectively called the CREST syndrome (**Figure 15**) [33].



Figure 15. Systemic sclerosis (scleroderma).

5.4. Angioedema (angioneurotic edema)

Angioedema is a diffuse edematous swelling of the soft tissues that most commonly involves the subcutaneous and submucosal connective tissues but may affect the gastrointestinal or respiratory tract, occasionally with fatal results. The disorder has been referred to as **Quincke's disease**, after the clinician who initially related the changes to an alteration in vascular permeability. The outdated term **angioneurotic edema** also has been used because affected patients often complained of a choking sensation and were labeled neurotic. The most common cause is mast cell degranulation, which leads to histamine release and the typical clinical alterations. IgE-mediated hypersensitivity reactions caused by drugs, foods, plants, dust, and inhalants produce mast cell degranulation and are fairly common. Contact allergic reactions to foods, cosmetics, topical medications, and even dental rubber dams have been found responsible. Mast cell degranulation can even result from physical stimuli, such as heat, cold, exercise, emotional stress, solar exposure, and significant vibration. Angioedema also can result from activation of the complement pathway. This may be hereditary or acquired. Two rare autosomal dominant hereditary forms are seen: type I and type II. Type I, comprising 85% of the hereditary cases, is caused by a quantitative reduction in the inhibitor that prevents the transformation of C1 to C1 esterase. Without adequate levels of C1 esterase inhibitor (C1-INH), C1 esterase cleaves C4 and C2 and results in angioedema. Type II exhibits normal levels of C1-INH, but the inhibitor is dysfunctional. The acquired type of C1-INH deficiency is seen in association with certain types of lymphoproliferative diseases (Caldwell syndrome) or in patients who develop specific autoantibodies. In lymphoproliferative diseases, monoclonal antibodies directed against the tumor cells activate C1 and lead to consumption of C1-INH.

An unusual pattern of drug reaction that can produce severe forms of angioedema that are not mediated by IgE is the type associated with use of drugs called angiotensin-converting enzyme (ACE) inhibitors (**Figure 16**) [34–36].



Figure 16. Angioedema.

6. Blistering (bullous) disorders

6.1. Pemphigus

Pemphigus is a rare autoimmune blistering disorder resulting from loss of normal intercellular attachments within the epidermis and the squamous mucosal epithelium. There are three major variants: pemphigus vulgaris (the most common type), pemphigus foliaceus, and paraneoplastic pemphigus.

Pemphigus vulgaris is a rare disorder that occurs most commonly in the elderly and more often in women than men. Lesions are painful, particularly when ruptured, and secondary infections are common. Most cases are associated with oropharyngeal involvement at some point in their course. Most patients require immunosuppressive therapy, sometimes for the remainder of their lives. Medications can cause pemphigus, and when they do, patients most often present with pemphigus foliaceus rather than pemphigus vulgaris. There is also an unusual endemic form of pemphigus foliaceus in South America (fogo selvagem) that is putatively associated with the bite of a black fly.

Pemphigus vulgaris, by far the most common type, involves both mucosa and skin, especially on the scalp, face, axillae, groin, trunk, and points of pressure. The lesions are superficial flaccid vesicles and bullae that rupture easily, leaving deep and often extensive erosions covered with a serum crust.

Pemphigus foliaceus, a rare, more benign form of pemphigus, results in bullae confined to skin, with only infrequent involvement of mucous membranes. The blisters in this disorder

are superficial, such that more limited zones of erythema and crusting of ruptured blisters are seen (**Figure 17**) [37–39].



Figure 17. Pemphigus vulgaris.

6.2. Bullous pemphigoid

Bullous pemphigoid is another distinctive acquired blistering disorder with an autoimmune basis. Blistering in bullous pemphigoid is triggered by the linear deposition of IgG antibodies and complement in the epidermal basement membrane. The bullae do not rupture as readily as in pemphigus and, if uncomplicated by infection, heal without scarring. The disease tends to follow a remitting and relapsing course and responds to topical or systemic immunosuppressive agents. Gestational pemphigoid (also known as herpes gestationis, a misnomer) is a clinically distinct subtype that appears suddenly during the second or third trimester of pregnancy. It is also caused by autoantibodies against BPAG. It typically resolves after childbirth but may recur with future pregnancies (**Figure 18**) [40].



