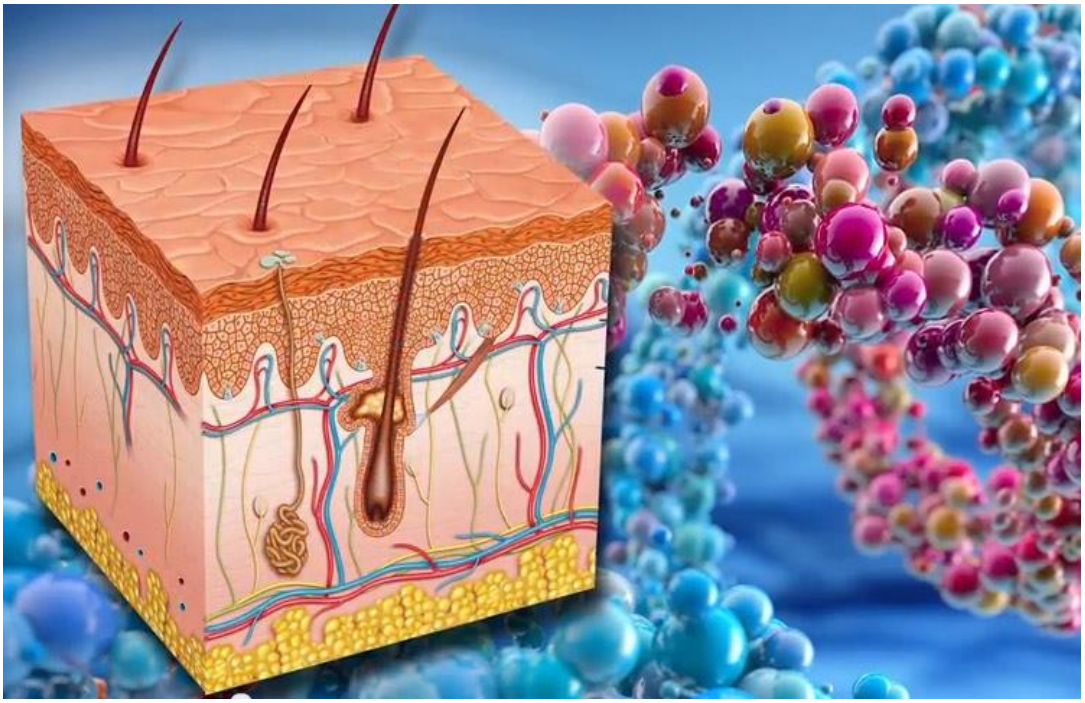
ADKHAMJON PAKIRDINOV

# CUTANEOUS SIGNS AND DIAGNOSIS. DERMATOSES RESULTING FROM PHYSICAL FACTORS. PRURITUS AND NEUROCUTANEOUS DERMATOSES



KAFOLAT TAFAKKUR
ANDIJAN – 2024

**THE MINISTRY OF HEALTH CARE OF REPUBLIC OF UZBEKISTAN**

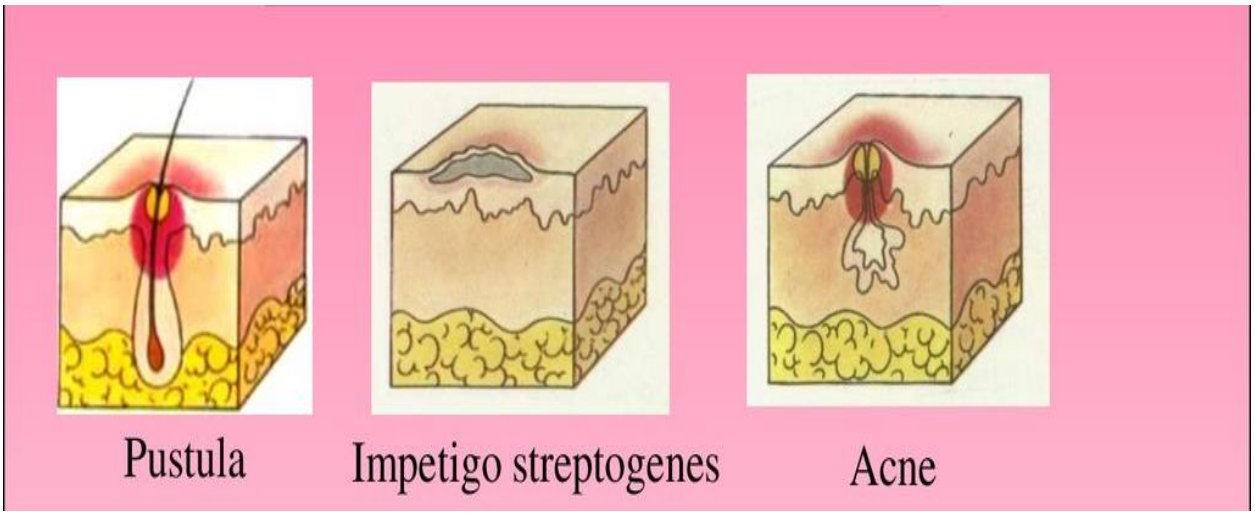
**THE CENTER FOR DEVELOPMENT OF MEDICAL EDUCATION**

**ANDIJAN STATE MEDICAL INSTITUTE**

**THE DEPARTMENT OF DERMATOLOGY AND VENEREOLOGY**

# CUTANEOUS SIGNS AND DIAGNOSIS. DERMATOSES RESULTING FROM PHYSICAL FACTORS. PRURITUS AND NEUROCUTANEOUS DERMATOSES

(FOR RESIDENTS, CLINICAL INTERNS, TREATMENT AND PEDIATRICS STUDENTS)




**KAFOLAT TAFAKKUR**
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# CUTANEOUS SIGNS AND DIAGNOSIS

In some cases, the appearance of skin lesions may be so distinctive that the diagnosis is clear at a glance. In other cases, subjective symptoms and clinical signs in themselves are inadequate, and a complete history and laboratory examinations, including a biopsy, are essential to arrive at a diagnosis.

The same disease may show variations under different conditions and in different individuals. The appearance of the lesions may have been modified by previous treatment or obscured by extraneous influences, such as scratching or secondary infection. Subjective symptoms may be the only evidence of a disease, as in pruritus, and the skin appearance may be generally unremarkable. Although history is important, the diagnosis in dermatology is most frequently made based on the objective physical characteristics and location or distribution of one or more lesions that can be seen or felt. Therefore, careful physical examination of the skin is paramount in der- matologic diagnosis.

## CUTANEOUS SIGNS

Typically, most skin diseases produce or present with lesions that have more or less distinct characteristics. They may be uniform or diverse in size, shape, and color, and may be in different stages of evolution or involution. The original lesions are known as the primary lesions, and identification of such lesions is the most important aspect of the dermatologic physical examination. They may continue to full development or be modified by regression, trauma, or other extraneous factors, producing secondary lesions.

## PRIMARY LESIONS

Primary lesions are of the following forms: macules (or patches), papules (or plaques), nodules, tumors, wheals, vesicles, bullae, and pustules.

## MACULES (MACULAE, SPOTS)

Macules are variously sized, circumscribed changes in skin color, without elevation or depression (nonpalpable). They may be circular, oval, or irregular, and may be distinct in outline or fade into the surrounding skin. Macules may constitute the whole or part of the eruption, or may be merely an early phase. If the lesions become slightly raised, they are then designated papules or, sometimes, morbilliform eruptions (Fig. 1).

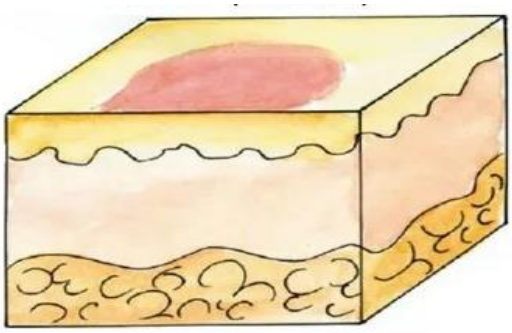


**Fig. 1. Macules**

## PATCHES

A patch is a large macule, 1 cm or greater in diameter, as may be seen in nevus flammeus or vitiligo (Fig. 2).

**Fig. 2. Patches**

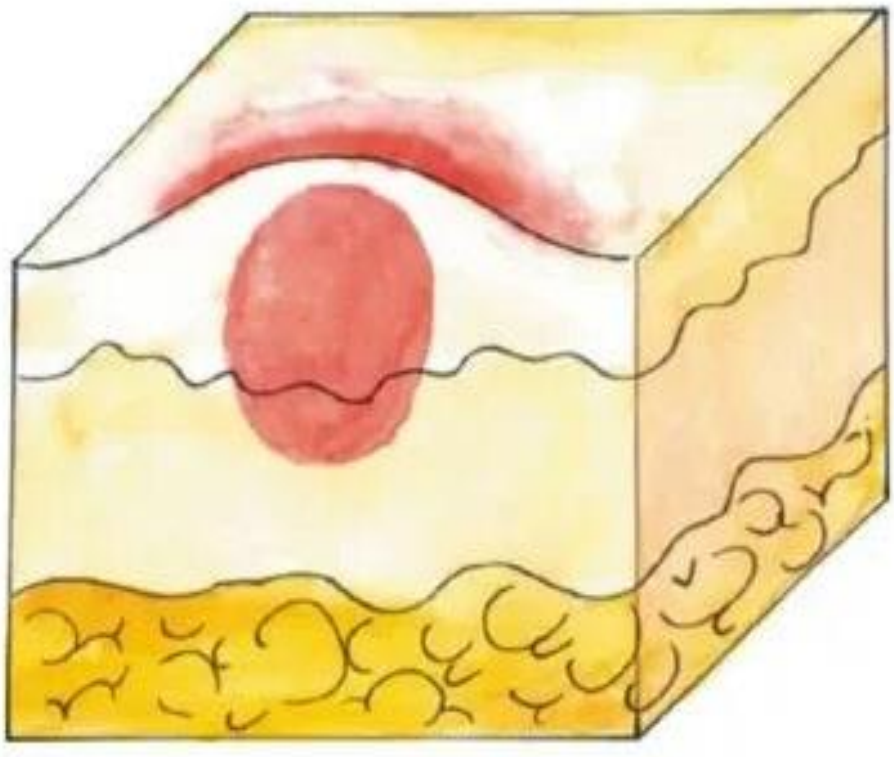
## PAPULES

Papules are circumscribed, solid elevations with no visible fluid, varying in size from a pinhead to 1 cm. They may be acuminate, rounded, conical, flat-topped, or umbilicated, and may appear white (as in milium), red (as in eczema), yellowish (as in xanthoma), or black (as in melanoma).

Papules are generally centered in the dermis and may be concentrated at the orifices of the sweat ducts or at the hair follicles. They may be of soft or firm consistency. The surface may be smooth or rough. If capped by scales, they are known as squamous papules, and the eruption is called papulosquamous.

Some papules are discrete and irregularly distributed, as in papular urticaria, whereas others are grouped, as in lichen nitidus. Some persist as papules, whereas those of the inflammatory type may progress to vesicles and even to pustules, or may erode or ulcerate before regression takes place.

The term maculopapular should not be used. There is no such thing as a maculopapule, but there may be both macules and papules in an eruption. Most typically such eruptions are morbilliform (Fig. 3).



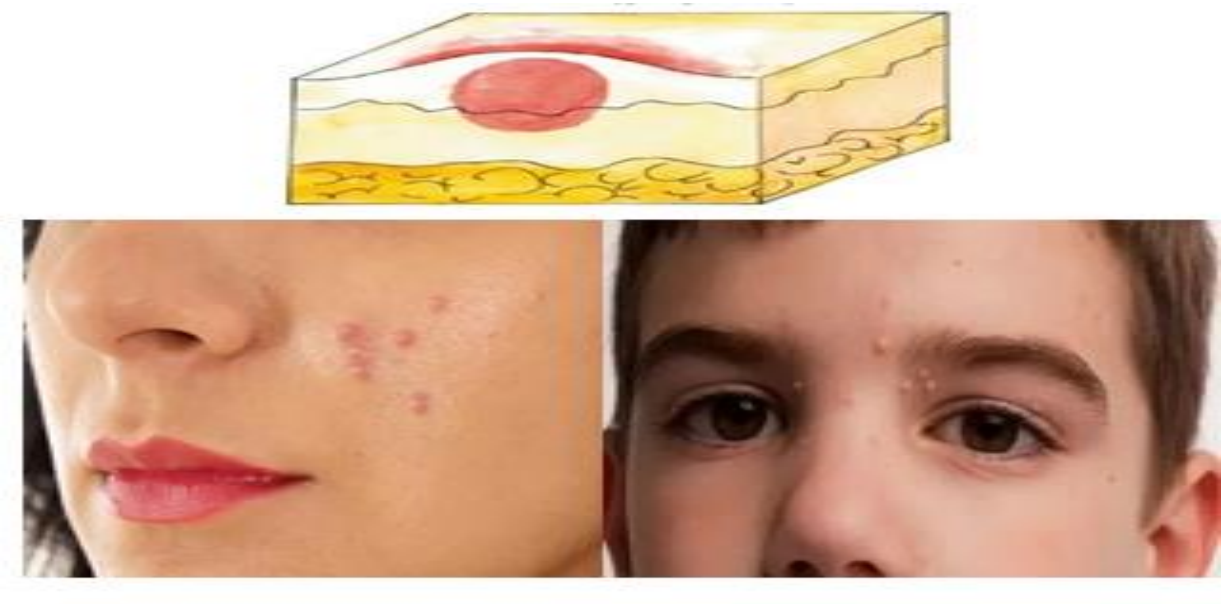


**Fig. 3. Papules**

## PLAQUES

A plaque is a broad papule (or confluence of papules), 1 cm or more in diameter. It is generally flat, but may be centrally depressed. The center of a plaque may be normal skin.

## NODULES

Nodules are morphologically similar to papules, but they are larger than 1 cm in diameter. They most frequently are centered in the dermis or subcutaneous fat (Fig. 4.).

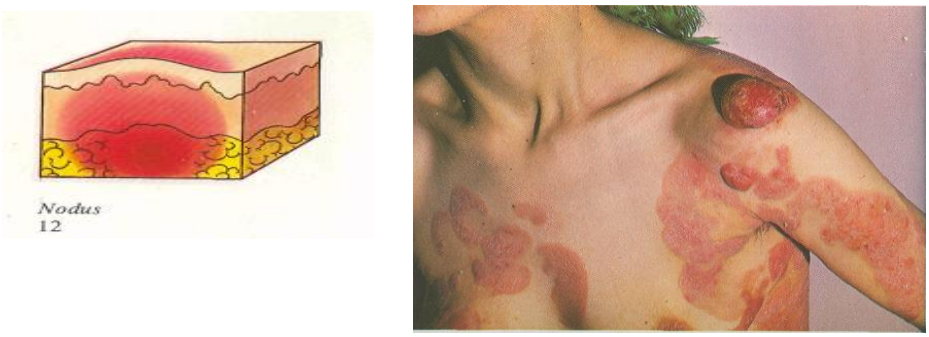



**Fig. 4.** Nodules

## TUMORS

Tumors are soft or firm and freely movable or fixed masses of various sizes and shapes (but in general greater than 2 cm in diameter). General usage dictates that the word "tumor" means a neoplasm. They may be elevated or deep-seated, and in some instances are pedunculated (fibromas). Tumors have a tendency to be rounded. Their consistency depends on the constituents of the lesion. Some tumors remain stationary indefinitely, whereas others increase in size or break down.

## WHEALS (HIVES)

Wheals are evanescent, edematous, plateau-like elevations of various sizes. They are usually oval or of arcuate contours, pink to red, and surrounded by a "flare" of macular erythema. They may be discrete or may coalesce. These lesions often develop quickly. Because the wheal is the prototypic lesion of urticaria, diseases in which wheals are prominent are frequently described as "urticarial" (e.g. urticarial vasculitis). Dermatographism, or pressure-induced whealing, may be evident **(**Fig. 5).

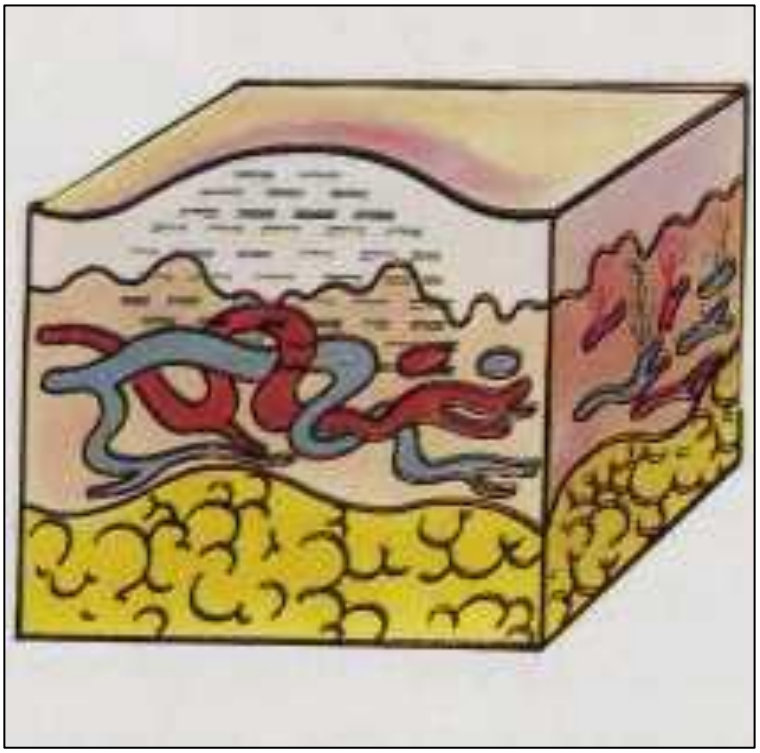


**Fig. 5.** Wheals

## VESICLES (BLISTERS)

Vesicles are circumscribed, fluid-containing, epidermal elevations, 1-10 mm in size. They may be pale or yellow from serous exudate, or red from serum mixed with blood. The apex may be rounded, acuminate, or umbilicated as in eczema her- peticum. Vesicles may be discrete, irregularly scattered, grouped as in herpes zoster, or linear as in allergic contact dermatitis from urushiol (poison ivy/oak). Vesicles may arise directly or from a macule or papule, and generally lose their identity in a short time, breaking spontaneously or developing into bullae through coalescence or enlargement, or developing into pustules. When the contents are of a seropuru- lent character, the lesions are known as vesicopustules. Vesicles consist of either a single cavity (unilocular) or several compartments (multilocular) containing fluid (Fig. 6).

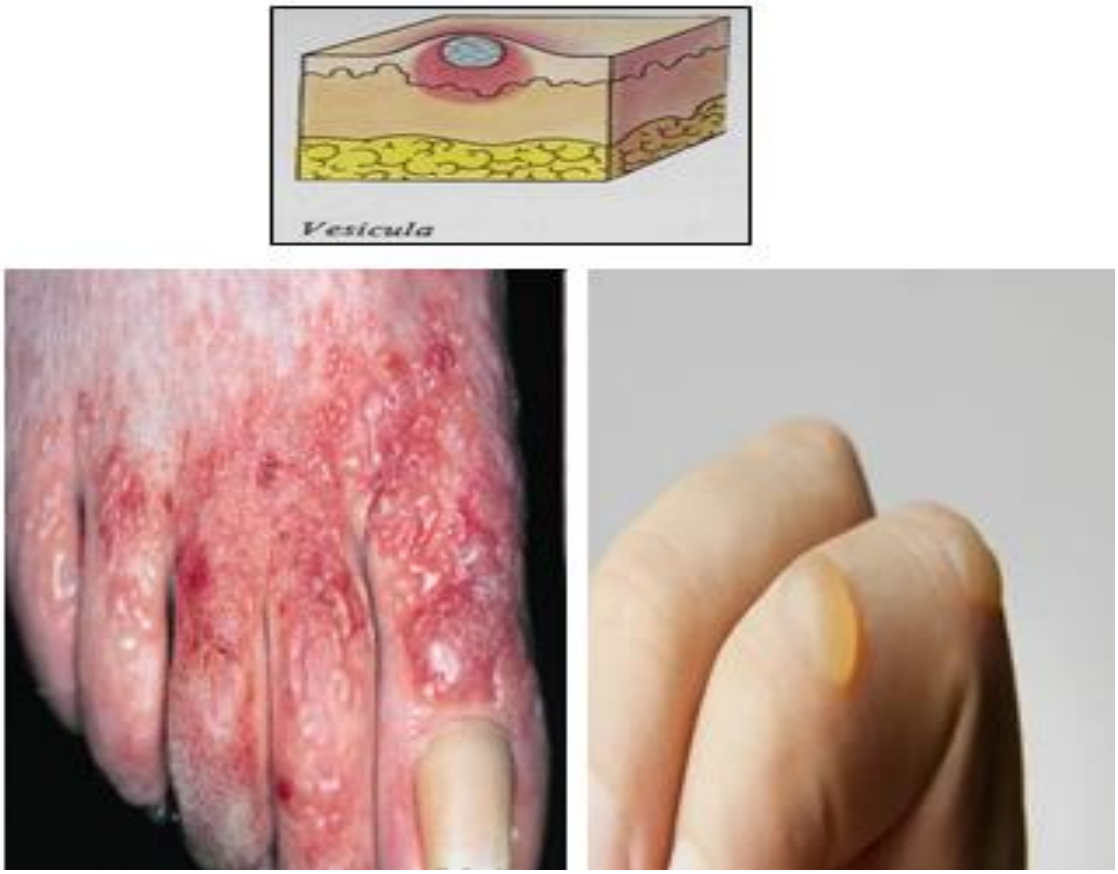



**Fig. 6.** Vesicles

## BULLAE

Bullae are rounded or irregularly shaped blisters containing serous or seropurulent fluid. They differ from vesicles only in size, being larger than 1 cm. They are usually unilocular but may be multilocular. Bullae may be located superficially in the epidermis, so that their walls are flaccid and thin, and subject to rupture spontaneously or from slight injury. After rupture, remnants of the thin walls may persist and, together with the exudate, may dry to form a thin crust; or the broken bleb may leave a raw and moist base, which may be covered with sero-purulent or purulent exudate. More rarely, irregular vegetations may appear on the base (as in pemphigus vegetans). When the bullae are subepidermal, they are tense, and ulcera- tion and scarring may result.

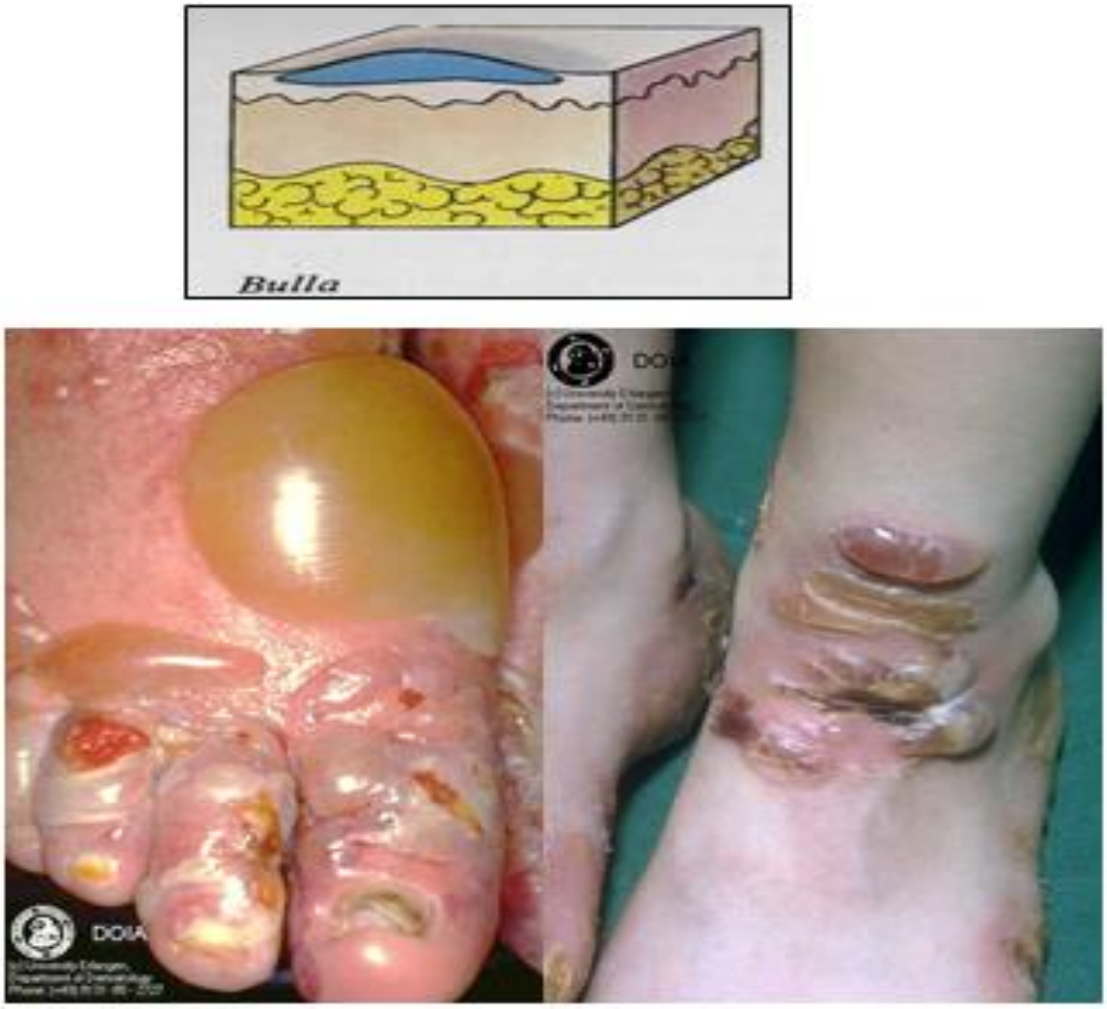



**Fig. 7.** Bullae

Nikolsky's sign refers to the diagnostic maneuver of putting lateral pressure on unblistered skin in a bullous eruption and having the epithelium shear off. Asboe-Hansen's sign refers to the extension of a blister to adjacent unblistered skin when pressure is put on the top of the blister. Both of these signs demonstrate the principle that in some diseases the extent of microscopic vesiculation is more than is evident by simple inspection. These findings are useful in evaluating the severity of pemphigus vulgaris and severe bullous drug reactions. Hemorrhagic bullae are common in pemphigus, herpes zoster, severe bullous drug reactions, and lichen sclerosus. The cellular contents of bullae may be useful in cytologically confirming the diagnosis of pemphigus, herpes zoster and herpes simplex (Fig. 7).

