7 - Dermatologic Disorders

Chapter 71. Approach to the Dermatologic Patient

Introduction

History and physical examination are adequate for diagnosing many skin lesions. Some require biopsy or other testing.

Important information to obtain from history includes

• Personal or family history of atopy (suggesting atopic dermatitis)

• Occupational exposures (contact dermatitis)

• Long-term exposure to sunlight or other forms of radiation (benign and malignant skin tumors)

• Systemic disease (diabetes and *Candida* or tinea, hepatitis C and cryoglobulinemia)

• Sexual history (syphilis and gonorrhea)

• Use of drugs (Stevens-Johnson syndrome, toxic epidermal necrolysis)

• Travel history (Lyme disease, skin infections)

A negative history is as important as a positive history. The history of the particular skin lesions is also important, including time and site of initial appearance, spread, change in appearance, and triggering factors.

Visual inspection is the central evaluation tool; many skin disorders are diagnosed by the characteristic appearance or morphology of the lesions.

Description of Skin Lesions

An extensive language has been developed to standardize the description of skin lesions, including

• Primary morphology (lesion type)

• Secondary morphology (configuration)

• Texture

• Distribution

• Color

Rash is a general term for a temporary skin eruption.

Primary Morphology

Macules are flat, nonpalpable lesions usually < 10 mm in diameter. Macules represent a change in color and are not raised or depressed compared to the skin surface. A patch is a large macule. Examples include freckles, flat moles, tattoos, port-wine stains, and the rashes of rickettsial infections, rubella, measles, and some allergic drug eruptions.

Papules are elevated lesions usually < 10 mm in diameter that can be felt or palpated. Examples include nevi, warts, lichen planus, insect bites, seborrheic and actinic keratoses, some lesions of acne, and skin cancers. The term maculopapular is often loosely and improperly used to describe many red skin rashes;

because this term is nonspecific and easily misused, it should be avoided.

Plaques are palpable lesions > 10 mm in diameter that are elevated or depressed compared to the skin surface. Plaques may be flat topped or rounded. Lesions of psoriasis and granuloma annulare commonly form plaques.

Nodules are firm papules or lesions that extend into the dermis or subcutaneous tissue. Examples include cysts, lipomas, and fibromas.

Vesicles are small, clear, fluid-filled blisters < 10 mm in diameter. Vesicles are characteristic of herpes infections, acute allergic contact dermatitis, and some autoimmune blistering disorders (eg, dermatitis herpetiformis).

Bullae are clear fluid-filled blisters > 10 mm in diameter. These may be caused by burns, bites, irritant or allergic contact dermatitis, and drug reactions. Classic autoimmune bullous diseases include pemphigus vulgaris and bullous pemphigoid. Bullae also may occur in inherited disorders of skin fragility.

Pustules are vesicles that contain pus. Pustules are common in bacterial infections and folliculitis and may arise in some inflammatory disorders including pustular psoriasis.

Urticaria (wheals or hives—see Plate 53) is characterized by elevated lesions caused by localized edema. Wheals are a common manifestation of hypersensitivity to drugs, stings or bites, autoimmunity, and, less commonly, physical stimuli including temperature, pressure, and sunlight. The typical wheal lasts < 24 h.

Scales are heaped-up accumulations of horny epithelium that occur in disorders such as psoriasis, seborrheic dermatitis, and fungal infections. Pityriasis rosea and chronic dermatitis of any type may be scaly.

Crusts (scabs) consist of dried serum, blood, or pus. Crusting can occur in inflammatory or infectious skin diseases (eg, impetigo).

Erosions are open areas of skin that result from loss of part or all of the epidermis. Erosions can be traumatic or can occur with various inflammatory or infectious skin diseases. An excoriation is a linear erosion caused by scratching, rubbing, or picking.

Ulcers result from loss of the epidermis and at least part of the dermis. Causes include venous stasis dermatitis, physical trauma with or without vascular compromise (eg, from decubitus ulcers, peripheral arterial disease), infections, and vasculitis.

Petechiae are nonblanchable punctate foci of hemorrhage. Causes include platelet abnormalities (eg, thrombocytopenia, platelet dysfunction), vasculitis, and infections (eg, meningococcemia, Rocky Mountain spotted fever, other rickettsioses).

Purpura is a larger area of hemorrhage that may be palpable. Palpable purpura is considered the hallmark of leukocytoclastic vasculitis. Purpura may indicate a coagulopathy. Large areas of purpura may be called ecchymoses or, colloquially, bruises.

Atrophy is thinning of the skin, which may appear dry and wrinkled, resembling cigarette paper. Atrophy may be caused by chronic sun exposure, aging, and some inflammatory and neoplastic skin diseases, including cutaneous T-cell lymphoma and lupus erythematosus. Atrophy also may result from long-term use of potent topical corticosteroids.

Scars are areas of fibrosis that replace normal skin after injury. Some scars become hypertrophic or thickened and raised. Keloids are hypertrophic scars that extend beyond the original wound margin.

Telangiectases are foci of small, permanently dilated blood vessels that are most often idiopathic but may occur in rosacea, systemic diseases (especially systemic sclerosis), or inherited diseases (eg,

ataxia-telangiectasia, hereditary hemorrhagic telangiectasia) or after long-term therapy with topical fluorinated corticosteroids.

Secondary Morphology (Configuration)

Configuration is the shape of single lesions and the arrangement of clusters of lesions.

Linear lesions take on the shape of a straight line and are suggestive of some forms of contact dermatitis, linear epidermal nevi, and lichen striatus.

Annular lesions are rings with central clearing. Examples include granuloma annulare, some drug eruptions, some dermatophyte infections (eg, ringworm), and secondary syphilis.

Nummular lesions are circular or coin-shaped; an example is nummular eczema.

Target (bull's-eye or iris) lesions appear as rings with central duskiness and are classic for erythema multiforme.

Serpiginous lesions have linear, branched, and curving elements. Examples include some fungal and parasitic infections (eg, cutaneous larva migrans).

Reticulated lesions have a lacy or networked pattern. Examples include cutis marmorata and livedo reticularis.

Herpetiform describes grouped papules or vesicles arranged like those of a herpes simplex infection.

Zosteriform describes lesions clustered in a dermatomal distribution similar to herpes zoster.

Texture

Some skin lesions have visible or palpable texture that suggests a diagnosis.

Verrucous lesions have an irregular, pebbly, or rough surface. Examples include warts and seborrheic keratoses.

Lichenification is thickening of the skin with accentuation of normal skin markings; it results from repeated rubbing.

Induration, or deep thickening of the skin, can result from edema, inflammation, or infiltration, including by cancer. Indurated skin has a hard, resistant feeling. Induration is characteristic of panniculitis, some skin infections, and cutaneous metastatic cancers.

Umbilicated lesions have a central indentation and are usually viral. Examples include molluscum contagiosum and herpes simplex.

Xanthomas, which are yellowish, waxy lesions, may occur in lipid disorders.

Location and Distribution

It is important to note whether

• Lesions are single or multiple

• Particular body parts are affected (eg, palms or soles, scalp, mucosal membranes)

• Distribution is random or patterned, symmetric or asymmetric

• Lesions are on sun-exposed or protected skin

Although few patterns are pathognomonic, some are consistent with certain diseases.

Psoriasis frequently affects the scalp, extensor surfaces of the elbows and knees, umbilicus, and the gluteal cleft.

Lichen planus frequently arises on the wrists, forearms, genitals, and lower legs.

Vitiligo may be patchy and isolated or may group around the distal extremities and face.

Chronic cutaneous lupus erythematosus has characteristic lesions on sun-exposed skin of the face, especially the forehead, nose, and the conchal bowl of the ear.

Hidradenitis suppurativa involves skin containing a high density of apocrine glands, including the axillae, groin, and under the breasts.

Color

Red skin (erythema) can result from many different inflammatory or infectious diseases. Cutaneous tumors are often pink or red. Superficial vascular lesions such as port-wine stains may appear red.

Orange skin is most often seen in hypercarotenemia, a usually benign condition of carotene deposition after excess dietary ingestion of β-carotene.

Yellow skin is typical of jaundice, xanthelasmas and xanthomas, and pseudoxanthoma elasticum.

Green fingernails suggest *Pseudomonas aeruginosa* infection.

Violet skin may result from cutaneous hemorrhage or vasculitis. Vascular lesions or tumors, such as Kaposi's sarcoma and hemangiomas, can appear purple. A lilac color of the eyelids or heliotrope eruption is characteristic of dermatomyositis.

Shades of blue, silver, and gray can result from deposition of drugs or metals in the skin, including minocycline, amiodarone, and silver (argyria). Ischemic skin appears purple to gray in color. Deep dermal nevi appear blue.

Black skin lesions may be melanocytic, including nevi and melanoma. Black eschars are collections of dead skin that can arise from vascular infarction, which may be caused by infection (eg, anthrax, angioinvasive fungi including *Rhizopus*, meningococcemia), calciphylaxis, arterial insufficiency, or vasculitis.

Other Clinical Signs

Dermatographism is the appearance of an urticarial wheal after focal pressure (eg, stroking or scratching the skin) in the distribution of the pressure. Up to 5% of normal patients may exhibit this sign, which is a form of physical urticaria.

Darier's sign refers to rapid swelling of a lesion when stroked. It occurs in patients with urticaria pigmentosa or mastocytosis.

Nikolsky's sign is epidermal shearing that occurs with gentle lateral pressure on seemingly uninvolved skin in patients with toxic epidermal necrolysis and some autoimmune bullous diseases.

Auspitz sign is the appearance of pinpoint bleeding after scale is removed from plaques in psoriasis.

Koebner phenomenon describes the development of lesions within areas of trauma (eg, caused by scratching, rubbing, injury). Psoriasis frequently exhibits this phenomenon, as may lichen planus.

Diagnostic Tests

Diagnostic tests are indicated when the cause of a skin lesion or disease is not obvious from history and physical examination alone (for patch testing, see p. 667).

Biopsy: A skin biopsy can be done by a primary care physician. One procedure is a punch biopsy, in which a tubular punch (diameter usually 4 mm) is inserted into deep dermal or subcutaneous tissue to obtain a specimen, which is snipped off at its base. More superficial lesions may be biopsied by shaving with a scalpel or razor blade. Bleeding is controlled by aluminum chloride solution or electrodesiccation; large incisions are closed by sutures. Larger or deeper biopsies can be done by excising a wedge of skin with a scalpel. All pigmented lesions should be excised deeply for histologic evaluation of depth; superficial biopsies are often inadequate. Diagnosis and cure are achieved simultaneously for most small tumors by complete excision that includes a small border of normal skin.

Scrapings: Skin scrapings help diagnose fungal infections and scabies. For fungal infection, scales are taken from the border of the lesion and placed onto a microscope slide. Then a drop of 10 to 20% potassium hydroxide (KOH) is added. Hyphae, budding yeast, or both confirm the diagnosis of tinea or candidiasis. For scabies, scrapings are taken from suspected burrows and placed directly under a coverslip with mineral oil; findings of mites, feces, or eggs confirm the diagnosis.

Wood's light: Wood's light (black light) can help distinguish hypopigmentation from depigmentation (depigmentation of vitiligo fluoresces ivory-white and hypopigmented lesions do not). Erythrasma fluoresces bright orangered. Tinea capitis caused by *Microsporum canis* and *Microsporum audouinii* fluoresces a light, bright green. (NOTE: Most tinea capitis in the US is caused by *Trichophyton* species, which do not fluoresce.) The earliest clue to cutaneous *Pseudomonas* infection (eg, in burns) may be green fluorescence.

Tzanck testing: Tzanck testing can be used to diagnose viral disease, such as herpes simplex and herpes zoster, and is done when active intact vesicles are present. Tzanck testing cannot distinguish between herpes simplex and herpes zoster infections. An intact blister is the preferred lesion for examination. The blister roof is removed with a sharp blade, and the base of the unroofed vesicle is scraped with a #15 scalpel blade. The scrapings are transferred to a slide and stained with Wright's stain or Giemsa stain. Multinucleated giant cells are a sign of herpes infection.

Diascopy: Diascopy is used to determine whether a lesion is vascular (inflammatory) or nonvascular (nevus) or hemorrhagic (petechia or purpura). A microscope slide is pressed against a lesion to see whether it blanches. Hemorrhagic lesions and nonvascular lesions do not blanch; inflammatory lesions do. Diascopy is sometimes used to identify sarcoid skin lesions, which, when tested, turn an apple jelly color.

Itching

(Pruritus)

Itching is a symptom that can cause significant discomfort and is one of the most common reasons for consultation with a dermatologist. Itching leads to scratching, which can cause inflammation, skin degradation, and possible secondary infection. The skin can become lichenified, scaly, and excoriated.

Pathophysiology

Itch can be prompted by diverse stimuli, including light touch, vibration, and wool fibers. There are a number of chemical mediators as well as different mechanisms by which the sensation of itch occurs.

Mediators: Histamine is one of the most significant mediators. It is synthesized and stored in mast cells in the skin and is released in response to various stimuli. Other mediators (eg, neuropeptides) can either cause the release of histamine or act as pruritogens themselves, thus explaining why antihistamines ameliorate some cases of itching and not others. Opioids have a central pruritic action as well as

stimulating the peripherally mediated histamine itch.

Mechanisms: There are 4 mechanisms of itch:

• Dermatologic—typically caused by inflammatory or pathologic processes (eg, urticaria, eczema)

• Systemic—related to diseases of organs other than skin (eg, cholestasis)

• Neuropathic—related to disorders of the CNS or peripheral nervous system (eg, multiple sclerosis)

• Psychogenic—related to psychiatric conditions

Intense itching stimulates vigorous scratching, which in turn can cause secondary skin conditions (eg, inflammation, excoriation, infection), which can lead to more itching. However, scratch can temporarily reduce the sensation of itch by activating inhibitory neuronal circuits.

Etiology

Itching can be a symptom of a primary skin disease or, less commonly, a systemic disease (see Table 71-1).

[**Table 71-1.** Some Causes of Itching]

Skin disorders: Many skin disorders cause itching. The most common include

• Dry skin

• Atopic dermatitis (eczema)

• Contact dermatitis

• Fungal skin infections

Systemic disorders: In systemic disorders, itching may occur with or without skin lesions. However, when itching is prominent without any identifiable skin lesions, systemic disorders and drugs should be considered more strongly. Systemic disorders are less often a cause of itching than skin disorders, but some of the more common causes include

• Allergic reaction (eg, to foods, drugs, bites and stings)

• Cholestasis

• Chronic renal failure

Less common systemic causes of itching include hyperthyroidism, hypothyroidism, diabetes, iron deficiency, dermatitis herpetiformis, and polycythemia vera.

Drugs: Drugs can cause itching as an allergic reaction or by directly triggering histamine release (most commonly morphine, some IV contrast agents).

Evaluation

History: History of present illness should determine onset of itching, initial location, course, duration, patterns of itching (eg, nocturnal or diurnal, intermittent or persistent, seasonal variation), and whether any rash is present. A careful drug history should be obtained; both oral (eg, opioids, cocaine, aspirin, prescription and OTC) and topical (eg, hydrocortisone, benadryl, moisturizers) drugs are included. History also should include any factors that make the itching better or worse.

Review of systems should seek symptoms of causative disorders, including steatorrhea and right upper quadrant pain (cholestasis); constitutional symptoms of fever, weight loss, and night sweats (cancer); intermittent weakness, numbness, tingling, and visual disturbances or loss (multiple sclerosis); irritability, sweating, weight loss, and palpitations (hyperthyroidism) or depression, dry skin, and weight gain (hypothyroidism); urinary frequency, excessive thirst, and weight loss (diabetes); and headache, pica, hair thinning, and exercise intolerance (iron deficiency anemia).

Past medical history should identify known causative disorders (eg, renal disease, cholestatic disorder, cancer being treated with chemotherapy) and the patient's emotional state. Social history should focus on family members with similar itching and skin symptoms (eg, scabies, pediculosis); relationship of itching to occupation or exposures to plants, animals, or chemicals; and history of recent travel.

Physical examination: Physical examination begins with a review of clinical appearance for signs of jaundice, weight loss or gain, and fatigue. Close examination of the skin should be done, taking note of presence, morphology, extent, and distribution of lesions. Cutaneous examination also should make note of signs of secondary infection (eg, erythema, swelling, warmth, yellow or honey-colored crusting).

The examination should make note of significant adenopathy suggestive of cancer. Abdominal examination should focus on organomegaly, masses, and tenderness (cholestatic disorder or cancer). Neurologic examination focuses on weakness, spasticity, or numbness (multiple sclerosis).

Red flags: The following findings are of particular concern:

• Constitutional symptoms of weight loss, fatigue, and night sweats

• Extremity weakness, numbness, or tingling

• Abdominal pain and jaundice

• Urinary frequency, excessive thirst, and weight loss

Interpretation of findings: Generalized itching that begins shortly after use of a drug is likely caused by that drug. Localized itching (often with rash) that occurs in the area of contact with a substance is likely caused by that substance. However, many systemic allergies can be difficult to identify because patients typically have consumed multiple different foods and have been in contact with many substances before developing itching. Similarly, identifying a drug cause in a patient taking several drugs may be difficult. Sometimes the patient has been taking the offending drug for months or even years before developing a reaction.