Figure 18. Bullous pemphigoid.

6.3. Dermatitis herpetiformis

Dermatitis herpetiformis is another type of autoimmune blistering disorder characterized by extremely pruritic urticaria and grouped vesicles. The disease affects predominantly males, often in the third and fourth decades of life. In up to 80% of cases, it occurs in association with celiac disease; conversely, only a small minority of patients with celiac disease develop dermatitis herpetiformis. Similar to celiac disease, dermatitis herpetiformis responds to a gluten-free diet. The lesions of dermatitis herpetiformis are bilateral, symmetrical, and grouped and preferentially involve the extensor surfaces, elbows, knees, upper back, and buttocks. Initially, neutrophils accumulate selectively at the tips of dermal papillae, forming small microabscesses. The basal cells overlying these microabscesses show vacuolization and focal dermoepidermal separation that ultimately coalesce to form a true subepidermal blister (Figure 19) [41].



Figure 19. Dermatitis herpetiformis.

7. Benign and premalignant epithelial lesions and nevi

7.1. Melanocytic nevus

Strictly speaking, the term “nevus” denotes any congenital lesion of the skin. Melanocytic nevus, however, refers to any benign congenital or acquired neoplasm of melanocytes. There are numerous types of melanocytic nevi, with varied appearances. Although these lesions usually are of only cosmetic concern, they can become irritating or mimic melanoma, requiring their surgical removal (Figure 20).

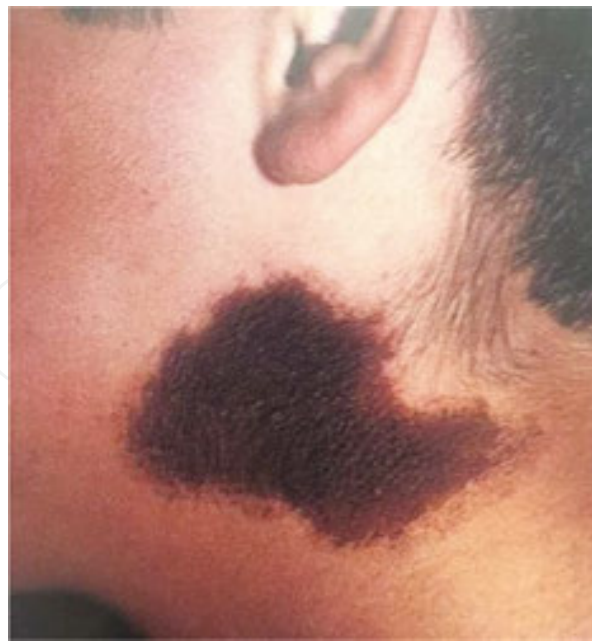


Figure 20. Melanocytic nevus.

7.2. Dysplastic nevus

Dysplastic nevi may be sporadic or familial. The latter ones are important clinically because they are considered potential precursors of melanoma. As with conventional melanocytic nevi, activating NRAS or BRAF mutations are commonly found in dysplastic nevi and are believed to have a pathogenic role. Unlike ordinary nevi, dysplastic nevi have a tendency to occur on body surfaces not exposed to the sun as well as on sun-exposed sites. Familial dysplastic nevus syndrome is strongly associated with melanoma, as the lifetime risk for the development of melanoma in affected persons is close to 100%. In sporadic cases, only individuals with 10 or more dysplastic nevi appear to be at an increased risk for melanoma (**Figure 21**) [42].



Figure 21. Dysplastic nevus.

7.3. Actinic keratosis

Actinic keratosis is sun-damaged skin with hyperkeratosis that exposure to ionizing radiation, industrial hydrocarbons, and arsenicals may induce similar lesions. Actinic keratoses are usually less than 1 cm in diameter (**Figure 22**). The lips may also develop similar lesions (termed “actinic cheilitis”) [43–47].



Figure 22. Actinic keratosis.

7.4. Seborrheic keratosis

Seborrheic keratoses are characterized by round, flat, coin-like, and waxy plaques that vary in diameter from millimeters to several centimeters and occur most frequently in middle-aged individuals. They arise spontaneously and are particularly numerous on the trunk, although the extremities, head, and neck may also be involved (**Figure 23**) [47, 48].