## PUSTULES

Pustules are small elevations of the skin containing purulent material (usually necrotic inflammatory cells). They are similar to vesicles in shape and usually have an inflammatory areola. They are usually white or yellow centrally, but may be red if they also contain blood. They may originate as pustules or may develop from papules or vesicles, passing through transitory early stages, during which they are known as papulopustules or vesicopustules (Fig. 8).

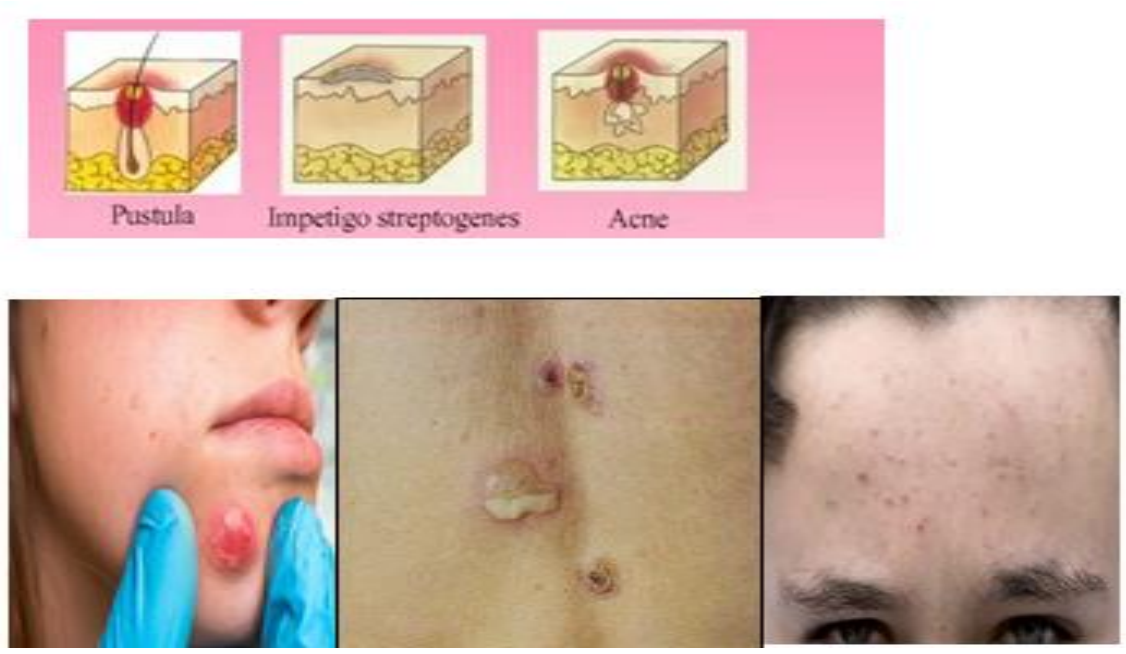



**Fig. 8. Pustules**

## SECONDARY LESIONS

Secondary lesions are of many kinds; the most important are scales, crusts, erosions, ulcers, fissures, and scars.

## SCALES (EXFOLIATION)

Scales are dry or greasy laminated masses of keratin. The body ordinarily is constantly shedding imperceptible tiny, thin fragments of stratum corneum. When the formation of epidermal cells is rapid or the process of normal keratinization is interfered with, pathologic exfoliation results, producing scales. These vary in size, some being fine, delicate, and branny, as in tinea versicolor, others being coarser, as in eczema and ichthyosis, while still others are stratified, as in psoriasis. Large sheets of desquamated epidermis are seen in toxic epidermal necrolysis, staphylococcal scalded skin syndrome, and infection-associated (toxinmediated) desquamations, such as scarlet fever. Scales vary in color from white-gray to yellow or brown from the admixture of dirt or melanin. Occasionally, they have a silvery sheen from trapping of air between their layers; these are micaceous scales, characteristic of psoriasis. When scaling occurs, it usually implies that there is some pathologic process in the epidermis, and parakeratosis is often present histologically.

## CRUSTS (SCABS)

Crusts are dried serum, pus, or blood, usually mixed with epithelial and sometimes bacterial debris. They vary greatly in size, thickness, shape, and color, according to their origin, composition, and volume. They may be dry, golden yellow, soft, friable, and superficial, as in impetigo; yellowish, as in favus; thick, hard, and tough, as in thirddegree burns; or lamellated, elevated, brown, black, or green masses, as in late syphilis. The latter have been described as oystershell (ostra- ceous) crusts and are known as rupia. When crusts become detached, the base may be dry or red and moist (Fig. 9).

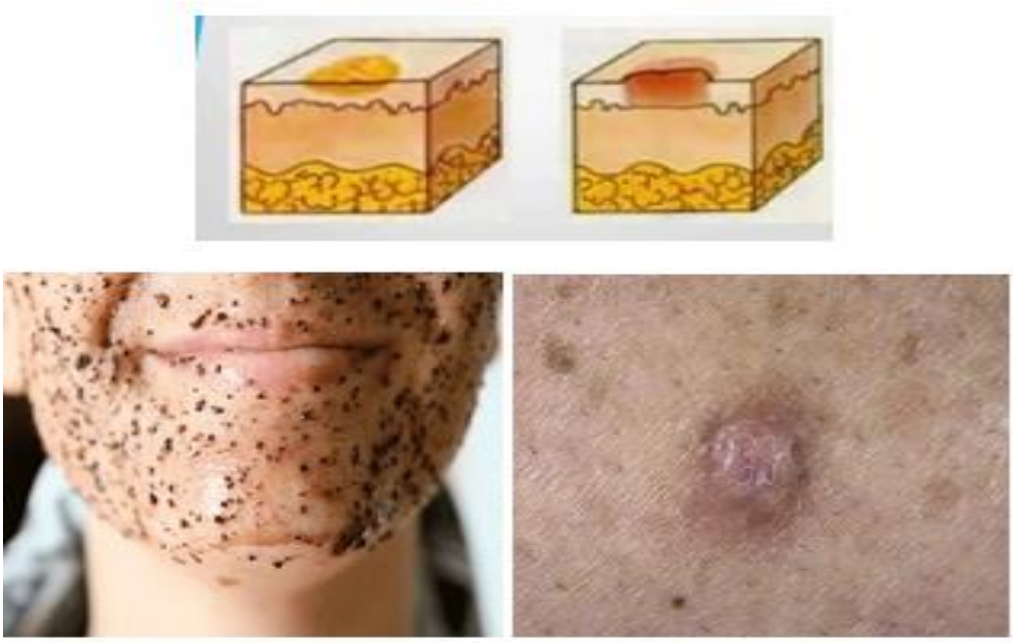


**Fig. 9. Crusts**

## EXCORIATIONS AND ABRASIONS (SCRATCH MARKS)

An excoriation is a punctate or linear abrasion produced by mechanical means, usually involving only the epidermis but not uncommonly reaching the papillary layer of the dermis. Excoriations are caused by scratching with the fingernails in an effort to relieve itching in a variety of diseases. If the skin damage is the result of mechanical trauma or constant friction, the term abrasion may be used. Frequently there is an inflammatory areola around the excoriation or a covering of yellowish dried serum or red dried blood. Excoriations may provide access for pyogenic microorganisms and the formation of crusts, pustules, or cellulitis, occasionally associated with enlargement of the neighboring lymphatic glands. In general, the longer and deeper excoriations are, the more severe was the pruritus that provoked them. Lichen planus is an exception, however, in which pruritus is severe, but excoriations are rare (Fig. 10).

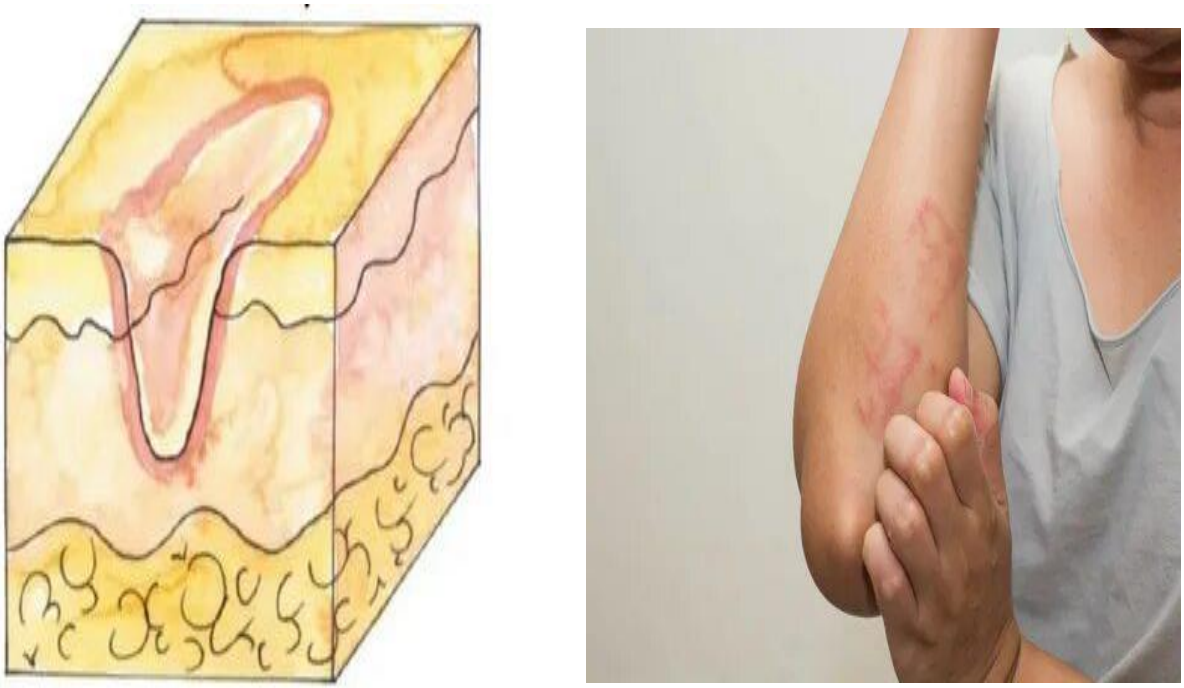
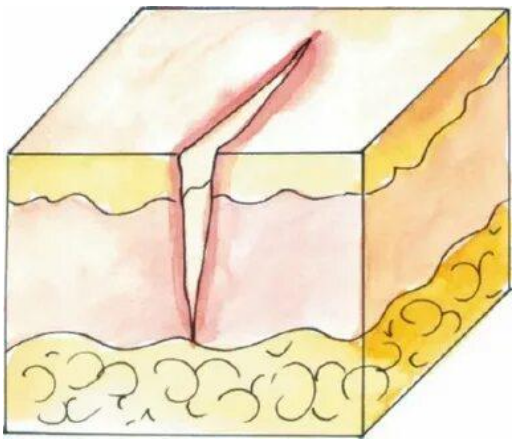


**Fig. 10. Excoriations**

## FISSURES (CRACKS, CLEFTS)

A fissure is a linear cleft through the epidermis or into the dermis. These lesions may be single or multiple, and vary from microscopic to several centimeters in length with sharply defined margins. They may be dry or moist, red, straight, curved, irregular, or branching. They occur most commonly when the skin is thickened and inelastic from inflammation and dryness, especially in regions subjected to frequent movement. Such areas are the tips and flexural creases of the thumbs, fingers, and palms; the edges of the heels; the clefts between the fingers and toes; at the angles of the mouth; the lips; and about the nares, auricles, and anus. When the skin is dry, exposure to cold, wind, water, and cleaning products (soap, detergents) may produce a stinging, burning sensation, indicating microscopic fissuring is present. This may be referred to as chapping, as in "chapped lips." When fissuring is present, pain is often produced by movement of the parts, which opens or deepens the fissures or forms new ones (Fig. 11).



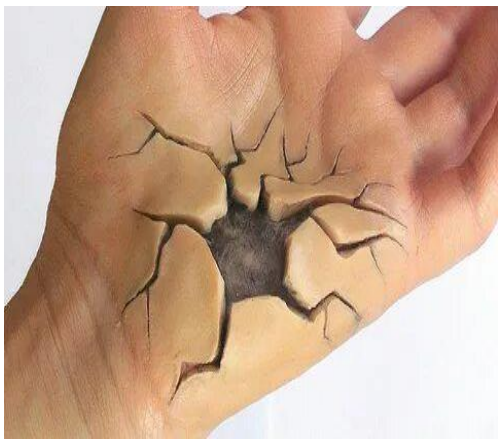
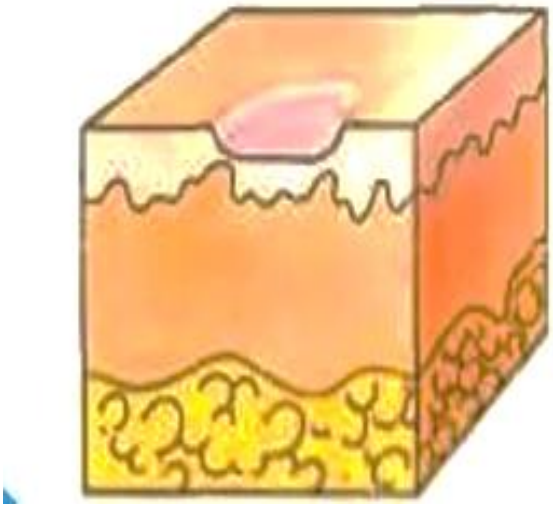


**Fig. 11. Fissures**

## EROSIONS

Loss of all or portions of the epidermis alone, as in impetigo or herpes zoster or simplex after vesicles rupture, produces an erosion. It may or may not become crusted, but it heals without a scar (Fig. 12).



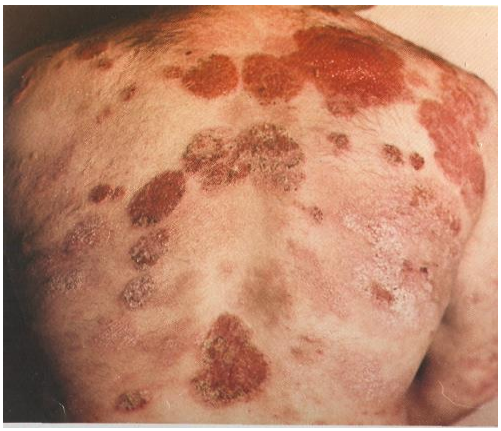
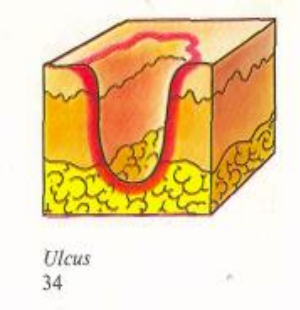


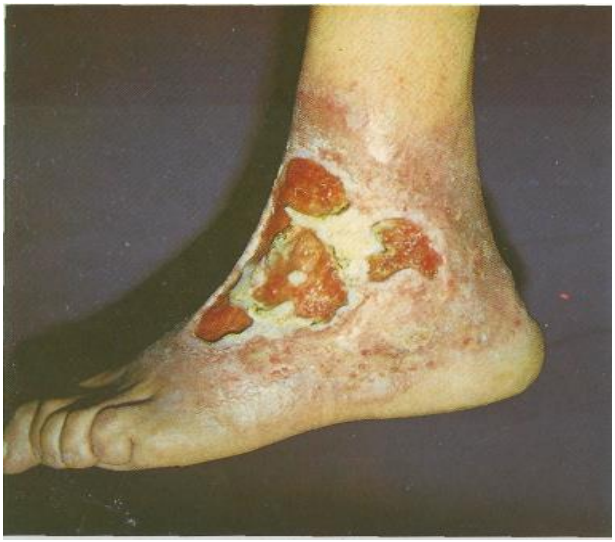
**Fig. 12. Erosions**

## ULCERS

Ulcers are rounded or irregularly shaped excavations that result from complete loss of the epidermis plus some portion of the dermis. They vary in diameter from a few millimeters to several centimeters. They may be shallow, involving little beyond the epidermis, as in dystrophic epidermolysis bullosa, the base being formed by the papillary layer, or they may extend deep into the dermis, subcutaneous tissues, or deeper, as with leg ulcers. They heal with scarring.

# ULCERS



## SCARS

Scars are composed of new connective tissue that replaced lost substance in the dermis or deeper parts as a result of injury or disease, as part of the normal reparative process. Their size and shape are determined by the form of the previous destruction. Scarring is characteristic of certain inflammatory processes and is therefore of diagnostic value. The pattern of scarring may be characteristic of a particular disease. Lichen planus and discoid lupus erythematosus, for example, have inflammation that is in relatively the same area anatomically, yet discoid lupus characteristically causes scarring as it resolves, whereas lichen planus rarely results in scarring of the skin. Both processes, however, cause scarring of the hair follicles when they occur on the scalp. Scars may be thin and atrophic, or the fibrous elements may develop into neoplastic overgrowths, as in keloids. Some individuals and some areas of the body, such as the anterior chest, are especially prone to scarring. Scars may be smooth or rough, pliable or firm, and tend at first to be pink or violaceous, later becoming white, glistening, and rarely, hyperpigmented.

Scars are persistent but tend to become less noticeable in the course of time. At times, and especially in certain anatomic locations (central chest), they grow thick, tough, and corded, forming a hypertrophic scar or keloid.

## GENERAL DIAGNOSIS

Interpretation of the clinical picture may be difficult, because identical manifestations may result from widely different causes. Moreover, the same etiologic factors may give rise to a great diversity of eruptions. There is one great advantage in dermatology: namely, that of dealing with an organ that can be seen and felt. Smears and cultures may be readily made for bacteria and fungi. Biopsy and histologic examination of skin lesions are usually very minor procedures, making histopathology an important component of the evaluation in many clinical situations. Given the ease of histologic confirmation of diagnoses in skin diseases, the threshold for biopsy should be low. This is especially true of inflammatory dermatoses, potentially infectious conditions, and skin disorders in immunosuppressed and hospitalized patients where clinical morphology may be atypical. Once therapy is begun empirically, histologic features may be altered by the treatment, making pathologic diagnosis more difficult.

## HISTORY

Knowledge of the patient's age, health, occupation, hobbies, and living conditions, and of the onset, duration, and course of the disease, and its response to previous treatment are important. The family history of similar disorders and other related diseases may be useful.

A complete drug history is one of the most important aspects of a thorough history. This includes prescription and over the counter medications, supplements, and herbal products. Drug reactions are frequently seen and may simulate many different diseases. Anti-inflammatory agents (steroidal or nonsteroidal), antibiotics, antihypertensives, antiarrhythmics, cholesterol- lowering agents, antiepileptics, and antidepressants may all produce cutaneous disorders. All may

simulate entities not usually attributed to drugs. It is equally important to inquire about topical agents that have been applied to the skin and mucous membranes for medicinal or cosmetic purposes, for these agents may cause cutaneous or systemic reactions.

Other illnesses, travel abroad, the patient's environment at home and at work, seasonal occurrences and recurrences of the disease, and the temperature, humidity, and weather exposure of the patient are all important items in a dermatologic history. Habitation in certain parts of the world predisposes to distinctive diseases for that particular geographic locale. San Joaquin Valley fever (coccidioidomycosis), Hansen's disease, leishmaniasis, and histoplasmosis are examples. Sexual orientation and practices may be relevant, as in genital ulcer diseases, human immunodeficiency virus (HIV) infection, and infestations (e.g. scabies, pubic lice).

## EXAMINATION

Examination should be conducted in a well-lit room. Natural sunlight is the ideal illumination. Fluorescent bulbs that produce wavelengths of light closer to natural sunlight than standard fluorescent bulbs are commercially available. Abnormalities of melanin pigmentation, e.g. vitiligo and melasma, are more clearly visible under ultraviolet (UV) light. A Wood's light (365 nm) is most commonly used and is also valuable for the diagnosis of some types of tinea capitis, tinea versicolor, and erythrasma.

A magnifying lens is of inestimable value in examining small lesions. It may be necessary to palpate the lesion for firmness and fluctuation; rubbing will elucidate the nature of scales; scraping will reveal the nature of the lesion's base. Pigmented lesions, especially in infants, should be rubbed in an attempt to elicit Darier's sign (whealing), as seen in urticaria pigmentosa. Dermoscopy is an essential part of the examination of pigmented lesions.

The entire eruption must be seen to evaluate distribution and configuration. This is optimally done by having the patient completely undress and viewing

him/her from a distance to take in the whole eruption at once. "Peek a boo" examination, by having the patient expose one anatomic area after another while remaining clothed, is not optimal because the examination of the skin will be incomplete and the overall distribution is hard to determine. After the patient is viewed at a distance, individual lesions are examined to identify primary lesions and to determine the evolution of the eruption and the presence of secondary lesions.

## DIAGNOSTIC DETAILS OF LESIONS DISTRIBUTION

Lesions may be few or numerous, and in arrangement they may be discrete or may coalesce to form patches of peculiar configuration. They may appear over the entire body, or follow the lines of cleavage (pityriasis rosea), dermatomes (herpes zoster), or lines of Blaschko (epidermal nevi). Lesions may form groups, rings, crescents, or unusual linear patterns. A remarkable degree of bilateral symmetry is characteristic of certain diseases such as dermatitis herpetiformis, vitiligo, and psoriasis.

## EVOLUTION

Some lesions appear fully evolved. Others develop from smaller lesions, then may remain the same during their entire existence (e.g. warts). When lesions succeed one another in a series of crops, as they do in varicella and dermatitis herpeti- formis, a polymorphous eruption results with lesions in various stages of development or involution all present at the same time.

## INVOLUTION

Certain lesions disappear completely, whereas others leave characteristic residual pigmentation or scarring. Residual dys- pigmentation, although a significant cosmetic issue, is not considered a scar. The pattern in which lesions involute may be useful in diagnosis, e.g. the typical keratotic papule of pityriasis lichenoides varioliformis acuta.

## GROUPING

Grouping is a characteristic of dermatitis herpetiformis, herpes simplex, and herpes zoster. Small lesions arranged around a large one are said to be in a corymbose arrangement. Concentric annular lesions are typical of borderline Hansen's disease and erythema multiforme. These are sometimes said to be in a cockade pattern, like the tricolor cockade hats worn by French revolutionists. Flea and other arthropod bites are usually grouped and linear (breakfastlunch and dinner sign). Grouped lesions of various sizes may be termed agminated.

## CONFIGURATION

Certain terms are used to describe the configuration that an eruption assumes either primarily or by enlargement or coalescence. Lesions in a line are called linear, and they may be confluent or discrete. Lesions may form a complete circle (annular) or a portion of a circle (arcuate or gyrate), or may be composed of several intersecting portions of circles (polycyclic). If the eruption is not straight but does not form parts of circles, it may be serpiginous . Round lesions may be small, like drops, called guttate; or larger, like a coin, called nummular. Unusual configurations that do not correspond to these patterns or to normal anatomic or embryonic patterns should raise the possibility of an exogenous dermatosis or factitia.

## COLOR

The color of the skin is determined by melanin, oxyhemoglobin, reduced hemoglobin, and carotene. Not only do the proportions of these components affect the color, but their depth within the skin, the thickness of the epidermis, and hydration also play a role. The Tyndall effect modifies the color of skin and of lesions by the selective scattering of light waves of different wavelengths. The blue nevus and Mongolian spots are examples of this light dispersion effect, in which brown melanin in the dermis appears blue-gray.

The color of lesions may be very valuable as a diagnostic factor. Dermatologists should be aware that there are many shades of pink, red, and

purple, each of which tends to suggest a diagnosis or disease group. Interface reactions such as lichen planus or lupus erythematosus are described as violaceous. Lipid-containing lesions are yellow, as in xanthomas or steatocystoma multiplex. The orangered (salmon) color of pityriasis rubra pilaris is characteristic. The constitutive color of the skin determines the quality of the color one observes with a specific disorder. In darkskinned persons, erythema is hard to perceive. Pruritic lesions in African-Americans may evolve to be small, shiny, flattopped papules with a violaceous hue (due to the combination of erythema and pigmentary incontinence). These lichenified lesions would be suspected of being lichenoid by the untrained eye, but are in fact eczematous.

Patches lighter in color than the normal skin may be completely depigmented or have lost only part of their pigment (hypopigmented). This is an important distinction, since certain conditions are or may be hypopigmented, such as tinea versicolor, nevus anemicus, Hansen's disease, hypomelanotic macules of tuberous sclerosis, hypomelanosis of Ito, seborrheic dermatitis, and idiopathic guttate hypomelanosis. True depigmentation should be distinguished from this; it suggests vitiligo, nevus depigmentosus, halo nevus, scleroderma, morphea, or lichen sclerosus.