If an etiology is not immediately obvious, the appearance and location of skin lesions can suggest a diagnosis (see Table 71-1).

In the minority of patients in whom no skin lesions are evident, a systemic disorder should be considered. Some disorders that cause itching are readily apparent on evaluation (eg, chronic renal failure, cholestatic jaundice). Other systemic disorders that cause itching are suggested by findings (see Table 71-1). Rarely, itching is the first manifestation of significant systemic disorders (eg, polycythemia vera, certain cancers, hyperthyroidism).

Testing: Many dermatologic disorders are diagnosed clinically. However, when itching is accompanied by discrete skin lesions of uncertain etiology, biopsy can be appropriate. When an allergic reaction is suspected but the substance is unknown, skin testing (either prick or patch testing depending on suspected etiology) is often done. When a systemic disorder is suspected, testing is directed by the suspected cause and usually involves CBC; liver, renal, and thyroid function measurements; and appropriate evaluation for underlying cancer.

Treatment

Any underlying disorder is treated. Supportive treatment involves the following (see also

Table 71-2):

• Local skin care

• Topical treatment

• Systemic treatment

Skin care: Itching due to any cause benefits from use of cool or lukewarm (but not hot) water when bathing, mild or moisturizing soap, limited bathing duration and frequency, frequent lubrication, humidification of dry air, and avoidance of irritating or tight clothing. Avoidance of contact irritants (eg, wool clothing) also may be helpful.

Topical drugs: Topical drugs may help localized itching. Options include lotions or creams that contain camphor and/or menthol, pramoxine, or corticosteroids. Corticosteroids are effective in relieving itch caused by inflammation but should be avoided for conditions that have no evidence of inflammation. Topical diphenhydramine and doxepin should be avoided because they may sensitize the skin.

Systemic drugs: Systemic drugs are indicated for generalized itching or local itching resistant to topical agents. Antihistamines, most notably hydroxyzine, are effective, especially for nocturnal itch, and are most commonly used. Sedating antihistamines must be used cautiously in elderly patients during the day because they can lead to falls; newer nonsedating antihistamines such as loratadine, fexofenadine, and cetirizine can be useful for daytime itching. Other drugs include doxepin (typically taken at night due to high level of sedation), cholestyramine (for renal failure, cholestasis, polycythemia vera), opioid antagonists such as naltrexone (for biliary pruritus), and possibly gabapentin (for uremic pruritus).

Physical agents that may be effective for itching include ultraviolet phototherapy.

Geriatrics Essentials

Xerotic eczema is very common among elderly patients. It is especially likely if itching is primarily on the lower extremities.

Severe, diffuse itching in the elderly should raise concern for cancer, especially if another etiology is not immediately apparent.

When treating the elderly, sedation can be a significant problem with antihistamines. Use of nonsedating antihistamines during the day and sedating antihistamines at night, liberal use of topical ointments and corticosteroids (when appropriate), and consideration of ultraviolet phototherapy can help avoid the complications of sedation.

Key Points

• Itching is usually a symptom of a skin disorder or systemic allergic reaction but can result from a systemic disorder.

• If skin lesions are not evident, systemic causes should be investigated.

• Skin care (eg, limiting bathing, avoiding irritants, moisturizing regularly, humidifying environment) should be observed.

• Symptoms can be relieved by topical or systemic drugs.

Urticaria

(Hives; Wheals)

Urticaria is migratory, well-circumscribed, erythematous, pruritic plaques on the skin (see Plate 53).

Urticaria also may be accompanied by angioedema, which results from mast cell and basophil activation in the deeper dermis and subcutaneous tissues and manifests as edema of the face and lips, extremities, or genitals. Angioedema can be life-threatening if airway obstruction occurs because of laryngeal edema or tongue swelling.

Pathophysiology

Urticaria results from the release of histamine, bradykinin, kallikrein, and other vasoactive substances from mast cells and basophils in the superficial dermis, resulting in intradermal edema caused by capillary and venous vasodilation and occasionally caused by leukocyte infiltration.

The process can be immune mediated or nonimmune mediated.

Immune-mediated mast cell activation includes

- Type I hypersensitivity reactions, in which allergen-bound IgE antibodies bind to high-affinity cell surface receptors on mast cells and basophils

- Autoimmune disorders, in which antibodies to an IgE receptor functionally cross-link IgE receptors and cause mast cell degranulation

Nonimmune-mediated mast cell activation includes

- Direct nonallergic activation of mast cells by certain drugs

- Drug-induced cyclooxygenase inhibition that activates mast cells by poorly understood mechanisms

[**Table 71-2.** Some Therapeutic Approaches to Itching]

- Activation by physical or emotional stimuli; mechanism is poorly understood but possibly involves the release of neuropeptides that interact with mast cells

Etiology

Urticaria is classified as acute (< 6 wk) or chronic (> 6 wk); acute cases (70%) are more common than chronic (30%).

Acute urticaria (see Table 71-3) most often results from

- Type I hypersensitivity reactions

A presumptive trigger (eg, drug, food ingestion, insect sting, infection) occasionally can be identified.

Chronic urticaria most often results from

- Idiopathic causes

- Autoimmune disorders

Chronic urticaria often lasts months to years, eventually resolving without a cause being found.

Evaluation

Because there are no definitive diagnostic tests for urticaria, evaluation largely relies on history and physical examination.

History: History of present illness should include a detailed account of the individual episodes of urticaria, including distribution, size, and appearance of lesions; frequency of occurrence; duration of individual lesions; and any prior episodes. Activities and exposures during, immediately before, and within the past 24 h of the appearance of urticaria should be noted. Clinicians specifically should ask about recent exercise; exposure to potential allergens (see Table 71-3), insects, or animals; new laundry detergent or soaps; new foods; recent infections; or recent stressful life events. The patient should be asked about the duration between any suspected trigger and the appearance of urticaria and which particular triggers are suspected. Important associated symptoms include pruritus, rhinorrhea, swelling of the face and tongue, and dyspnea.

Review of systems should seek symptoms of causative disorders, including fever, fatigue, abdominal pain, and diarrhea (infection); heat or cold intolerance, tremor, or weight change (autoimmune thyroiditis); joint pain (cryoglobulinemia, SLE); malar rash (SLE); dry eyes and dry mouth (Sjogren's syndrome); cutaneous ulcers and hyperpigmented lesions after resolution of urticaria (urticarial vasculitis); small pigmented papules (mastocytosis); lymphadenopathy (viral illness, cancer, serum sickness); acute or chronic diarrhea (viral or parasitic enterocolitis); and fevers, night sweats, or weight loss (cancer).

Past medical history should include a detailed allergy history, including known atopic conditions (eg, allergies, asthma, eczema) and known possible causes (eg, autoimmune disorders, cancer). All drug use should be reviewed, including OTC drugs and herbal products, specifically any agents particularly associated with urticaria (see Table 71-3). Family history should elicit any history of rheumatoid disease, autoimmune disorders, or cancer. Social history should cover any recent travel and any risk factors for transmission of infectious disease (eg, hepatitis, HIV).

Physical examination: Vital signs should note the presence of bradycardia or tachycardia and tachypnea. General examination should immediately seek any signs of respiratory distress and also note cachexia, jaundice, or agitation.

Examination of the head should note any swelling of the face, lips, or tongue; scleral icterus; malar rash; tender and enlarged thyroid; lymphadenopathy; or dry eyes and dry mouth. The oropharynx should be inspected and the sinuses should be palpated and transilluminated for signs of occult infection (eg, sinus infection, tooth abscess).

Abdominal examination should note any masses, hepatomegaly, splenomegaly, or tenderness. Neurologic examination should note any tremor or hyperreflexia or hyporeflexia. Musculoskeletal examination should note the presence of any inflamed or deformed joints.

Skin examination should note the presence and distribution of urticarial lesions as well as any cutaneous ulceration, hyperpigmentation, small papules, or jaundice. Urticarial lesions usually appear as well-demarcated transient swellings involving the dermis. These swellings are typically red and vary in size from pinprick to covering wide areas. Some lesions can be very large. In other cases, smaller urticarial lesions may become confluent. However, skin lesions also may be absent at the time of the visit. Maneuvers to evoke physical urticaria can be done during the examination, including exposure to vibration (tuning fork), warmth (tuning fork held under warm water), cold (stethoscope or chilled tuning fork), water, or pressure (lightly scratching an unaffected area with a fingernail).

Red flags: The following findings are of particular concern:

• Angioedema (swelling of the face, lips, or tongue)

[**Table 71-3.** Some Causes of Urticaria]

• Stridor, wheezing, or other respiratory distress

• Hyperpigmented lesions, ulcers, or urticaria that persist > 48 h

• Signs of systemic illness (eg, fever, lymphadenopathy, jaundice, cachexia)

Interpretation of findings: Acute urticaria is nearly always due to some defined exposure to a drug or physical stimulus or an acute infectious illness. However, the trigger is not always clear from the history, particularly because allergy may develop without warning to a previously tolerated substance.

Most **chronic urticaria** is idiopathic. The next most common cause is an autoimmune disorder. The causative autoimmune disorder is sometimes clinically apparent. Urticarial vasculitis sometimes is associated with connective tissue disorders (particularly SLE or Sjogren's syndrome). In urticarial vasculitis, urticaria is accompanied by findings of cutaneous vasculitis; it should be considered when the urticaria are painful rather than pruritic, last > 48 h, do not blanch, or are accompanied by vesicles or purpura.

Testing: Usually, no testing is needed for an isolated episode of urticaria unless symptoms and signs suggest a specific disorder (eg, infection).

Unusual, recurrent, or persistent cases warrant further evaluation. Referral for allergy skin testing should be done, and routine laboratory tests should consist of CBC, blood chemistries, liver function tests, and thyroid-stimulating hormone (TSH). Further testing should be guided by symptoms and signs (eg, of autoimmune disorders) and any abnormalities on the screening tests (eg, hepatitis serologies and ultrasonography for abnormal liver function tests; ova and parasites for eosinophilia; cryoglobulin titer for elevated liver function tests or elevated creatinine; thyroid autoantibodies for abnormal TSH).

Skin biopsy should be done if there is any uncertainty as to the diagnosis or if wheals persist > 48 h (to rule out urticarial vasculitis).

Clinicians should not recommend the patient do an empiric challenge (eg, "Try such and such again and see whether you get a reaction") because subsequent reactions may be more severe.

Treatment

Any identified causes are treated or remedied. Implicated drugs or foods should be stopped.

Nonspecific symptomatic treatment (eg, taking cool baths, avoiding hot water and scratching, and wearing loose clothing) may be helpful.

Drugs: Antihistamines remain the mainstay of treatment. They must be taken on a regular basis, rather than as needed. Newer oral antihistamines often are preferred because of once-daily dosing and because some are less sedating. Appropriate choices include

• Cetirizine 10 mg once/day

• Fexofenadine 180 mg once/day

• Desloratadine 5 mg once/day

• Levocetirizine 5 mg once/day

Older oral antihistamines (eg, hydroxyzine 10 to 25 mg q 4 to 6 h; diphenhydramine 25 to 50 mg q 6 h) are sedating but inexpensive and also quite effective.

Systemic corticosteroids (eg, prednisone 30 to 40 mg po once/day) are given for severe symptoms but should not be used long term. Topical corticosteroids or antihistamines are not beneficial.

Angioedema: Patients who have angioedema involving the oropharynx or any involvement of the airway should receive epinephrine 0.3 mL of 1:1000 solution sc and be admitted to the hospital. On discharge, patients should be supplied with and trained in the use of an auto-injectable epinephrine pen.

Geriatrics Essentials

The older oral antihistamines (eg, hydroxyzine, diphenhydramine) are sedating and can cause confusion, urinary retention, and delirium. They should be used cautiously to treat urticaria in elderly patients.

Key Points

• Urticaria can be caused by allergic or nonallergic mechanisms.

• Most acute cases are caused by an allergic reaction to a specific substance.

• Most chronic cases are idiopathic or result from autoimmune disease.

• Treatment is based on severity; nonsedating antihistamines and avoidance of triggers are first-line options.

• Topical corticosteroids and antihistamines are not beneficial.

• Concomitant systemic symptoms require a thorough evaluation for the etiology.

Skin Manifestations of Internal Disease

The skin frequently serves as a marker for underlying internal disease. The type of lesion typically relates to a specific disease or type of disease.

Internal cancer: Of patients with dermatomyositis, about 50% have associated breast, lung, ovarian, and GI cancers.

Acute onset of multiple seborrheic keratoses (Leser-Trelat sign) may indicate underlying internal cancer, particularly adenocarcinoma. However, because of the high prevalence of seborrheic keratoses in healthy adults, this sign may be overdiagnosed.

Acute febrile neutrophilic dermatosis is associated with hematologic cancer.

Acanthosis nigricans (see Plate 24) that is associated with cancer can be of rapid onset and particularly widespread. Pruritus without a clearly associated dermatitis may indicate occult cancer, often lymphoma.

Paraneoplastic pemphigus is a relatively rare autoimmune blistering disease that has been associated with various cancers, including leukemias.

The carcinoid syndrome (flushing and erythema of the neck) is associated with carcinoid tumor.

Erythema gyratum repens is a rare eruption consisting of concentric erythematous lesions, resembling wood grain, which has been associated with various cancers.

Endocrinopathies: Many skin findings are associated with endocrinopathies but are not specific.

Patients with diabetes mellitus may have acanthosis nigricans, necrobiosis lipoidica, perforating disorders, and scleredema adultorum.

Thyroid disease, both hypothyroidism and hyperthyroidism, can affect hair, nails, and skin.

Cushing's disease causes striae distensae, moon facies, and skin fragility.

Addison's disease is characterized by hyperpigmentation that is accentuated in skin creases and areas of trauma.

GI disorders: Skin conditions commonly associated with GI disorders include

- Pyoderma gangrenosum: Inflammatory bowel disease
- Lichen planus and porphyria cutanea tarda: Hepatitis C infection
- Diffuse hyperpigmentation, or bronze diabetes: Hemochromatosis
- Erythema nodosum: Inflammatory bowel disease, sarcoidosis, and various infections
- Eruptive xanthomas: Elevated serum triglycerides

Chapter 72. Principles of Topical Dermatologic Therapy

Introduction

Topical dermatologic treatments include

• Cleansing agents

• Absorbents

• Anti-infective agents

• Anti-inflammatory agents

• Astringents (drying agents that precipitate protein and shrink and contract the skin)

• Emollients (skin hydrators and softeners)

• Keratolytics (agents that soften, loosen, and facilitate exfoliation of the squamous cells of the epidermis)

Vehicles

Topical therapies can be delivered in various vehicles, which include

• Powders

• Liquids

• Combinations of liquid and oil

The vehicle influences a therapy's effectiveness and may itself cause adverse effects (eg, contact or irritant dermatitis). Generally, aqueous preparations are drying (because the liquid evaporates) and are used in acute inflammatory conditions. Oil-based preparations are moisturizing and are preferred for chronic inflammation.

Powders: Inert powders may be mixed with active agents (eg, antifungals) to deliver therapy. They are prescribed for lesions in moist or intertriginous areas.

Liquids: Liquid vehicles include

• Baths and soaks

• Solutions

• Lotions

• Gels

Baths and soaks are used when therapy must be applied to large areas, such as with extensive contact dermatitis or atopic dermatitis.

Solutions are ingredients dissolved in a solvent, usually ethyl alcohol, propylene glycol, polyethylene glycol, or water. Solutions are convenient to apply (especially to the scalp for disorders such as psoriasis or seborrhea) but tend to be drying. Two common solutions are Burow's solution and Domeboro's solution.

Lotions are water-based emulsions. They are easily applied to hairy skin. Lotions cool and dry acute inflammatory and exudative lesions, such as contact dermatitis, tinea pedis, and tinea cruris.

Gels are ingredients suspended in a solvent thickened with polymers. Gels are often more effective for controlled release of topical agents. They are often used in acne, rosacea, and psoriasis of the scalp.

Combination vehicles: Combinations include

• Creams

• Ointments

Combination vehicles usually contain oil and water but may also contain propylene or polyethylene glycol.

Creams are semi-solid emulsions of oil and water. They are used for moisturizing and cooling and when exudation is present. They vanish when rubbed into skin.

Ointments are oil based (eg, petrolatum) with little if any water. Ointments are optimal lubricants and increase drug penetration because of their occlusive nature; a given concentration of drug is generally more potent in an ointment. They are preferred for lichenified lesions and lesions with thick crusts or heaped-up scales, including psoriasis and lichen simplex chronicus. Ointments are less irritating than creams for erosions or ulcers.

Dressings

Dressings protect open lesions, facilitate healing, increase drug absorption, and protect the patient's clothing.

Nonocclusive dressings: The most common are gauze dressings. They maximally allow air to reach the wound, which is often preferred in healing, and allow the lesion to dry. Nonocclusive dressings wetted with solution, usually saline, are used to help cleanse and debride thickened or crusted lesions. The dressings are applied wet and removed after the solution has evaporated (wet-to-dry dressings); materials from the skin then adhere to the dressing.