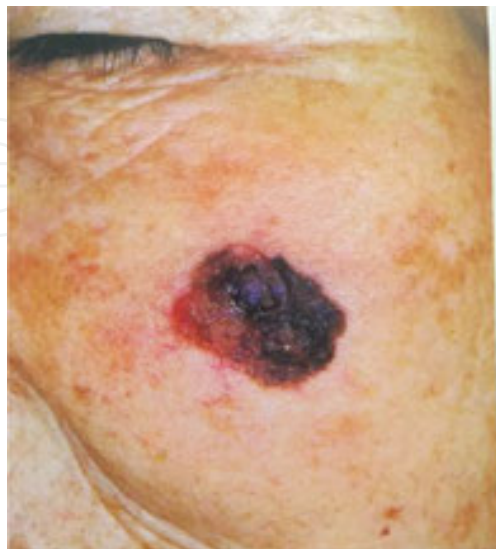


Figure 23. Seborrheic keratosis.

7.5. Keratoacanthoma

Keratoacanthoma is a self-limited epithelial proliferation with a strong clinical and histopathological similarity to well-differentiated squamous cell carcinoma. Indeed, many dermatopathologists consider it to represent an extremely well-differentiated squamous cell carcinoma. Cutaneous lesions presumably arise from the infundibulum of hair follicles. An association with sun damage is suggested by the fact that most solitary lesions are found on sun-exposed skin in older adults. Additional potential contributing factors include tar exposure, HPV, immunosuppression, certain drugs (e.g., BRAF inhibitors and tyrosine kinase inhibitors), tattooing, and burns or other trauma. Keratoacanthoma-like lesions have been produced in animals by the cutaneous application of carcinogens. Keratoacanthoma shows a male predilection and rarely occurs before 45 years of age. Almost 95% of solitary lesions involve sun-exposed skin, and 8% of all cases involve the outer edge of the vermilion border of the lips, with equal frequency on the upper and lower lips (**Figure 24**) [49, 50].



Figure 24. Keratoacanthoma.

8. Malignant epidermal tumors

8.1. Basal cell carcinoma

Basal cell carcinoma is the most common invasive cancer in humans, reaching nearly 1 million cases per year in the United States. It is a slow-growing tumor that rarely metastasizes. The vast majority of cases are recognized at an early stage and cured by local excision. However, a small number of tumors (<0.5%) are locally aggressive and potentially disfiguring or exceedingly rarely that they may metastasize to distant sites. They occur at sun-exposed sites in lightly pigmented elderly adults. As with squamous cell carcinoma, the incidence of basal cell carcinoma is increased in the setting of immunosuppression and in disorders of DNA repair, such as xeroderma pigmentosum. Basal cell carcinomas usually present as pearly papules containing prominent dilated subepidermal blood vessels (telangiectasias) (**Figure 25**) [51, 52].



Figure 25. Basal cell carcinoma.

8.2. Squamous cell carcinoma

Squamous cell carcinoma is the second most common tumor arising on sun-exposed sites in older people. The most important cause of cutaneous squamous cell carcinoma is DNA damage induced by exposure to UV light. Other risk factors for squamous cell carcinoma include industrial carcinogens (tars and oils), chronic ulcers and draining osteomyelitis, old burn scars, ingestion of arsenicals, ionizing radiation, and (in the oral cavity) tobacco and betel nut chewing (**Figure 26**) [53].



Figure 26. Squamous cell carcinoma.

8.3. Malignant melanoma

Melanoma is the most deadly of all skin cancers and is strongly linked to acquired mutations caused by exposure to UV radiation in sunlight. It is a relatively common neoplasm that can be cured if it is detected and treated when it is in its earliest stages. The great preponderance of melanoma arises in the skin; other sites of origin include the oral and anogenital mucosal surfaces (i.e., oropharynx as well as gastrointestinal and genitourinary tracts), esophagus,

meninges, and the uvea of the eye. Today, as a result of increased public awareness of the signs of cutaneous melanoma, most are cured surgically. Melanoma has two growth phases: radial and vertical. Radial growth describes the horizontal spread of melanoma within the epidermis and superficial dermis. During this initial stage, the tumor cells seem to lack the capacity to metastasize. Tumors in radial growth phase fall into several clinicopathological classes, including lentigo maligna, usually presenting as an indolent lesion on the face of older men that may remain in the radial growth phase for several decades; superficial spreading, the most common type of melanoma, usually involving sun-exposed skin; and acral/mucosal lentiginous melanoma, which is unrelated to sun exposure. In vertical growth phase, the tumor cells invade downward into the deeper dermal layers as an expansile mass (**Figures 27 and 28**) [54–57].