Hyperpigmentation may result from epidermal or dermal causes. It may be related to either increased melanin or deposition of other substances. Epidermal hyperpigmentation occurs in nevi, melanoma, cafeaulait spots, melasma, and lentigines. These lesions are accentuated when examined with a Wood's light. Dermal pigmentation occurs subsequent to many inflammatory conditions (postinflammatory hyperpigmentation) or from deposition of metals, medications, medication-melanin complexes, or degenerated dermal material (ochronosis). These conditions are not enhanced when examined by a Wood's light. The hyperpigmentation following inflammation is most commonly the result of dermal melanin deposition, but in some conditions, such as lichen aureus, is caused by iron. Dermal iron deposition appears more yellowbrown or golden than dermal melanin.

## CONSISTENCY

Palpation is an essential part of the physical examination of lesions. Does the lesion blanch on pressure? If not, it may be purpuric. Is it fluctuant? If so, it may have free fluid in it. Is it cold or hot? If there is a nodule or tumor, does it sink through a ring into the panniculus, like a neurofibroma? Is it hard enough for calcification to be suspected, merely very firm, like a keloid or dermatofibroma, or branny, like scleredema?

## HYPERESTHESIA/ANESTHESIA

Certain conditions may be associated with increased or decreased sensation. For example, the skin lesions of borderline and tuberculoid Hansen's disease typically are anesthetic in their centers. In neuropathic conditions (such as notalgia paresthetica), the patient may perceive both pruritus and hyperesthesia. Neurally mediated itch may be accompanied by other neural sensations such as heat or burning. The combination of pruritus with other neural symptoms suggests the involvement of nerves in the pathological process.

## HAIR, NAILS, AND ORAL MUCOSA

Involvement of hair-bearing areas by certain skin disorders causes characteristic lesions. Discoid lupus, for example, causes scarring alopecia with characteristic dyspigmentation (Fig. 2-9). On the skin the lesions may be much less characteristic. Diffuse hair loss may be seen in certain conditions such as acrodermatitis enteropathica, and may be a clue to the diagnosis. In addition, loss of hair within a skin lesion may be suggestive of the correct diagnosis, e.g. the alopecia seen in the tumid plaques of follicular mucinosis.

Some skin disorders cause characteristic changes of the nails, even when the periungual tissue is not involved. The pitting seen in psoriasis and alopecia areata may be useful in confirming these diagnoses when other findings are not characteristic. In addition, the nails and adjacent structures may be the sole site of pathology, as in candidal paronychia.

The complete skin examination includes examination of the oral mucosa. Oral lesions are characteristically found in viral syndromes (exanthems), lichen planus, HIV-associated Kaposi sarcoma, and autoimmune bullous diseases (pemphigus vulgaris).

## DERMATOSES RESULTING FROM PHYSICAL FACTORS

The body requires a certain amount of heat, but beyond definite limits, insufficient or excessive amounts are injurious. The local action of excessive heat causes burns or scalds; on the other hand, undue cold causes chilblains, frostbite, and congelation. Thresholds of tolerance exist in all body structures sensitive to electromagnetic wave radiation of varying frequencies, such as xrays and ultraviolet (UV) rays. The skin, which is exposed to so many external physical forces, is more subject to injuries caused by them than is any other organ.

## HEAT INJURIES THERMAL BURNS

### Thermal burns

Injury of varying intensity may be caused by the action of excessive heat on the skin. If this heat is extreme, the skin and underlying tissue may be destroyed. The changes in the skin resulting from dry heat or scalding are classified in four degrees.

- *First-degree burns* of the skin result merely in an active congestion of the superficial blood vessels, causing erythema that may be followed by epidermal desquamation (peeling). Ordinary sunburn is the most common example of a first-degree burn. The pain and increased surface heat may be severe, and it is not rare to have some constitutional reaction if the involved area is large.
- *Second-degree burns* are subdivided into superficial and deep forms.
  - In the superficial type there is a transudation of serum from the capillaries, which causes edema of the superficial tissues. Vesicles and blebs are formed by the serum gathering beneath the outer layers of the epidermis. Complete recovery without scarring is usual in burns of this kind.

- The deep second-degree burn is pale and anesthetic. Injury to the reticular dermis compromises blood flow and destroys appendages, so that healing takes over

  1 month to occur and results in scarring.

- *Third-degree burns* involve loss of tissue of the full thickness of the skin, and often some of the subcutaneous tissues. Since the skin appendages are destroyed, there is no epithelium available for regeneration of the skin. An ulcerating wound is produced, which in healing leaves a scar.
- *Fourth-degree burns* involve the destruction of the entire skin and subcutaneous fat with any underlying tendons.

Both third- and fourth-degree burns require grafting for closure. All third and fourth-degree burns are followed by constitutional symptoms of varied gravity, their severity depending on the size of the involved surface, the depth of the burn, and particularly the location of the burned surface. The more vascular the involved area, the more severe the symptoms.

The prognosis is poor for any patient in whom a large area of skin surface is involved, particularly if more than twothirds of the body surface has been burned. Women, infants, and toddlers all have an increased risk of death from burns when compared to men. Excessive scarring, with either keloidlike scars or flat scars with contractures, may produce deformities and dysfunctions of the joints, as well as chronic ulcerations due to impairment of local circulation. Delayed post-burn blistering may occur in partialthickness wounds and skingraft donor sites. It is most common on the lower extremities, and is self-limited. Burn scars may be the site of development of carcinoma or sarcoma. With modern reconstructive surgery these unfortunate end results can be minimized.

## TREATMENT

Immediate first aid for minor thermal burns consists of prompt cold applications (ice water, or cold tap water if no ice is at hand), continued until pain does not return on stopping them.

The vesicles or blebs of second-degree burns should not be opened but should be protected from injury, since they form a natural barrier against contamination by microorganisms. If they become tense and unduly painful, the fluid may be evacuated under strictly aseptic conditions by puncturing the wall with a sterile needle, allowing the blister to collapse on to the underlying wound. Excision of full-thickness and deep dermal wounds that will not reepithelialize within 3 weeks reduces wound infections, shortens hospital stays, and improves survival. Additionally, contractures and functional impairment may be mitigated by such early intervention and grafting. The most superficial wounds may be dressed with greasy gauze, while silver-containing dressings are used for their antiobitic properties in intermediate wounds. Fluid resuscitation, treatment of inhalation injury and hypercatabolism, monitoring and early intervention of sepsis, and intensive care management in a burn center are all recommended in large partialthickness wounds and full-thickness burns.

## ELECTRICAL BURNS

Electrical burns may occur from contact or as a flash exposure.

A contact burn is small but deep, causing some necrosis of the underlying tissues. Low-voltage injuries usually occur in the home, are treated conservatively, and generally heal well. Oral commissure burns may require reconstructive procedures. Highvoltage burns are often occupational; internal damage may be masked by little surface skin change, and be complicated by subtle and slowly developing sequelae. Early surgical intervention to improve circulation and repair vital tissues is helpful in limiting loss of the extremity. Flash burns usually cover a large area and, being similar to any surface burn, are treated as such. Lightning may cause burns after a direct strike, where an entrance and an exit wound are visible. This is the most lethal type of strike, and cardiac arrest or other internal injuries may occur. Other types of strike are indirect and result in burns that are either:

- linear in areas on which sweat was present
- in a feathery or arborescent pattern, which is believed to be pathognomonic
- punctate with multiple, deep, circular lesions

- thermal burns from ignited clothing or heated metal. These may occur if the patient was speaking on a cellphone or listening to an iPod when struck.

## HOT TAR BURNS

Polyoxyethylene sorbitan in neosporin ointment or sunflower oil is an excellent dispersing agent that facilitates the removal of hot tar from burns.

## MILIARIA

Miliaria, the retention of sweat as a result of occlusion of eccrine sweat ducts, produces an eruption that is common in hot, humid climates, such as in the tropics and during the hot summer months in temperate climates. *Staphylococcus epider- midis,* which produces an extracellular polysaccharide substance, induces miliaria in an experimental setting. This polysaccharide substance may obstruct the delivery of sweat to the skin surface. The occlusion prevents normal secretion from the sweat glands, and eventually pressure causes rupture of the sweat gland or duct at different levels. The escape of sweat into the adjacent tissue produces miliaria. Depending on the level of the injury to the sweat gland or duct, several different forms are recognized.

## MILIARIA CRYSTALLINA (SUDAMINA)

Miliaria crystallina is characterized by small, clear, superficial vesicles with no inflammatory reaction. It appears in bedridden patients in whom fever produces increased perspiration or in situations in which clothing prevents dissipa- tion of heat and moisture, as in bundled children. The lesions are generally asymptomatic and their duration is shortlived because they tend to rupture at the slightest trauma. One patient with postexercise itching was found to have miliaria crystallina; it resolved spontaneously. Drugs such as isotretinoin, bethanechol and doxorubicin may induce it. The lesions are selflimited; no treatment is required.

## MILIARIA RUBRA (PRICKLY HEAT)

The lesions of miliaria rubra appear as discrete, extremely pruritic, erythematous papulovesicles accompanied by a sensation of prickling, burning, or

tingling. They later may become confluent on a bed of erythema. The sites most frequently affected are the antecubital and popliteal fossae, trunk, inframammary areas (especially under pendulous breasts), abdomen (especially at the waistline), and inguinal regions; these sites frequently become macerated because evaporation of moisture has been impeded. Exercise-induced itching may also be caused by miliaria rubra. The site of injury and sweat escape is in the prickle cell layer, where spongiosis is produced.

## MILIARIA PUSTULOSA

Miliaria pustulosa is preceded by another dermatitis that has produced injury, destruction, or blocking of the sweat duct. The pustules are distinct, superficial, and independent of the hair follicle. The pruritic pustules occur most frequently on the intertriginous areas, flexure surfaces of the extremities, scrotum, and back of bedridden patients. Contact dermatitis, lichen simplex chronicus, and intertrigo are some of the associated diseases, although pustular miliaria may occur several weeks after these diseases have subsided. Recurrent episodes may be a sign of type I pseudohypoaldosteronism, as saltlosing crises may precipitate miliaria pustulosa or rubra, with resolution after stabilization.

## MILIARIA PROFUNDA

Non-pruritic, fleshcolored, deepseated, whitish papules characterize this form of miliaria. It is asymptomatic, usually lasts only 1 h after overheating has ended, and is concentrated on the trunk and extremities. Except for the face, axillae, hands, and feet, where there may be compensatory hyperhidrosis, all the sweat glands are nonfunctional. The occlusion is in the upper dermis. This form is observed only in the tropics and usually follows a severe bout of miliaria rubra.

## POSTMILIARIAL HYPOHIDROSIS

Postmiliarial hypohidrosis results from occlusion of sweat ducts and pores, and may be severe enough to impair an individual's ability to perform sustained work in a hot environment. Affected persons may show decreasing efficiency,

irritability, anorexia, drowsiness, vertigo, and headache; they may wander in a daze. It has been shown that hypohidrosis invariably follows miliaria, and that the duration and severity of the hypohidrosis are related to the severity of the miliaria. Sweating may be depressed to half the normal amount for as long as 3 weeks.

## TROPICAL ANHIDROTIC ASTHENIA

This is a rare form of miliaria with longlasting poral occlusion, which produces anhidrosis and heat retention.

## TREATMENT

The most effective treatment for miliaria is to place the patient in a cool environment. Even a single night in an airconditioned room helps to alleviate the discomfort. Next best is the use of circulating air fans to cool the skin. Anhydrous lanolin resolves the occlusion of pores and may help to restore normal sweat secretions. Hydrophilic ointment also helps to dissolve keratinous plugs and facilitates the normal flow of sweat. Soothing, cooling baths containing colloidal oatmeal or cornstarch are beneficial if used in moderation. Mild cases may respond to dusting powders, such as cornstarch or baby talcum powder.

## ERYTHEMA AB IGNE

Erythema ab igne is a persistent erythema or the coarsely reticulated residual pigmentation resulting from itthat is usually produced by long exposure to excessive heat without the production of a burn. It begins as a mottling caused by local hemostasis and becomes a reticulated erythema, leaving pigmentation. Multiple colors are simultaneously present in an active patch, varying from pale pink to old rose or dark purplishbrown. After the cause is removed, the affection tends to disappear gradually, but sometimes the pigmentation is permanent.

Histologically, an increased amount of elastic tissue in the dermis is noted. The changes in erythema ab igne are similar to those of actinic elastosis. Interface dermatitis and epithelial atypia may be noted.

Erythema ab igne occurs on the legs as a result of habitually warming them in front of open fireplaces, space heaters, or car heaters. Similar changes may be

produced at sites of an electric heating pad application such as the low back, or the upper thighs with laptop computers. The condition occurs also in cooks, silversmiths, and others exposed over long periods to direct moderate heat.

Epithelial atypia, which may lead to Bowen's disease and squamous cell carcinoma, has rarely been reported to occur overlying erythema ab igne. Treatment with 5-fluorouracil (5-FU) or imiquimod cream may be effective in reversing this epidermal alteration.

The use of emollients containing a-hydroxy acids or a cream containing fluocinolone acetonide 0.01%, hydroquinone 4%, and tretinoin 0.05% may help reduce the unsightly pigmentation.

## COLD INJURIES

Exposure to cold damages the skin by at least three mechanisms.

- Reduced temperature directly damages the tissue, as in frostbite and cold immersion foot.
- Vasospasm of vessels perfusing the skin prevents adequate perfusion of the tissue and causes vascular injury and consequent tissue injury (pernio, acrocyanosis, and frostbite).
- In unusual circumstances, adipose tissue is predisposed to damage by cold temperatures due to fat composition or location (cold panniculitis, see Chapter 23).

Outdoor workers and recreationalists, the armed forces, alcoholics, and the homeless are particularly likely to suffer cold injuries.

## ACROCYANOSIS

Acrocyanosis is a persistent blue discoloration of the entire hand or foot worsened by cold exposure. The hands and feet may be hyperhidrotic. It occurs chiefly in young women. Cyanosis increases as the temperature decreases and changes to erythema with elevation of the dependent part. The cause is unknown. Smoking should be avoided. Acrocyanosis is distinguished from Raynaud syndrome by its persistent nature (as opposed to the episodic nature of Raynaud) and lack of tissue damage (ulceration, distal fingertip resorption).

Acrocyanosis with swelling of the nose, ears, and dorsal hands may occur after inhalation of butyl nitrite. Interferona 2a may induce it. Repeated injection of the dorsal hand with narcotic drugs may produce lymphedema and an appearance similar to the edematous phase of scleroderma. This socalled puffy hand syndrome may include erythema or a bluish discoloration of the digits. Patients with anorexia nervosa frequently manifest acrocyanosis as well as perniosis, livedo reticularis and acral coldness. It may improve with weight gain.

Acral vascular syndromes may also be a sign of malignancy. In 47% of the 66 reported cases the diagnosis of cancer coincided with the onset of the acral disease. These are most likely to be vasospastic or occlusive; however, acrocyanosis has also been reported.

## CHILBLAINS (PERNIO)

Chilblains constitute a localized erythema and swelling caused by exposure to cold. Blistering and ulcerations may develop in severe cases. In people predisposed by poor peripheral circulation, even moderate exposure to cold may produce chilblains. Cryoglobulins, cryofibrinogens or cold agglutinins may be present and pathogenic. Chilblainlike lesions may occur in discoid and systemic lupus erythematosus (chilblain lupus) or as a presenting sign of leukemia cutis. The chronic use of crack cocaine and its attendant peripheral vasoconstriction will lead to perniosis with cold, numb hands and atrophy of the digital fat pads, especially of the thumbs and index fingers, as well as nail curvature.

Chilblains occur chiefly on the hands, feet, ears, and face, especially in children; onset is enhanced by dampness. A variant occurs on the lateral thighs in women equestrians who ride on cold damp days (equestrian perniosis). Tight-fitting jeans with a low waistband may produce this type of cold injury on the hips. Wading across cold streams may produce similar lesions. Erythrocyanosis crurum has been used to describe similar cases. Lesions of cold injury of the lateral thighs can be nodular.

Patients with chilblains are often unaware of the cold injury when it is occurring, but later burning, itching, and redness call it to their attention. The

affected areas are bluishred, the color partially or totally disappearing on pressure, and are decidedly cool to the touch. Sometimes the extremities are clammy because of excessive sweating. As long as the damp cold exposure continues, new lesions will continue to appear and lesions may resolve slowly. Investigation into an underlying cause should be undertaken in cases that are recurrent, chronic, extending into warm seasons or poorly responsive to treatment.

Perniosis histologically demonstrates a lymphocytic vasculitis. There is dermal edema, and a superficial and deep perivascular, tightly cuffed, lymphocytic infiltrate. The infiltrate involves the vessel walls and is accompanied by characteristic "fluffy" edema of the vessel walls.

## TREATMENT

The affected parts should be protected against further exposure to cold or dampness. If the feet are affected, woolen socks should be worn at all times during the cold months. Because patients are often not conscious of the cold exposure that triggers the lesions, appropriate dress must be stressed, even if patients say they do not sense being cold. Since central cooling triggers peripheral vasoconstriction, keeping the whole body (not just the affected extremity) warm is critical. Heating pads may be used judiciously to warm the parts. Smoking is strongly discouraged.

Nifedipine, 20 mg three times a day, has been effective. Vasodilators such as nicotinamide, 500 mg three times a day, or dipyridamole, 25 mg three times a day, or the phosphodi- esterase inhibitor sildenafil, 50 mg twice daily, may be used to improve circulation. Pentoxifylline may be effective. Spontaneous resolution occurs without treatment in 1-3 weeks. Systemic corticoid therapy is useful in chilblain lupus erythematosus.

## FROSTBITE

When soft tissue is frozen and locally deprived of blood supply, the damage is called frostbite. The ears, nose, cheeks, fingers, and toes are most often affected. The frozen part painlessly becomes pale and waxy. Various degrees of tissue destruction similar to those caused by burns are encountered. These are erythema and edema, vesicles and bullae, superficial gangrene, deep gangrene,

and injury to muscles, tendons, periosteum, and nerves. The degree of injury is directly related to the temperature and duration of freezing. African Americans are at increased risk of frostbite.

## TREATMENT

Early treatment of frostbite before swelling develops should consist of covering the part with clothing or with a warm hand or other body surface to maintain a slightly warm temperature so that adequate blood circulation can be maintained. Rapid rewarming in a water bath between 37 and 43°C (100-110°F) is the treatment of choice for all forms of frostbite. Rewarming should be delayed until the patient has been removed to an area where there is no risk of refreezing. Slow thawing results in more extensive tissue damage. Analgesics, unless contraindicated, should be administered because of the considerable pain experienced with rapid thawing. When the skin flushes and is pliable, thawing is complete. The use of tissue plasminogen activator to lyse thrombi decreases the need for amputation if given within 24 h of injury. Supportive measures such as bed rest, a highprotein/highcalorie diet, wound care, and avoidance of trauma are imperative. Any rubbing of the affected part should be avoided, but gentle massage of proximal portions of the extremity that are not numb may be helpful.

After swelling and hyperemia have developed, the patient should be kept in bed with the affected limb slightly flexed, elevated, and at rest. Exposing the affected limb to air at room temperature relieves pain and helps prevent tissue damage. Protection by a heat cradle may be desirable.

The use of anticoagulants to prevent thrombosis and gangrene during the recovery period has been advocated. Pentoxifylline, ibuprofen, and aspirin may be useful adjuncts. Antibiotics should be given as a prophylactic measure against infection and tetanus immunization should be updated. Recovery may take many months. Injuries that affect the proximal phalanx or the carpal or tarsal area, especially when accompanied by a lack of radiotracer uptake on bone scan, have a high likelihood of requiring amputation. Whereas prior cold injury is a major risk

factor for recurrent disease, sym- pathectomy may be preventative against repeated episodes. Arthritis may be a late complication.

## TRENCH FOOT

Trench foot results from prolonged exposure to cold, wet conditions without immersion or actual freezing. The term is derived from trench warfare in World War I, when soldiers stood, sometimes for hours, in trenches with a few inches of cold water in them. Fishermen, sailors, and shipwreck survivors are sometimes seen with this condition. The lack of circulation produces edema, paresthesias, and damage to the blood vessels. Gangrene may occur in severe cases. Treatment consists of removal from the causal environment, bed rest, and restoration of the circulation. Other measures, such as those used in the treatment of frostbite, should be employed.

## WARM WATER IMMERSION FOOT

Exposure of the feet to warm, wet conditions for 48 h or more may produce a syndrome characterized by maceration, blanching, and wrinkling of the soles and sides of the feet (Fig. 3-10). Itching and burning with swelling may persist for a few days after removal of the cause, but disability is temporary. It was commonly seen in military service members in Vietnam but has also been seen in persons wearing insulated boots.

This condition should be differentiated from tropical immersion foot, seen after continuous immersion of the feet in water or mud at temperatures above 22°C (71.6°F) for 2-10 days. This was known as "paddy foot" in Vietnam. It involves erythema, edema, and pain of the dorsal feet, as well as fever and adenopathy. Resolution occurs 3-7 days after the feet have been dried.

Warm water immersion foot can be prevented by allowing the feet to dry for a few hours in every 24 or by greasing the soles with a silicone grease once a day. Recovery is usually rapid if the feet are thoroughly dry for a few hours.

## SUNBURN AND SOLAR ERYTHEMA

The solar spectrum has been divided into different regions by wavelength. The parts of the solar spectrum important in photomedicine include UV radiation (below 400 nm), visible light (400-760 nm), and infrared radiation (beyond 760 nm). Visible light has limited biologic activity, except for stimulating the retina. Infrared radiation is experienced as radiant heat. Below 400 nm is the UV spectrum, divided into three bands: UVA, 320-400 nm; UVB, 280-320 nm; and UVC, 200280 nm. UVA is divided into two subcategories: UVA I (340400 nm) and UVA II (320-340 nm). Virtually no UVC reaches the earth's surface because it is absorbed by the ozone layer above the earth.

The minimal amount of a particular wavelength of light capable of inducing erythema on an individual's skin is called the minimal erythema dose (MED). Although the amount of UVA radiation is 100 times greater than UVB radiation during midday hours, UVB is up to 1000 times more erythemogenic than UVA, and so essentially all solar erythema is caused by UVB. The most biologically effective wavelength of radiation from the sun for sunburn is 308 nm. UVA does not play a significant role in solar erythema and sunburn; however, in the case of druginduced photosensitivity, UVA is of major importance.

The amount of UV exposure increases at higher altitudes, is substantially larger in temperate climates in the summer months, and is greater in tropical regions. UVA may be reflected somewhat more than UVB from sand, snow, and ice. While sand and snow reflect as much as 85% of the UVB, water allows 80% of the UV to penetrate up to 3 feet. Cloud cover, although blocking substantial amounts of visible light, is a poor UV absorber. During the middle 4-6 h of the day, the intensity of UVB is 2-4 times greater than in the early morning and late afternoon.

## CLINICAL SIGNS AND SYMPTOMS

Sunburn is the normal cutaneous reaction to sunlight in excess of an erythema dose. UVB erythema becomes evident at around 6 h after exposure and

peaks at 12-24 h, but the onset is sooner and the severity greater with increased exposure. The erythema is followed by tenderness, and in severe cases, blistering, which may become confluent. Discomfort may be severe; edema commonly occurs in the extremities and face; chills, fever, nausea, tachycardia, and hypotension may be present. In severe cases such symptoms may last for as long as a week. Desquamation is common about a week after sunburn, even in areas that have not blistered.

After UV exposure, skin pigment undergoes two changes: immediate pigment darkening (IPD, Meirowsky phenomenon) and delayed melanogenesis. IPD is maximal within hours after sun exposure and results from metabolic changes and redistribution of the melanin already in the skin. It occurs after exposure to long-wave UVB, UVA, and visible light. With large doses of UVA, the initial darkening is prolonged and may blend into the delayed melanogenesis. IPD is not photo- protective. Delayed tanning is induced by the same wave - lengths of UVB that induce erythema, begins 2-3 days after exposure, and lasts 10-14 days. Delayed melanogenesis by UVB is mediated through the production of DNA damage and the formation of cyclobutane pyrimidine dimers (CPD). Therefore, although UVB-induced delayed tanning does provide some protection from further solar injury, it is at the expense of damage to the epidermis and dermis. Hence, tanning is not recommended for sun protection. Commercial sunbedinduced tanning, while increasing skin pigment, does not increase UVB MED, and is therefore not protective for UVB damage. An individual's inherent baseline pigmentation, ability to tan, and the ease with which he/she burns are described as his/her "skin type." Skin type is used to determine starting doses of phototherapy and sunscreen recommendations, and reflects the risk of development of skin cancer and photoaging.

Exposure to UVB and UVA causes an increase in the thickness of the epidermis, especially the stratum corneum. This increased epidermal thickness leads to increased tolerance to further solar radiation. Patients with vitiligo may increase their UV exposure without burning by this mechanism.