Occlusive dressings: Occlusive dressings increase the absorption and effectiveness of topical therapy. Most common are transparent films such as polyethylene (plastic household wrap) or flexible, transparent, semi-permeable dressings. Hydrocolloid dressings can be applied with a gauze cover in patients with cutaneous ulceration. Zinc oxide gelatin (Unna's paste boot) is an effective occlusive dressing for patients with stasis dermatitis and ulcers. Plastic tape impregnated with flurandrenolide, a corticosteroid, can be used for isolated or recalcitrant lesions.

Occlusive dressings applied over topical corticosteroids to increase absorption are sometimes used to treat psoriasis, atopic dermatitis, skin lesions of lupus erythematosus, and chronic hand dermatitis, among other conditions. Systemic absorption of topical corticosteroids may occur and cause

• Development of miliaria

• Skin atrophy

• Striae

• Bacterial or fungal infections

• Adrenal suppression

• Acneiform eruptions

Other occlusive dressings are used to protect and help heal open wounds, such as burns (see p. 3242).

Categories and Indications

Major categories of topical agents include

• Cleansing

• Moisturizing

• Drying

• Anti-inflammatory

• Antimicrobial

• Keratolytic

• Astringent

• Antipruritic

Cleansing agents: The principal cleansing agents are soaps, detergents, and solvents. Soap is the most popular cleanser, but synthetic detergents are also used. Baby shampoos are usually well tolerated around the eyes and for cleansing wounds and abrasions; they are useful for removing crusts and scales in psoriasis, eczema, and other forms of dermatitis. However, acutely irritated, weeping, or oozing lesions are most comfortably cleansed with water or isotonic saline.

Water is the principal solvent for cleansing. Organic solvents (eg, acetone, petroleum products, propylene glycol) are very drying, can be irritating, and cause irritant or, less commonly, allergic contact dermatitis. Removal of hardened tar and dried paint from the skin may require a petrolatum-based ointment or commercial waterless cleanser.

Moisturizing agents: Moisturizers (emollients) restore water and oils to the skin and help to maintain skin hydration. They typically contain glycerin, mineral oil, or petrolatum and are available as lotions, creams, ointments, and bath oils. Stronger moisturizers contain urea 2%, lactic acid 5 to 12%, and glycolic acid 10% (higher concentrations are used as keratinolytics, eg, for ichthyosis). They are most effective when applied to already moistened skin (ie, after a bath or shower).

Drying agents: Excessive moisture in intertriginous areas (eg, between the toes; in the intergluteal cleft, axillae, groin, and inframammary areas) can cause irritation and maceration. Powders dry macerated skin and reduce friction by absorbing moisture. However, some powders tend to clump and can be irritating if they become moist. Cornstarch and talc are most often used. Although talc is more effective, talc may cause granulomas if inhaled and is no longer used in baby powders. Cornstarch may promote fungal growth. Aluminum chloride solutions are another type of drying agent (often useful in hyperhidrosis).

Anti-inflammatory agents: Topical anti-inflammatory agents are either corticosteroids or noncorticosteroids.

Corticosteroids are the mainstay of treatment for most noninfectious inflammatory dermatoses. Lotions are useful on intertriginous areas and the face. Gels are useful on the scalp and in management of contact dermatitis. Creams are useful on the face and in intertriginous areas and for management of inflammatory dermatoses. Ointments are useful for dry scaly areas and when increased potency is required. Corticosteroid-impregnated tape is useful to protect an area from excoriation. It also increases corticosteroid absorption and therefore potency.

Topical corticosteroids range in potency from mild (class VII) to superpotent (class I—see Table 72-1). Intrinsic differences in potency are attributable to fluorination or chlorination (halogenation) of the compound.

Topical corticosteroids are generally applied 2 to 3 times daily, but high-potency formulations may require

application only once/day or even less frequently. Most dermatoses are treated with mid-potency to high-potency formulations; mild formulations are better for mild inflammation and for use on the face or intertriginous areas, where systemic absorption is more likely. All agents can cause skin atrophy, striae, and acneiform eruptions when used for > 1 mo. This effect is particularly problematic on the thinner skin of the face or genitals. Corticosteroids also promote fungal growth. Contact dermatitis in reaction to preservatives and additives is also common with prolonged use. Contact dermatitis to the corticosteroid itself may also occur. Perioral dermatitis occurs with mid-potency or high-potency formulations used on the face but is uncommon with mild formulations. High-potency formulations may cause adrenal suppression when used in children, over extensive skin surfaces, or for long periods. Relative contraindications include conditions in which infection plays an underlying role and acneiform disorders.

Noncorticosteroid anti-inflammatory agents include tar preparations. Tar comes in the form of crude coal tar and is indicated for psoriasis. Adverse effects include irritation, folliculitis, staining of clothes and furniture, and photosensitization. Contraindications include infected skin. Several herbal products are commonly used in commercial products, although their effectiveness has not been well established. Among the most popular are chamomile and calendula.

Antimicrobials: Topical antimicrobials include

• Antibiotics

• Antifungals

• Insecticides

• Nonspecific antiseptic agents

Antibiotics have few indications. Topical clindamycin and erythromycin are used as primary or adjunctive treatment for acne vulgaris in patients who do not warrant or tolerate oral antibiotics. Mupirocin has excellent gram-positive (*Staphylococcus aureus*, streptococci) coverage and can be used to treat impetigo when deep tissues are not affected. OTC antibiotics such as bacitracin and polymyxin are often used in postoperative care of a skin biopsy site and to prevent infection in scrapes, minor burns, and excoriations. Topical neomycin causes contact dermatitis more frequently than other antibiotics. The use of topical antibiotics and washing with antiseptic soaps in healing wounds may, however, actually slow healing.

Antifungals are used to treat candidiasis, a wide variety of dermatophytoses, and other fungal infections (see
Table 82-1 on p. 704).

Insecticides (eg, permethrin, malathion) are used treat lice infestation and scabies (see
Table 83-1 on p. 712).

Nonspecific antiseptic agents include iodine solutions (eg, povidone iodine, clioquinol), gentian violet, silver preparations (eg, silver nitrate, silver sulfadiazine), and zinc pyrithione. Iodine is indicated for presurgical skin preparation. Gentian violet is used when an inexpensive chemically and physically stable antiseptic/antimicrobial is needed. Silver preparations are effective in treating burns and ulcers and have strong antimicrobial

[**Table 72-1.** Relative Potency of Selected Topical Corticosteroids]

properties; several wound dressings are impregnated with silver. Zinc pyrithione is an antifungal and a common ingredient in shampoos used to treat dandruff due to psoriasis or seborrheic dermatitis. Healing wounds should generally not be treated with topical antiseptics other than silver because they are irritating and tend to kill fragile granulation tissue.

Keratolytics: Keratolytics soften and facilitate exfoliation of epidermal cells. Examples include 3 to 6% salicylic acid and urea. Salicylic acid is used to treat psoriasis, seborrhea, acne, and warts. Adverse

effects are burning and systemic toxicity if large areas are covered. It should rarely be used in children and infants. Urea is used to treat plantar keratodermas and ichthyosis. Adverse effects are irritation and intractable burning. It should not be applied to large areas.

Astringents: Astringents are drying agents that precipitate protein and shrink and contract the skin. The most commonly used astringents are aluminum acetate (Burow's solution) and aluminum sulfate plus Ca acetate (Domeboro's solution). Usually applied with dressings or as soaks, astringents are used to treat infectious eczema, exudative skin lesions, and pressure ulcers. Witch hazel is a popular OTC astringent.

Antipruritics: Doxepin is a topical antihistamine that is effective in treating itching of atopic dermatitis, lichen simplex chronic dermatitis, and nummular dermatitis. Topical benzocaine and diphenhydramine (present in certain OTC lotions) are sensitizing and not recommended. Other antipruritics include camphor 0.5 to 3%, menthol 0.1 to 0.2%, pramoxine hydrochloride, and eutectic mixture of local anesthetics (EMLA), which contain equal parts lidocaine and prilocaine in an oil-in-water vehicle. Topical antipruritics are preferred over systemic drugs (eg, oral antihistamines) when smaller surface areas of skin are affected and pruritus is not intractable. Calamine lotion is soothing but not specifically antipruritic.

Chapter 73. Acne and Related Disorders

Introduction

Acne vulgaris is a common skin problem, affecting most adolescents and many adults. Perioral dermatitis and rosacea can produce similar lesions.

Acne Vulgaris

Acne vulgaris (acne) is the formation of comedones, papules, pustules, nodules, and/or cysts as a result of obstruction and inflammation of pilosebaceous units (hair follicles and their accompanying sebaceous gland). It most often affects adolescents. Diagnosis is by examination. Treatment is a variety of topical and systemic agents intended to reduce sebum production, infection, and inflammation and to normalize keratinization.

Pathophysiology

Acne occurs when pilosebaceous units become obstructed with plugs of sebum and desquamated keratinocytes, then colonized and sometimes infected with the normal skin anaerobe *Propionibacterium acnes*. Manifestations differ depending on whether *P. acnes* stimulates inflammation in the follicle; acne can be noninflammatory or inflammatory.

Comedones, uninfected sebaceous plugs impacted within follicles, are the signature of noninflammatory acne. Comedones are termed open or closed depending on whether the follicle is dilated or closed at the skin surface. Inflammatory acne comprises papules, pustules, nodules, and cysts.

Papules appear when lipases from *P. acnes* metabolize triglycerides into free fatty acids (FFA), which irritate the follicular wall. Pustules occur when active *P. acnes* infection causes inflammation within the follicle. Nodules and cysts occur when rupture of follicles due to inflammation, physical manipulation, or harsh scrubbing releases FFAs, bacteria, and keratin into tissues, triggering soft-tissue inflammation.

Etiology

The most common trigger is puberty, when surges in androgen stimulate sebum production and hyperproliferation of keratinocytes. Other triggers include hormonal changes that occur with pregnancy or throughout the menstrual cycle; occlusive cosmetics, cleansing agents, and clothing; and humidity and sweating. Associations between acne exacerbation and diet (eg, chocolate), inadequate face washing, masturbation, and sex are unfounded. Some studies question an association with milk products. Acne may improve in summer months because of sunlight's anti-inflammatory effects. Proposed associations between acne and hyperinsulinism require further investigation.

Symptoms and Signs

Cystic acne can be painful; other types cause no physical symptoms but can be a source of significant emotional distress. Lesion types frequently coexist at different stages.

Comedones appear as whiteheads or blackheads. Whiteheads (closed comedones) are flesh-colored or whitish palpable lesions 1 to 3 mm in diameter; blackheads (open comedones) are similar in appearance but with a dark center.

Papules and pustules are red lesions 2 to 5 mm in diameter. In both, the follicular epithelium becomes damaged with accumulation of neutrophils and then lymphocytes. When the epithelium ruptures, the comedo contents elicit an intense inflammatory reaction in the dermis. Relatively deep inflammation produces papules. Pustules are more superficial.

Nodules are larger, deeper, and more solid than papules. Such lesions resemble inflamed epidermoid cysts, although they lack true cystic structure.

Cysts are suppurative nodules. Rarely cysts become infected and form abscesses. Long-term cystic acne can cause scarring that manifests as tiny, deep pits (icepick scars), larger pits, shallow depressions, or areas of hypertrophic scar.

Acne conglobata is the most severe form of acne vulgaris, affecting men more than women. Patients have abscesses, draining sinuses, fistulated comedones, and keloidal and atrophic scars. The back and chest are severely involved. The arms, abdomen, buttocks, and even the scalp may be affected.

Acne fulminans is acute, febrile, ulcerative acne, characterized by the sudden appearance of confluent abscesses leading to hemorrhagic necrosis. Leukocytosis and joint pain and swelling may also be present.

Pyoderma faciale (also called rosacea fulminans) occurs suddenly on the midface of young women. It may be analogous to acne fulminans. The eruption consists of erythematous plaques and pustules, involving the chin, cheeks, and forehead.

Diagnosis

• Assessment for contributing factors (eg, hormonal, mechanical, or drug-related)

• Determination of severity (mild, moderate, severe)

• Assessment of psychosocial impact

Diagnosis is by examination. Differential diagnosis includes rosacea (in which no comedones are seen), corticosteroid-induced acne (which lacks comedones and in which pustules are usually in the same stage of development), perioral dermatitis (usually with a more perioral and periorbital distribution), and acneiform drug eruptions. Acne severity is graded mild, moderate, or severe based on the number and type of lesions; a standardized system is outlined in
Table 73-1.

Prognosis

Acne of any severity usually remits spontaneously by the early to mid-20s, but a substantial minority of patients, usually women, may have acne into their 40s; options for treatment may be limited because of child-bearing. Many adults occasionally develop mild, isolated acne lesions. Noninflammatory and mild inflammatory acne usually heals without scars. Moderate to severe inflammatory acne heals but often leaves scarring. Scarring is not only physical; acne may be a huge emotional stressor for adolescents who may withdraw, using the acne as an excuse to avoid difficult personal adjustments. Supportive counseling for patients and parents may be indicated in severe cases.

Treatment

• Comedones: Topical tretinoin

• Mild inflammatory acne: Topical antibiotics, benzoyl peroxide, or both

• Moderate acne: Oral antibiotics

• Severe acne: Oral isotretinoin

• Cystic acne: Intralesional triamcinolone

Treatments are directed at reducing sebum production, comedone formation, inflammation, and infection (see
Fig. 73-1). Selection of

[**Table 73-1.** Classification of Acne Severity]

[**Fig. 73-1.** How various drugs work in treating acne.]

treatment is generally based on severity; options are summarized in Table 73-2. Affected areas should be cleansed daily, but extra washing, use of antibacterial soaps, and scrubbing confer no added benefit. Changes in diet are also unnecessary and ineffective, although moderation of milk intake might be considered for treatment-resistant adolescent acne. Peeling agents such as sulfur, salicylic acid, and resorcinol are minor therapeutic adjuncts.

Treatment should involve educating the patient and tailoring the plan to one that is realistic for the patient. Treatment failure can frequently be attributed to lack of adherence to the plan and also to lack of follow-up. Consultation with a specialist may be necessary.

Mild acne: Single-agent therapy is generally sufficient for comedonal acne; papulopustular acne generally requires dual therapy (eg, the combination of tretinoin with benzoyl peroxide or topical antibiotics). Treatment should be continued for 6 wk or until lesions respond. Maintenance treatment may be necessary to maintain control.

A mainstay of treatment for comedones is daily topical tretinoin as tolerated. Daily adapalene gel, tazarotene cream or gel, azelaic acid cream, and glycolic or salicylic acid in propylene glycol are alternatives for patients who cannot tolerate topical tretinoin. Adverse effects include erythema, burning, stinging, and peeling. Adapalene and tazarotene are retinoids; like tretinoin, they tend to be somewhat irritating and photosensitizing. Azelaic acid has comedolytic and antibacterial properties by an unrelated mechanism and may be synergistic with retinoids.

Mild inflammatory acne should be treated with topical benzoyl peroxide, topical antibiotics (eg, erythromycin, clindamycin), glyolic acid, or a combination. Combination preparations of these agents may help limit development of resistance. None have significant adverse effects other than drying and irritation (and rare allergic reactions to benzoyl peroxide). Topical retinoids are often used concomitantly.

Physical extraction of comedones using a comedo extractor is an option for patients unresponsive to topical treatment. Comedo extraction may be done by a physician, nurse, or physician assistant. One end of the comedo extractor is like a blade or bayonet that punctures the closed comedo. The other end exerts pressure to extract the comedo.

Oral antibiotics (eg, tetracycline, minocycline, doxycycline, erythromycin) can be used when wide distribution of lesions makes topical therapy impractical.

Moderate acne: Moderate acne responds best to oral systemic therapy with antibiotics. Antibiotics effective for acne include tetracycline, minocycline, erythromycin, and doxycycline. Full benefit takes ≥ 12 wk. Topical therapy as for mild acne is usually used concomitantly with oral antibiotics.

Tetracycline is usually a good first choice: 250 or 500 mg bid (between meals and at bedtime) for 4 wk or until lesions respond, after which it may be reduced to the lowest effective dose. Rarely, dosage must be increased to

[**Table 73-2.** Drugs Used to Treat Acne]

500 mg qid. After control is achieved, it is reasonable to attempt to taper and discontinue the oral antibiotic and continue topical therapy for control. Because relapse often follows short-term treatment, therapy may need to be continued for months to years, although for maintenance tetracycline 250 or 500 mg once/day is often sufficient. Minocycline 50 or 100 mg bid causes fewer GI adverse effects, is easier to take, and is less likely to cause photosensitization, but it is the most costly option. Erythromycin and doxycycline are considered 2nd-line drugs because both can cause GI adverse effects, and doxycycline is a frequent photosensitizer. Subantimicrobial doses of doxycycline have also been proven effective for acne and rosacea.