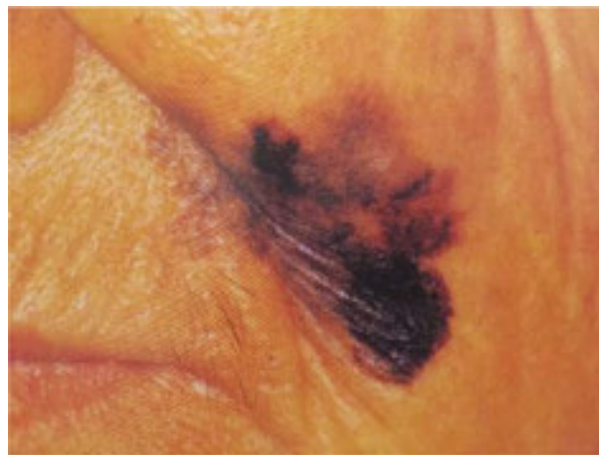


Figure 27. Melanoma.



Figure 28. Lentigo maligna melanoma.

9. Miscellaneous

9.1. Sturge-Weber syndrome

Sturge-Weber syndrome is a rare, nonhereditary developmental condition that is characterized by a hamartomatous vascular proliferation involving the tissues of the brain and face. Patients with this disease are born with a dermal capillary vascular malformation of the face known as a port-wine stain or nevus flammeus because of its deep purple color. This port-wine stain usually has a unilateral distribution along one or more segments of the trigeminal nerve. Occasionally, patients have bilateral involvement or additional port-wine lesions elsewhere on the body. Only 8% to 10% of patients with facial port-wine nevi will have Sturge-Weber syndrome. Risk for the condition occurs primarily in patients with involvement along the distribution of the ophthalmic branch of the trigeminal nerve (V1). If the port-wine stain involves the entire distribution of V1, the risk for neurological and ocular involvement is 78% (Figure 29) [58–62].



Figure 29. Sturge-Weber syndrome.

9.2. Paederus dermatitis

Paederus dermatitis (also known as night burn) is a peculiar irritant dermatitis following contact with an insect belonging to the genus *Paederus* and its fluid, which contains a blistering toxic amide, the chemical pederin. The dermatitis is characterized by erythematous-bullous lesions of sudden onset on exposed areas of the body: the neck is the most common site involved, followed by the face (Figures 30 and 31) [63].



Figure 30. *Paederus* dermatitis.



Figure 31. *Paederus* insect.

9.3. Melasma

Melasma is an acquired symmetrical hyperpigmentation of the sun-exposed skin of the face and neck. Its exact cause is unknown, but UV light exposure and hormonal influences appear to be important etiological factors. Studies suggest that UV light stimulates production of dermal stem cell factor and α -melanocyte-stimulating hormone, resulting in proliferation of melanocytes and increased melanin production. Melasma classically is associated with pregnancy. In addition, an association with oral contraceptives, hormone replacement therapy, thyroid disorders, phototoxic medications, antiepileptic agents, and cosmetics has been described. Several studies suggest a genetic predisposition. The condition most commonly

affects medium- to dark-complexioned persons—particularly Asian and Hispanic women. In the United States, melasma affects more than 5 million individuals. It typically appears in adult women as bilateral brown or grayish cutaneous macules that range from a few millimeters to more than 2 cm in diameter. Lesions develop slowly with sun exposure and primarily involve the skin of the midface, forehead, upper lip, chin, mandibular ramus region, and (rarely) the arms. The pigmentation may remain faint or darken over time. Melasma only rarely affects men (**Figure 32**) [64–68].



Figure 32. Melasma.

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