## TREATMENT

Once redness and other symptoms are present, treatment of sunburn has limited efficacy. The damage is done and the inflammatory cascades are triggered. Prostaglandins, especially of the E series, are important mediators. Aspirin (ASA) and nonsteroidal anti-inflammatory drugs (NSAIDs), including indomethacin, have been studied, as well as topical and systemic steroids. Medium potency (class II) topical steroids applied 6 h after the exposure (when erythema first appears) give a small reduction in signs and symptoms. Since oral NSAIDs and systemic steroids have been tested primarily prior to or immediately after sun exposure, there is insufficient evidence to recommend their routine use, except immediately after solar overexposure. Therefore treatment of sunburn should be supportive, with pain management (using acetaminophen, ASA, or NSAIDs), plus soothing topical emollients or corticosteroid lotions. In general, a sunburn victim experiences at least 1 or 2 days of discomfort and even pain before much relief occurs.

## PROPHYLAXIS

Sunburn is best prevented. Use of the UV index, published daily by the National Weather Service for many US cities and found in newspapers, facilitates taking adequate precautions to prevent solar injury. Numerous educational programs have been developed to make the public aware of the hazards of sun exposure. Despite this, sunburn and excessive sun exposure continue to occur in the US and Western Europe, especially in white persons under the age of 30, among whom more than 50% report at least one sunburn per year. Sun protection programs have four messages:

- Avoid midday sun.
- Seek shade.
- Wear protective clothing.
- Apply a sunscreen.

The period of highest UVB intensity, between 9 am and 3-4 pm, accounts for the vast majority of potentially hazardous UV exposure. This is the time when

the angle of the sun is less than 45° or when a person's shadow is shorter than his/her height. In temperate latitudes it is almost impossible to burn if these hours of sun exposure are avoided. Trees and artificial shade provide substantial protection from UVB. Foliage in trees provides the equivalent of sun protection factor (SPF) 4-50, depending on the density of the greenery. Clothing can be rated by its ability to block UVB radiation. The scale of measure is the UV protection factor (UPF) (analogous to SPF in sunscreens). Although it is an in vitro measurement, as with SPF, it correlates well with the actual protection the product provides in vivo. In general, denser weaves, older, washed clothing, and loosefitting clothing screen UVB more effectively. Wetting a fabric may substantially reduce its UPF. Laundering a fabric in a Tinosorb-containing material (SunGuard) will add substantially to the UPF of the fabric. Hats with at least a 4-inch brim all around are recommended.

A sunscreen's efficacy in blocking the UVB (sunburn- inducing) radiation is expressed as an SPF. This is the ratio of the number of MEDs of radiation required to induce erythema through a film of sunscreen (2 mg/cm$^2$), compared with unprotected skin. Most persons apply sunscreens in too thin a film, so the actual "applied SPF" is about half that on the label. Sunscreening agents include UV-absorbing chemicals (chemical sunscreens) and UV-scattering or blocking agents (physical sunscreens). Available sunscreens, especially those of high SPFs (>30), usually contain both chemical sunscreens (such as p-aminobenzoic acid [PABA], PABA esters, cinna- mates, salicylates, anthranilates, benzophenones, benzylidene camphors such as ecamsule [Mexoryl], dibenzoylmethanes [Parsol 1789, in some products present as a multicompound technology Helioplex], and Tinosorb [S/M]) and physical agents (zinc oxide or titanium dioxide). They are available in numerous formulations, including sprays, gels, emollient creams, and wax sticks. Sunscreens may be water-resistant (maintaining their SPF after 40 min of water immersion) or waterproof (maintaining their SPF after 80 min of water immersion).

For skin types I-III (see Table 3-1), daily application of a sunscreen with an SPF of 30 in a facial moisturizer, foundation, or aftershave is recommended. For outdoor exposure, a sunscreen of SPF 30 or higher is recommended for regular use. In persons with severe photosensitivity and at times of high sun exposure, high-intensity sunscreens of SPF 30+ with inorganic blocking agents may be required. Application of the sunscreen at least 20 min before and 30 min after sun exposure has begun is recommended. This dual application approach will reduce the amount of skin exposure by two- to threefold over a single application. Sunscreen should be reapplied after swimming or vigorous activity or toweling. Sunscreen failure occurs mostly in men, due to failure to apply it to all the sunexposed skin, or failure to reapply sunscreen after swimming. Sunscreens may be applied to babies (under 6 months) on limited areas. Vitamin D supplementation may be recommended with the most stringent sun-protection practices.

Photoaging and cutaneous immunosuppression are mediated by UVA as well as UVB. For this reason, sunscreens with improved UVA coverage have been developed (Parsol 1789, Mexoryl, Tinosorb). The UVA protection does not parallel the SPF on the label. If UVA protection is sought, a combination sunscreen with inorganic agents and UVA organic sunscreens (identified by name in the list of ingredients) is recommended.

## EPHELIS (FRECKLE) AND LENTIGO

Freckles are small (<0.5 cm) brown macules that occur in profusion on the sun-exposed skin of the face, neck, shoulders, and backs of the hands. They become prominent during the summer when exposed to sunlight and subside, sometimes completely, during the winter when there is no exposure. Blonds and red-heads with blue eyes and of Celtic origin (skin types I or II) are especially susceptible. Ephelides may be genetically determined and may recur in successive generations in similar locations and patterns. They usually appear around age 5.

Ephelis must be differentiated from lentigo simplex. The lentigo is a benign discrete hyperpigmented macule appearing at any age and on any part of the body,

including the mucosa. The intensity of the color is not dependent on sun exposure. The solar lentigo appears at a later age, mostly in persons with long-term sun exposure. The backs of the hands and face (especially the forehead) are favored sites.

Histologically, the ephelis shows increased production of melanin pigment by a normal number of melanocytes. Otherwise, the epidermis is normal, whereas the lentigo has elongated rete ridges that appear to be clubshaped.

Freckles and solar lentigines are best prevented by appropriate sun protection. Cryotherapy, topical retinoids, hydroquinone, and lasers are effective in the treatment of solar lentigines.

## PHOTOAGING (DERMATOHELIOSIS)

The characteristic changes induced by chronic sun exposure are called photoaging or dermatoheliosis. An individual's risk for developing these changes correlates with his/her skin type. Risk for melanoma and nonmelanoma skin cancer is also related to skin type. The most susceptible to the deleterious effects of sunlight are those of skin type I blueeyed, faircomplexioned persons who do not tan. They are frequently of Irish or other Celtic or Anglo-Saxon descent. Individuals who have developed photoaging have the genetic susceptibility and have had sufficient actinic damage to develop skin cancer, and therefore require more frequent and careful cutaneous examinations.

Chronic sun exposure and chronologic aging are additive. Cigarette smoking is also important in the development of wrinkles; hence the inability of observers to distinguish solarinduced from smokinginduced skin aging accurately. The areas primarily affected by photoaging are those regularly exposed to the sun: the V area of the neck and chest, back and sides of the neck, face, backs of the hands and extensor arms, and in women the skin between the knees and ankles. The skin becomes atrophic, scaly, wrinkled, inelastic, or leathery with a yellow hue (Milian citrine skin). In some persons of Celtic ancestry, dermatoheliosis produces profound epidermal atrophy without wrinkling, resulting in an almost translucent appearance of the skin through which hyperplastic sebaceous glands and

prominent telangiectasias are seen. These persons are at high risk for nonmelanoma skin cancer. Pigmentation is uneven, with a mixture of poorly demarcated hyperpigmented and white atrophic macules observed. The photodamaged skin appears generally darker because of these irregularities of pigmentation; added to this is dermal hemosiderosis from actinic purpura. Solar lentigines occur on the face and dorsa of the hands.

Many of the textural and tinctorial changes in sundamaged skin are caused by alterations in the upper dermal elastic tissue and collagen. This process is called solar (actinic) elas- tosis, which imparts a yellow color to the skin. Many clinical variants of solar elastosis have been described, and an affected individual may simultaneously have many of these changes. Small yellowish papules and plaques may develop along the sides of the neck. They have been variably named striated beaded lines (the result of sebaceous hyperplasia) or fibroelastolytic papulosis of the neck, which is caused by solar elastosis. At times, usually on the face or chest, this elastosis may form a macroscopic, translucent papule with a pearly color that may closely resemble a basal cell carcinoma (Dubreuilh elastoma, actinic elastotic plaque). Similar plaques may occur on the helix or antihelix of the ear (elastotic nodules of the ear). Poikiloderma of Civatte refers to reticulate hyperpigmentation with telangiectasia, and slight atrophy of the sides of the neck, lower anterior neck, and V of the chest. The submental area, shaded by the chin, is spared (Fig. 3-13). Poikiloderma of Civatte frequently presents in fairskinned men and women in their mid- to late thirties or early forties. Cutis rhomboidalis nuchae (sailor's or farmer's neck) is characteristic of long-term, chronic sun exposure. The skin on the back of the neck becomes thickened, tough, and leathery, and the normal skin markings are exaggerated. Nodular elastoidosis with cysts and comedones occurs on the inferior periorbital and malar skin (Favre-Racouchot syndrome) on the forearms (actinic comedonal plaque) or helix of the ear. These lesions appear as thickened yellow plaques studded with comedones and keratinous cysts. Telangiectasias over the cheeks, ears, and sides of the neck may develop. Because of the damage to the connective tissue of the dermis, skin fragility is prominent, and patients note skin

tearing from trivial injuries. Most commonly, patients complain that even minimal trauma to their extensor arms leads to an ecchymosis, a phenomenon called actinic purpura. As the ecchymoses resolve, dusky brown macules remain for months, increasing the mottled appearance of the skin. White stellate pseudoscars on the forearms are a frequent complication of this enhanced skin fragility. In some patients, soft, fleshcolored to yellow papules and nodules coalesce on the forearms to form a cordlike band extending from the dorsal to the flexural surfaces (solar elastotic bands).

UVB and UVA radiation induce reactive oxygen species (ROS) and hydrogen peroxide. Acting through activator protein (AP)-1, transcription of various matrix-degrading enzymes is upregulated, specifically matrix metalloproteinase (MMP)-1 (collagenase), MMP-3 (stromelysin 1), and MMP-9 (gelatinase). MMP-1 cleaves a critical site on collagens types I and III, creating collagen fragments which are further degraded by MMP-3 and 9. Collagen fragments plus downregulation of procollagen promoters through AP-1 lead to a marked decrease in new collagen formation in UV-exposed skin. In darkly pigmented persons, UV exposure does not activate MMP-1, in part explaining the protective effect of skin pigmentation against photoaging. In chronologically aged skin, due perhaps to ROS generation, MMP-1 levels are also increased through AP-1, and collagen fragments are increased four-fold. Thus, chronologic aging and photoaging may be mediated through an identical biochemical mechanism.

Histologically, chronically sunexposed skin demonstrates homogenization and a faint blue color of the connective tissue of the upper reticular dermis, socalled solar elastosis. This "elastotic" material is derived largely from elastic fibers, stains with histochemical stains for elastic fibers, and demonstrates marked increased deposition of fibulin-2 and its breakdown products. Types I and III collagen are decreased. Characteristically, there is a zone of normal connective tissue immediately below the epidermis and above the elastotic material.

## COLLOID MILIUM

There are two forms of colloid milium: adult and juvenile. Cases of "nodular" colloid degeneration or "paracolloid" may represent severe presentations of adult colloid milium or cases of nodular amyloidosis, but these cases are few in number and reports of them occurred prior to technologies that could have better elucidated their etiology. Pigmented forms of colloid milium associated with hydroquinone use represent ochronosislike pigmentation. In both the adult and juvenile forms of colloid milium, the primary skin lesion is a translucent, fleshcolored, or slightly yellow 1-5 mm papule. Minimal trauma may lead to purpura due to vascular fragility. Histologically, the colloid consists of intradermal, amorphous fissured eosinophilic material. In adult colloid milium lesions appear in the sunexposed areas of the hands, face, neck, forearms, and ears in middleaged and older adults, usually men. Lesions often coalesce into plaques, and may rarely be verrucous. Petrochemical exposures have been associated with adult colloid milium. Lesions have been induced by sunbed exposure, and can be unilateral, usually in commercial drivers. Adult colloid milium may be considered a papular variant of solar elastosis. The colloid material is derived from elastic fibers, and solar elastosis is found adjacent to the areas of colloid degeneration histologically.

Juvenile colloid milium is much rarer. It develops before puberty and there may be a family history. The lesions are similar to the adult form, but appear initially on the face, later extending to the neck and hands. Sun exposure also appears to be important in inducing lesions of juvenile colloid milium. Juvenile colloid milium, ligneous conjunctivitis, and ligneous periodontitis may appear in the same patient and are probably of similar pathogenesis. Histologically, juvenile colloid milium can be distinguished from adult colloid milium by the finding of keratinocyte apoptosis in the overlying epidermis. The colloid material in juvenile colloid milium is derived from the apoptotic keratinocytes and stains for cytokeratin. Treatment with fractional photothermolysis is effective.

## PREVENTION AND TREATMENT

Since both UVB and UVA are capable of inducing the tissue- destructive biochemical pathways implicated in photoaging, sun protection against both portions of the UV spectrum is the primary prevention required against photoaging. Because photoaging, like other forms of radiation damage, appears to be cumulative, reducing the total lifetime UV exposure is the goal. The guidelines outlined above for sunburn prophylaxis should be followed.

The regular use of emollients or moisturizing creams on the areas of sun damage will reduce scaling and may improve fragility by making the skin more pliable. a-Hydroxy acids may improve skin texture when used in lower, nonirritating concentrations. Topical tretinoin, adapalene, and tazarotene can improve the changes of photoaging. Changes are slow and irritation may occur. Chemical peels, resurfacing techniques, laser and other light technologies for the treatment of vascular alterations, pigmented lesions, and dermal alterations, botulinum toxins and soft tissue augmentation are all used to treat the consequences of photoaging. The surgical and laser treatments of photoaging are discussed in Chapter 38.

## PHOTOSENSITIVITY

Photosensitivity disorders include cutaneous reactions that are chemically induced (from an exogenous source), metabolic (inborn errors such as the porphyrias, resulting in the production of endogenous photosensitizers), idiopathic, and light- exacerbated (genetic and acquired). Phototoxicity and the idiopathic disorders are discussed below; the other conditions are covered elsewhere.

## CHEMICALLY INDUCED PHOTOSENSITIVITY

A number of substances known as photosensitizers may induce an abnormal reaction in skin exposed to sunlight or its equivalent. The result may be a markedly increased sunburn response without allergic sensitization called phototoxicity. Phototoxicity may occur from both externally applied (phyto-photodermatitis and berloque dermatitis) and internally administered chemicals

(phototoxic drug reaction). In contrast, photoallergic reactions are true allergic sensitizations triggered by sunlight, produced either by internal administration (photoallergic drug reaction) or by external contact (photoallergic contact dermatitis). Chemicals capable of inducing phototoxic reactions may also produce photoallergic reactions.

In the case of external contactants, the distinction between phototoxicity and photoallergy is usually straightforward. The former occurs on initial exposure, has an onset of less than 48 h, occurs in the vast majority of persons exposed to the phototoxic substance and sunlight, and shows a histologic pattern similar to sunburn. By contrast, photoallergy occurs only in sensitized persons, may have a delayed onset (up to 14 days-the period of initial sensitization), and shows histologic features of allergic contact dermatitis.

## ACTION SPECTRUM

Chemicals known to cause photosensitivity (photosensitizers) are usually resonating compounds with a molecular weight of less than 500. Absorption of radiant energy (sunlight) by the photosensitizer produces an excited state, which in returning to a lower energy state gives off energy through fluorescence, phosphorescence, charge transfer, heat, or formation of free radicals. Each photosensitizing substance absorbs only specific wavelengths of light, called its absorption spectrum. The specific wavelengths of light that evoke a photosensitive reaction are called the action spectrum. The action spectrum is included in the absorption spectrum of the photosensitizing chemical. The action spectrum for photoallergy is mostly in the long ultraviolet (UVA) region and may extend into the visible light region (320-425 nm).

Photosensitivity reactions occur only when there is sufficient concentration of the photosensitizer in the skin, and the skin is exposed to a sufficient intensity and duration of light in the action spectrum of that photosensitizer. The intensity of the photosensitivity reaction is, in general, dosedependent and is worse with a greater dose of photosensitizer and greater light exposure.

## PHOTOTOXIC REACTIONS

A phototoxic reaction is a nonimmunologic reaction that develops after exposure to a specific wavelength and intensity of light in the presence of a photosensitizing substance. It is a sunburn type reaction, with erythema, tenderness, and even blistering occurring only on the sunexposed parts. This type of reaction can be elicited in many persons who have no previous history of exposure or sensitivity to that particular substance, but individual susceptibility varies widely. In general, to elicit a phototoxic reaction, a considerably greater amount of the photosensitizing substance is necessary than that needed to induce a photoallergic reaction. The erythema begins (like any sunburn) within 2-6 h but worsens for 48-96 h before beginning to subside. Exposure of the nailbed may lead to onycholysis, called photo-onycholysis. Phototoxic reactions, especially from topically applied photosensitizers, may cause marked hyperpigmentation, even without significant preceding erythema. The action spectrum for most phototoxic reactions is in the UVA range.

## PHOTOTOXIC TAR DERMATITIS

Coal tar, creosote, crude coal tar, or pitch, in conjunction with sunlight exposure, may induce a sunburn reaction associated with a severe burning sensation (tar "smarts" or "flashes"). Since these volatile hydrocarbons may be airborne, the patient may give no history of touching tar products. The burning and erythema may continue for 1-3 days. While up to 70% of white persons exposed to such a combination develop this reaction, persons with type V and VI skin are protected by their constitutive skin pigmentation. Following the acute reaction, hyper- pigmentation occurs, which may persist for years. Coal tar or its derivatives may be found in cosmetics, drugs, dyes, insecticides, and disinfectants.

## PHYTOPHOTODERMATITIS

Furocoumarins in many plants may cause a phototoxic reaction when they come in contact with skin that is exposed to UVA light. This is called phytophotodermatitis. Several hours after exposure, a burning erythema occurs,

followed by edema and the development of vesicles or bullae. An intense residual hyperpigmentation results that may persist for weeks or months. The intensity of the initial phototoxic reaction may be mild and may not be recalled by the patient despite significant hyperpigmentation. Fragrance products containing bergapten, a component of oil of bergamot, will produce this reaction. If a fragrance containing this 5-methoxypsoralen or other furocoumarin is applied to the skin prior to exposure to the sun or tanning lights, berloque dermatitis may result. This hyperpig- mentation, which may be preceded by redness and edema, occurs primarily on the neck and face. Artificial bergapten free bergamot oil and laws limiting the use of furocoumarins in Europe and the US have made this a rare condition. However, "Florida Water" and "Kananga Water" colognes, formerly popular in the Hispanic, African American, and Caribbean communities, contain this potent photosensitizer and can still be ordered online, as can other aromatherapy products containing furocoumarins.

Most phototoxic plants are in the families Umbelliferae, Rutaceae (rue), Compositae, and Moraceae. Incriminated plants include agrimony, angelica, atrillal, bavachi, buttercup, common rice, cowslip, dill, fennel, fig, garden and wild carrot, garden and wild parsnip, gas plant, goose foot, zabon, lime and Persian lime, lime bergamot, masterwort, mustard, parsley, St John's wort, and yarrow. In Hawaii the anise - scented mokihana berry *(Pelea anisata)* was known to natives for its phototoxic properties (the mokihana burn). It is a member of the rue family. Home tanning solutions containing fig leaves can produce phytophotodermatitis. These may be widespread and severe enough to require burn unit management.

Occupational disability from exposure to the pink rot fungus *(Sclerotinia sclerotiorum),* present on celery roots, occurs in celery farmers. In addition, disease-resistant celery contains furocoumarins and may produce phytophotodermatitis in grocery workers. Usually not enough sensitizing furocou- marin is absorbed from dietary exposure; however, ingested herbal remedies may cause sytemic phototoxicity.

Dermatitis bullosa striata pratensis (grass or meadow dermatitis) is a phytophotodermatitis caused by contact not with grass, but with yellowflowered meadow parsnip or a wild, yellowflowered herb of the rose family. The eruption consists of streaks and bizarre configurations with vesicles and bullae that heal with residual hyperpigmentation. The usual cause is sunbathing in fields containing the phototoxic plants. Similarly, tourists in the tropics will sometimes rinse their hair with lime juice outdoors and streaky hyperpigmentation of the arms and back will result where the lime juice runs down.

Blistering phytophotodermatitis must be differentiated from rhus dermatitis. The vesicles and bullae of rhus are not necessarily limited to the sun-exposed areas, and itching is the most prominent symptom. Lesions continue to occur in rhus dermatitis for a week or more. In phytophotodermatitis the reaction is limited to sun-exposed sites, a burning pain appears within 48 h, and marked hyperpigmentation results. The asymmetry, atypical shapes, and streaking of the lesions are helpful in establishing the diagnosis. These features may, however, lead to a misdiagnosis of child abuse.

Treatment of a severe, acute reaction is similar to the management of a sunburn, with cool compresses, mild analgesics if required, and topical emollients. Use of topical steroids and strict sun avoidance immediately following the injury may protect against the hyperpigmentation. The hyperpigmenta- tion is best managed by "tincture of time."

## IDIOPATHIC PHOTOSENSITIVITY DISORDERS

This group includes the photosensitivity diseases for which no cause is known. They are not associated with external photosensitizers (except for some cases of chronic actinic dermatitis) or inborn errors of metabolism.

## POLYMORPHOUS LIGHT ERUPTION

Polymorphous light eruption (PLE, PMLE) is the most common form of photosensitivity. In various studies among Northern European white persons, a history of PLE can be elicited in between 5% and 20% of the adult population. It

represents about onequarter of all photosensitive patients in referral centers. All races and skin types can be affected. The onset is typically in the first four decades of life and females outnumber males by 2 or 3 : 1. The pathogenesis is unknown, but a family history may be elicited in between 10% and 50% of patients. It has been reported by some investigators that 1020% of patients with PLE may have positive antinuclear antigens (ANAs) and a family history of lupus erythematosus. Photosensitive systemic lupus erythematosus (SLE) patients may give a history of PLE-like eruptions for years before the diagnosis of SLE is made. PLE patients should be followed for the development of symptoms of SLE.

Clinically, the eruption may have several different morphologies, although in the individual patient the morphology is usually constant. The papular (or erythematopapular) variant is the most common, but papulovesicular, eczematous, ery- thematous, and plaque-like lesions also occur. Plaque-like lesions are more common in elderly patients and may closely simulate lupus erythematosus, with indurated, erythematous, fixed lesions. In African Americans, a pinpoint papular variant has been observed, closely simulating lichen nitidus but showing spongiotic dermatitis histologically. Scarring and atrophy do not occur; however, in darkly pigmented races, marked postinflammatory hyper- or hypopigmentation may be present. In some patients, pruritus only without an eruption may be reported (PLE sine eruptione). Some of these patients will develop typical PLE later in life.

The lesions of PLE appear most typically 1-4 days after exposure to sunlight. Patients may report itching and erythema during sun exposure, and development of lesions within the first 24 h. A change in the amount of sun exposure appears to be more critical than the absolute amount of radiation. Patients living in tropical climates may be free of eruption, only to develop disease when they move to temperate zones, where there is more marked seasonal variation in UV intensity. Areas of involvement include the face, the V area of the chest, neck, and arms. In general, for each individual certain areas are predisposed. However, typically, areas protected during the winter, such as the extensor

forearms, are particularly affected, whereas areas exposed all year (face and dorsa of hands) may be relatively spared. The eruption appears most commonly in the spring. Often the eruption improves with continued sun exposure (hardening) so that patients may be clear of the condition in the summer or autumn.

An unusual variant of PLE is juvenile spring eruption of the ears. This occurs most commonly in boys aged 5-12 years, but may also be found in young adult males. It presents in the spring, often after sun exposure on cold but sunny days. Large outbreaks may occur in boys' schools. The typical lesions are grouped small papules or papulovesicles on the helices. Lesions may form visible vesicles and crusting. It is selflimited and does not scar. UVA is the inducing spectrum, and some patients also have lesions of PLE elsewhere. The histologic picture is identical to that of PLE.

Histologically, a perivascular, predominately T-cell, infiltrate is present in the upper and mid dermis. There is often edema and endothelial swelling, with occasional neutrophils. Epidermal changes are variable, with spongiosis and exocytosis the changes most often observed. Occasionally, a virtual absence of findings microscopically may paradoxically be reported and has been referred to as pauci-inflammatory photodermatitis.

The reported action spectrum of PLE varies, possibly depending on the different ethnic backgrounds of reported populations. UVA is most often responsible; however, UVB and both wavelengths in combination are also frequently necessary. Patients often report eruptions following sun exposure through window glass. Visible light sensitivity can also occur, albeit very rarely. Women more commonly than men are sensitive to UVA only, and men are more commonly sensitive to visible light. Men, although the minority of PLE patients, tend to have more severe PLE and broader wavelengths of sensitivity. Most patients react more in affected sites, and in some, lesions can only be induced in affected areas. Phototesting produces variable results. Schornagel et al reported that one protocol, which produced positive results in 83% of tested patients, used four exposures of UVB, UVA, or a combination in previously affected sites.

However, the light sources are not readily available and reported protocols vary widely. In clinical practice the diagnosis is usually made clinically.

In the differential diagnosis of PLE, the following should be considered: lupus erythematosus, photosensitive drug eruption, prurigo nodularis, and photoallergic contact dermatitis. Histopathologic examination, ANA testing, and direct immunofluorescence (DIF) are helpful in distinguishing these diseases. Serologic testing alone may not distinguish PLE from SLE, due to the possibility of positive ANA tests in PLE patients. Lupus erythematosus may present initially with photosensitivity before other features of lupus erythematosus occur.