Long-term use of antibiotics may cause a gram-negative pustular folliculitis around the nose and in the center of the face. This uncommon superinfection may be difficult to clear and is best treated with oral isotretinoin after discontinuing the oral antibiotic. Ampicillin is an alternative treatment for gram-negative folliculitis. In women, prolonged antibiotic use can cause candidal vaginitis; if local and systemic therapy does not eradicate this problem, antibiotic therapy for acne must be stopped.

Severe acne: Oral isotretinoin is the best treatment for patients with moderate acne in whom antibiotics are unsuccessful and for those with severe inflammatory acne. Dosage of isotretinoin is usually 1 mg/kg once/day for 16 to 20 wk, but the dosage may be increased to 2 mg/kg once/day. If adverse effects make this dosage intolerable, it may be reduced to 0.5 mg/kg once/day. After therapy, acne may continue to improve. Most patients do not require a 2nd course of treatment; when needed, it should be resumed only after the drug has been stopped for 4 mo. Retreatment is required more often if the initial dosage is low (0.5 mg/kg). With this dosage (which is very popular in Europe), fewer adverse effects occur, but prolonged therapy is usually required.

Isotretinoin is nearly always effective, but use is limited by adverse effects, including dryness of conjunctivae and mucosae of the genitals, chapped lips, arthralgias, depression, elevated lipid levels, and the risk of birth defects if treatment occurs during pregnancy. Hydration with water followed by petrolatum application usually alleviates mucosal and cutaneous dryness. Arthralgias (mostly of large joints or the lower back) occur in about 15% of patients. Increased risk for depression and suicide is much publicized but probably rare. CBC; liver function; and fasting glucose, triglyceride, and cholesterol levels should be determined before treatment. Each should be reassessed at 4 wk and, unless abnormalities are noted, need not be repeated until the end of treatment. Triglycerides rarely increase to a level at which the drug should be stopped. Liver function is seldom affected. Because isotretinoin is teratogenic, women of childbearing age are urged to use 2 methods of contraception for 1 mo before treatment, during treatment, and for at least 1 mo after stopping treatment. Pregnancy tests should be done before beginning therapy and monthly until 1 mo after therapy stops.

Intralesional injection of 0.1 mL triamcinolone acetonide suspension 2.5 mg/mL (the 10 mg/mL suspension must be diluted) is indicated for patients with firm (cystic) acne who seek quick clinical improvement and to reduce scarring. Local atrophy may occur but is usually transient. For isolated, very boggy lesions, incision and drainage are often beneficial but may result in residual scarring.

Other forms of acne: Pyoderma faciale is treated with oral corticosteroids and isotretinoin. Acne fulminans is treated with oral corticosteroids and systemic antibiotics. Acne conglobata is treated with oral isotretinoin if systemic antibiotics fail. For acne with endocrine abnormalities, antiandrogens are indicated. Spironolactone, which has some antiandrogen effects, is sometimes prescribed to treat acne at a dose of 50 to 100 mg po once/day. Cyproterone acetate is used in Europe. When other measures fail, an estrogen-progesterone-containing contraceptive may be tried; therapy ≥ 6 mo is needed to evaluate effect.

Scarring: Small scars can be treated with chemical peels, laser resurfacing, or dermabrasion. Deeper, discrete scars can be excised. Wide, shallow depressions can be treated with subcision or collagen injection. Collagen implants are temporary and must be repeated every few years.

Perioral Dermatitis

Perioral dermatitis is an erythematous, papulopustular facial eruption that resembles acne and/or rosacea but typically starts around the mouth.

A variety of causes have been proposed, including exposure to topical corticosteroids and/or fluoride in water and toothpaste, but the etiology is unknown. Despite its name, perioral dermatitis is not a true dermatitis. It primarily affects women of childbearing age and children. The eruption classically starts at the nasolabial folds and spreads perioralally sparing a zone around the vermilion border of the lips. But the eruption can also spread periorbitally and to the forehead.

Diagnosis is by appearance; perioral dermatitis is distinguished from acne by the absence of comedones and from rosacea by the latter's lack of lesions around the mouth and eyes. Seborrheic dermatitis and

contact dermatitis must be excluded. Biopsy, which is generally not clinically necessary, shows spongiosis and a lymphohistiocytic infiltrate affecting vellus hair follicles. In the lupoid variant, granulomas may be present.

Treatment is to stop fluorinated dental products and topical corticosteroids (if being used) and then either use topical antibiotics (eg, erythromycin 2% or metronidazole 0.75% gel or cream bid), or oral tetracycline 250 to 500 mg po bid (between meals) for 4 wk, tapered to the lowest effective dose. Alternative oral antibiotics include doxycycline 50 to 100 mg bid and minocycline 50 to 100 mg bid. In contrast to acne, antibiotics can usually be stopped. Reasons for efficacy of antibiotics are unclear given the absence of evidence of infection. Isotretinoin has been successfully used to treat granulomatous perioral dermatitis.

Rosacea

Rosacea (acne rosacea) is a chronic inflammatory disorder characterized by facial flushing, telangiectasias, erythema, papules, pustules, and in severe cases, rhinophyma (see Plate 43). Diagnosis is based on the characteristic appearance and history. Treatment depends on severity and includes topical metronidazole, topical and oral antibiotics, rarely isotretinoin, and, for severe rhinophyma, surgery.

Rosacea most commonly affects patients aged 30 to 50 with fair complexions, most notably those of Irish and Northern European descent, but it affects and is probably under-recognized in darker-skinned patients.

Etiology

The etiology is unknown, although associations with abnormal vasomotor control, impaired facial venous drainage, an increase in follicle mites (*Demodex folliculorum*), and *Helicobacter pylori* infection have been proposed. People with rosacea may have elevated levels of small antimicrobial peptides that are part of the body's natural defense system. People with rosacea may also have higher than normal levels of cathelicidin as well as another group of enzymes called stratum corneum tryptic enzymes.

Symptoms and Signs

Rosacea is limited to the face and scalp and manifests in 4 phases:

• Prerosacea phase

• Vascular phase

• Inflammatory phase

• Late stage

In the prerosacea phase, patients describe embarrassing flushing and blushing, often accompanied by uncomfortable stinging. Common reported triggers for these flares include sun exposure, emotional stress, cold or hot weather, alcohol, spicy foods, exercise, wind, cosmetics, and hot baths or hot drinks. These symptoms persist throughout other phases of the disorder.

In the vascular phase, patients develop facial erythema and edema with multiple telangiectases, possibly as a result of persistent vasomotor instability.

An inflammatory phase often follows, in which sterile papules and pustules (leading to the designation of rosacea as adult acne) develop.

Some patients go on to develop late-stage rosacea, characterized by coarse tissue hyperplasia of the cheeks and nose (rhinophyma) caused by tissue inflammation, collagen deposition, and sebaceous gland hyperplasia.

The phases of rosacea are usually sequential. Some patients go directly into the inflammatory stage, bypassing the earlier stages. Treatment may cause rosacea to return to an earlier stage. Progression to the late stage is not inevitable.

Ocular rosacea often accompanies facial rosacea and manifests as some combination of blepharoconjunctivitis, iritis, scleritis, and keratitis, causing itching, foreign body sensation, erythema, and edema of the eye.

Diagnosis

• Clinical evaluation

Diagnosis is based on the characteristic appearance; there are no specific diagnostic tests. The age of onset and absence of comedones help distinguish rosacea from acne. Differential diagnosis includes acne vulgaris, SLE, sarcoidosis, photodermatitis, drug eruptions (particularly from iodides and bromides), granulomas of the skin, and perioral dermatitis.

Treatment

• Avoidance of triggers

• Consideration of topical or oral antibiotics

• Consideration of isotretinoin if antibiotics are unsuccessful

• Consideration of dermabrasion and tissue excision for rhinophyma

Primary initial treatment of rosacea involves avoidance of triggers (including use of sunscreen). Antibiotics may be used for inflammatory disease. The objective of treatment is control of symptoms, not cure.

Metronidazole cream 1%, lotion (0.75%), or gel (0.75%) and azelaic acid 20% cream, applied bid, are equally effective; 2.5% benzoyl peroxide, applied once/day or bid, can be added for improved control. Less effective alternatives include sodium sulfacetamide 10%/sulfur 5% lotion; clindamycin 1% solution, gel, or lotion; and erythromycin 2% solution, all applied bid. Many patients require indefinite treatment for chronic control.

Oral antibiotics are indicated for patients with multiple papules or pustules and for those with ocular rosacea; options include tetracycline 250 to 500 mg bid, doxycycline 50 to 100 mg bid, minocycline 50 to 100 mg bid, and erythromycin 250 to 500 mg bid. Dose should be reduced to the lowest one that controls symptoms once a beneficial response is achieved. Recalcitrant cases may respond to oral isotretinoin. Subantimicrobial doses of doxycycline are also effective for acne and rosacea.

Techniques for treatment of rhinophyma include dermabrasion and tissue excision; cosmetic results are good.

Chapter 74. Bullous Diseases

Introduction

Bullae are elevated, fluid-filled blisters ≥ 5 mm in diameter. Bullous diseases include bullous pemphigoid, dermatitis herpetiformis, epidermolysis bullosa acquisita, herpes gestationis (pemphigoid gestationis—see p. 2666), linear IgA disease, pemphigus vulgaris, and pemphigus foliaceus. Staphylococcal scalded skin syndrome (see p. 701) and toxic epidermal necrolysis (see p. 689) also cause bullae.

Bullous Pemphigoid

Bullous pemphigoid is an autoimmune skin disorder causing chronic, pruritic bullous eruptions in elderly patients. Diagnosis is by skin biopsy. Corticosteroids are used initially. Most patients require long-term maintenance therapy, for which a variety of drugs can be used.

In bullous pemphigoid, antibodies are directed against the basement membrane zone of the epidermis, causing separation between the epidermis and dermis. Bullous pemphigoid must be distinguished from pemphigus vulgaris (see p. 658), a much more serious disease.

Symptoms and Signs

Characteristic tense bullae develop on normal-appearing or erythematous skin, most often in flexural areas. Nikolsky's sign, in which lateral pressure on skin adjacent to a blister causes epidermal detachment, is negative. Bullous pemphigoid can manifest initially as hives with annular, dusky-red, edematous lesions, with or without peripheral vesicles. Itching is common, usually without other symptoms. Oral lesions occur in about one third of patients but heal rapidly.

Diagnosis

• Skin biopsy and antibody titers

Patients should have a skin biopsy and serum antibody titers for hemidesmosomal BP antigens BP230 (BPAg1) and BP180 (BPAg2).

Bullous pemphigoid must be differentiated from pemphigus vulgaris (see Table 74-1), linear IgA disease, erythema multiforme, drug-induced eruptions, benign mucous membrane pemphigoid, paraneoplastic pemphigoid, dermatitis herpetiformis, and epidermolysis bullosa acquisita.

Prognosis

Prognosis is good, and the disorder usually subsides within months to years; however, the disorder is potentially fatal, especially in the elderly and debilitated patients, with death being caused by infection and sepsis or the effects of the drugs.

Treatment

• Corticosteroids, topical or oral

• Anti-inflammatory drugs

Mild bullous pemphigoid sometimes resolves without treatment, but resolution usually

[**Table 74-1.** Distinguishing Pemphigoid from Pemphigus Vulgaris]

takes months or years. Patients with more severe disease receive prednisone 60 to 80 mg po once/day, which can be tapered to a maintenance level of ≤ 10 to 20 mg/day after several weeks. Most patients achieve remission after 2 to 10 mo. Occasional new lesions in elderly patients do not require increasing the prednisone dosage.

The disorder occasionally responds to a combination of tetracycline or minocycline and nicotinamide. Other treatment options include dapsone, sulfapyridine, erythromycin, and tetracycline used alone for their anti-inflammatory rather than their antibiotic properties. IV immune globulin has been used occasionally. For patients with generalized and recalcitrant disease, immunosuppressants such as azathioprine, cyclophosphamide, rituximab, and cyclosporine may be used. However, use of immunosuppressants for bullous pemphigoid is controversial.

Dermatitis Herpetiformis

Dermatitis herpetiformis is a cutaneous manifestation associated with gluten sensitivity. It produces a chronic eruption characterized by clusters of intensely pruritic vesicles, papules, and urticaria-like lesions. The cause is autoimmune. Diagnosis is by skin biopsy with direct immunofluorescence testing. Treatment is usually with dapsone or sulfapyridine and a gluten-free diet.

This disease usually manifests in patients 30 to 40 yr old (but may occur from age 2 to 90 yr) and is rare in blacks and Asians.

More than 90% of affected patients have a gluten-sensitive enteropathy, which is often asymptomatic. Dermatitis herpetiformis develops in 15 to 25% of patients with celiac sprue. Patients have a slightly higher incidence of other autoimmune disorders, including type 1 diabetes mellitus, sarcoidosis, SLE, and thyroid abnormalities. The incidence of enteropathy-associated T-cell lymphoma is also increased.

The term herpetiformis refers to the clustered appearance of the lesions rather than a relationship to herpesvirus.

Symptoms and Signs

Onset is usually gradual. Vesicles, papules, and urticaria-like lesions are usually distributed symmetrically on extensor aspects (elbows, knees, sacrum, buttocks, occiput). Vesicles and papules occur in about one third of patients. Itching and burning are severe, and scratching often obscures the primary lesions with eczematization of nearby skin, leading to an erroneous diagnosis of eczema. NSAIDs and iodides may worsen the rash.

Diagnosis

• Skin biopsy

Diagnosis is based on skin biopsy and direct immunofluorescence testing of a lesion and adjacent normal-appearing skin. Granular IgA deposition in the dermal papillary tips is invariably present and important for diagnosis. Patients should be evaluated for celiac sprue (see p. 158).

Treatment

• Gluten-free diet

• Dapsone

Strict adherence to a gluten-free diet for a prolonged time (eg, 6 to 12 mo) controls the disease in some patients, obviating or reducing the need for drug therapy. When drugs are needed, dapsone generally results in remarkable improvement. Initial dosages of dapsone are 25 to 50 mg po once/day in adults and 0.5 mg/kg in children. Usually, this dose dramatically relieves symptoms, including itching, within 1 to 3 days; if it does, the dose is continued. If no improvement occurs, the dose can be increased every week, up to 300 mg/day. Most patients can be maintained on 50 to 150 mg/day, and some require as little as 25 mg/wk. After initial therapy and stabilization of the disease, the majority of patients can be maintained on a strict gluten-free diet. Although less effective, sulfapyridine may be used as an alternative for patients who cannot tolerate dapsone. Initial oral dosage is 500 mg bid, increasing by 1 g/day q 1 to 2 wk until

disease is controlled. Maintenance dosage varies from 500 mg twice/wk to 1000 mg once/day. Colchicine is another treatment option. Treatment continues until lesions resolve.

In patients with G6PD deficiency, dapsone may cause severe hemolysis. Patients receiving dapsone or sulfapyridine should have a baseline CBC; CBC is then done weekly for 4 wk, then every 2 to 3 wk for 8 wk, and every 12 to 16 wk thereafter. Hemolytic anemia and methemoglobinemia are the most frequently encountered adverse effects. CNS or liver toxicity is rare. If dapsone therapy causes considerable hemolysis, significant cardiopulmonary problems, or peripheral neuropathy, sulfapyridine may be used. Sulfapyridine usually does not induce significant hemolysis.

Epidermolysis Bullosa Acquisita

Epidermolysis bullosa acquisita is a chronic autoimmune mucocutaneous disease causing blistering and skin fragility.

Epidermolysis bullosa acquisita usually appears in adults. Bullous lesions may develop on normal-appearing skin spontaneously or may be caused by minor trauma. The trauma-prone areas of the skin, such as the extensor surfaces of elbows, knees, ankles, and buttocks, are most commonly affected. Pain and scarring are common. Because the hands and feet are often involved, disability can be significant. Occasionally, mucosa of eyes, mouth, or genitals is involved. Laryngeal and esophageal involvement also occurs. Diagnosis is by skin biopsy. Lesions respond poorly to corticosteroids. Mild disease may be treated with colchicine, but more severe disease may require cyclosporine or immune globulin.

Linear Immunoglobulin A Disease

Linear immunoglobulin A (IgA) disease is an uncommon bullous disease distinguished from bullous pemphigoid and dermatitis herpetiformis by the linear deposits of IgA in the basement membrane zone.

Linear IgA disease occurs in adults and children. The childhood form is most frequently termed chronic bullous disease of childhood.

In linear IgA disease, vesicular or bullous skin lesions occur frequently in a clustered (herpetiform) arrangement. There is a predilection for flexural areas (eg, inguinal crease). As in dermatitis herpetiformis, severe burning and pruritus of cutaneous lesions are prominent features. It was previously considered a form of dermatitis herpetiformis but has no concomitant gluten-sensitive enteropathy and immunopathology. Also, genetic studies indicate that linear IgA disease is a separate disorder. Drug-induced linear IgA disease, most commonly associated with vancomycin, has been reported.

Diagnosis is by skin biopsy. Dapsone is the treatment of choice. Doses should be similar to those used for dermatitis herpetiformis (see p. 657), and CBC monitoring should follow the same parameters. Other treatment options include glucocorticoids (systemic, topical, and intralesional), cyclophosphamide, azathioprine, colchicine, tetracycline and nicotinamide, and cyclosporine.