Therapeutically, most patients with mild disease can be managed by avoiding the sun and using barrier protection and high-SPF, broadspectrum sunscreens. It is critical that the sunblocks contain specific absorbers of longwave UVA (Parsol 1789, Mexoryl, zinc oxide, and titanium dioxide). Sunblocks containing more than one of these agents are more effective. Since UVA is the most common triggering wavelength, good UVA coverage is critical. Most patients do not apply an adequate amount of sunscreen for it to be optimally effective. DermaGard film can be applied to windows at home and in the car to block the transmission of nearly all UBV and UVA, while allowing visible light to be transmitted. Degradation does occur so it should be replaced every 5 years. These measures of photoprotection are critical for all patients, since they are free of toxicity and reduce the amount and duration of other therapies required. Patient education is important in the management of this disease, and phototesting may be required to convince the patient that he/she is UV-sensitive. It will also determine the action spectrum.

The use of topical tacrolimus ointment at night or twice daily, combined with the above measures for sun avoidance and the use of sunscreens, controls many of these patients. At times topical steroids, frequently of super or high potency in several daily to weekly pulses, are necessary to control the pruritus and clear the eruption. Antihistamines (hydroxyzine, diphenhydramine, or doxepin) may be used for pruritus. Systemic corticosteroids in short courses may be

necessary, especially in the spring. In patients whose condition is not controlled by the above measures, hardening in the spring with UVB, narrow-band UVB, or psoralen + UVA (PUVA) can dramatically decrease the sun sensitivity of patients with PLE, and up to 80% of patients can be controlled with phototherapy. In the most sensitive patients, systemic steroids may be needed at the inception of the phototherapy. Systemic hydroxychloroquine sulfate, 200-400 mg/day, may be used. It has a delayed onset and is best instituted in the late winter to prevent spring outbreaks. Chloroquine or quinacrine may be effective if hydroxychloroquine is not, but in general antimalarials are inferior to phototherapy. In the most severe cases, management with azathioprine, cyclosporine, thalidomide, or mycophenolate mofetil may be considered. If these agents are used in a patient considered to have PLE, an evaluation for chronic actinic dermatitis should be performed, as patients with PLE rarely require these agents.

## ACTINIC PRURIGO

Actinic prurigo probably represents a variant of PLE; it is most commonly seen in Native Americans of North and Central America and Colombia. The incidence in Mexico has been reported to be between 1.5% and 3.5%. It has been reported in Europe, Australia, and Japan as well. The female to male ratio is 2 - 6 : 1. Actinic prurigo in Native Americans in the US begins before age 10 in 45% of cases and before age 20 in 72%. Up to 75% of cases have a positive family history (hereditary PLE of Native Americans). In Europe, 80% of cases occur before age 10. In the Inuit Canadian population onset is later and frequently in adulthood.

In childhood, lesions begin as small papules or papulovesicles that crust and become impetiginized. They are intensely pruritic and frequently excoriated. In children, the cheeks, distal nose, ears, and lower lip are typically involved. Cheilitis may be the initial and only feature for years. Conjunctivitis is seen in 10-20% of patients (limbal-type vernal catarrah). Lesions of the arms and legs are also common and usually exhibit a prurigo nodule-like configuration. The eruption may extend to involve sunprotected areas, especially the buttocks, but lesions in these

areas are always less severe. In adults, chronic, dry papules and plaques are most typical, and cheilitis and crusting occur less frequently. Skin lesions tend to persist throughout the year in the tropics, although they are clearly worse during periods of increased sun exposure. In temperate and highlatitude regions, lesions occur from March through the summer and substantially remit in the winter. Hardening, as seen with PLE, does not occur. In up to 60% of patients with actinic prurigo that presents before the age of 20, the condition improves or resolves within 5 years, whereas adults usually have the disease throughout life.

Initial therapy is identical to that for PLE. Thalidomide has been used effectively and safely over many years in this condition. In cases refractory to or intolerant of thalidomide, cyclosporine A can be very effective. Topical cyclosporine A 2% was effective in controlling limbal lesions in one case of actinic prurigo-associated conjunctivitis.

## BRACHIORADIAL PRURITUS

PLE may present initially and only on the brachioradial area. This type of brachioradial eruption was the initial pattern of brachioradial pruritus described and was termed solar pruritus. The majority of cases of brachioradial pruritus, and especially those characterized by severe, refractory, intractable pruritus and secondary severe lichenification, are now felt to represent a form of neuropathic pruritus, related to cervical spine disease (see Chapter 4). Sunlight may be an eliciting factor and cervical spine disease a predisposing factor in patients with brachioradial pruritus. To identify those patients in whom photosensitivity plays a prominent role, a high-SPF (UVA/UVB) sunscreen should be applied to one arm only for several weeks. In cases of PLE this usually leads to improvement of that one arm, as compared to the contralateral unprotected arm. In patients with primarily neuropathic disease, sunscreen application leads to minimal improvement.

## SOLAR URTICARIA

Solar urticaria is most common in females aged 20-40 years. Within seconds to minutes after light exposure, typical urticarial lesions appear and resolve in 1-2 h, rarely lasting more than 24 h. Delayed reactions rarely occur. Chronically exposed sites may have some reduced sensitivity. In severe attacks, syncope, bronchospasm, and anaphylaxis may occur Patients with solar urticaria may be sensitive to wavelengths over a broad spectrum. The wavelengths of sensitivity and the minimal urticarial doses may vary with anatomic site and over time within the same patient. UVA sensitivity is the most common, but visible light sensitivity is also frequently reported. The photosensitivity can be passively transferred, and irradiation of the patient's serum with the activating wavelength followed by reinjection will create a wheal in the patient, but not in an unaffected patient. This suggests the presence of a circulating photoinducible allergen to which the individual patient with solar urticaria is sensitive. In some patients an inhibition spectrum may be identified which inhibits the binding of the endogenous photoallergen to mast cells.

Solar urticaria is virtually always idiopathic. Rarely, medications including tetracycline (but not minocycline), chlorpromazine, progestational agents, and repirinast have been reported to induce solar urticaria. Erythropoietic protopor- phyria and very rarely porphyria cutanea tarda may present with lesions simulating solar urticaria. There are rare reports of solar urticaria in lupus erythematosus.

The diagnosis of solar urticaria is usually straightforward from the history. Phototesting is useful to determine the wavelengths of sensitivity, and to ascertain the minimal urticarial dose (MUD) if UVA desensitization is being considered.

Because many patients have sensitivity in the UVA or even visible range, standard sunscreens are of limited benefit but broad-spectrum sunscreens should be instituted. Antihistamines, especially the nonsedating H1 agents lorata- dine, cetirizine HCl, and fexofenadine, may increase the MUD 10-fold or more. Higher doses, twice or more the standard recommendation, may be required (e.g. 180 mg

of fexofena- dine twice a day). These, plus sun avoidance and broadspectrum sunscreens, are the first-line therapy. PUVA or increasing UVA exposures are effective in more difficult cases, the former having greater efficacy. Rush hardening may induce UVA tolerance, allowing patients to begin PUVA therapy. PUVA is effective, even if the patient is not sensitive to UVA. Cyclosporine A (4.5 mg/kg/day) and intravenous immunoglobulin (IVIG; 0.4 g/kg/day for 5 days repeated monthly) have been anecdotally reported as effective. For the most difficult cases, plasmapheresis may be used to remove the circulating photoallergen, allowing PUVA to be given leading to remission.

## HYDROA VACCINIFORME

Hydroa vacciniforme is a rare, chronic photodermatosis with onset in childhood. Boys and girls are equally represented, but boys present earlier and have disease on average for a longer time. There is a bimodal onset (between ages 1 and 7 and between 12 and 16). The natural history of the typical disorder is for it to remit spontaneously before age 20, but rare cases in young adults do occur. Within 6 h of exposure stinging begins. At 24 h or sooner erythema and edema appear, followed by the characteristic 2-4 mm vesicles. Over the next few days these lesions rupture, become centrally necrotic, and heal with a smallpoxlike scar. Lesions tend to appear in crops with disease-free intervals. The ears, nose, cheeks, and extensor arms and hands are affected. Subungual hemorrhage or oral ulcerations may occur.

Histologically, early lesions show intraepidermal vesiculation and dermal edema that evolves into a subepidermal blister. Necrotic lesions show reticular degeneration of keratinocytes, with epidermal necrosis flanked by spongiosis with a dense perivascular infiltrate of neutrophils and lymphocytes. Dermal vessels may be thrombosed, simulating vasculitis. Lesions may be reproduced by repetitive UVA, with the action spectrum in the 330-360 nm range.

The differential diagnosis includes PLE, actinic prurigo, and erythropoietic protoporphyria. Porphyrin levels are normal in hydroa vacciniforme. In erythropoietic protoporphyria the burning typically begins within minutes of sun

exposure, and over time patients develop diffuse, thickened, waxlike scarring, rather than the smallpoxlike scars of hydroa vacciniforme. Histologic evaluation is useful in distinguishing these two conditions. Treatment is principally to avoid sunlight exposure and to use broadspectrum sunscreens that block in the UVA range. Prophylactic narrowband UVB phototherapy in the early spring may be effective.

A subset of children and, less commonly, adults with photosensitive hydroa vacciniforme-like skin lesions manifest facial swelling, indurated nodules or progressive ulcers, fever and liver damage. Hypersensitivity to mosquito bites may also be seen. These patients may develop Epstein-Barr virus (EBV)-associated NK/T-cell lymphomas and die of this or of a hemo- phagocytic syndrome. The hydroa vacciniforme-like skin lesions may precede the diagnosis of the lymphoma by up to a decade, and initially the patient may appear to have typical hydroa vacciniforme of the selflimited type. This, then, is a disease spectrum, with both typical and severe hydroa vac- ciniforme being EBV-associated. Treatment of the lymphoma may lead to clearing of these lesions.

## CHRONIC ACTINIC DERMATITIS

Chronic actinic dermatitis represents the end stage of progressive photosensitivity in some patients. It has replaced the terms persistent light reactivity, actinic reticuloid, photosensitive eczema, and chronic photosensitivity dermatitis. The basic components of this disease are:

- a persistent, chronic, eczematous eruption in the absence of exposure to known photosensitizers
- usually broad-spectrum photosensitivity with decreased MED to UVA and/or UVB, and at times visible light
- histology consistent with a chronic dermatitis, with or without features of lymphoma.

Clinically, the disease predominantly affects middleaged or elderly men. In the US, patients with skin types V and VI may be disproportionately affected. Skin

lesions consist of edematous, scaling, thickened patches and plaques that tend to be confluent. Lesions occur primarily or most severely on the exposed skin and may spare the upper eyelids, behind the ears, and the bottoms of wrinkles. Involvement of unexposed sites often occurs, progressing to erythroderma in the most severe cases. Marked depigmentation resembling vitiligo may result. Patients may not realize their condition is exacerbated by exposure to light. It may persist in all seasons.

The pathogenesis of this syndrome is unknown. In some patients a preceding topical or oral photosensitizer may be implicated, but the condition fails to improve with discontinuation of the inciting agent. In about onethird of patients, photopatch testing yields a positive response to previously applied agents, especially musk ambrette, sunscreen ingredients, and hexachlorophene. Patch testing to standard agents may have a positive result in about 30% of patients, but no particular relevance is found. However, in up to 85% of European patients, sesquiterpene lactone contact sensitivity from Compositae has been identified. In addition, more than 75% of men over the age of 60 with sesquiterpene lactone sensitivity have abnormal phototesting results. CD8 (suppressor/cytotoxic) T cells are disproportionately represented in the cutaneous infiltrates in the majority of cases, and less commonly, in the peripheral blood. IgE levels may be elevated.

In this clinical setting the diagnosis of chronic actinic dermatitis is established by histologic evaluation and phototest- ing. Phototesting often reproduces the lesions. Around 65% of patients are sensitive to UVA, UVB, and visible light; 22% to UVA and UVB; and 5% to UVB or UVA only. The finding of photosensitivity to UVA and UVB helps to differentiate chronic actinic dermatitis from drug-induced photosensitivity, which usually exhibits only UVA photosensitivity. PLE, photoallergic contact dermatitis, airborne contact dermatitis, and mycosis fungoides or Sezary syndrome must be excluded. PLE is excluded by the broad-spectrum reduced MED in chronic actinic dermatitis, although some patients may begin with a PLE-like disease that later meets the criteria for chronic actinic dermatitis. Contact dermatitis is excluded by patch and

photopatch testing. Mycosis fungoides may be difficult to differentiate from chronic actinic dermatitis in cases with atypical histology. Phototesting is critical in these cases. Mycosis fungoides will manifest a T-cell receptor rearrangement in lesional skin or peripheral blood and usually shows a CD4 (helper) T-cell predominance.

Therapy for chronic actinic dermatitis includes identifying possible topical photosensitizers by photopatch testing and scrupulously avoiding them. Maximum sun avoidance and broadspectrum sunscreens are essential. Topical tacrolimus is useful in some patients. Topical and systemic steroids are effective in some cases, but chronic toxicity of systemic steroids limits chronic usage. Azathioprine, 50-200 mg/day, is the most reproducibly effective treatment and may be required annually during periods of increased sun intensity. Lowdose PUVA can be attempted, but is often not tolerated, even when used with topical and systemic steroids. Hydroxyurea, 500 mg twice a day, benefited one patient. Cyclosporine A, thalido- mide, and mycophenolate mofetil may also be utilized. Immunosuppressive agents may allow patients to tolerate PUVA therapy. With careful management about 1 in 10 patients will lose their photosensitivity within 5 years, 1 in 5 by 10 years, and half of patients by 15 years.

## PHOTOSENSITIVITY AND HIV INFECTION

Photosensitivity resembling PLE, actinic prurigo, or chronic actinic dermatitis is seen in about 5% of human immunodeficiency virus (HIV)-infected persons. In general, photosensitivity is seen when the CD4 count is below 200 (often below 50), except in persons with a genetic predisposition (Native Americans). Photosensitivity may be the initial manifestation of HIV disease. African American patients are disproportionately represented among patients with HIV photosensitivity. Photosensitivity may be associated with ingestion of a photosensitizing medication, especially NSAIDs or trimethoprim-sulfamethoxazole, but the skin eruption often does not improve even when the medication is discontinued. Histologically, the lesions may show subacute or chronic dermatitis, often with a dense dermal infiltrate with many eosinophils.

Histology identical to PLE, lichen planus or lichen nitidus may also occur. When the CD4 count is below 50, especially in black patients, chronic actinic dermatitis with features of actinic prurigo is typical. Widespread vitiliginous lesions may develop. Therapy is difficult, but thalidomide may be beneficial

## RADIODERMATITIS

The major target within the cell by which radiation damage occurs is the DNA. The effects of ionizing radiation on the cells depend on the amount of radiation, its intensity (exposure rate), and the characteristics of the individual cell. Rapidly dividing cells and anaplastic cells in general have increased radiosensitivity when compared with normal tissue. When radiation therapy is delivered, it is frequently fractionated-divided into small doses. This allows the normal cells to recover between doses.

When the dose is large, cell death results. In small amounts, the effect is insidious and cumulative. Mitosis is arrested temporarily, with consequent retardation of growth. The exposure rate affects the number of chromosome breaks. The more rapid the delivery of a certain amount of radiation, the greater the number of chromosome breaks. The number of breaks is also increased by the presence of oxygen.

## ACUTE RADIODERMATITIS

When an "erythema dose" of ionizing radiation is given to the skin, there is a latent period of up to 24 h before visible erythema appears. This initial erythema lasts 2-3 days but may be followed by a second phase beginning up to 1 week after the exposure and lasting up to 1 month. When the skin is exposed to a large amount of ionizing radiation, an acute reaction develops, the extent of which will depend on the amount, quality, and duration of exposure. Such radiation reaction occurs in the treatment of malignancy and in accidental over- exposure. The reaction is manifested by initial erythema, followed by a second phase of erythema at 3-6 days. Vesiculation, edema, and erosion or ulceration may occur, accompanied by pain. The skin develops a dark color that may be mistaken for hyperpigmentation, but that desquamates. This type of radiation injury may

subside in several weeks to several months, again depending on the amount of radiation exposure. Skin that receives a large amount of radiation will never return to normal. It will lack adnexal structures, be dry, atrophic, and smooth, and be hypopigmented or depigmented. Cutaneous necrosis may complicate yttrium-90 synovectomy, a treatment given for chronic synovitis.

## EOSINOPHILIC, POLYMORPHIC, AND PRURITIC ERUPTION ASSOCIATED WITH RADIOTHERAPY

This polymorphic, pruritic eruption arising several days to several months after radiotherapy for cancer tends to favor the extremities. Acral excoriations, erythematous papules, vesicles, and bullae occur. It is not necessarily limited to the areas of radiation treatment. Histologically, a superficial and deep perivascular lymphohistiocytic infiltrate with eosinophils is present. Topical steroids, antihistamines, and UVB are all effective, and spontaneous resolution also occurs.

## CHRONIC RADIODERMATITIS

Chronic exposure to "suberythema" doses of ionizing radiation over a prolonged period will produce varying degrees of damage to the skin and its underlying parts after a variable latent period ranging from several months to several decades. It may also occur on the back or flank after fluoroscopy and roentgenography for diagnostic purposes.

Telangiectasia, atrophy, and hypopigmentation with residual focal increased pigment (freckling) may appear. The skin becomes dry, thin, smooth, and shiny. The nails may become striated, brittle, and fragmented. The capacity to repair injury is substantially reduced, resulting in ulceration from minor trauma. The hair becomes brittle and sparse. In more severe cases these chronic changes may be followed by radiation keratoses and carcinoma. Additionally, subcutaneous fibrosis, thickening, and binding of the surface layers to deep tissues may present as tender, erythematous plaques 6-12 months after radiation therapy. It may resemble erysipelas or inflammatory metastases.

## RADIATION CANCER

After a latent period averaging 20-40 years, various malignancies may develop. Most frequent are basal cell carcinoma (BCC), followed by squamous cell carcinoma (SCC). These may appear in sites of prior radiation, even if there is no evidence of chronic radiation damage. Sun damage may be additive to radiation therapy, increasing the appearance of nonmelanoma skin cancers. SCCs arising in sites of radiation therapy metastasize more frequently than purely suninduced SCCs. In some patients, either type of tumor may predominate. Location plays some role; SCCs are more common on the arms and hands, whereas BCCs are seen on the head and neck and lumbosacral area. Other radiation-induced cancers include angiosarcoma, malignant fibrous histiocytoma, sarcomas, and thyroid carcinoma. The incidence of malignant neoplasms increases with the passage of time.

## TREATMENT

Acute radiodermatitis may be reduced with a topical corticosteroid ointment combined with an emollient cream applied twice a day and instituted at the onset of therapeutic radiotherapy. Chronic radiodermatitis without carcinoma requires little or no attention except protection from sunlight and the extremes of heat and cold. Careful cleansing with mild soap and water, the use of emollients, and, on occasion, hydrocortisone ointment are the only requirements for good care.

The early removal of precancerous keratoses and ulcerations is helpful in preventing the development of cancers. For radiation keratoses treatment with cryosurgery, 5-FU, imiquimod cream, or topical 5-aminolaevulinic acid-photodynamic therapy may be sufficient. If the keratosis feels infiltrated, a biopsy is indicated. Radiation ulcerations should be studied by excisional or incisional biopsy if they have been present for 3 or more months. Complete removal by excision is frequently required to obtain healing and exclude focal carcinoma in the ulceration. Radiationinduced nonmelanoma skin cancers are managed by standard methods. The higher risk of metastasis from radiation-induced SCCs mandates careful follow-up and regular regional lymph node evaluation.

## MECHANICAL INJURIES

Mechanical factors may induce distinctive skin changes. Pressure, friction, and the introduction of foreign substances (such as by injection) are some of the means by which skin injuries may occur.

## CALLUS

Callus is a nonpenetrating, circumscribed hyperkeratosis produced by pressure. It occurs on parts of the body subject to intermittent pressure, particularly the palms and soles, and especially the bony prominences of the joints. Those engaged in various sports, certain occupations, or other repetitive activity develop callosities of distinctive size and location as stigmata. Examples of these are surfer's nodules, boxer's knuckle pads, jogger's toe, rower's rump, tennis toe, jogger's nipple, prayer callus, neck callosities of violinists, bowler's hand, and Russell's sign. The latter are calluses, small lacerations or abrasions on the dorsum of the hand overlying the metacarpophalangeal and interphalangeal joints, and are seen as a clue to the diagnosis of bulimia nervosa.

The callus differs from the clavus in that it has no penetrating central core and it is a more diffuse thickening. It tends to disappear spontaneously when the pressure is removed. Most problems are encountered with calluses on the soles. Ill-fitting shoes, orthopedic problems of the foot caused by aging or a deformity of the foot exerting abnormal pressure, and high activity level are some of the etiologic factors to be considered in painful callosities of the feet.

Padding to relieve the pressure, paring of the thickened callus, and the use of keratolytics, such as 40% salicylic acid plasters, are some of the effective means of relieving painful callosities. Twelve percent ammonium lactate lotion or a urea-containing cream is often helpful

## CLAVUS (CORNS)

Corns are circumscribed, horny, conical thickenings with the base on the surface and the apex pointing inward and pressing on subjacent structures. There

are two varieties: the hard corns, which occur on the dorsa of the toes or on the soles, and the soft corns, which occur between the toes and are softened by the macerating action of sweat. In a hard corn, the surface is shiny and polished and, when the upper layers are shaved off, a core is noted in the densest part of the lesion. It is this core that causes a dull/boring or sharp/lancinating pain by pressing on the underlying sensory nerves. Corns arise at sites of friction or pressure, and when these causative factors are removed, they spontaneously disappear. Frequently, a bony spur or exostosis is present beneath both hard and soft corns of long duration, and unless this exostosis is removed cure is unlikely. The soft interdigital corn usually occurs in the fourth interdigital space of the foot. Frequently, there is an exostosis at the metatarsalphalangeal joint that causes pressure on the adjacent toe. These are soft, soggy, and macerated so that they appear white. Treatment by simple excision may be effective.

Plantar corns must be differentiated from plantar warts, and in most cases this can be done with confidence only by paring off the surface keratin until either the pathognomonic elongated dermal papillae of the wart with its blood vessels, or the clear horny core of the corn can be clearly seen. Porokeratosis plantaris discreta is a sharply marginated, coneshaped, rubbery lesion that commonly occurs beneath the metatarsal heads. Multiple lesions may occur. It has a 3:1 female predominance, is painful, and is frequently confused with a plantar wart or corn. Keratosis punctata of the creases may be seen in the creases of the digits of the feet, where it may be mistaken for a corn.

The relief of pressure or friction by corrective footwear or the application of a ring of soft felt wadding around the region of the corn will often bring a good result. Soaking the feet in hot water and paring the surface by means of a scalpel blade or pumice stone leads to symptomatic improvement. Salicylic acid is successful when carefully and diligently used. After careful paring of the corn with emphasis on removing the center core, 40% salicylic acid plaster is applied. Soaking the foot for half an hour before reapplying the medication enhances the effect. After 48 h the plaster is removed, the white macerated skin is rubbed off,

and a new plaster is reapplied. This is continued until the corn is gone. It should be stressed that removal of any underlying bony abnormality, if present, is often necessary to effect a cure.

## PSEUDOVERRUCOUS PAPULES AND NODULES

These striking 2-8 mm, shiny, smooth, red, moist, flat-topped, round lesions in the perianal area of children are considered to be a result of encopresis or urinary incontinence. There is a similarity to lesions affecting urostomy patients. Protection of the skin will help eliminate them. Similar lesions have been described in women who repeatedly apply Vagisil to the groin

## CORAL CUTS

A severe type of skin injury may occur from the cuts of coral skeletons. The abrasions and cuts are painful, and local therapy may sometimes provide little or no relief. Healing may take months. As a rule, if secondary infection is guarded against, such cuts heal as well as any others. The possibility of *Mycobacterium marinum* infection must be considered in persistent lesions.

## PRESSURE ULCERS (DECUBITUS)

The bedsore, or decubitus, is a pressure ulcer produced anywhere on the body by prolonged pressure. The pressure sore is caused by ischemia of the underlying structures of the skin, fat, and muscles as a result of sustained and constant pressure. Usually, it occurs in chronically debilitated persons who are unable to change position in bed. The bony prominences of the body are the most frequently affected sites. Around 95% of all pressure ulcers develop on the lower body, with 65% in the pelvic area and 30% on the legs. The ulcer usually begins with erythema at the pressure point; in a short time a "punched - out" ulcer develops. Necrosis with a grayish pseudomem- brane is seen, especially in the untreated ulcer. Potential complications of pressure ulcers include sepsis, local infection, osteomyelitis, fistulas, and SCC.

Over 100 risk factors have been identified, with diabetes mellitus, peripheral vascular disease, cerebrovascular disease, sepsis, and hypotension being prominent. Pressure ulcers are graded according to a fourstage system, with the earliest being recognized by changes in one or more of the following: skin temperature, tissue consistency, and/or sensation. The lesion first appears as an area of persistent redness. Stage II is a superficial ulcer involving the epidermis and/or dermis, with the deeper stage III ulcers damaging the subcutaneous fat, and in stage IV, the muscle, bone, tendon, or joint capsule.

Prevention relies on redistributing pressure at a minimum interval of 2 h. Treatment consists of relief of the pressure on the affected parts by frequent change of position, meticulous nursing care, and the use of airfilled products, liquidfilled flotation devices, or foam products. Other measures include ulcer care, management of bacterial colonization and infection, operative repair if necessary, continual education, the ensuring of adequate nutrition, management of pain, and provision of psychosocial support.

Ulcer care is critical. Debridement may be accomplished by sharp, mechanical, enzymatic, and/or autolytic measures. In some cases operative care will be required. Stable heel ulcers are an exception; they do not need debridement if only a dry eschar is present. Wounds should be cleaned initially and each dressing changed by a nontraumatic technique. Normal saline rather than peroxide or povidoneiodine is best. Selection of a dressing should ensure that the ulcer tissue remains moist and the surrounding skin dry.

Occlusive dressings include over 300 marketed products. They are generally classified as film, alginates, foams, hydro- gels, hydrofibers, and hydrocolloid dressings. Transparent films are only used for stage II ulcers, as they only provide light drainage, while hydrofibers are utilized only for fullthickness stage III and IV ulcers. Surgical debridement with reconstructive procedures may be necessary. Adjuvant therapies such as ultrasound, laser, UV, hyperbaric oxygen, electrical stimulation, radiant heat, the application of growth factors, cultured keratinocyte

grafts, skin substitutes, and miscellaneous topical and oral agents are being investigated to determine their place in the treatment of these ulcers.

At times anaerobic organisms colonize these ulcers and cause a putrid odor. The topical application of metronidazole eliminates this odor within 36 h.

## FRICTION BLISTERS

The formation of vesicles or bullae may occur at sites of combined pressure and friction, and may be enhanced by heat and moisture. The feet of military recruits in training, the palms of oarsmen who have not yet developed protective calluses, and the fingers of drummers ("drummer's digits") are examples of those at risk. The size of the bulla depends on the site of the trauma. If the skin is tense and uncomfortable, the blister should be drained, but the roof should not be completely removed as it may act as its own dressing.

In studies focusing on the prevention of friction blister of the feet in long-distance runners and soldiers, acrylic fiber socks with drying action have been found to be effective. Additionally, pretreatment with a 20% solution of aluminum chloride hexa- hydrate for at least 3 days has been shown to reduce foot blisters significantly after prolonged hiking, but at the expense of skin irritation. Emollients decrease the irritation, but reduce the overall effectiveness of the treatment.

## FRACTURE BLISTERS

These blisters overlie sites of closed fractures, especially the ankle and lower leg. They appear a few days to 3 weeks after the injury, and are felt to be caused by vascular compromise. They may create complications such as infection and scarring, especially if bloodfilled or when present in diabetics. They generally heal spontaneously in 5-14 days but may cause delay of surgical reduction of the fracture.

## SCLEROSING LYMPHANGIITIS

This lesion is a cordlike structure encircling the coronal sulcus of the penis, or running the length of the shaft, that has been attributed to trauma during vigorous sexual play. It results from a superficial thrombophlebitis and thus has been renamed Mondor's disease of the penis. Treatment is not necessary; it follows a benign, self-limiting course.

## BLACK HEEL

Synonyms for black heel include talon noir and calcaneal petechiae. A sudden shower of minute, black, punctate macules occurs most often on the posterior edge of the plantar surface of one or both heels, but sometimes distally on one or more toes. Black heel is often seen in basketball, volleyball, tennis, or lacrosse players. Seeming confluence may lead to mimicry of melanoma. The bleeding is caused by shearing stress of sports activities. Paring with a No 15 blade and performing a guaiac test will confirm the diagnosis. Treatment is unnecessary.

## SUBCUTANEOUS EMPHYSEMA

Free air occurring in the subcutaneous tissues is detected by the presence of cutaneous crepitations. Gasproducing organisms, especially *Clostridia*, and leakage of free air from the lungs or gastrointestinal tract are the most common causes. Samlaska et al reviewed the wide variety of causes of subcutaneous emphysema, including penetrating and nonpenetrating injuries, iatrogenic causes occurring during various procedures in hospitalized patients, spontaneous pneumomediastinum such as may occur with a violent cough, childbirth, asthma, Boerhaave syndrome (esophageal rupture after vomiting), or the Heimlich maneuver, intra-abdominal causes, such as inflammatory bowel disease, cancer, perirectal abscess, pancreatitis, or cystitis, dental procedures when using air pressure instruments and highspeed drills, and factitial disease.

## TRAUMATIC ASPHYXIA

Cervicofacial cyanosis and edema, multiple petechiae of the face, neck, and upper chest, and bilateral subconjunctival hemorrhage may occur after prolonged crushing injuries of the thorax or upper abdomen. Such trauma reverses blood flow in the superior vena cava or its tributaries.

## PAINFUL FAT HERNIATION

Also called painful piezogenic pedal papules, this rare cause of painful feet represents fat herniations through thin fascial layers of the weightbearing parts of the heel. These dermatoceles become apparent when weight is placed on the heel and disappear as soon as the pressure is removed. These fat herniations are present in many people but the majority experience no symptoms. However, extrusion of the fat tissue together with its blood vessels and nerves may initiate pain on prolonged standing. Avoidance of prolonged standing wil obviously relieve this pain. Other options include taping of the foot, use of compression stockings, or use of plastic heel cups or padded orthotics to restrict the herniations. Laing et al found 76% of 29 subjects had pedal papules, and interestingly, by placing pressure on the wrists, found 86% to have piezogenic wrist papules.

## NARCOTIC DERMOPATHY

Heroin (diacetylmorphine) is a narcotic prepared for injection by dissolving the heroin powder in boiling water and then injecting it. The favored route of administration is intravenous. This results in thrombosed, cordlike, thickened veins at the sites of injection. Subcutaneous injection ("skin popping") can result in multiple, scattered ulcerations, which heal with discrete atrophic scars. In addition, amphetamines, cocaine, and other drugs may be injected. Subcutaneous injection may result in infections, complications of bacterial abscess and cellulites, or sterile nodules, apparently acute foreign body reactions to the injected drug, or the adulterants mixed with it. These lesions may ulcerate. Chronic persistent, firm

nodules, a combination of scar and foreign body reaction, may result. If cocaine is being injected, it may cause ulcers because of its direct vasospastic effect. Addicts will continue to inject heroin and cocaine into the chronic ulcer bed.

The cutaneous manifestations of injection of heroin and other drugs also include camptodactylia, edema of the eyelids, persistent nonpitting edema of the hands, urticaria, abscesses, atrophic scars, and hyperpigmentation. Pentazocine abuse leads to a typical clinical picture of tense, woody fibrosis, irregular punched-out ulcerations, and a rim of hyperpigmen- tation at the sites of injections. Extensive calcification may occur within the thickened sites.

## FOREIGN BODY REACTIONS

### TATTOO

Tattoos result from the introduction of insoluble pigments into the skin. They may be traumatic, cosmetic, or medicinal in nature, and be applied by a professional or an amateur. Pigment is applied to the skin and then needles pierce the skin to force the material into the dermis. Pigments utilized may be carmine, indigo, vermilion, India ink, chrome green, magnesium (lilac color), Venetian red, aluminum, titanium (white color) or zinc oxide, lead carbonate, copper, iron, logwood, cobalt blue, cinnabar (mercuric sulfide), and cadmium sulfide. Cadmium, cobalt, mercury, and lead are not often used; however, occasional photosensitive reactions to cadmium, which was used for yellow color or to brighten the cinnabar red, are still seen. Tattoo-associated dermopathies may be reactive (allergic, lichenoid, granulomatous, or photosensitive) or infective (inoculation of syphilis, infectious hepatitis, tuberculosis, HIV, warts, molluscum and Hansen's disease), or may induce a Koebner response in patients with active lichen planus or psoriasis. Discoid lupus erythematosus has been reported to occur in the redpigmented portion of tattoos. Occasionally, the tattoo marks may become keloidal. Severe allergic reactions to "temporary tattoos" (painting of pigments such as henna on the surface of the skin) occur when the allergen phenylenediamine is added to make the color more dramatic.

Red tattoos are the most common cause of delayed reactions, with the histologic findings typically showing a lichenoid process. Occasionally, a pseudolymphomatous reaction may occur in red tattoos. Dermatitis in areas of red (mercury), green (chromium), or blue (cobalt) have been described in patients who are patch test-positive to these metals. Sarcoidal, foreign body, and allergic granulomatous reactions may also occur within tattoos. Aluminum may induce such reactions.

Treatment of such reactions is with topical or intralesional steroids. Excision is also satisfactory when the lesions are small enough and situated so that ellipsoid excisions are feasible. They may also be successfully treated with the Q-switched 532 nm neodymium:YAG laser, although generalized allergic reactions occasionally occur with this modality; prevention by treatment with oral steroids and antihistamines has been suggested. Tattoo darkening and nonresponse to laser treatment are not uncommon. Caution must be used when treating fleshcolored and pink-red tattoos, as they may darken after treatment. This is likely due to the reduction of ferric oxide to ferrous oxide. White ink, composed mostly of titanium dioxide, is commonly used to brighten green, blue, yellow, and purple tattoos. Laser irradiation reduces titanium to a bluecolored pigment. Test areas are recommended when treating lightcolored facial tattoos. $CO_2$ resurfacing lasers used conservatively are an alternative to the Q-switched lasers in such patients. A full discussion of laser treatment of tattoos appears in Chapter 38.

## PARAFFINOMA (SCLEROSING LIPOGRANULOMA)

At one time the injection of oils into the skin for cosmetic purposes, such as the smoothing of wrinkles and the augmentation of breasts, was popular. Paraffin, camphorated oil, cottonseed or sesame oil, mineral oil, and beeswax may produce plaquelike indurations with ulcerations after a time lapse of months up to as many as 40 years. Several reports document penile paraffinomas caused by selfinjection. When vaseline gauze or a topical ointment is used to dress unsutured wounds, lipogranulomas or inflammatory mild erysipelaslike lesions with marked

tenderness may occur. Present treatment methods for sclerosing lipogranuloma are unsatisfactory. Surgical removal must be wide and complete.

## GRANULOMAS

### Silicone granuloma

Liquid silicones, composed of long chains of dimethyl siloxy groups, are biologically inert. They have been used for the correction of wrinkles, for the reduction of scars, and for the building up of atrophic depressed areas of the skin. Many case reports detail granulomatous reactions to silicone, some with migration and reactive nodules at points distant from the injection site. As acupuncture needles are coated with silicone, granulomas may occur at the entry points of the needle. The incidence of the nodular swellings, which may be quite destructive and treatmentresistant, remains unknown. It is clear that, if used, medical-grade silicone injected in small volumes should be the rule and that it should not be injected into the penis or the glandular tissue of the breast. For breast augmentation, silicone may be used as silastic implants. If trauma causes rupture of the bag, subcutaneous fibrotic nodules often develop. Human adjuvant disease and sclerodermatous reactions after such events have been reported; however, large reviews have failed to establish an etiologic link to silicone and connective tissue disease. Treatment of silicone granulomas is often not successful. Surgical removal may lead to fistulas, abscesses, and marked deformity. Both minocycline, 100 mg twice a day for several months, and imiquimod cream have been anecdotally useful. Bioplastique consists of polymerized silicone particles dispersed in a gel carrier. When used for lip augmentation, nodules may develop. Histologically, these are foreign body granulomas.

## MERCURY GRANULOMA

Mercury may cause foreign body giant cell or sarcoidal type granulomas, pseudolymphoma, or membranous fat necrosis. It is usually identifiable as egg-shaped, extracellular, dark grey to black irregular globules. The gold lysis test is positive in tissues. Energy-dispersive radiographic spectros- copy may be done

and will identify mercury by the characteristic emission spike. Such testing may be helpful in identifying any foreign substance suspected to have been implanted accidentally or intentionally by the patient. Systemic toxicity or embolus may develop from mercury and may result in death. Therefore excision is necessary and can be accomplished under x-ray guidance.

## BERYLLIUM GRANULOMA

This is seen as a chronic, persistent, granulomatous inflammation of the skin with ulceration that may follow accidental laceration, usually in an occupational setting.

## ZIRCONIUM GRANULOMA

A papular eruption involving the axillae is sometimes seen as an allergic reaction in those shaving their armpits and using a deodorant containing zirconium. Although zirconium was eliminated from aerosol type deodorants in 1978, aluminum-zirconium complex is present in some antiperspi- rants. Additionally, various poison ivy lotions contain zirconium compounds. The lesions are brownish-red, dome-shaped, shiny papules. This is an acquired, delayed type, allergic reaction resulting in a granuloma of the sarcoidal type. After many months the lesions involute spontaneously.

## SILICA GRANULOMA

Automobile and other types of accidents may produce tattooing of dirt (silicon dioxide) into the skin, which induces silica granulomas. These present commonly as black or blue papules or macules arranged in a linear fashion. At times the granulomatous reaction to silica may be delayed for many years, with the ensuing reaction being both chronic and disfiguring. They may be caused by amorphous or crystalline silicon dioxide (quartz), magnesium silicate (talcum), or complex polysilicates (asbestos). Talc granulomas of the skin and peritoneum may develop after surgical operations from the talcum powder used on surgical gloves. Silica granulomas have a statistical association with systemic sarcoidosis, and silica may act as a stimulus for granuloma formation in patients with latent

sarcoidosis. Removal of these granulomas is fraught with difficulties. The best method of care is immediate and complete removal to prevent these reactions. Excision and systemic steroids have been used but recurrences are common. Some reactions may subside spontaneously after 1-12 months. Dermabrasion is a satisfactory method for the removal of dirt accidentally embedded into the skin of the face or scalp.

## CARBON STAIN

Discoloration of the skin from embedded carbon usually occurs in children from the careless use of firearms or firecrackers, or from a puncture wound by a pencil, which may leave a permanent black mark of embedded graphite, easily mistaken for a metastatic melanoma. Narcotic addicts who attempt to clean needles by flaming them with a lighted match may tattoo the carbon formed on the needle as it is inserted into the skin. The carbon is deposited at various depths, which produces a connective tissue reaction and even keloids. Carbon particles may be removed immediately after their deposition using a toothbrush and forceps. This expeditious and meticulous early care results in the best possible cosmetic result. If the particles are left in place long enough, they are best removed using the Q-switched neodymium:YAG laser at 1064 nm. Suzuki reported success in 50 of 51 treated tattoos with an average of 1.7 treatments. However, microexplosions producing poxlike scars have occurred with each laser pulse. Alternatively, dermabrasion may be used. Injected or filler substances utilized for facial rejuvenation may produce foreign body or sarcoidal granulomas. Palpable thickening and nodules, which may occasionally be painful, have been reported to collagen, hyaluronic acid and acrylic hydrogels, polylactic acid, polyalkylimide and polymethylmethacrylate microspheres. The reaction may be delayed for years; at times patients are reluctant to admit to these prior cosmetic interventions and frequently cannot name the filler used. Topical, intralesional, or systemic steroids, at times augmented by tacrolimus, or minocycline or doxycycline have been reported to be helpful medical interventions.

# PRURITUS AND NEUROCUTANEOUS DERMATOSES.

## PRURITUS

Pruritus, commonly known as itching, is a sensation exclusive to the skin. It may be defined as the sensation that produces the desire to scratch. Pruritogenic stimuli are first responded to by keratinocytes, which release a variety of mediators, and fine intraepidermal C-neurons filaments. Approximately 5% of the afferent unmyelinated C neurons respond to pruritogenic stimuli. Itch sensations in these nerve fiber endings in the subepidermal area are transmitted via the lateral spino- thalamic tract to the brain. Here a variety of foci generate both stimulatory and inhibitory responses. The sum of this complicated set of interactions appears to determine the quality and intensity of itch.

Itching may be elicited by many normally occurring stimuli, such as light touch, temperature change, and emotional stress. Chemical, mechanical, and electrical stimuli may also elicit itching. The brain may reinterpret such sensations as being painful or causative of burning or stinging sensations. A large group of neuromediators have been identified. Some of the most important mediators are histamine, serotonin, tryptate, opioid peptides, substance P, prostaglandins such as PGE2, acetylcholine, cytokines such as interleukin (IL)-2, and a variety of neuropeptides and vasoactive peptides. Investigation is ongoing to discover the relative importance of each of these and to determine under which clinical circumstances therapeutic targeting of these molecules will lead to relief of symptoms.

Itch has been classified into four primary categories: prurito- ceptive, or that initiated by skin disorders, itch caused by systemic disorders, neuropathic itch due to disorders of the central or peripheral nervous systems, and psychogenic itch (the type observed in parasitophobia). An overlap or mixture of these may be causative in any individual patient.

## PATTERNS OF ITCHING

There are wide variations from person to person, and in the same person there may be a variation in reactions to the same stimulus. Heat will usually aggravate preexisting pruritus. Stress, absence of distractions, anxiety, and fear may all enhance itching. It is apt to be most severe at the time of undressing for bed. Severe pruritus, with or without prior skin lesions, may be paroxysmal in character with a sudden onset, often severe enough to awaken the patient. It may stop instantly and completely as soon as pain is induced by scratching. However, the pleasure of scratching is so intense that the patient despite the realization that he/she is damaging the skin is often unable to stop short of inflicting such damage. Itching of this distinctive type is characteristic of a select group of dermatoses: lichen simplex chronicus, atopic dermatitis, num- mular eczema, dermatitis herpetiformis, neurotic excoriations, eosinophilic folliculitis, uremic pruritus, subacute prurigo, paraneoplastic itch (usually secondary to lymphoma), and prurigo nodularis. In general, only these disorders produce such intense pruritus and scratching as to induce bleeding. In individual cases, other diseases may manifest such severe symptoms.

## TREATMENT

General guidelines for therapy of the itchy patient include keeping cool, and avoidance of hot baths or showers and of wool clothing. The latter is a nonspecific irritant, as is xerosis. Many patients note itching increases after showers, when they wash with soap and then dry roughly. Using soap only in the axilla and inguinal area, patting dry, and applying a moisturizer will often help avoid such exacerbations. Patients often use an ice bag or hot water to calm pruritus; however, hot water can irritate the skin, is effective only for short periods, and over time exacerbates the condition.

Relief of pruritus with topical remedies may be achieved with topical anesthetic preparations. Many contain benzocaine, which may produce contact

sensitization. Pramoxine in a variety of vehicles, lidocaine 5% ointment, EMLA ointment (a eutectic mixture of lidocaine and prilocaine) and lidocaine gel are preferred anesthetics that may be quite useful in localized conditions. EMLA and lidocaine may be toxic if applied to large areas. Topical antihistamines are generally not recommended, although doxepin cream may be effective for mild pruritus when used alone. Doxepin cream may cause contact allergy or a burning sensation, and somnolence may occur when doxepin is used over large areas. Topical lotions that contain menthol or camphor feel cool and improve pruritus. Others with specific ceramide content designed to mimic that of the normal epidermal barrier are useful. Capsaicin, by depleting substance P, can be effective, but the burning sensation present during initial use frequently causes patients to discontinue its use. Topical steroids and calcineurin inhibitors effect a decrease in itching via their anti-inflammatory action, and therefore are of limited efficacy in neurogenic, psycho- genic and systemic disease-related pruritus. Phototherapy with ultraviolet (UV) B, UVA, and PUVA may be useful in a variety of dermatoses and pruritic disorders. Many oral agents are available to treat pruritus. The most frequently utilized by nondermatologists are the antihistamines. Firstgeneration H antihistamines, such as hydroxyzine and diphenhydramine, may be helpful in nocturnal itching, but their efficacy as antipruritics in many disorders, with the exception of urticaria and mastocytosis, is disappointing. Doxepin is an exception in that it has the ability to reduce anxiety and depression, and has utility in several pruritic disorders. Sedating antihistamines should be prescribed cautiously because of their impairment of cognitive ability. The nonsedating antihistamines and $H_2$ blockers are only effective in urticaria and mast cell disease. Opioids are involved in itch induction. In general, activation of opioid receptors stimulates itch, while κ-opioid receptor stimulation inhibits itch perception; however, the interaction is complex. Additionally, opioid altering agents such as naltrexone, naloxone, nalfurafine, and butorphanol have significant side effects and varying modes of delivery (intravenous, intranasal, and oral). Initial reports of utility in one condition are often followed by conflicting reports

on further study. Specific recommendations in selected pruritic conditions are detailed in those sections. They appear most useful for cholestatic pruritus. Central reduction of itch perception may be effected by anticonvulsants and antidepressants. Gabapentin and pregabalin are examples of the former, while mirtazapine, paroxetine, sertraline, and fluoxetine are examples of the latter. Ondansetron, a serotonin receptor antagonist, had initial reports of efficacy in some pruritic disorders; however, more detailed investigation has revealed its utility to be minimal. Finally thalidomide, through a variety of direct neural effects, immunomodulatory actions and hypnosedative effects, is also useful in selected patients.

## INTERNAL CAUSES OF PRURITUS

Itching may be present as a symptom in a number of internal disorders. The intensity and duration of itching vary from one disease to another. Among the most important internal causes of itching are liver disease, especially obstructive and hepatitis C (with or without evidence of jaundice or liver failure), renal failure, hypo- and hyperthyroidism, hematopoietic diseases such as iron deficiency anemia, polycythemia vera, neoplastic diseases such as lymphoma (especially Hodgkin disease), leukemia, and myeloma, internal solid tissue malignancies, intestinal parasites, carcinoid, multiple sclerosis, acquired immunodeficiency syndrome (AIDS), and neuropsychiatric diseases, with anorexia nervosa prominent among the latter. Diabetes mellitus is frequently listed as an internal cause of pruritus but most individuals with diabetes do not itch. If a diabetic patient has pruritus with no primary skin lesions, other causes of pruritus should be investigated.

The pruritus of Hodgkin disease is usually continuous and at times is accompanied by severe burning. The incidence of pruritus is between 10% and 30% and is the first symptom of this disease in 7% of patients. Its cause is unknown. The pruritus of leukemia, except for chronic lymphocytic leukemia, has a tendency to be less severe than in Hodgkin disease.

Internal organ cancer may be found in patients with generalized pruritus that is unexplained by skin lesions. However, no significant overall increase of malignant neoplasms can be found in patients with idiopathic pruritus. A suggested work-up for chronic, generalized pruritus includes taking a complete history, performing a thorough physical examination and carrying out the following laboratory tests: a complete blood count (CBC) and differential, thyroid, liver, and renal panels, hepatitis C serology, an human immunodeficiency virus (HIV) antibody (if risk factors are present), urinalysis, stool for occult blood, serum protein electrophoresis, and chest xray evaluation. Presence of eosinophilia on the CBC is a good screen for parasitic diseases, but if the patient has been on systemic corticosteroids, blood eosinophilia may not be a reliable screen for parasitic diseases and stool samples for ova and parasites should be submitted. Additional radio- logic studies or specialized testing, as indicated for the patient's age and as dictated by the history and physical findings, should be performed. A biopsy for direct immunofluorescence can occasionally be helpful to detect dermatitis herpetiformis or pemphigoid.

## CHRONIC KIDNEY DISEASE

Chronic kidney disease (CKD) is the most common systemic cause of pruritus; 20-80% of patients with chronic renal failure itch. The pruritus is often generalized, intractable, and severe; however, dialysis-associated pruritus may be episodic, mild, or localized to the dialysis catheter site, face, or legs.

The mechanism of pruritus associated with CKD is multifactorial. Xerosis, secondary hyperparathyroidism, increased serum histamine levels, hypervitaminosis A, iron deficiency anemia, and neuropathy have been implicated. Complications such as Kyrle disease, acquired perforating disease, lichen simplex chronicus, and prurigo nodularis may develop and contribute to the degree and severity of pruritus.

CKD-associated pruritus responds well to narrow-band UVB phototherapy but often recurs after discontinuation. Many patients have concomitant xerosis, and aggressive use of emollients, including soaking and smearing, may help them.

Gabapentin given three times weekly at the end of hemodialysis sessions can be effective, but its renal excretion is decreased in CKD so a low initial dose of 100 mg after each session with slow upward titration is recommended. In recalcitrant disease, the options include colestyramine, 5 g twice a day, or activated charcoal, 6 g/day. Naltrexone, topical tacrolimus and ondansetron were reported to be useful in initial trials, but subsequent studies indicate they are ineffective. Thalidomide, topical capsaicin, intranasal butorphanol, and intravenous lidocaine are less practical options. Renal transplantation will eliminate pruritus.

## BILIARY PRURITUS

Chronic liver disease with obstructive jaundice may cause severe generalized pruritus, and 20-50% of patients with jaundice have pruritus. This itching is probably caused by central mechanisms, as suggested by elevated central nervous system (CNS) opioid peptide levels, downregulation of opioid peptide CNS receptors, and the reported therapeutic effectiveness of naloxone, butorphanol, naltrexone, or nalmefene. Opioid withdrawaltype reactions may occur. The serum-conjugated bile acid levels do not correlate with the severity of pruritus.

## PRIMARY BILIARY CIRRHOSIS

Primary biliary cirrhosis occurs almost exclusively in women older than 30 years of age. Itching may begin insidiously and be the presenting symptom in a quarter to one half of patients. With time, extreme pruritus develops in nearly 80% of patients. This almost intolerable itching is accompanied by jaundice and a striking melanotic hyperpigmentation of the entire skin; the patient may turn almost black, except for a hypopigmented "butterfly" area in the upper back. Eruptive xanthomas, plane xanthomas of the palms, xanthelasma, and tuberous xanthomas over the joints may be seen.

Dark urine, steatorrhea, and osteoporosis occur frequently. Serum bilirubin, alkaline phosphatase, serum ceruloplasmin, serum hyaluronate, and cholesterol values are increased. The antimitochondrial antibody test is positive. The disease is usually relentlessly progressive with the development of hepatic failure. Several cases have been accompanied by scleroderma.