Pemphigus Vulgaris

Pemphigus vulgaris is an uncommon, potentially fatal, autoimmune disorder characterized by intraepidermal blisters and extensive erosions on apparently healthy skin and mucous membranes. Diagnosis is by skin biopsy with direct immunofluorescence testing. Treatment is with corticosteroids and sometimes immunosuppressants.

Pemphigus vulgaris usually occurs in middle-aged or elderly patients and is rare in children. One variant, paraneoplastic pemphigus, occurs in older patients with cancer (primarily lymphoreticular); outcome is poor.

The disorder is characterized by the presence of autoantibodies directed against intercellular adhesion molecules desmoglein-1 and desmoglein-3 in the epidermis. They are Ca-dependent cadherins, involved in adhesion and cell signaling between epidermal cells. Acantholysis results from either direct inhibition of

function of the desmogleins by autoantibody binding or from autoantibody-induced cell signaling that results in down-regulation of cell-cell adhesion and formation of blisters. These autoantibodies are present in both serum and skin during active disease. Any area of stratified squamous epithelium may be affected, including mucosal surfaces.

Symptoms and Signs

The primary lesions are flaccid bullae of various sizes (see Plate 41), but often skin or mucosa just shears off, leaving painful erosions. Lesions typically occur first in the mouth, where they rupture and remain as chronic, often painful, erosions for variable periods before the skin is affected; dysphagia and poor oral intake are common. Lesions also may occur in the upper esophagus. Cutaneous bullae typically arise from normal-appearing skin, rupture, and leave a raw area and crusting. Itching is usually absent. Open skin lesions often become infected. If large portions of the body are affected, fluid and electrolyte loss may be significant.

Diagnosis

• Clinical evaluation

• Biopsy with direct immunofluorescence testing

• Sometimes titers of antibodies against desmoglein-3 or desmoglein-1

Pemphigus vulgaris should be suspected in patients with any bullous disorder or chronic mucosal ulceration. It must be differentiated from other chronic oral ulcers and from other bullous dermatoses (eg, pemphigus foliaceus, bullous pemphigoid, mucous membrane pemphigoid, drug eruptions, toxic epidermal necrolysis, erythema multiforme, dermatitis herpetiformis, bullous contact dermatitis). Two physical signs in pemphigus vulgaris are helpful:

• Lateral pressure on skin adjacent to a blister causes epidermal detachment (Nikolsky's sign).

• Pressure on a blister can cause the blister to extend to adjacent skin (Asboe-Hansen sign).

Biopsy of the edge of a fresh lesion and of a nearby area of normal skin is required; light microscopy and direct immunofluorescence testing are usually diagnostic. Serum antibodies (eg, to desmoglein-3) can be used for diagnosis and for differentiating from pemphigus foliaceus; serial titers can help follow disease activity.

Prognosis

Before systemic corticosteroids were used, pemphigus vulgaris was usually fatal; most patients died within 5 yr of disease onset. Even with treatment, pemphigus vulgaris is a serious disorder with an inconsistent and unpredictable response to treatment, a prolonged course, and virtually inevitable adverse drug effects.

Treatment

• Corticosteroids, oral or IV

• Sometimes immunosuppressants

• Sometimes plasmapheresis and IV immune globulin (IVIG)

Referral to a dermatologist with expertise in treating this disorder is recommended. Hospitalization is required initially for all but the most minor cases. Cleansing and dressing of open skin lesions is similar to that done for partial-thickness burns (eg, reverse isolation, hydrocolloid or silver sulfadiazine dressings —see p. 3246).

Drug treatment aims to decrease the production of autoantibodies and stop the eruption of new lesions. The mainstay is systemic corticosteroids. Some patients with few lesions may respond to oral prednisone 20 to 30 mg once/day, but most require 1.0 mg/kg once/day as an initial dose. Some clinicians begin with even higher doses, which may slightly hasten initial response but does not appear to improve outcome. If new lesions continue to appear after 5 to 7 days, IV pulse therapy with methylprednisolone 1 g once/day can be tried.

Immunosuppressants such as methotrexate, cyclophosphamide, azathioprine, gold, mycophenolate mofetil, cyclosporine, or rituximab can reduce the need for corticosteroids and thus minimize the undesirable effects of long-term corticosteroid use. Plasmapheresis and high-dose IVIG to reduce antibody titers have also been effective.

Once no new lesions have appeared for 7 to 10 days, corticosteroid dose should be tapered monthly by about 10 mg/day (tapering continues more slowly once 20 mg/day is reached). A relapse requires a return to the starting dose. If the patient has been stable after a year, a trial without treatment can be attempted but must be closely monitored.

Pemphigus Foliaceus

Pemphigus foliaceus is a generally benign blistering disorder. It is characterized by splitting high in the epidermis, causing erosions to form on the skin.

Pemphigus foliaceus usually occurs in middle-aged patients. Foci of high incidence occur in South America, especially Brazil.

The primary lesion is a flaccid bulla. However, because splitting occurs high in the epidermis, bullae are rarely seen; the blisters are so fragile that they rupture. Clinically, scaly, crusted cutaneous erosions, often on an erythematous base, can be seen. Mucosal surfaces are not usually involved. In one variant, pemphigus erythematosus, lesions occur on light-exposed skin and are often similar to those of cutaneous lupus erythematosus.

Diagnosis is by biopsy of a lesion and neighboring normal skin and by serum antibody titers against the cell adhesion molecule desmoglein 1 (160 kd). Because the disorder is much more benign than pemphigus vulgaris, treatment is generally less aggressive. Superpotent topical corticosteroids may be sufficient in some patients. Others require oral prednisone and additional immunosuppressants. A combination of tetracycline 500 mg qid and nicotinamide 1.5 g/day has been effective in some patients. Plasmapheresis is an option for severe disease.

Chapter 75. Cornification Disorders

Introduction

Cornification disorders include calluses, corns, ichthyosis, and keratosis pilaris.

Calluses and Corns

(Tylomas; Helomas; Clavi)

Calluses and corns are circumscribed areas of hyperkeratosis at a site of intermittent pressure or friction. Calluses are more superficial, cover broader areas of skin, and usually asymptomatic. Corns are deeper, more focal, and frequently painful. Diagnosis is by appearance. Treatment is with manual abrasion with or without keratolytics. Prevention involves altering biomechanics, such as changing footwear. Rarely, surgery is required.

Calluses and corns are caused by intermittent pressure or friction, usually over a bony prominence (eg, heel, metatarsal heads).

Corns consist of a sharply circumscribed keratinous plug, pea-sized or slightly larger, which extends through most of the underlying dermis. An underlying adventitial bursitis may develop. Hard corns occur over prominent bony protuberances, especially on the toes and plantar surface. Soft corns occur between the toes. Most corns result from poorly fitting footwear, but small seed-sized corns on non-weight-bearing aspects of the soles and palms may represent inherited keratosis punctata.

Calluses lack a central plug and have a more even appearance. They usually occur on the hands or feet but may occur elsewhere, especially in a person whose occupation entails repeated trauma to a particular area (eg, the mandible and clavicle of a violinist).

Symptoms and Signs

Calluses are usually asymptomatic but, if friction is extreme, may become irritated, causing mild burning discomfort. At times, the discomfort may mimic that of interdigital neuralgia.

Corns may be painful or tender when pressure is applied. A bursa or fluid-filled pocket sometimes forms beneath a corn.

Diagnosis

• Clinical evaluation

A corn may be differentiated from a plantar wart or callus by paring away the horny skin. After paring, a callus shows smooth translucent skin, whereas a wart (see p. 715) appears sharply circumscribed, sometimes with soft macerated tissue or with central black dots (bleeding points) representing thrombosed capillaries. A corn, when pared, shows a sharply outlined yellowish to tan translucent core that interrupts the normal architecture of the papillary dermis. Interdigital neuralgia can be ruled out by the absence of interspace pain on palpation.

Treatment

• Manual removal

• Keratolytics

• Cushioning

• Altering foot biomechanics

A nail file, emery board, or pumice stone used immediately after bathing is often a practical way to manually remove hyperkeratotic tissue. Keratolytics (eg, 17% salicylic acid in collodion, 40% salicylic acid plasters, 40% urea) can also be used, taking care to avoid applying the agents to normal skin. Normal skin may be protected by covering it with petrolatum before application of the keratolytic.

Cushioning and altering foot biomechanics can help prevent corns and help treat existing corns. Although difficult to eliminate, pressure on the affected surface should be reduced and redistributed. For foot lesions, soft, well-fitting shoes are important; they should have a roomy toe box so that toes can move freely in the shoe. Stylish shoes often prevent this freedom of motion. Shoes that increase discomfort of a lesion should be eliminated from the wardrobe. Pads or rings of suitable shapes and sizes, moleskin or foam-rubber protective bandages, arch inserts (orthotics), or metatarsal plates or bars may help redistribute the pressure. For corns and calluses on the ball of the foot, an orthotic should not be full length but should extend only to the ball or part of the shoe immediately behind the corn or callus. Surgical off-loading or removal of the offending bone is rarely necessary.

Patients who have a tendency to develop calluses and corns may need the regular services of a podiatrist. Patients with impaired peripheral circulation, especially if associated with diabetes, require expert care.

Ichthyosis

Ichthyosis is scaling and flaking of skin ranging from mild but annoying dryness (xeroderma) to severe disfiguring disease (inherited ichthyosis). Ichthyosis can also be a sign of systemic disease. Diagnosis is clinical. Treatment involves emollients and sometimes oral retinoids.

Xeroderma: Xeroderma (xerosis), or dry skin, is neither inherited nor associated with systemic abnormalities. Dry skin results from loss of the water content of the skin, resulting in fine white scales. Risk factors for xerosis include the following:

• Residence in a dry, cold climate

• Older age

• Atopic dermatitis

• Frequent bathing, particularly if using harsh soaps

Inherited ichthyoses: Inherited ichthyoses, which are characterized by excessive accumulation of scale on the skin surface, are classified according to clinical and genetic criteria (see Table 75-1). Some occur in isolation without

[**Table 75-1.** Clinical and Genetic Features of Some Inherited Ichthyoses]

associated abnormalities (eg, ichthyosis vulgaris, X-linked ichthyosis, lamellar ichthyosis, epidermolytic hyperkeratosis [bullous congenital ichthyosiform erythroderma]). Other ichthyoses are part of a syndrome that involves multiple organs. For instance, Refsum's disease (see p. 3024) and Sjogren-Larsson syndrome (hereditary intellectual disability and spastic paralysis caused by a defect in fatty aldehyde dehydrogenase) are autosomal recessive conditions with skin and extracutaneous organ involvement. A dermatologist should assist in diagnosis and management, and a medical geneticist should be consulted for genetic counseling.

Acquired ichthyosis: Ichthyosis may be an early manifestation of some systemic disorders (eg, leprosy, hypothyroidism, lymphoma, AIDS). Some drugs cause ichthyosis (eg, nicotinic acid, triparanol, butyrophenones). The dry scaling may be fine and localized to the trunk and legs, or it may be thick and widespread. Biopsy of ichthyotic skin is usually not diagnostic of the systemic disorder; however, there are exceptions, most notably sarcoidosis, in which a thick scaling may appear on the legs, and biopsy usually shows the typical granulomas.

Treatment

• Minimization of exacerbating factors

• Moisturization and keratolytics

• Sometimes infection prophylaxis

When ichthyosis is caused by a systemic disorder, abatement is greatest if the primary disorder can be corrected. Otherwise, treatment is symptomatic, including using emollients and keratolytics and avoiding drying.

Moisturization and keratolytics: In any ichthyosis, there is impaired epidermal barrier function, and moisturizers should be applied immediately after bathing. Substances that are applied to the skin may have increased absorption. For example, hexachlorophene products should not be used because of increased absorption and toxicity.

An emollient, preferably plain petrolatum, mineral oil, or lotions containing urea or α-hydroxy acids (eg, lactic, glycolic, and pyruvic acids), should be applied twice daily, especially after bathing while the skin is still wet. Blotting with a towel removes excess applied material.

Ichthyosis typically responds well to propylene glycol. To remove scale (eg, if ichthyosis is severe), patients can apply a preparation containing 40 to 60% propylene glycol in water under occlusion (eg, a thin plastic film or bag), every night after hydrating the skin (eg, by bathing or showering); in children, the preparation should be applied twice daily without occlusion. Occlusion should be maintained overnight. After scaling has decreased, less frequent application is required. Other useful keratolytics include ceramide-based creams, 6% salicylic acid gel, hydrophilic petrolatum and water (in equal parts), and the α-hydroxy acids in various bases. Topical calcipotriol cream has been used with success; however, this vitamin D derivative can result in hypercalcemia when used over broad areas, especially in small children.

Retinoids are effective in treating ichthyosis. Oral synthetic retinoids are effective for most ichthyoses. Acitretin (see p. 679) is effective in treating most forms of inherited ichthyosis. In lamellar ichthyosis, 0.1% tretinoin cream or oral isotretinoin may be effective. The lowest effective dose should be used. Long-term (1 yr) treatment with oral isotretinoin has resulted in bony exostoses in some patients, and other long-term adverse effects may arise. (CAUTION: *Oral retinoids are contraindicated in pregnancy because of their teratogenicity, and acitretin should be avoided in women of childbearing potential because of its teratogenicity and long half-life.)*

Infection prophylaxis: Patients with epidermolytic hyperkeratosis may need long-term treatment with cloxacillin 250 mg po tid or qid or erythromycin 250 mg po tid or qid, as long as thick intertriginous scaling is present, to prevent bacterial superinfection from causing painful, foul-smelling pustules. Regularly using soaps containing chlorhexidine may also reduce the bacteria, but these soaps tend to dry the skin.

Keratosis Pilaris

Keratosis pilaris is a disorder of keratinization in which horny plugs fill the openings of hair follicles.

Keratosis pilaris is common. The cause is unknown, but there is often an autosomal dominant inheritance. Multiple small, pointed, keratotic follicular papules appear mainly on the lateral aspects of the upper arms, thighs, and buttocks. Facial lesions may also occur, particularly in children. Lesions are most prominent in cold weather and sometimes abate in the summer. Skin may appear red. The problem is mainly cosmetic, but the disorder may cause itching or, rarely, follicular pustules.

Treatment is usually unnecessary and often unsatisfactory. Hydrophilic petrolatum and water (in equal parts), cold cream, or petrolatum with 3% salicylic acid may help flatten the lesions. Buffered lactic acid (ammonium lactate) lotions or creams, urea creams, 6% salicylic acid gel, or 0.1% tretinoin cream may also be effective. Acid creams should be avoided in young children because of burning and stinging.

Pulse-dye laser has been used successfully to treat facial redness.

Chapter 76. Dermatitis

Introduction

Dermatitis is superficial inflammation of the skin characterized by redness, edema, oozing, crusting, scaling, and sometimes vesicles. Pruritus is common. Eczema is a term often used interchangeably with dermatitis.

Atopic Dermatitis

Atopic dermatitis (AD) is an immune-mediated inflammation of the skin arising from an interaction between genetic and environmental factors. Recent research suggests that a heritable epidermal barrier defect is a primary cause, and defects in the *filaggrin* gene have been specifically implicated. Pruritus is the primary symptom; skin lesions range from mild erythema to severe lichenification. Diagnosis is by history and examination. Treatment is moisturizers, avoidance of allergic and irritant triggers, and often topical corticosteroids. Atopic dermatitis frequently resolves completely by age 30.

Etiology

AD primarily affects children in urban areas or developed countries; at least 5% of children in the US are affected. Like asthma, it may be linked to proallergic/proinflammatory T-cell immune responses. Such responses are becoming more common in developed countries because trends toward smaller families, cleaner indoor environments, and early use of vaccinations and antibiotics deprive children of the early exposure to infections and allergens that otherwise suppress proallergic T cells and thereby induce tolerance to various antigens.

Pathophysiology

AD can be divided into 2 forms:

• Extrinsic: IgE-mediated (70 to 80% of cases)

• Intrinsic: Non-IgE-mediated (20 to 30% of cases)

Extrinsic AD: This form occurs when environmental exposures trigger immunologic, usually allergic (ie, IgE-mediated), reactions in genetically susceptible people. Common environmental triggers include

• Foods (eg, milk, eggs, soy, wheat, peanuts, fish)

• Airborne allergens (eg, dust mites, molds, dander)

• *Staphylococcus aureus* colonization on skin due to deficiencies in endogenous antimicrobial peptides

• Topical products (eg, cosmetics)

AD is common within families, suggesting a genetic component. Many patients with AD have a mutation in the gene encoding for the filaggrin protein, which is a component of the cornified cell envelope produced by differentiating keratinocytes. Also, research has shown that skin affected by AD is deficient in ceramides, which increases transepidermal water loss.

Intrinsic AD: This form is not mediated by IgE. Intrinsic AD is nonfamilial and idiopathic, and its pathophysiology is generally not well understood.