To treat the pruritus, opioid antagonists, such as naltrexone, 50 mg/day, have proven efficacy but significant side effects. Additionally, colestyramine, 4 g 1-3 times a day, UVB twice weekly, and rifampin, 300-450 mg/day, have been reported to be effective. The latter should be used with caution as it may cause hepatitis. Ondansetron was not effective in a controlled trial. Liver transplantation is the definitive treatment for end- stage disease and provides dramatic relief from the severe pruritus.

## POLYCYTHEMIA VERA

More than one third of patients with polycythemia vera report pruritus; it is usually induced by temperature changes or several minutes after bathing. The cause is unknown.

Aspirin has been shown to provide immediate relief from itching; however, there is a risk of hemorrhagic complications, and low doses are recommended. PUVA and narrow-band UVB are also effective. A marked improvement is noted after an average of six treatments, while a complete remission occurs within 2-10 weeks in 8 of 10 treated patients. Paroxetine, most prevalent. Other intestinal parasites such as *Taenia solium*, *T. saginata*, amebiasis, and *Strongyloides stercoralis* may produce pruritus. Pediculosis pubis may cause anal itching; however, attention is focused by the patient on the pubic area, where itching is most severe. Scabies may be causative, but will usually also involve the finger webs, wrists, axillae, areolae, and genitals.

Seborrheic dermatitis of the anal area may cause pruritus ani. It usually also involves other areas, such as the inguinal regions, scalp, chest, and face. Similarly, lichen planus may involve the perianal region. Anal psoriasis may cause itching. The perianal lesions are usually sharply marginated, and psoriatic lesions may be present on other parts of the body. Other frequent sites for psoriasis should be examined, such as the fingernails.

A thorough examination for malignancies should be carried out; extramammary Paget's disease is easily overlooked. Lumbosacral radiculopathy

may be present, as assessed by radiographs and nerve conduction studies; paravertebral blockade may help these patients.

### TREATMENT

Meticulous toilet care should be followed, no matter what the cause of the itching. After defecation, the anal area should be cleansed with soft cellulose tissue paper and, whenever possible, washed with mild soap and water. Cleansing with wet toilet tissue is advisable in all cases. Medicated cleansing pads, such as Tucks, should be used regularly. A variety of moist toilet tissue products are now available. Contact allergy to preservatives in these products is occasionally a problem. An emollient lotion, Balneol, is helpful for cleansing without producing irritation.

Except in psychogenic pruritus ani, once the etiologic agent has been identified, a rational and effective treatment regimen may be started. Topical corticosteroids are effective for most noninfectious types of pruritus ani; however, use of topical tacrolimus ointment will frequently suffice and is safer. Pramoxine hydrochloride, a nonsteroidal topical anesthetic, is also often effective, especially in a lotion form combined with hydrocortisone. In pruritus ani, as well as in pruritus scroti and vulvae, it is sometimes best to discontinue all topical medications and treat with plain water sitz baths at night, followed immediately by plain petrolatum applied over wet skin. This soothes the area, provides a barrier, and eliminates contact with potential allergens and irritants.

## PRURITUS SCROTI

The scrotum of an adult is relatively immune to dermatophyte infection, but it is a favorite site for circumscribed neurodermatitis (lichen simplex chronicus). Psychogenic pruritus is probably the most frequent type of itching seen. Why it preferentially affects this area, or in women the vulva, is unclear. Lichenification may result, be extreme, and persist for many years despite intensive therapy.

Infectious conditions may complicate or cause pruritus on the scrotum but are less common than idiopathic scrotal pru ritus. Fungal infections, except candidiasis, usually spare the scrotum. When candidal infection affects the scrotum, burning rather than pruritus is frequently the primary symptom. The scrotum is eroded, weepy, or crusted. The scrotum may be affected to a lesser degree in cases of pruritus ani, but this pruritus usually affects the midline, extending from the anus along the midline to the base of the scrotum, rather than the dependent surfaces of the scrotum, where pruritus scroti usually occurs. Scrotal pruritus may be associated with allergic contact dermatitis from topical medications, including topical steroidal agents.

Topical corticosteroids are the mainstay of treatment, but caution should be exercised. The "addicted scrotum syndrome" may be caused by the use of high-potency topical steroidal agents. Although this is usually seen after chronic use, even short-term high-potency steroid medications may produce it. The scrotum is frequently in contact with inner thigh skin, producing areas of occlusion, which increases the penetration of topical steroidal agents. If topical steroids are utilized in this area, those of low potency are favored. As with facial skin, high-potency steroids used on the scrotum can result in addictive skin; every time the patient attempts to taper off the steroid, severe burning and redness occur. Topical tacrolimus ointment is useful in overcoming the effects of overuse of potent topical steroids. Another alternative is gradual tapering to less and less potent corticosteroids. Other useful nonsteroidal alternatives include topical pramoxine, doxepin, or simple petrolatum, the latter applied after a sitz bath as described for pruritus ani.

## PRURITUS VULVAE

The vulva is a common site for pruritus of different causes. Pruritus vulvae is the counterpart of pruritus scroti. In a prospective series of 141 women with chronic vulvar symptoms, the most common causes were unspecified dermatitis (54%), lichen sclerosus (13%), chronic vulvovaginal candidiasis (10%),

dysesthetic vulvodynia (9%), and psoriasis (5%). In prepubertal children such itching is most frequently irritant in nature and they generally benefit from education about improved hygienic measures.

Vaginal candidiasis is a frequent cause of pruritus vulvae. This is true especially during pregnancy and when oral antibiotics are taken. The inguinal, perineal, and perianal areas may be affected. Microscopic examination for *Candida albicans* and cultures for fungus should be performed. *Trichomonas vaginitis* may cause vulvar pruritus. For the detection of *T. vaginalis*, examination of vaginal secretions is often diagnostic. The organism is recognized by its motility, size (somewhat larger than a leukocyte), and piriform shape.

Contact dermatitis from sanitary pads, contraceptives, douche solutions, fragrance, colophony, corticosteroids, and a partner's condoms may account for vulvar pruritus. Urinary incontinence should also be considered. Lichen sclerosus is another frequent cause of pruritus in the genital area in middleaged and elderly women. Lichen planus may involve the vulva, resulting in pruritus and mucosal changes, including resorption of the labia minora and atrophy.

When burning rather than itching predominates, the patient should be evaluated for signs of sensory neuropathy.

## TREATMENT

Candidiasis is treated with topical anticandidal agents. A single 150 mg dose of fluconazole is effective for acute candidiasis, but chronic disease with pruritus may require 150 mg/day for 5 days, followed by 150 mg/week for several months. *Trichomonas* infection is best treated with oral metronidazole or by vaginal gel or inserts. Lichen sclerosus responds best to pulsed dosing of high-potency topical steroids or to topical tacrolimus or pimecrolimus. Topical steroidal agents and topical tacrolimus may be used to treat psychogenic pruritus or irritant or allergic reactions. Highpotency topical steroids are effective in treating lichen planus, but other options are also available. Topical lidocaine, topical pramoxine, or an oral tricyclic antidepressant may be helpful in select cases. Any chronic skin disease that does not appear to be responding to therapy should prompt a biopsy. Referral

to a physician specializing in vulvar diseases should be considered for patients whose condition is unresponsive to therapy. In chronic idiopathic forms hypnosis therapy may be useful.

## PUNCTA PRURITICA (ITCHY POINTS)

"Itchy points" consists of one or two intensely itchy spots in clinically normal skin, sometimes followed by the appearance of seborrheic keratoses at exactly the same site. Others believe puncta pruritica is a variant of notalgia paresthetica. Curettage, cryosurgery, or punch biopsy of the itchy points may cure the condition.

## AQUAGENIC PRURITUS AND AQUADYNIA

Aquagenic pruritus is itching evoked by contact with water of any temperature. Degranulation of mast cells and increased concentration of histamine and acetylcholine in the skin after contact with water are found. In most cases there is severe, prickling discomfort within minutes of exposure to water or on cessation of exposure to water, and there is often a family history of similar symptoms.

Aquagenic pruritus must be distinguished from xerosis or asteatosis and an initial trial of "soaking and smearing," as described for winter itch above, is recommended. The condition may be associated with polycythemia vera, hyper-eosinophilic syndrome, juvenile xanthogranuloma, and myelodysplastic syndrome. Treatment options include the use of antihistamines, systemic steroids, sodium bicarbonate dissolved in bath water, propranolol, naltrexone, and UVB or psoralen + UVA (PUVA) phototherapy. One patient found tight-fitting clothing settled the symptoms after only 5 minutes.

Shelley et al reported two patients with widespread burning pain that lasted 15-45 min after water exposure. They called this reaction aquadynia and consider the disorder a variant of aquagenic pruritus. Clonidine and propranolol seemed to provide some relief.

## SCALP PRURITUS

Pruritus of the scalp, especially in elderly persons, is rather common. Lack of excoriations, scaling, or erythema excludes inflammatory causes of scalp pruritus such as seborrheic dermatitis, psoriasis, dermatomyositis or lichen simplex chronicus. Most such cases remain idiopathic, but some represent chronic folliculitis. Treatment is challenging. Topical tar shampoos, salicylic acid shampoos, corticosteroid topical gels, mousse, shampoos, and liquids, and in severe cases with localized itch, an intralesional injection of corticosteroid suspension can sometimes provide relief. Minocycline or oral antihistamines may be helpful. In other patients, low doses of anti- depressants, such as doxepin, are useful.

## DRUG-INDUCED PRURITUS

Medications should be considered a possible cause of protracted pruritus with or without a skin eruption. For instance, pruritus is frequently present after opioid use. Also chloroquine and amodiaquine produce pruritus in many patients treated for malaria.

Hydroxyethyl starch (HES) is used as a volume expander, a substitute for human plasma. One-third of all patients treated will develop severe pruritus with long latency of onset (3-15 weeks) and persistence. Up to 30% of patients have localized symptoms. Antihistamines are ineffective. HES deposits are found in the skin of all patients tested, distributed in dermal macrophages, endothelial cells of blood and lymph vessels, perineural cells, endoneural macrophages of larger nerve fascicles, keratinocytes, and Langerhans cells. Substance P release from macrophages is not increased, and basophil degranulation test results are negative, suggesting that the actions of HES-induced pruritus result from the direct stimulation of cutaneous nerves.

## CHRONIC PRURITIC DERMATOSES OF UNKNOWN CAUSE

Prurigo simplex is the preferred term for the chronic itchy idiopathic dermatosis described below. Papular dermatitis, subacute prurigo, "itchy red bump" disease, and Rosen papular eruption in black men most likely represent variations of prurigo simplex. The term prurigo continues to lack nosologic precision.

Prurigo is characterized by the lesion known as the prurigo papule, which is dome-shaped and topped with a small vesicle. The vesicle is usually present only transiently because of its immediate removal by scratching, so that a crusted papule is more frequently seen. Prurigo papules are present in various stages of development and are seen mostly in middleaged or elderly persons of both sexes. The trunk and extensor surfaces of the extremities are favorite sites, symmetrically distributed. Other areas include the face, neck, lower trunk, and buttocks. The lesions usually appear in crops, so that papulovesicles and the late stages of scarring may be seen at the same time.

The histopathology of prurigo simplex is nonspecific, but often suggests an arthropod reaction. Spongiosis accompanied by a perivascular mononuclear infiltrate with some eosinophils is often found.

Many conditions may cause pruritic erythematous papules. Scabies, atopic dermatitis, insect bite reactions, papular urticaria, dermatitis herpetiformis, contact dermatitis, pityriasis lichenoides et varioliformis acuta (PLEVA), transient acantho- lytic dermatosis (TAD), papuloerythroderma of Ofuji, dermatographism, and physical urticarias should be considered. Biopsy may be helpful in differentiating dermatitis herpeti- formis, PLEVA, TAD, and, on occasion, unsuspected scabies.

### TREATMENT

The medications for initial treatment of prurigo simplex and its variants should be topical corticosteroids and oral antihis- tamines. Early in the disease process, moderate-strength steroids should be used; if the condition is found to be unresponsive, a change to highpotency forms is indicated. Rebound may occur.

Intralesional injection of triamcinolone will eradicate individual lesions. For more recalcitrant disease, UVB or PUVA therapy may be beneficial.

## PRURIGO PIGMENTOSA

Prurigo pigmentosa is a rare dermatosis of unknown cause characterized by the sudden onset of erythematous papules or vesicles that leave reticulated hyperpigmentation when they heal. The condition mainly affects Japanese. Only a few cases have been reported in white persons. Men outnumber women 2:1. The mean age of onset is 25. It is associated with weight loss, dieting, anorexia, diabetes, and ketonuria. It is exacerbated by heat, sweating, and friction, and thus occurs most commonly in the winter and spring. The areas most frequently involved are the upper back, nape, clavicular region, and chest. Mucous membranes are spared. Histology of early lesions shows neutrophils in the dermal papillae and epidermis. Following this, a lichenoid dermatitis with variable psoriasiform hyperplasia occurs. Direct immunofluorescence yields negative findings. The cause is unknown. Minocycline, 100-200 mg/day, is the treatment of choice. Dapsone and alteration of the diet are also effective but topical steroids are not. Recurrence and exacerbations are common.

## PAPULOERYTHRODERMA OF OFUJI

A rare disorder most commonly found in Japan, papuloerythroderma of Ofuji is characterized by pruritic papules that spare the skinfolds, producing bands of uninvolved cutis, the socalled deckchair sign. Frequently there is associated blood eosinophilia. This condition is considered by some to be a form of erythroderma in the elderly and by others to be a paraneoplastic syndrome. Skin biopsies reveal a dense lymphohistio- cytic infiltrate, eosinophils in the papillary dermis, and increased Langerhans cells. Reported malignancies include T-cell lymphomas, B-cell lymphomas, Sezary syndrome, and visceral carcinomas. Not enough cases have been reported to determine a true association with cancer. Other associations are hepatitis C infection and medication reactions to aspirin, ranitidine, and furosemide.

The differential diagnosis is the same as for prurigo simplex. Systemic steroids are the treatment of choice, and may result in long-term remissions. Topical steroids, tar derivatives, emollients, systemic retinoids, cyclosporine, and PUVA may also be therapeutic.

## LICHEN SIMPLEX CHRONICUS

This is also known as circumscribed neurodermatitis. As a result of longcontinued rubbing and scratching, more vigorously than a normal pain threshold would permit, the skin becomes thickened and leathery. The normal markings of the skin become exaggerated, so that the striae form a crisscross pattern, and between them a mosaic is produced composed of flattopped, shiny, smooth, quadrilateral facets. This change, known as lichenification, may originate on seemingly normal skin or may develop on skin that is the site of another disease, such as atopic or allergic contact dermatitis or ringworm. Such underlying etiologies should be sought and, if found, treated specifically. Paroxysmal pruritus is the main symptom.

Circumscribed, lichenified, pruritic patches may develop on any part of the body; however, the disease has a predilection for the back and sides of the neck, and the extremities, especially the wrists and ankles. At times, the eruption is decidedly papular, resembling lichen planus; in other instances, the patches are excoriated, slightly scaly or moist, and, rarely, nodular.

Several distinctive types are recognized. Lichen simplex nuchae often occurs on the back of the neck. It is not unusual to find this area excoriated and bleeding. Nodular neurodermatitis of the scalp consists of multiple pruritic and excoriated papules and may be called prurigo of the scalp. The nodules or papules may ooze and form crusts and scales. The vulva, scrotum, and anal area can be sites of severe neurodermatitis. Genital and anal areas, however, are seldom involved at the same time. An upper eyelid, the orifice of one or both ears, or a palm or sole may also be involved; the ankle flexure is also a favorite site. Persistent rubbing of the shins or upper back may result in dermal deposits of

amyloid and the subsequent development of lichen and macular amyloidosis, respectively.

To what extent mechanical trauma plays a role in producing the original irritation is not known. The onset of this derma tosis is usually gradual and insidious. Chronic scratching of a localized area is a response to unknown factors; however, stress and anxiety have long been thought important.

## TREATMENT

Essentially, cessation of pruritus is the goal. It is important to stress the need for the patient to avoid scratching the areas involved if the sensation of itch is ameliorated. Recurrences are frequent, even after the most thorough treatment, and there are instances in which the clearance of one lesion will see the onset of another elsewhere.

High-potency agents, such as clobetasol propionate, diflorasone diacetate, or betamethasone dipropionate cream or ointment, should be used initially but not indefinitely because of the potential for steroidinduced atrophy. Occlusion of medium-potency steroids may be beneficial. Use of a steroidcontaining tape to provide both occlusion and anti-inflammatory effects may have benefit. Treatment can be shifted to the use of mediumto lowerstrength topical steroid creams as the lesions resolve. Topical doxepin, capsaicin, or pimecrolimus cream or tacrolimus ointment provides significant antipruritic effects and is a good adjunctive therapy.

Botulinum toxin type A injection was curative in three patients within 2-4 weeks.

Intralesional injections of triamcinolone suspension, using a concentration of 5 or (with caution) 10 mg/mL, may be required. Too superficial injection invites the twin risks of epidermal and dermal atrophy and depigmentation, which may last for many months. The suspension should not be injected into infected lesions for fear of causing abscesses. In the most severe cases, complete occlusion with an Unna boot may break the cycle.

## PRURIGO NODULARIS

Prurigo nodularis is a disease with multiple itching nodules situated chiefly on the extremities, especially on the anterior surfaces of the thighs and legs. A linear arrangement is common. The individual lesions are peasized or larger, firm, and erythematous or brownish. When fully developed, they become verrucous or fissured. The course of the disease is chronic and the lesions evolve slowly. Itching is severe but usually confined to the lesions themselves. Bouts of extreme pruritus often occur when these patients are under stress. Prurigo nodularis is one of the disorders in which the pruritus is characteristically paroxysmal: intermittent, unbearably severe, and relieved only by scratching to the point of damaging the skin, usually inducing bleeding and often scarring.

The cause of prurigo nodularis is unknown; multiple factors may contribute, including atopic dermatitis, anemia, hepatic diseases (including hepatitis C), HIV disease, pregnancy, renal failure, lymphoproliferative disease, photodermatitis, gluten enteropathy, stress, and insect bites. Pemphigoid nodularis may be confused with prurigo nodularis clinically.

The histologic findings are those of compact hyperkeratosis, irregular acanthosis, and a perivascular mononuclear cell infiltrate in the dermis. Dermal collagen may be increased, especially in the dermal papillae, and subepidermal fibrin may be seen, both evidence of excoriation. In cases associated with renal failure, transepidermal elimination of degenerated collagen may be found.

### TREATMENT

Treatment is challenging. Local measures include antipruritic lotions and emollients. Administration of antihistamines, antidepressants or anxiolytics is of moderate benefit in allaying symptoms. The initial treatment of choice is intralesional or topical administration of steroids. Usually, superpotent topical products are required, but at times lowerstrength preparations used with occlusion may be beneficial. The use of steroids in tape (Cordran) and prolonged occlusion with semipermeable dressings, such as are used for treating nonhealing wounds, can be useful in limited areas. Intralesional steroids will usually eradicate

individual lesions, but unfortunately many patients have too extensive disease for these local measures. PUVA has also been shown to be effective in some cases. Vitamin $D_3$ ointment, calcipotriene ointment, or tacrolimus ointment applied topically twice a day may be therapeutic and steroidsparing. Isotretinoin, 1 mg/kg/day for 2-5 months, may benefit some patients.

Good results have been obtained with thalidomide and cyclosporine. With thalidomide the onset may be rapid or slow and sedation may occur. The initial dose is 100 mg/day, titered to the lowest dose required. Patients treated with thalidomide are at risk of developing a dosedependent neuropathy at cumulative doses of 40-50 g. Combination therapy with sequential UVB and thalidomide may be better than either alone. Cyclosporine at doses of 3-4.5 mg/kg/day has also been shown to be effective in treating recalcitrant disease. Cryotherapy has been used adjunctively.

## PSYCHODERMATOLOGY

There are purely cutaneous disorders that are psychiatric in nature, their cause being directly related to psychopathologic causes in the absence of primary dermatologic or other organic causes. Delusions of parasitosis, neurotic excoriations, factitial dermatitis, and trichotillomania compose the major categories of psychodermatology. The differential diagnosis for these four disorders is two fold, requiring the exclusion of organic causes and the definition of a potential underlying psychologic disorder. Other delusional disorders include bromidrosiphobia and body dysmorphic disorder.

Psychosis is characterized by the presence of delusional ideation, which is defined as a fixed misbelief that is not shared by the patient's subculture. Monosymptomatic hypochondriacal disorder is a form of psychosis characterized by delusions regarding a particular hypochondriacal concern. In contrast to schizophrenia, there are no other mental deficits, such as auditory hallucination, loss of interpersonal skills, or presence of other inappropriate actions. Patients with monosymptomatic hypochondriacal psychosis often function appropriately in

social settings, except for a single fixated belief that there is a serious problem with their skin or other parts of their body.

## SKIN SIGNS OF PSYCHIATRIC ILLNESS

The skin is a frequent target for the release of emotional tension. Selfinjury by prolonged, compulsive repetitious acts may produce various mutilations, depending on the act and site of injury. Selfbiting may be manifested by biting the nails (onychophagia), skin (most frequently the forearms, hands, and fingers) and lip. Dermatophagia is a habit or compulsion, which may be conscious or subconscious. Bumping of the head produces lacerations and contusions, which may be so severe as to produce cranial defects and lifethreatening complications. Compulsive repetitive hand- washing may produce an irritant dermatitis of the hands.

Bulimia, with its self-induced vomiting, results in Russell's sign crusted papules on the dorsum of the dominant hand from cuts by the teeth. Clenching of the hand produces swelling and ecchymosis of the fingertips and subungual hemorrhage. Selfinflicted lacerations may be of suicidal intent. Liplicking produces increased salivation and thickening of the lips. Eventually the perioral area becomes red and produces a distinctive picture resembling the exaggerated mouth makeup of a clown. Pressure produced by binding the waistline tightly with a cord will eventually lead to atrophy of the subcutaneous tissue.

Psychopharmacologic agents, especially the newer atypical antipsychotic agents, and behavioral therapy alone or in combination with these agents are the treatments of choice.

## DELUSIONS OF PARASITOSIS

Delusions of parasitosis (delusional parasitosis, Ekbom syndrome, acarophobia, dermatophobia, parasitophobia, entomophobia, or pseudoparasitic dysesthesia) are firm fixations in a person's mind that he or she suffers from a parasitic infestation of the skin. At times close contacts may share the delusion.

The belief is so fixed that the patient may pick small pieces of epithelial debris from the skin and bring them to be examined, always insisting that the offending parasite is contained in such material. Samples of alleged parasites enclosed in assorted containers, paper tissue, or sandwiched between adhesive tape are so characteristic that it is referred to as the "matchbox sign." Usually, the only symptom is pruritus or a stinging, biting, or crawling sensation. Intranasal formication, or a crawling sensation of the nasal mucosa, is common in this condition. Cutaneous findings may range from none to excoriations, prurigo nodularis, and frank ulcerations.

Frequently, these patients have paranoid tendencies. Women are affected 2:1 over men, often during middle or old age. The condition has been reported to be associated with schizophrenia, bipolar disorders, depression, anxiety disorders, and obsessional states, but is usually a monosymptomatic hypochondriacal disorder. A variety of organic causes have been suggested, including cocaine and amphetamine abuse, dementia, malignancies, cerebrovascular disease, multiple sclerosis, and vitamin $B_{12}$ deficiency. Some of these may produce cutaneous symptoms, particularly pruritus, which may contribute to the delusion.

The differential diagnosis is influenced by the cutaneous findings and history. Initial steps should be directed at excluding a true infestation, such as scabies, or an organic cause. A thorough history, particularly in reference to therapeutic and recreational drug use (amphetamines and cocaine), review of systems, and physical examination should be performed. Morgellons disease is considered by many simply to be another name for delusions of parasitosis. Patients complain of crawling, biting, burning or other sensations which cause them to be intensely anxious. Often granules or fibers are provided by the patient for analysis. Many patients have associated psychiatric conditions.

A skin biopsy is frequently performed, more to reassure the patient than to uncover occult skin disease. Screening laboratory tests to exclude systemic disorders should be obtained: a CBC, urinalysis (UA), liver function tests (LFTs), thyroid function tests (TFTs), iron studies, and serum $B_{12}$, folate, and electrolyte

levels. Multiple sclerosis may present with dysesthesia, which may at times be mistaken for infestation. Once organic causes have been eliminated, the patient should be evaluated to determine the cause of the delusions. Schizophrenia, monosymptomatic hypochondriacal psychosis, psychotic depression, dementia, and depression with somatization are considerations in the differential diagnosis.

Management of this difficult problem varies. While referral to a psychiatrist may be considered best for the patient, most frequently the patient will reject suggestions to seek psychiatric help. The dermatologist is cautioned against confronting the patient with the psychogenic nature of the disease. It is preferable to develop trust, which will usually require several visits. If pharmacologic treatment is undertaken, the patient may accept it if the medication is presented as one which will alter the perception of this bothersome sensation. Pimozide was the longstanding treatment of choice, but is associated with a variety of side effects, including stiffness, restlessness, prolongation of the Q-T interval, and extrapyramidal signs. Patients often respond to relatively low dosages, in the 1-4 mg range, which limits these problems. Pimozide is an antipsychotic medication approved for the treatment of Tourette syndrome and patients should understand the labeling prior to obtaining the drug. Newer atypical antipsychotic agents, such as risperidone, and olanzapine, have fewer side effects and are now considered the appropriate first-line agents for the treatment of delusions of parasitosis. With appropriate pharmacologic intervention it is likely that 25-50% of patients will remit.

## NEUROTIC EXCORIATIONS

Many persons have unconscious compulsive habits of picking at themselves, and at times the tendency is so persistent and pronounced that excoriations of the skin are produced. The lesions are caused by picking, digging, or scraping, and they usually occur on parts readily accessible to the hands. These patients admit their actions induce the lesions, but cannot control their behavior.

The excavations may be superficial or deep and are often linear. The bases of the ulcers are clean or covered with a scab. Righthanded persons tend to produce lesions on their left side and lefthanded persons on their right side. There is evidence of past healed lesions, usually with linear scars, or rounded hyperor hypopigmented lesions, in the area of the active excoriations. The face, upper arms, and upper back are favorite sites for these excoriations. Sometimes the focus is on acne lesions, producing acne excoriee.

Most of these patients are otherwise healthy adults. They usually lead normal lives. The organic differential diagnosis is vast and includes any condition that may manifest with excoriations. The most common psychopathologies associated with neurotic excoriations are depression, obsessivecompulsive disorder, and anxiety.

The treatment of choice is doxepin because of its antidepres- sant and antipruritic effects; doses are slowly increased to 100 mg or higher, if tolerated. Many alternatives to doxepin may be indicated, especially in those affected by an obsessive- compulsive component. These include clomipramine, paroxetine, fluoxetine, and sertraline. Other drugs with utility include desipramine, buspirone, and quick-acting benzodiazepines. Treatment is difficult, often requiring a combined psychiatric and pharmacologic intervention. It is important to establish a constructive patient therapist alliance. Training in diversion strategies during "scratching episodes" may be helpful. An attempt should be made to identify specific conflicts or stres- sors preceding onset. The therapist should concentrate on systematic training directed at the behavioral reaction pattern. There should be support and advice given with regard to the patient's social situation and interpersonal relations.

## FACTITIOUS DERMATITIS (DERMATITIS ARTEFACTA)

Factitious dermatitis is the term applied to self-inflicted skin lesions made consciously and often with the intent to elicit sympathy, escape responsibilities, or collect disability insurance. Most patients are adults in midlife, with women more

often affected than men by a 3 : 1 ratio. The vast majority have multiple lesions and are unemployed or on sick leave. These skin lesions are provoked by mechanical means or by the application or injection of chemical irritants and caustics. The lesions may simulate other dermatoses but usually have a distinctive, geometric, bizarre appearance, whose shape and arrangement frequently are not encountered in any other affection. The lesions are generally distributed on parts easily reached by the hands and have a tendency to be linear and arranged regularly and symmetrically. They are rarely seen on the right hand, right wrist or right arm unless the patient is lefthanded.

When chemicals are used, red streaks or guttate marks are often seen beneath the principal patch, where drops of the chemical have accidentally run or fallen on the skin. According to the manner of production, the lesions may be erythematous, vesicular, bullous, ulcerative, or gangrenous. The more common agents of destruction used are the fingernails, pointed instruments, hot metal; chemicals such as carbolic, nitric, or acetic acid; caustic potash or soda, turpentine, table salt, urine, and feces. The lesions are likely to appear in crops. At times the only sign may be the indefinitely delayed healing of an operative wound, which is purposely kept open by the patient. Tight cords or clothing tied around an arm or leg may produce factitious lymphedema, which may be mistaken for postphlebitic syndrome or nerve injury, as well as other forms of chronic lymphedema.

Subcutaneous emphysema, manifesting as cutaneous crepitations, may be factitial in origin. Recurrent migratory subcutaneous emphysema involving the extremities, neck, chest, or face can be induced through injections of air into tissue with a needle and syringe. Circular pockets and bilateral involvement without physical findings that suggest a contiguous spread from a single source suggest a factitial origin. Puncturing the buccal mucosa through to facial skin with a needle and puffing out the cheeks can produce alarming results. Neck and shoulder crepitation is also a complication in manic patients that results from hyperventilation and breath-holding.

The organic differential diagnosis depends on the cutaneous signs manifested (e.g. gas gangrene for patients with factitious subcutaneous emphysema, and the various forms of lymphedema for factitious lymphedema). Considerations for psycho- pathology include malingering, borderline personality disorders, and psychosis.

Proof of diagnosis is sometimes difficult. Occlusive dressings may be necessary to protect the lesions from ready access by the patient. It is usually best not to reveal any suspicion of the cause to the patient and to establish the diagnosis definitely without the patient's knowledge. If the patient is hospitalized, a resourceful, cooperative nurse may be useful in helping to establish the diagnosis. When injection of foreign material is suspected, examination of biopsy material by spec- troscopy may reveal talc or other foreign material. Treatment should ideally involve psychotherapy, but most frequently the patient promptly rejects the suggestion and goes to another physician to seek a new round of treatment. It is best for the dermatologist to maintain a close relationship with the patient and provide symptomatic therapy and nonjudgmental support. Pimozide or atypical antipsychotic agents in low dose have been used with some success. High doses of selective serotonin reuptake inhibitors (SSRIs) may also be beneficial. Consultation with an experienced psychiatrist is prudent.

## TRICHOTILLOMANIA

Trichotillomania (trichotillosis or neuromechanical alopecia) is a neurosis characterized by an abnormal urge to pull out the hair. The sites involved are generally the frontal region of the scalp, eyebrows, eyelashes, and the beard. There are irregular areas of hair loss, which may be linear or bizarrely shaped. Uncommonly, adults may pull out pubic hair. The classic presentation is the "Friar Tuck" form of vertex and crown alopecia. Hairs are broken and show differences in length. The pulled hair may be ingested and occasionally the trichobezoar will cause obstruction. When the tail extends from the main mass in the stomach to the small or large intestine, Rapunzel syndrome is the diagnosis. The nails may show

evidence of onychophagy (nail biting), but no pits are present. The disease is seven times more common in children than in adults, and girls are affected 2.5 times more often than boys.

This disease often develops in the setting of psychosocial stress in the family, which may revolve around school problems, sibling rivalry, moving to a new house, hospitalization of a parent, or a disturbed parentchild relationship.

Differentiation from alopecia areata is possible because of the varying lengths of broken hairs present, the absence of nail pitting, and the microscopic appearance of the twisted or broken hairs as opposed to the tapered fractures of alopecia areata. Other organic disorders to consider are androgenic alopecia, tinea capitis, monilethrix, pili torti, pseudopelade of Brocq, traction alopecia, syphilis, nutritional deficiencies, and systemic disorders such as lupus and lymphoma. If necessary, a biopsy can be performed and is usually quite helpful. It reveals traumatized hair follicles with perifollicular hemorrhage, fragmented hair in the dermis, empty follicles, and deformed hair shafts (trichomalacia). Multiple catagen hairs are typically seen. An alternative technique to biopsy, particularly for children, is to shave a part of the involved area and observe for regrowth of normal hairs. The differential diagnosis for underlying psychopathology is obsessive-compulsive disorder (most common), depression, and anxiety.

In children the diagnosis should be addressed openly, and referral to a child psychiatrist for behavioral therapy should be encouraged. In adults with the problem, psychiatric impairment may be severe. Pharmacotherapy with clomipramine was found most effective of the studied medications, but fluoxetine, venlafaxine, and olanzapine have proven effective in some patients. Trichobezoars require surgical removal.

## DERMATOTHLASIA

Dermatothlasia is a cutaneous neurosis characterized by a patient's uncontrollable desire to rub or pinch themselves to form bruised areas on the skin, sometimes as a defense against pain elsewhere.

## BROMIDROSIPHOBIA

Bromidrosiphobia (delusions of bromhidrosis) is a monosymptomatic delusional state in which a person is convinced that his or her sweat has a repugnant odor that keeps other people away. The patient is unable to accept any evidence to the contrary. Threequarters of patients with bromidrosiphobia are male, with an average age of 25. Atypical antipsychotic agents or pimozide may be beneficial. It may be an early symptom of schizophrenia.

## BODY DYSMORPHIC DISORDER (DYSMORPHIC SYNDROME, DYSMORPHOPHOBIA)

Body dysmorphic disorder is the delusion of having an ugly body part. It is most common in young adults of either sex. The concern is frequently centered about the nose, mouth, genitalia, breasts, or hair. Objective evaluation will reveal a normal appearance or slight defect. Patients may manifest obsessional features, spending large amounts of time inspecting the area. Depression may present a risk of suicide. Therapy with SSRIs may help those who manifest this obsessive-compulsive disease. Those more severely affected have delusions that may lead to requests for repeated surgeries of the site, and require antipsychotic medications.

## NEUROCUTANEOUS DERMATOSES SCALP DYSESTHESIA

Cutaneous dysesthesia syndromes are characterized by pain and burning sensations without objective findings. Many patients report coexisting pruritus or transient pruritus associated with the dysesthesia. Scalp dysesthesia occurs primarily in middle-aged to elderly women. A psychiatric cause or overlay is frequently associated and treatment with lowdose antidepressants is often helpful.

## BURNING MOUTH SYNDROME (GLOSSODYNIA, BURNING TONGUE)

Burning mouth syndrome (BMS) is divided into two forms: a primary type characterized by a burning sensation of the oral mucosa without a dental or

medical cause, and secondary BMS. A number of conditions, such as lichen planus, candi- diasis, vitamin or nutritional deficiencies such as low $B_{12}$, iron or folate, hypoestrogenism, parafunctional habits, diabetes, dry mouth, contact allergies, cranial nerve injuries, and medication side effects, may cause secondary BMS. Identification of such underlying conditions and treatment directed at them will result in relief of secondary BMS.

Primary BMS occurs most commonly in postmenopausal women. They are particularly prone to a feeling of burning of the tongue, mouth, and lips, with no objective findings. Symptoms vary in severity but are more or less constant. Patients with burning mouth syndrome often complain that multiple oral sites are involved. Management with topical applications of clonazepam, capsaicin, doxepin, or lidocaine can help. Oral administration of a-lipoic acid, SSRIs or tricyclic antidepressants, amisulpride, anticonvulsants, or benzodiazepines has been reported to be effective. The most commonly used, best studied, and most often successful therapy is provided by the antidepressant medications, and many patients have other symptoms of depression as well.

Burning lips syndrome may be a separate entity; it appears to affect both men and women equally and occurs in individuals between the ages of 50 and 70 years. The labial mucosa may be smooth and pale, and the minor salivary glands of the lips are frequently dysfunctional. Treatment with a-lipoic acid showed improvement in 2 months in a doubleblind controlled study.

## VULVODYNIA

Vulvodynia is defined as vulvar discomfort, usually described as burning pain, occurring without medical findings. It is chronic, defined as lasting 3 months or longer. Two subtypes are seen, the localized and generalized subsets. Both may occur only when provoked by physical contact, as a spontaneous pain, or mixed in type. Vulvar pain secondary to many underlying disorders may occur, but when candidal infections, endometriosis, neoplastic conditions, referred pain from myalgic muscles, contact dermatitis, hypoestrogenism, neurologic etiologies, or

prior radiotherapy are the cause, these are treated appropriately and the patient's condition is not categorized as vulvodynia.

The typical patient is a nulligravid married woman in her late thirties. Up to 15% of women seen in some gynecologic practices may be affected. Dyspareunia may completely prevent sexual intercourse. This problem and the chronic pain may lead to compromise of interpersonal relations. They may be exacerbated by stress, depression, or anxiety, or may lead to such conditions over time. A male counterpart may be seen and has been called the burning genital skin syndrome or dysesthetic peno-/scrotodynia.

Treatment should always include patient education and psychological support. Topical anesthetics and lubricants, such as petrolatum, applied before intercourse may be tried initially. Elimination of irritants, treatment of atopy with topical tacrolimus (allowing for the discontinuance of topical steroids which have usually been tried without success), and the use of antihistamines for dermatographism may be helpful. Vulvodynia is considered among the chronic pain syndromes that can have a psychological impact. Treatment then centers on the use of tricyclic and SSRI antidepressants, and neuroleptics, chiefly gabapentin or pregabalin. Other interventions such as botulinum toxin A, montelukast, and surgery may be considered in individual cases, but the evidence for any of the above therapies is limited.

## NOTALGIA PARESTHETICA

Notalgia paresthetica is a unilateral sensory neuropathy characterized by infrascapular pruritus, burning pain, hyperalgesia, and tenderness, often in the distribution of the second to sixth thoracic spinal nerves. A pigmented patch localized to the area of pruritus is often found. This is due to postinflammatory change. Macular amyloidosis may be produced by chronic scratching. In the majority of cases, degenerative changes in the corresponding vertebrae leading to spinal nerve impingement are seen.

Topical capsaicin has been shown to be effective; however, relapse occurs in most patients within 4 weeks of discontinuing its use. The area of involvement may be injected intradermally with 4 U of botulinum toxin type A spaced 2 cm apart. Excellent long-term results may occur and injections may be repeated as necessary. The topical lidocaine patch may provide relief. Paravertebral blocks, oxycarbazepine, ultrasound, and physiotherapy are useful interventions when a structural change in the vertebrae is found to be the cause.

## BRACHIORADIAL PRURITUS

This condition is characterized by itching localized to the brachioradial area of the arm. To relieve the burning, stinging, or even painful quality of the itch, patients will frequently use ice packs. Cervical spine pathology is frequently found on radiographic evaluation. Searching for causes of the abnormality should include discussion of spinal injury, such as trauma, arthritis, or chronic repetitive microtrauma, whiplash injury, or assessment for a tumor in the cervical spinal column. Patients often present in the spring and report that UV light precipitates the pruritus. Cervical spine disease may then be a predisposing factor, with sunlight the eliciting factor.

Interventions of value include gabapentin, carbamazepine, topical capsaicin, cervical spine manipulation, neck traction, anti-inflammatory medications, physical therapy, or surgical resection of a cervical rib.

## MERALGIA PARESTHETICA (ROTH-BERNHARDT DISEASE)

This affection is a variety of paresthesia, with persistent numbness and periodic transient episodes of burning or lancinating pain on the anterolateral surface of the thigh. The lateral femoral cutaneous nerve innervates this area and is subject to entrapment and compression along its course. Sensory mononeuropathies besides notalgia and meralgia paresthetica include mental and intercostal neuropathy and cheiralgia, gonyalgia, and digitalgia paresthetica.

Meralgia paresthetica occurs most frequently in middleaged, obese men. Alopecia localized to the area innervated by the lateral femoral nerve may be a skin sign of this disease. External compression may occur from tightfitting clothing, cell phones or other heavy objects in the pockets or worn on belts, or seatbelt injuries from automobile accidents. Internal compression from arthritis of the lumbar vertebrae, a herniated disk, pregnancy, intraabdominal disease that increases intrapelvic pressure, iliac crest bone graft harvesting, diabetes, neuroma, and rarely, a lumbar spine or pelvic tumor have been reported causes in individual cases.

The diagnostic test of choice is somatosensory evoked potentials of the lateral femoral cutaneous nerve. Local anesthetics, such as use of a lidocaine patch, nonsteroidal antiinflammatories, rest, and avoidance of aggravating factors may lead to improvement. Gabapentin is useful in various neuropathic pain disorders. If such interventions fail and a nerve block rapidly relieves symptoms, then local infiltration with corticosteroids is indicated. Surgical decompression of the lateral femoral cutaneous nerve can produce good to excellent outcomes, but should be reserved for patients with intractable symptoms who responded to nerve blocks but not corticosteroids. If the nerve block does not result in symptom relief, CT scans of the lumbar spine and pelvic and lower abdominal ultrasound examinations to assess for tumors are indicated.

## COMPLEX REGIONAL PAIN SYNDROME

Encompassing the descriptors reflex sympathetic dystrophy, causalgia, neuropathic pain, and Sudek syndrome, complex regional pain syndrome (CRPS) is characterized by burning pain, hyperesthesia, and trophic disturbances resulting from injury to a peripheral nerve. It most commonly occurs in one of the upper extremities, although leg involvement is frequent. The most common symptom is burning pain aggravated by movement or friction. The skin of the involved extremity becomes shiny, cold, and atrophic, and may profusely perspire. Additional cutaneous manifestations include bullae, erosions, edema,

telangiectases, hyperpigmentation, ulcerations, and brownishred patches with linear fissures.

The intensity of the pain varies from trivial burning to a state of torture accompanied by extreme hyperesthesia and, frequently, hyperhidrosis. The part not only is subject to an intense burning sensation, but also a touch or a tap of the finger causes exquisite pain. Exposure to the air is avoided with a care that seems absurd, and the patient walks carefully, carrying the limb tenderly with the sound hand. Patients are tremulous and apprehensive, and keep the hand constantly wet, finding relief in the moisture rather than in the temperature of the application. A condition resembling permanent chilblains or even trophic ulcers may be present.

CRPS usually begins with severe, localized, burning pain, focal edema, muscle spasm, stiffness or restricted mobility, and vasospasm affecting skin color and temperature. This may be followed by a diffusion of the pain and edema, diminished hair growth, brittle nails, joint thickening, and onset of muscle atrophy. Finally, irreversible trophic changes, intractable pain involving the entire limb, flexor contractures, marked atrophy of the muscles, severe limitation in joint and limb mobility, and severe osteoporosis result.

There may be a precipitating event, such as a crush injury, laceration, fracture, sprain, burn, or surgery that produces some degree of softtissue or nerve complex injury. Causes include fractures, peripheral revascularization of the extremities, hypothermic insult, myocardial infarction, peripheral nerve injury, and multiple sclerosis. Associations with Munchausen syndrome and factitial ulcerations have also been reported. Not all patients will have all of the features of CRPS, and an early diagnosis improves the chance of cure. The five major components are pain, edema, dysregulation of autonomic function, alterations in motor function, and dystrophic changes. A three-phase technetium bone scan is helpful in confirming the diagnosis of CRPS in patients who fail to meet all five of these criteria. Consultation with a neurologist or an anesthesiologist specializing in pain is advisable. Osteoporosis is a frequent complication, and studies using pamidronate, a powerful inhibitor of bone absorption, have been shown to improve

symptoms of pain, tenderness, and swelling significantly. Tricyclic anti-depressants and antipsychotic agents are often helpful. Transcutaneous electrical nerve stimulation and deep brain stimulation may also be useful. Paravertebral block or sym- pathectomy is most effective, but not without potential complications.

## TRIGEMINAL TROPHIC LESIONS

Interruption of the peripheral or central sensory pathways of the trigeminal nerve may result in a slowly enlarging, unilateral, uninflamed ulcer on ala nasi or adjacent cheek skin. The nasal tip is spared. It may infrequently occur elsewhere on the face. Onset of ulceration varies from weeks to several years after trigeminal nerve injury. Biopsy to exclude tumor or a variety of granulomatous or infective etiologies is usually indicated. Selfinflicted trauma to the anesthetic skin is believed to be the cause, and the appropriate treatment is to prevent this by occlusion or with the initiation of psychotropic medicine. It is usually successful, but scarring may be severe.

## MAL PERFORANS PEDIS

Also known as neuropathic ulceration or perforating ulcer of the foot, mal perforans is a chronic ulcerative disease seen on the sole in conditions that result in loss of pain sensation at a site of constant trauma. The primary cause lies in either the posterolateral tracts of the cord (in arteriosclerosis and tabes dorsalis), lateral tracts (in syringomyelia), or peripheral nerves (in diabetes or Hansen's disease).

In most cases, mal perforans begins as a circumscribed hyperkeratosis, usually on the ball of the foot. This lesion becomes soft, moist, and malodorous, and later exudes a thin, purulent discharge. A slough slowly develops and an indo-lent, necrotic ulcer is left that lasts indefinitely. Whereas the neuropathy renders the ulceration painless and walking continues, plantar ulcers in this situation have

a surrounding thick callus. Deeper perforation and secondary infection often lead to osteomyelitis of the metatarsal or tarsal bones.

Treatment should consist of relief of pressure on the ulcer through use of a totalcontact cast and debridement of the surrounding callosity. Removable cast walkers and half-shoes were significantly less effective means of offloading in a randomized clinical trial. Administration of local and systemic antibiotics is sometimes helpful.

## SCIATIC NERVE INJURY

Serious sciatic nerve injury can result from improperly performed injections into the buttocks. Older patients are more susceptible to injectioninduced sciatic nerve injury because of their decreased muscle mass and/or debilitating diseases. The most common scenario for nerve damage is improper needle placement. Other common causes of sciatic neuropathy are hip surgery complications, hip fracture and dislocation, and compression by benign and malignant tumors. A paralytic foot drop is the most common finding. There is sensory loss and absence of sweating over the distribution of the sciatic nerve branches. The skin of the affected extremity becomes thin, shiny, and often edematous.

Surgical exploration, guided by nerve action potentials, with repair of the sciatic nerve is worthwhile in selected cases.

## SYRINGOMYELIA

Also known as Morvan's disease, syringomyelia results from cystic cavities inside the cervical spinal cord, due to alterations of cerebrospinal fluid flow. Compression of the lateral spinal tracts produces sensory and trophic changes on the upper extremities, particularly in the fingers. The disease begins insidiously and gradually causes muscular weakness, hyperhidrosis, and sensory disturbances, especially in the thumb and index and middle fingers. The skin changes are characterized by dissociated anesthesia with loss of pain and temperature sense but with retention of tactile sense. Burns are the most frequent lesions noted. Bullae,

warts, and trophic ulcerations occur on the fingers and hands, and ultimately there are contractures and gangrene. Other unusual features may be hypertrophy of the limbs, hands, or feet, and asymmetric scalp hair growth with a sharp midline demarcation. The disease must be differentiated chiefly from Hansen's disease. Unlike Hansen's disease, syringomyelia does not interfere with sweating or block the flare around a histamine wheal. Early surgical treatment allows for improvement of symptoms and prevents progression of neurologic deficits.

## HEREDITARY SENSORY AND AUTONOMIC

## NEUROPATHIES (HSAN)

A number of inherited conditions are characterized by sensory dysfunctions and varying degrees of autonomic alterations. From a dermatologic standpoint, altered pain and temperature sensation, selfmutilating behavior, and sweating abnormalities may be present. Two of them are discussed below.

### FAMILIAL DYSAUTONOMIA (RILEY-DAY SYNDROME)

Familial dysautonomia (HSAN III) is characterized by defective lacrimation, decreased pain sensation, impaired temperature and blood pressure regulation, and absent tendon reflexes. Skin and oral manifestations include hyperhidrosis, a transient erythema, predominantly on the trunk, acrocyanosis of the hands, absence of fungiform and circumvallate papillae of the tongue, and measurable deficiencies in taste from water and sweet, bitter, and salty stimuli. Dental features may be prominent and include hypersalivation and orodental trauma progressing to self-mutilation.

This neurodegenerative disease is inherited as an autosomalrecessive trait, most often in Jewish families. The Schirmer test for lacrimal dysfunction is positive. The intradermal histamine test shows a diminished flare, and immersion of the hands in water at 40°C (104°F) causes erythematous mottling of the skin. The mutation in Riley-Day syndrome is in the IK-B (IKBKAP) associated protein, a subunit of *Elongator*. This leads to a tissuespecific abnormality in splicing of

premRNA. Splicing defects are estimated to be responsible for up to 15% of human diseases. Treatment is supportive; however, there is hope that kinetin, a cytokinin, will prove to be a helpful treatment, as in vitro studies have shown it can rescue the mRNA splicing defect of Riley-Day syndrome.

HSAN type IV is an autosomalrecessive disorder characterized by anhidrosis, recurrent hyperpyrexia, absence of the pain sensation, selfmutilating behavior, and mental retardation. Repeated injuries produce ulcers, most commonly of the acral and oral tissues. Secondary infection of the digits with osteomyelitis is not an infrequent complication. The disease has been found to be caused by mutations and polymorphisms in the *TRKA (NTRK1)* gene, which is present on chromosome 1 and encodes for the receptor tyrosine kinase for nerve growth factor. Treatment of this disorder is supportive. Care should be taken to avoid burning, scratching, and the various other traumatic events that can happen in ordinary living.

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# CONTENT

# ANDIJON DAVLAT TIBBIYOT INSTITUTI

# GUVOHNOMA

**ANDIJON – 2024**

# O‘QUV ADABIYOTINING NASHR RUXSATNOMASI

O‘zbekiston Respublikasi Oliy ta’lim, fan va innovatsiyalar vazirligi, Andijon davlat tibbiyot instituti rektorining 2024 yil “01” martdagi “01/08/490-Sh”–sonli buyrug‘iga asosan

***A.Paqirdinov***
(muallifning familiyasi, ismi-sharifi)

***Davolash ishi - 60910200***
**(ta’lim yo‘nalishi (mutaxassisligi)**

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talabalari (o‘quvchilari) uchun tavsiya etilgan.

***Cutaneous signs and diagnosis dermatoses resulting from physical factors. Pruritus and neurocutaneous dermatoses***
*nomli o‘quv qo‘llanmasi*
(o‘quv adabiyotining nomi va turi: darslik, o‘quv qo‘llanma)

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O‘zbekiston Respublikasi Vazirlar Mahkamasi tomonidan litsenziya berilgan nashriyotlarda nashr etishga ruxsat berildi.

Rektor _____ M.M.Madazimov
(imzo)

Ro‘yxatga olish raqami:
46

# NOTE

**O‘QUV QO‘LLANMA**

# ADKHAMJON PAKIRDINOV

# “CUTANEOUS SIGNS AND DIAGNOSIS. DERMATOSES RESULTING FROM PHYSICAL FACTORS. PRURITUS AND NEUROCUTANEOUS DERMATOSES"

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