Symptoms and Signs

Manifestations of intrinsic and extrinsic AD are similar. AD usually appears in infancy, typically by 3 mo. In the acute phase, lasting 1 to 2 mo (see

Plate 27), red, weeping, crusted lesions appear on the face and spread to the neck, scalp, extremities, and abdomen. In the chronic phase (see
Plate 28), scratching and rubbing create skin lesions (typically erythematous macules and papules that lichenify with continued scratching). Lesions typically appear in antecubital and popliteal fossae and on the eyelids, neck, and wrists and may occasionally become generalized. Lesions slowly resolve to dry scaly macules (xerosis) that can fissure and facilitate exposure to irritants and allergens. In older children and adults, intense pruritus is the key feature. Patients have a reduced threshold for perceiving itch, and itch worsens with allergen exposures, dry air, sweating, local irritation, wool garments, and emotional stress.

Complications: Secondary bacterial infections, especially staphylococcal and streptococcal, and regional lymphadenitis are common.

Eczema herpeticum (Kaposi's varicelliform eruption) is a diffuse herpes simplex infection occurring in patients with AD. It manifests as grouped vesicles in areas of active or recent dermatitis, although normal skin can be involved. High fever and adenopathy may develop after several days. Occasionally, this infection can become systemic, which may be fatal. Sometimes the eye is involved, causing a painful corneal lesion.

Fungal and nonherpetic viral skin infections (eg, common warts, molluscum contagiosum) can also occur.

Patients with long-standing AD may develop cataracts in their 20s or 30s.

Frequent use of topical products exposes the patient to many potential allergens, and contact dermatitis may aggravate and complicate AD, as may the generally dry skin that is common among these patients.

Diagnosis

• Clinical evaluation

• Sometimes testing for allergic triggers with skin prick testing or radioallergosorbent testing levels

Diagnosis is clinical (see
Table 76-1). AD is often hard to differentiate from other dermatoses (eg, seborrheic dermatitis, contact dermatitis, nummular dermatitis, psoriasis), although a family history of atopy and the distribution of lesions are helpful. For example, psoriasis is usually extensor rather than flexurally distributed, may involve the fingernails, and has a shinier (micaceous) scale. Seborrheic dermatitis affects the face (eg, nasolabial folds, eyebrows, glabellar region, scalp) most commonly. Nummular dermatitis is not flexural, and lichenification is rare. Because patients can still develop other skin disorders, not all subsequent skin problems should be attributed to AD.

There is no definitive laboratory test for AD. However, allergic precipitants of AD can be identified with skin testing, measurement of allergen-specific IgE levels, or both.

Prognosis

AD in children often abates by age 5 yr, although exacerbations are common throughout adolescence and into adulthood. Girls and patients with severe disease, early age of onset, family history, and associated rhinitis or asthma are more likely to have prolonged disease. Even in these patients, AD frequently resolves completely by age 30. AD may have long-term psychologic sequelae as children confront many challenges of living with a visible, sometimes disabling, skin disease during formative years.

[**Table 76-1.** Clinical Findings in Atopic Dermatitis*]

Treatment

• Supportive care (eg, moisturizers, symptomatic treatment for pruritus)

• Avoidance of precipitating factors

• Topical corticosteroids

• Sometimes immune modulators (most often topical but sometimes oral)

• Sometimes ultraviolet (UV) therapy

Treatment can usually be given at home, but patients who have exfoliative dermatitis (see p. 668), cellulitis, or eczema herpeticum may need to be hospitalized.

Supportive care: Skin care involves moisturizing. Bathing and hand washing should be infrequent, and lukewarm (not hot) water should be used; soap use should be minimized on dermatitic areas because it may be drying and irritating. Colloidal oatmeal baths can be helpful. When toweling dry, the skin should be blotted or patted dry rather than rubbed.

Body oils or emollients such as white petrolatum, vegetable oil, or hydrophilic petrolatum (unless the patient is allergic to lanolin) applied immediately after bathing may help retain skin moisture and reduce itching. Continuously wet dressings (not wet-to-dry) are an alternative for severe lesions. Coal tar cream or oil can be an effective topical anti-pruritic but also can be inconvenient because it stains clothing.

Antihistamines can help relieve pruritus. Options include hydroxyzine 25 mg po tid or qid (for children, 0.5 mg/kg q 6 h or 2 mg/kg in a single bedtime dose) and diphenhydramine 25 to 50 mg po at bedtime. Low-sedating H_1 receptor blockers, such as loratadine 10 mg po once/day, fexofenadine 60 mg po bid or 180 mg po once/day, and cetirizine 5 to 10 mg po once/day, may be useful, although their efficacy has not been defined. Doxepin (a tricyclic antidepressant also with H_1 and H_2 receptor blocking activity) 25 to 50 mg po at bedtime may also help, but its use is not recommended for children < 12 yr. Fingernails should be cut short to minimize excoriations and secondary infections.

Avoidance of precipitating factors: Household antigens can be controlled by using synthetic fiber pillows and impermeable mattress covers; washing bedding in hot water; removing upholstered furniture, soft toys, carpets, and pets (to reduce dust mites and animal dander); using air circulators equipped with high-efficiency particulate air (HEPA) filters in bedrooms and other frequently occupied living areas; and using dehumidifiers in basements and other poorly aerated damp rooms (to reduce molds). Reduction of emotional stress is useful but often difficult. Antistaphylococcal antibiotics, both topical (eg, mupirocin, fusidic acid) and oral (eg, dicloxacillin, cephalexin, erythromycin [all 250 mg qid]), can control *S. aureus* nasal colonization and are indicated in patients with severe disease unresponsive to specific therapies and positive nasal cultures. Extensive dietary changes intended to eliminate exposure to allergenic foods are unnecessary and probably ineffective; food hypersensitivities rarely persist beyond childhood.

Corticosteroids: Corticosteroids are the mainstay of therapy. Creams or ointments applied twice daily are effective for most patients with mild or moderate disease. Emollients are applied between corticosteroid applications and can be mixed with them to decrease the corticosteroid amount required to cover an area. Systemic corticosteroids (prednisone 60 mg or, for children 1 mg/kg, po once/day for short courses of 7 to 14 days) are indicated for extensive or refractory disease but should be avoided whenever possible, because disease often recurs and topical therapy is safer. Prolonged, widespread use of high-potency corticosteroid creams or ointments should be avoided in infants because adrenal suppression may ensue.

Other therapies: Tacrolimus and pimecrolimus are T-cell inhibitors effective for AD. They should be used when patients do not respond to corticosteroids and tar or when corticosteroid adverse effects such as skin atrophy, striae formation, or adrenal suppression is a concern. Tacrolimus or pimecrolimus cream is applied twice daily. Burning or stinging after application is usually transient and abates after a few days. Flushing is less common.

Repair of the stratum corneum and barrier function may help alleviate AD. Research has shown that skin affected by AD is particularly deficient in ceramides and that a deficiency in ceramides increases transepidermal water loss. Several ceramide-containing emollient products are considered helpful for AD

control.

Phototherapy is helpful for extensive AD. Natural sun exposure ameliorates disease in many patients, including children. Alternatively, therapy with ultraviolet A (UVA) or B (UVB) may be used. Narrowband UVB therapy is proving more effective than traditional broadband UVB therapy and is also effective in children. Psoralen plus UVA (PUVA—see p. 679) therapy is reserved for extensive, refractory AD. Adverse effects include sun damage (eg, PUVA lentigines, nonmelanoma skin cancer). Because of these adverse effects, PUVA is rarely indicated for children or young adults.

Systemic immune modulators effective in at least some patients include cyclosporine, interferon gamma, mycophenolate, methotrexate, and azathioprine. All downregulate or inhibit T-cell function and have anti-inflammatory properties. These agents are indicated for widespread, recalcitrant, or disabling AD that fails to abate with topical therapy and phototherapy.

Eczema herpeticum is treated with acyclovir. Infants receive 10 to 20 mg/kg IV q 8 h; older children and adults with mild illness may receive 200 mg po 5 times/day. Involvement of the eye is considered an ophthalmic emergency, and if eye involvement is suspected, an ophthalmology consult should be obtained.

Contact Dermatitis

Contact dermatitis (CD) is acute inflammation of the skin caused by irritants or allergens. The primary symptom is pruritus. Skin changes range from erythema to blistering and ulceration, often on or near the hands but occurring on any exposed skin surface. Diagnosis is by exposure history, examination, and sometimes skin patch testing. Treatment entails antipruritics, topical corticosteroids, and avoidance of causes.

Pathophysiology

CD is caused by irritants or allergens.

Irritant contact dermatitis (ICD): ICD accounts for 80% of all cases of CD. It is a nonspecific inflammatory reaction to substances contacting the skin; the immune system is not activated. Numerous substances are involved, including

• Chemicals (eg, acids, alkalis, solvents, metal salts)

• Soaps (eg, abrasives, detergents)

• Plants (eg, poinsettias, peppers)

• Body fluids (eg, urine, saliva)

Properties of the irritant (eg, extreme pH, solubility in the lipid film on skin), environment (eg, low humidity, high temperature, high friction), and patient (eg, very young or old) influence the likelihood of developing ICD. ICD is more common among patients with atopic disorders, in whom ICD also may initiate immunologic sensitization and hence allergic CD.

Phototoxic dermatitis (see p. 675) is a variant in which topical (eg, perfumes, coal tar) or ingested (eg, psoralens) agents generate damaging free radicals and inflammatory mediators only after absorption of ultraviolet light.

Allergic contact dermatitis (ACD): ACD is a type IV cell-mediated hypersensitivity reaction that has 2 phases:

• Sensitization to an antigen

• Allergic response after reexposure

In the sensitization phase, allergens are captured by Langerhans' cells (dendritic epidermal cells), which migrate to regional lymph nodes where they process and present the antigen to T cells. The process may be brief (6 to 10 days for strong sensitizers such as poison ivy) or prolonged (years for weak sensitizers such as sunscreens, fragrances, and glucocorticoids). Sensitized T cells then migrate back to the epidermis and activate on any reexposure to the allergen, releasing cytokines, recruiting inflammatory cells, and leading to the characteristic symptoms and signs of ACD.

In **autoeczematization**, epidermal T cells activated by an allergen migrate locally or through the circulation to cause dermatitis at sites remote from the initial trigger. However, contact with fluid from vesicles or blisters cannot trigger a reaction elsewhere on the patient or on another person.

Multiple allergens cause ACD (see Table 76-2), and cross-sensitization among agents is common (eg, between benzocaine and paraphenylenediamine). Cross-sensitization means that exposure to one substance can result in an allergic response after exposure to a different but related substance.

ACD variants include photoallergic CD and systemically induced ACD. In photoallergic CD (see p. 675), a substance becomes sensitizing only after it undergoes structural change triggered by ultraviolet light. Typical causes include aftershave lotions, sunscreens, and topical sulfonamides. Reactions may extend to non-sun-exposed skin. In systemically induced ACD, ingestion of an allergen after topical sensitization causes diffuse dermatitis (eg, oral diphenhydramine after sensitization with topical diphenhydramine).

Symptoms and Signs

ICD: ICD is more painful than pruritic. Signs range from mild erythema to hemorrhage, crusting, erosion, pustules, bullae, and edema.

ACD: In ACD, the primary symptom is intense pruritus; pain is usually the result of excoriation or infection. Skin changes range from transient erythema through vesiculation to severe swelling with bullae, ulceration, or both. Changes often occur in a pattern, distribution, or combination that suggests a specific exposure, such as linear streaking on an arm or leg (eg, from brushing against poison ivy) or circumferential erythema (under a wristwatch or waistband). Any surface may be involved, but hands are the most common surface due to handling and touching potential allergens. With airborne exposure (eg,

[**Table 76-2.** Causes of Allergic Contact Dermatitis]

perfume aerosols), areas not covered by clothing are predominantly affected. The dermatitis is typically limited to the site of contact but may later spread due to scratching and autoeczematization. In systemically induced ACD, skin changes may be distributed over the entire body.

Diagnosis

• Clinical evaluation

• Sometimes patch testing

CD can often be diagnosed by skin changes and exposure history. The patient's occupation, hobbies, household duties, vacations, clothing, topical drug use, cosmetics, and spouse's activities must be considered. The "use" test, in which a suspected agent is applied far from the original area of dermatitis, usually on the flexor forearm, is useful when perfumes, shampoos, or other home agents are suspected.

Patch testing is indicated when ACD is suspected and does not respond to treatment. In patch testing, standard contact allergens are applied to the upper back using adhesive-mounted patches containing minute amounts of allergen or plastic (Finn) chambers containing allergen held in place with porous tape. Thin-layer rapid use epicutaneous (TRUE) patch testing involves 2 adhesive strips that can be applied and interpreted by any provider. Skin under the patches is evaluated 48 and 96 h after application. False-positive results occur when concentrations provoke an irritant rather than an allergic reaction, when

reaction to one antigen triggers a nonspecific reaction to others, or with cross-reacting antigens. False-negative results occur when patch allergens do not include the offending antigen. Definitive diagnosis requires a history of exposure to the test agent in the original area of dermatitis.

Prognosis

Resolution may take up to 3 wk. Reactivity is usually lifelong. Patients with photoallergic CD can have flares for years when exposed to sun (persistent light reaction).

Treatment

• Avoidance of offending agents

• Supportive care (eg, cool compresses, dressings, antihistamines)

• Corticosteroids (most often topical but sometimes oral)

CD is prevented by avoiding the trigger; patients with photosensitive CD should avoid exposure to sun.

Topical treatment includes cool compresses (saline or Burow's solution) and corticosteroids; patients with mild to moderate ACD are given mid-potency topical corticosteroids (eg, triamcinolone 0.1% ointment or betamethasone valerate cream 0.1%). Oral corticosteroids (eg, prednisone 60 mg once/day for 7 to 14 days) can be used for severe blistering or extensive disease. Systemic antihistamines (eg, hydroxyzine, diphenhydramine) help pruritus; antihistamines with low anticholinergic potency, such as low-sedating H_1 blockers, are not as effective. Wet-to-dry dressings can soothe oozing blisters, dry the skin, and promote healing.

Exfoliative Dermatitis

(Erythroderma)

Exfoliative dermatitis is widespread erythema and scaling of the skin caused by preexisting skin disorders, drugs, cancer, or unknown causes. Symptoms and signs are pruritus, diffuse erythema, and epidermal sloughing. Diagnosis is clinical. Treatment involves corticosteroids and correction of the cause.

Exfoliative dermatitis is a manifestation of rapid epidermal cell turnover. Its cause is unknown, but it most often occurs in the context of preexisting skin disorders (eg, atopic dermatitis, contact dermatitis, seborrheic dermatitis, psoriasis, pityriasis rubra pilaris), use of drugs (eg, penicillin, sulfonamides, isoniazid, phenytoin, barbiturates), and cancer (eg, mycosis fungoides, leukemia, and, rarely, adenocarcinomas). Up to 25% of patients have no identifiable underlying disease.

Symptoms and Signs

Symptoms include pruritus, malaise, and chills. Diffuse erythema initially occurs in patches but spreads and involves all or nearly all of the body. Extensive epidermal sloughing leads to abnormal thermoregulation, nutritional deficiencies because of extensive protein losses, increased metabolic rate with a hypercatabolic state, and hypovolemia due to transdermal fluid losses.

Diagnosis

• Clinical evaluation

Diagnosis is by history and examination. Preexisting skin disease may underlie the extensive erythema and suggest a cause. Biopsy is often nonspecific but is indicated when mycosis fungoides is suspected. Blood tests may reveal hypoproteinemia, hypocalcemia, and iron deficiency, each a consequence of extensive protein, electrolyte, and RBC loss; however, these findings are not diagnostic.

Treatment

• Supportive care (eg, rehydration)

• Topical care (eg, emollients, colloidal oatmeal baths)

• Systemic corticosteroids for severe disease

The disease may be life threatening; hospitalization is often necessary. Any known cause is treated. Supportive care consists of correction of dehydration, correction of electrolyte abnormalities and nutritional deficiencies, and comprehensive wound care and dressings to prevent bacterial superinfection. Because drug eruptions and contact dermatitis cannot be ruled out by history alone, all drugs should be stopped if possible or changed. Skin care is with emollients and colloidal oatmeal baths. Weak topical corticosteroids (eg, 1 to 2.5% hydrocortisone ointment) may be used. Corticosteroids (prednisone 40 to 60 mg po once/day for 10 days, then tapered) are used for severe disease.

Prognosis depends on the cause. Cases related to drug reactions have the shortest duration, lasting 2 to 6 wk after the drug is withdrawn.

Hand and Foot Dermatitis

Hand and foot dermatitis is not a single disorder. Rather, it is a categorization of dermatitis that affects the hands and feet selectively due to one of several causes.

Patients often present with isolated dermatitis of the hands or feet. Causes include

• Contact dermatitis

• Fungal infection

• Psoriasis

• Scabies

Other causes include systemic viral infection in children (hand-foot-and-mouth disease—see p. 1426) or certain chemotherapies (hand-foot syndrome). Some cases are idiopathic.

Diagnosis can sometimes be inferred from location and appearance of the skin lesions (see Table 76-3).

Treatment of all forms of hand and foot dermatitis should be directed at the cause when possible. Topical corticosteroids or antifungals may be tried empirically. Patients should also avoid prolonged contact with water that would otherwise remove protective oils and lead to paradoxical drying of the skin.

Dyshidrotic dermatitis: Pruritic vesicles or bullae on the palms, sides of the fingers, or soles are characteristic of this disorder. Scaling, redness, and oozing often follow vesiculation. Pompholyx is a severe form with bullae. The cause is unknown, but fungal infection, contact dermatitis, and id reactions to tinea pedis can cause a similar clinical appearance and should be ruled out. Treatment includes topical corticosteroids, tacrolimus or pimecrolimus, oral antibiotics, and ultraviolet light.

Keratolysis exfoliativa: Painless patchy peeling of the palms, soles, or both is characteristic of this disorder. The cause is unknown; treatment is unnecessary because the condition is self-resolving.

Hyperkeratotic eczema: Thick yellow-brown plaques on the palms and sometimes soles are characteristic of this disorder. The cause is unknown. Treatment is with topical corticosteroids and keratolytics, oral psoralen plus ultraviolet A (PUVA), and retinoids.

Id reaction: The appearance of vesicles usually on the sides of the fingers in response to active

dermatitis elsewhere is characteristic of this disorder. The cause may be an allergic reaction.

Housewives' eczema: This irritant contact dermatitis affects people whose hands are frequently immersed in water. It is worsened by washing dishes, clothes, and babies because repeated exposure to even mild detergents and water or prolonged sweating under rubber gloves may irritate dermatitic skin or cause an irritant contact dermatitis.

Hand-foot syndrome: This disorder (also called acral erythema or palmar-plantar eryth-rodysesthesia) represents cutaneous toxicity caused by certain systemic chemotherapies (eg, capecitabine, cytarabine, fluorouracil, idarubicin, doxorubicin, taxanes, methotrexate, cisplatin, tegafur). Manifestations include pain, swelling, numbness, tingling, redness, and sometimes flaking or blistering of the palms or soles. Treatment is with oral or topical corticosteroids, topical dimethylsulfoxide, oral vitamin B_6 (pyridoxine), OTC analgesics (eg, acetaminophen, ibuprofen), and supportive measures (eg, cool compresses, minimizing manual tasks).

Lichen Simplex Chronicus

(Neurodermatitis)

Lichen simplex chronicus is eczema caused by repeated scratching; by several mechanisms, chronic scratching causes further itching, creating a vicious circle. Diagnosis is by examination.

[Table 76-3. Differential Diagnosis of Hand Dermatitis]

Treatment is through education and behavioral techniques to prevent scratching and corticosteroids and antihistamines.

Etiology

Lichen simplex chronicus is thickening of the skin with variable scaling that arises secondary to repetitive scratching or rubbing. Lichen simplex chronicus is not a primary process. Perceived pruritus in a specific area of skin (with or without underlying pathology) provokes rubbing and mechanical trauma, resulting in secondary lichenification and further pruritus. Lichen simplex chronicus frequently occurs in people with anxiety disorders and nonspecific emotional stress as well as in patients with any type of underlying chronic dermatitis.

Pathophysiology

The underlying pathophysiology is unknown but may involve alterations in the way the nervous system perceives and processes itchy sensations. Skin that tends toward eczematous conditions (eg, atopic dermatitis) is more prone to lichenification.

Symptoms and Signs

Lichen simplex chronicus is characterized by pruritic, dry, scaling, hyperpigmented, lichenified plaques in irregular, oval, or angular shapes. It involves easily reached sites, most commonly the legs, arms, neck, and upper trunk.

Diagnosis

• Clinical evaluation

Diagnosis is by examination. A fully developed plaque has an outer zone of discrete, brownish papules and a central zone of confluent papules covered with scales. Look-alike conditions include tinea corporis, lichen planus, and psoriasis; lichen simplex chronicus can be distinguished from these by potassium hydroxide wet mount and biopsy.

Treatment

• Education and behavioral techniques

• Corticosteroids (most often topical but sometimes intralesional)

• Antihistamines

Primary treatment is patient education about the effects of scratching and rubbing. Secondary treatment is topical corticosteroids (eg, triamcinolone acetonide, fluocinonide); surgical tape impregnated with flurandrenolide (applied in the morning and replaced in the evening) may be preferred because occlusion prevents scratching. Small areas may be locally infiltrated (intralesional injections) with a long-acting corticosteroid such as triamcinolone acetonide 2.5 mg/mL (diluted with saline), 0.3 mL/cm^2 of lesion; treatment can be repeated every 3 to 4 wk. Oral H_1-blocking antihistamines may be useful. Emollients may also be helpful.

Nummular Dermatitis

Nummular (discoid) dermatitis is inflammation of the skin characterized by coin-shaped or disc-shaped lesions. Diagnosis is clinical. Treatment may include antibiotics, corticosteroids, and ultraviolet light therapy.

Nummular dermatitis is most common among middle-aged patients and is often associated with dry skin, especially during the winter. The cause is unknown.

Symptoms and Signs

Discoid lesions often start as patches of confluent vesicles and papules that later ooze serum and form crusts. Lesions are eruptive, widespread, and pruritic. They are often more prominent on the extensor aspects of the extremities and on the buttocks but also appear on the trunk. Exacerbations and remissions may occur, and when they do, new lesions tend to reappear at the sites of healed lesions.

Diagnosis

Diagnosis is clinical based on the characteristic appearance and distribution of the skin lesions.

Treatment

• Supportive care

• Antibiotics

• Corticosteroids (most often topical, but sometimes intralesional or oral)

• Ultraviolet light therapy

No treatment is uniformly effective. Oral antibiotics (eg, dicloxacillin or cephalexin 250 mg qid) may be given, along with use of tap water compresses, especially when weeping and pus are present. Less inflamed lesions may respond to tetracycline 250 mg po qid, which has a beneficial (although not necessarily antibacterial) effect. Corticosteroid cream or ointment should be rubbed in 3 times daily. An occlusive dressing with a corticosteroid cream under polyethylene film or with flurandrenolide-impregnated tape can be applied at bedtime. Intralesional corticosteroid injections may be beneficial for the few lesions that do not respond to therapy. In more widespread, resistant, and recurrent cases, ultraviolet B radiation alone or oral psoralen plus ultraviolet A (PUVA) radiation may be helpful. Occasionally, oral corticosteroids are required, but long-term use should be avoided; a reasonable starting dose is prednisone 40 mg every other day.

Seborrheic Dermatitis

Seborrheic dermatitis (SD) is inflammation of skin that has a high density of sebaceous glands (eg, face, scalp, upper trunk). The cause is unknown, but *Pityrosporum ovale*, a normal skin organism, plays some role. SD occurs with increased frequency in patients with HIV and in those with certain neurologic disorders. SD causes occasional pruritus, dandruff, and yellow, greasy scaling along the hairline and on the face. Diagnosis is made by examination. Treatment is tar or other medicated shampoo and topical corticosteroids and antifungals.

Despite the name, the composition and flow of sebum are usually normal. The pathogenesis of SD is unclear, but its activity has been linked to the number of *Pityrosporum* yeasts present on the skin. The incidence and severity of disease seem to be affected by genetic factors, emotional or physical stress, and climate (usually worse in cold weather). SD may precede or be associated with psoriasis (called seborrhiasis). SD may be more common and more severe among patients with neurologic disorders (especially Parkinson's disease) or HIV/AIDS. Very rarely, the dermatitis becomes generalized.

Symptoms and Signs

Symptoms develop gradually, and the dermatitis is usually apparent only as dry or greasy diffuse scaling of the scalp (dandruff) with variable pruritus. In severe disease, yellow-red scaling papules appear along the hairline, behind the ears, in the external auditory canals, on the eyebrows, in the axillae, on the bridge of the nose, in the nasolabial folds, and over the sternum. Marginal blepharitis with dry yellow crusts and conjunctival irritation may develop. SD does not cause hair loss.

Neonates may develop SD with a thick, yellow, crusted scalp lesion (cradle cap); fissuring and yellow scaling behind the ears; red facial papules; and stubborn diaper rash. Older children may develop thick, tenacious, scaly plaques on the scalp that may measure 1 to 2 cm in diameter.

Diagnosis

• Clinical evaluation

Diagnosis is made by physical examination. SD may occasionally be difficult to distinguish from other disorders, including psoriasis, atopic dermatitis or contact dermatitis, tinea, and rosacea.

Treatment

• Topical therapy

Adults: In adults, zinc pyrithione, selenium sulfide, sulfur and salicylic acid, or tar shampoo should be used daily or every other day until dandruff is controlled and twice/wk thereafter. A corticosteroid lotion (eg, 0.01% fluocinolone acetonide solution, 0.025% triamcinolone acetonide lotion) can be rubbed into the scalp or other hairy areas twice daily until scaling and redness are controlled. For SD of the postauricular areas, nasolabial folds, eyelid margins, and bridge of the nose, 1% hydrocortisone cream is rubbed in 2 or 3 times daily, decreasing to once/day when SD is controlled; hydrocortisone cream is the safest corticosteroid for the face because fluorinated corticosteroids may cause adverse effects (eg, telangiectasia, atrophy, perioral dermatitis). In some patients, 2% ketoconazole cream or other topical imidazoles applied twice daily for 1 to 2 wk induce a remission that lasts for months. For eyelid margin seborrhea, a dilution of 1 part baby shampoo to 9 parts water is applied with a cotton swab.

Infants and children: In infants, a baby shampoo is used daily, and 1% hydrocortisone cream is rubbed in twice daily. For thick lesions on the scalp of a young child, 2% salicylic acid in olive oil or a corticosteroid gel is applied at bedtime to affected areas and rubbed in with a toothbrush. The scalp is shampooed daily until the thick scale is gone.

Stasis Dermatitis

Stasis dermatitis is inflammation of the skin of the lower legs caused by chronic venous insufficiency. Symptoms are itching, scaling, hyperpigmentation, and sometimes ulceration.

Diagnosis is clinical. Treatment is directed at the chronic venous insufficiency and preventing occurrence or progression of associated ulcers.

Stasis dermatitis occurs in patients with chronic venous insufficiency (see p. 2231) because pooled venous blood in the legs compromises the endothelial integrity in the microvasculature, resulting in fibrin leakage, local inflammation, and local cell necrosis.

Symptoms and Signs

Initially, hyperpigmentation and red-brown discoloration from RBC extravasation appear. Later, eczematous changes develop and manifest as erythema, scaling, weeping, and crusting (see Plate 46), all of which can be made worse by bacterial superinfection or by contact dermatitis caused by the many topical treatments often applied. When chronic venous insufficiency and stasis dermatitis are both inadequately treated, stasis dermatitis progresses to frank skin ulceration (see Plate 47), chronic edema, thickened fibrotic skin, or lipodermatosclerosis (a painful induration resulting from panniculitis, which, if severe, gives the lower leg an inverted bowling pin shape with enlargement of the calf and narrowing at the ankle).

Diagnosis

Diagnosis is clinical based on the characteristic appearance of the skin lesions and other signs of chronic venous insufficiency.

Treatment

• Elevation, compression, and dressings

• Sometimes topical or oral antibiotics

Chronic venous insufficiency must be adequately treated with leg elevation and compression stockings (see p. 2232). For acute stasis dermatitis (characterized by crusts, exudation, and superficial ulceration), continuous and then intermittent tap water compresses should be applied. For a weeping lesion, a hydrocolloid dressing may be best. For less acute dermatitis, a corticosteroid cream or ointment should be applied 3 times/day or incorporated into zinc oxide paste.

Ulcers are best treated with compresses and bland dressings (eg, zinc oxide paste); other dressings (eg, hydrocolloids) are also effective (see also p. 740). Ulcers in ambulatory patients may be healed with Unna's paste boot (zinc gelatin), the less messy zinc gelatin bandage, or a colloid dressing (all are available commercially). Colloid-type dressings used under elastic support are more effective than Unna's paste boot. It may be necessary to change the dressing every 2 or 3 days, but as edema recedes and the ulcer heals, once or twice/wk is sufficient. After the ulcer heals, an elastic support should be applied before the patient rises in the morning. Regardless of the dressing used, reduction of edema (usually with compression) is paramount for healing.

Oral antibiotics (eg, cephalosporins, dicloxacillin) are used to treat superimposed cellulitis. Topical antibiotics (eg, mupirocin, silver sulfadiazine) are useful for treating erosions and ulcers. When edema and inflammation subside, split-thickness skin grafts may be needed for large ulcers.

Complex or multiple topical drugs or OTC remedies should not be used. The skin in stasis dermatitis is more vulnerable to direct irritants and to potentially sensitizing topical agents (eg, antibiotics; anesthetics; vehicles of topical drugs, especially lanolin or wool alcohols).

Chapter 77. Reactions to Sunlight

Introduction

The skin may respond to excessive sunlight in several ways: various chronic changes (eg, dermatoheliosis, actinic keratoses), photosensitivity, or sunburn.

Ultraviolet (UV) radiation: Although the sun emits a wide range of UV electromagnetic radiation (ie, UVA, 320 to 400 nm; UVB, 280 to 320 nm; UVC, 100 to 280 nm), only UVA and UVB reach the earth's surface. The character and amount of such radiation vary greatly with the seasons and with changing atmospheric conditions. Exposure of skin to sunlight depends on multiple lifestyle factors, (eg, clothing, occupation), geographic factors (eg, altitude, latitude), and time of year (UV intensity is higher in summer).

Sunburn-producing rays (primarily wavelengths < 320 nm) are filtered out by glass and to a great extent by smoke and smog. Sunburn-producing rays may pass through light clouds, fog, or 30 cm of clear water, causing severe burns in unsuspecting people. Snow, sand, and water enhance exposure by reflecting the rays. Stratospheric ozone, which filters out shorter wavelengths of UV, is depleted by man-made chlorofluorocarbons (eg, in refrigerants and aerosols). A decreased ozone layer increases inadvertent exposure to UVA and UVB.

Sun-tanning lamps use artificial light that is more UVA than UVB. This UVA use is often advertised as a "safer" way to tan; however, many of the same long-term deleterious effects may occur as with UVB exposure, including photoaging and skin cancer. Quite simply, there is no "safe tan."

Pathophysiology

After exposure to sunlight, the epidermis thickens, and melanocytes produce the pigment melanin at an increased rate, causing tanning. Tanning provides some natural protection against future exposure. Exposure leads to both inactivation and loss of epidermal Langerhans' cells, which are immunologically important.

People differ greatly in their sensitivity and response to sunlight based on the amount of melanin in their skin. Skin is classified into 6 types (I to VI) in decreasing order of susceptibility to sun injury. Classification is based on skin color, UV sensitivity, and response to sun exposure. Skin type I is white to lightly pigmented, very sensitive to UV light, has no immediate pigment darkening, always burns easily, and never tans. Skin type VI is dark brown or black, least sensitive to UV light, has significant immediate pigment darkening, and tans profusely (deep black). Dark-skinned people are not immune to the effects of the sun and can become sunburned with strong or prolonged exposure. Long-term effects of UV exposure in dark-skinned people are the same as those in light-skinned people but are often delayed and less severe. People with blonde or red hair are especially susceptible to the acute and chronic effects of UV radiation. Uneven melanocyte activation occurs in many fair-haired people and results in freckling. There is no skin pigmentation in people with albinism (see p. 719) because of a defect in melanin metabolism. Patchy areas of depigmentation are present in patients with vitiligo (see p. 720) because of immunologic destruction of melanocytes.

Prevention

Avoidance: Simple precautions help prevent sunburn and the chronic effects of sunlight. These precautions are recommended for people of all skin types, particularly those who are fair skinned and burn easily. Exposure to bright midday sun should not be > 30 min, even for people with dark skin. In temperate zones, exposure is less hazardous before 10 AM and after 3 PM because more sunburn-producing wavelengths are filtered out. Fog and clouds do not reduce risk, and risk is increased at high altitude.

Clothing: Skin should be covered. Fabrics with a tight weave block the sun better than do those with a loose weave. Special clothing that provides high sun protection is commercially available. Broad-brimmed hats protect the face, ears, and neck. Regular use of UV-protective, wrap-around sunglasses helps shield

the eyes.

Sunscreens: Although sunscreens help protect the skin from sunburn and chronic sun damage, they do not always prevent damage. Older sunscreens tended to filter only UVB light, but many newer sunscreens are now "full spectrum" and effectively filter UVA light as well. In the US, the FDA rates sunscreens by sun protection factor (SPF): the higher the number, the greater the protection. Agents with SPF ≥ 15 are recommended. The SPF, however, only quantifies the protection against UVB exposure; there is no scale for UVA protection.

Sunscreens are available in a wide variety of formulations, including creams, gels, foams, sprays, and sticks. Self-tanning products do not provide significant protection from UV exposure.

Most sunscreens contain several agents that function as chemical screens, absorbing light or providing a physical screen that reflects or scatters light. Common chemical sunscreen agents mostly absorb UVB rays and include the aminobenzoates, which include *p*-aminobenzoic acid (PABA), salicylates, cinnamates, benzophenones (eg, avobenzone), and the anthrilates (an aminobenzoate derivative). Of these, the benzophenones are particularly effective at screening UVA rays.

Other sunscreens, called sunblocks, contain zinc oxide and titanium dioxide, which physically block both UVB and UVA rays. Micronized formulations of these products have significantly improved their cosmetic acceptability.

Sunscreen failure is common and usually results from insufficient application of the product, application too late (sunscreens should optimally be applied 30 min before exposure), or failure to reapply after swimming or exercise.

Allergic or photoallergic reactions to sunscreens must be distinguished from other photosensitive skin eruptions. Patch or photopatch testing with sunscreen components may be necessary to make the diagnosis. This testing is usually done by dermatologists with a particular expertise in allergic contact dermatitis.

Chronic Effects of Sunlight

Aging: Chronic exposure to sunlight ages the skin (dermatoheliosis, extrinsic aging), producing both fine and coarse wrinkles, rough leathery texture, mottled pigmentation, and telangiectasia. The atrophic effects in some people may resemble those seen after x-ray therapy (chronic radiation dermatitis).

Actinic keratoses: Actinic keratoses are precancerous changes in skin cells (keratinocytes) that are a frequent, disturbing consequence of many years of sun exposure. People with blonde or red hair, blue eyes, and skin type I or II are particularly susceptible.

The keratoses are usually pink or red, poorly marginated, and scaly on palpation, although some are light gray or pigmented, giving them a brown appearance. They should be differentiated from seborrheic keratoses (see p. 746), which increase in number and size with aging. Seborrheic keratoses tend to appear waxy and stuck-on but can often take on an appearance similar to actinic keratoses. Close inspection usually reveals distinguishing characteristics of the lesion. Unlike actinic keratoses, seborrheic keratoses also occur on non-sun-exposed areas of the body and are not premalignant.

Skin cancers (see p. 748)**:** The incidence of squamous cell carcinoma and basal cell carcinoma in fair, light-skinned people is directly proportional to the total annual sunlight in the area. Such lesions are especially common among people who were extensively exposed to sunlight as children and adolescents and among those who are chronically exposed to the sun as part of their profession or recreational activities (eg, athletes, farmers, ranchers, sailors, frequent sunbathers). Sun exposure also substantially increases the risk of malignant melanomas.

Treatment

Various combination therapies, including chemical peels, 5-fluorouracil (5-FU), topical α-hydroxy acids,

imiquimod, photodynamic therapy, and tretinoin, have been used to reduce carcinogenic changes and improve the cosmetic appearance of chronically sun-damaged skin. These therapies are often effective in ameliorating superficial skin changes (eg, coarse and fine wrinkles, irregular pigmentation, sallowness, roughness, minor laxity) but have a much less pronounced effect on deeper changes (eg, telangiectasias). Lasers are capable of treating both superficial and deep changes in the dermis and are used to treat cosmetic and precancerous skin changes. Many chemicals are used in OTC cosmetic products without significant evidence that they improve chronic changes of the skin caused by sunlight.

Actinic keratoses: There are several options, depending on the number and location of lesions.

• Liquid nitrogen

• Topical 5-FU

• Topical imiquimod

If only a few actinic keratoses are present, cryotherapy (freezing with liquid nitrogen) is the most rapid and satisfactory treatment.

If there are too many lesions to freeze, topical 5-FU applied to the affected area nightly or twice daily for 2 to 6 wk often clears the majority of lesions. Several strengths and formulations of 5-FU are commercially available. Many patients tolerate 0.5% 5-FU cream applied once/day for 4 wk on the face better than stronger concentrations. Actinic keratoses on the arms may require stronger concentrations, such as 5% cream. Topical 5-FU produces a brisk reaction, with redness, scaling, and burning, often affecting areas with no visible actinic keratoses. If the reaction is too brisk, application may be suspended for 1 to 3 days. Topical 5-FU has few significant adverse effects except for this unsightly and uncomfortable reaction, which can be masked by cosmetics and, when necessary, suppressed with topical corticosteroids. 5-FU should not be used to treat basal cell carcinomas, except those shown by biopsy to be of the superficial type.

A relatively new drug, imiquimod, is often used for treatment of actinic keratoses and superficial basal cell carcinomas. It stimulates the immune system to recognize and destroy cancerous skin lesions. For treatment of skin cancers, see Ch. 90.

Photosensitivity

Photosensitivity is a poorly understood cutaneous reaction to sunlight probably involving the immune system. It may be idiopathic or occur after exposure to certain drugs or chemicals, and it is sometimes a feature of systemic disorders (eg, SLE, porphyria, pellagra, xeroderma pigmentosum). Diagnosis is clinical. Treatment varies by type.

In addition to the acute and chronic effects of sunlight, a variety of unusual reactions may occur soon after only a brief sun exposure. Unless the cause is obvious, patients with pronounced photosensitivity should be evaluated for systemic or cutaneous disorders associated with light sensitivity such as SLE (see p. 305) and porphyria (see p. 807). Treatment for chemical photosensitivity is topical corticosteroids and avoidance of the causative substance.

Solar urticaria: In certain patients, urticaria develops at a site of sun exposure within a few minutes. Rarely, if large areas are involved, syncope, dizziness, wheezing, and other systemic symptoms may develop. Etiology is unclear but may involve endogenous skin constituents functioning as photoallergens, leading to mast cell degranulation as in other types of urticaria. Solar urticaria can be distinguished from other types of urticaria in that wheals in solar urticaria occur only on exposed skin after ultraviolet (UV) light exposure. Solar urticaria can be classified based on the component of the UV spectrum (UVA, UVB, and visible light) that produces them. Treatment can be difficult and may include H_1 blockers, antimalarial drugs, topical corticosteroids, sunscreens, and psoralen UV light (PUVA). The wheals of solar urticaria usually last just minutes to hours, but the disorder is chronic and can wax and wane over years.

Chemical photosensitivity: Over 100 substances, ingested or applied topically, are known to

predispose to cutaneous reactions following sun exposure. A limited number are responsible for most reactions (see Table 77-1). Reactions are divided into phototoxicity and photoallergy.

In **phototoxicity**, light-absorbing compounds directly generate free radicals and inflammatory mediators, causing tissue damage manifesting as pain and erythema (like sunburn). This reaction does not require prior sun exposure and can appear in any person, although reaction is highly variable. Typical causes of phototoxic reactions include topical (eg, perfumes, coal tar) or ingested (eg, tetracyclines, psoralen-containing plants) agents. Phototoxic reactions do not generalize to non-sun-exposed skin.

Photoallergy is a type IV (cell-mediated) immune response; light absorption causes structural changes in the drug or substance, allowing it to bind to tissue protein and function as a hapten. Prior exposure is required. Typical causes of photoallergic reactions include aftershave lotions, sunscreens, and sulfonamides. Reaction may extend to non-sun-exposed skin. Symptoms include erythema, pruritus, and sometimes vesicles.

[**Table 77-1.** Some Substances that Sensitize the Skin to Sunlight]

Polymorphous light eruption: These eruptions are unusual reactions to light that do not seem to be associated with systemic disease or drugs. Eruptions appear on sun-exposed areas, usually 30 min to several hours after exposure. Lesions are pruritic, erythematous, and often papular but may be papulovesicular or plaquelike. They are most common among women and people from northern climates when first exposed to spring or summer sun than among those exposed to sun year-round. Lesions subside within several days to 1 wk or so. Actinic prurigo is a similar (perhaps related) phenomenon with more nodular-appearing lesions that may persist year-round, worsening with sun exposure.

Diagnosis is made by history, skin findings, and exclusion of other sun-sensitivity disorders. Diagnosis sometimes requires reproduction of the lesions with artificial or natural sunlight when the patient is not using any potentially sensitizing drugs.

Often, lesions are self-limited and spontaneously improve as summer progresses. Treatment is by moderating sun exposure and applying topical corticosteroids. More severely affected patients may benefit from desensitization by graduated exposure to UV light with PUVA (see p. 679) or narrow band UVB (312 nm) phototherapy. Patients with disabling disease may require a course of oral immunosuppressive therapy such as prednisone, azathioprine, cyclosporine, or hydroxychloroquine.

Sunburn

Sunburn is characterized by erythema and sometimes pain and blisters caused by exposure to solar ultraviolet radiation. Treatment is similar to that for thermal burns, including cool compresses, NSAIDs, and, for severe cases, sterile dressings and topical antimicrobials. Prevention by sun avoidance and use of sunscreens is crucial.

Sunburn results from overexposure of the skin to ultraviolet (UV) radiation; wavelengths in the UVB spectrum (280 to 320 nm) cause the most pronounced effects.

Symptoms and Signs

Symptoms and signs appear in 1 to 24 h and, except in severe reactions, peak within 72 h. Skin changes range from mild erythema, with subsequent superficial scaling, to pain, swelling, skin tenderness, and blisters. Constitutional symptoms (eg, fever, chills, weakness, shock), similar to a thermal burn, may develop if a large portion of the body surface is affected; these symptoms may be caused by the release of inflammatory cytokines such as IL-1.

Secondary infection, blotchy pigmentation, and miliaria-like eruptions are the most common late complications. Exfoliated skin may be extremely vulnerable to sunlight for several weeks.

Treatment

• Supportive measures

Further exposure should be avoided until sunburn has completely subsided. Cold tap water compresses and oral NSAIDs help relieve symptoms, as may topical aloe vera. Topical corticosteroids are no more effective than cool compresses. Blistered areas should be managed similarly to other partial-thickness burns (see p. 3246), with sterile dressings and topical bacitracin or silver sulfadiazine. Ointments or lotions containing local anesthetics (eg, benzocaine) should be avoided because of the risk of allergic contact dermatitis.

Early treatment of extensive, severe sunburn with a systemic corticosteroid (eg, prednisone 20 to 30 mg po bid for 4 days for adults or teenagers) may decrease the discomfort, but this use is controversial.

Prevention

Simple precautions (eg, avoiding the sun especially during midday, wearing tightly woven clothing, using sunscreens) usually prevent most cases of sunburn (see p. 673).

Chapter 78. Psoriasis and Scaling Diseases

Introduction

Psoriasis, parapsoriasis, pityriasis rosea, pityriasis rubra pilaris, pityriasis lichenoides, lichen planus, and lichen sclerosus are dissimilar disorders grouped together because their primary lesions have similar characteristics: sharply marginated, scaling papules or plaques without wetness, crusts, fissures, and excoriations. Lesion appearance and distribution distinguish these diseases from each other.

Psoriasis

Psoriasis is an inflammatory disease that manifests most commonly as well-circumscribed, erythematous papules and plaques covered with silvery scales. Cause is unclear but seems to involve the immune system. Common triggers include trauma, infection, and certain drugs. Symptoms are usually minimal with occasional mild itching, but cosmetic implications may be major. Some people develop severe disease with painful arthritis. Diagnosis is based on appearance and distribution of lesions. Treatment is with emollients, vitamin D analogs, retinoids, tar, anthralin, corticosteroids, phototherapy, and, when severe, methotrexate, retinoids, immunomodulatory agents (biologics), or immunosuppressants.

Psoriasis is hyperproliferation of epidermal keratinocytes combined with inflammation of the epidermis and dermis. It affects about 1 to 5% of the population worldwide; light-skinned people are at greater risk. Peak onset is roughly bimodal, most often at ages 16 to 22 and at ages 57 to 60, but the disorder can occur at any age.

Etiology

The cause is unclear but involves immune stimulation of epidermal keratinocytes; T cells seem to play a central role. Family history is common, and certain genes and HLA antigens (Cw6, B13, B17) are associated with psoriasis. An environmental trigger is thought to evoke an inflammatory response and subsequent hyperproliferation of keratinocytes.

Well-identified triggers include

- Injury (Koebner phenomenon)
- Sunburn
- HIV
- β-Hemolytic streptococcal infection
- Drugs (especially β-blockers, chloroquine, lithium, ACE inhibitors, indomethacin, terbinafine, and interferon alfa)
- Emotional stress
- Alcohol consumption

Symptoms and Signs

Lesions are either asymptomatic or pruritic and are most often localized on the scalp, extensor surfaces of the elbows and knees, sacrum, buttocks, and penis. The nails, eyebrows, axillae, umbilicus, and perianal region may also be affected. The disease can be widespread, involving confluent areas of skin extending between these regions. Lesions differ in appearance depending on type.

Among the various subtypes (see Table 78-1), plaque psoriasis (psoriasis vulgaris or chronic plaque psoriasis) is the most common pattern;

lesions are discrete, erythematous papules or plaques covered with thick, silvery, shiny scales. Lesions appear gradually and remit and recur either spontaneously or with appearance and resolution of triggers.

Arthritis develops in 5 to 30% of patients and can be disabling (see p. 344); joint destruction may ultimately occur.

Psoriasis is rarely life-threatening but can affect a patient's self-image. Besides image, the sheer amount of time required to treat extensive skin or scalp lesions and to maintain clothing and bedding may adversely affect quality of life.

Diagnosis

• Clinical evaluation

• Rarely biopsy

Diagnosis is most often by clinical appearance and distribution of lesions. Differential diagnosis includes seborrheic dermatitis, dermatophytoses, cutaneous lupus erythematosus, eczema, lichen planus, pityriasis rosea, squamous cell carcinoma in situ (Bowen's disease, especially when on the trunk), lichen simplex chronicus, and secondary syphilis. Biopsy is rarely necessary and may not be diagnostic.

Disease is graded as mild, moderate, or severe based on the body surface area affected and how the lesions affect patients' quality of life. There are many more complex scoring systems for disease severity (eg, the Psoriasis Area and Severity Index), but these systems are useful mainly in research protocols.

Treatment

• Topical treatments

• Systemic treatments

• Ultraviolet (UV) light therapy

Treatment options are extensive and include emollients, salicylic acid, coal tar, anthralin, corticosteroids, vitamin D_3 analogs, methotrexate, topical and oral retinoids, topical and oral calcineurin inhibitors, immunosuppressants, immunomodulatory agents (biologics), and ultraviolet light therapy.

Topical treatments: Emollients include emollient creams, ointments, petrolatum, paraffin, and even hydrogenated vegetable (cooking) oils. They reduce scaling and are most effective when applied twice daily and immediately after bathing. Lesions may appear redder as scaling decreases or becomes more transparent. Emollients are safe and should probably always be used for mild to moderate plaque psoriasis.

Salicylic acid is a keratinolytic that softens scales, facilitates their removal, and increases absorption of other topical agents. It is especially useful as a component of scalp treatments; scalp scale can be quite thick.

Coal tar ointments, solutions, or shampoos are anti-inflammatory and decrease keratinocyte hyperproliferation via an unknown mechanism. They are typically applied at night and washed off in the morning. They can be used in combination with topical corticosteroids or with exposure to natural or artificial broad-band UVB light (280 to 320 nm) in slowly increasing increments (Goeckerman regimen).

Anthralin is a topical antiproliferative, anti-inflammatory agent. Its mechanism is unknown. Effective dose is 0.1% cream or ointment increased to 1% as tolerated. Anthralin may be irritating and should be used with caution in intertriginous areas; it also stains. Irritation and staining can be avoided

[**Table 78-1.** Subtypes of Psoriasis]

by washing off the anthralin 20 to 30 min after application. Using a liposome-encapsulated preparation may also avoid some disadvantages of anthralin.

Corticosteroids are usually used topically but may be injected into small or recalcitrant lesions. (CAUTION: *Systemic corticosteroids may precipitate exacerbations or development of pustular psoriasis and should not be used to treat psoriasis.*) Topical corticosteroids are used twice daily, sometimes with anthralin or coal tar applied at bedtime. Corticosteroids are most effective when used overnight under occlusive polyethylene coverings or incorporated into tape; a corticosteroid cream is applied without occlusion during the day. Corticosteroid potency (see p. 647) is selected according to the extent of involvement. As lesions abate, the corticosteroid should be applied less frequently or at a lower potency to minimize local atrophy, striae formation, and telangiectases. Ideally, after about 3 wk, an emollient should be substituted for the corticosteroid for 1 to 2 wk (as a rest period); this substitution limits corticosteroid dosage and prevents tachyphylaxis. Topical corticosteroid use can be expensive because large quantities (about 1 oz or 30 g) are needed for each application when a large body surface area is affected. Topical corticosteroids applied for long duration to large areas of the body may cause systemic effects and exacerbate psoriasis. For small, thick, localized, or recalcitrant lesions, high-potency corticosteroids are used with an occlusive dressing or flurandrenolide tape; these dressings are left on overnight and changed in the morning. Relapse after topical corticosteroids are stopped is often faster than with other agents.

Vitamin D_3 analogs (eg, calcipotriol, calcitriol) are topical vitamin D analogs that induce normal keratinocyte proliferation and differentiation; they can be used alone or in combination with topical corticosteroids. Some clinicians have patients apply calcipotriol on weekdays and corticosteroids on weekends.

Calcineurin inhibitors (eg, tacrolimus, pimecrolimus) are available in topical form and are generally well-tolerated. They are not as effective as corticosteroids but may avoid the complications of corticosteroids when treating facial and intertriginous psoriasis. They may be associated with an increased risk of lymphoma and skin cancer.

Tazarotene is a topical retinoid. It is less effective than corticosteroids as monotherapy but is a useful adjunct.

Systemic treatments: Methotrexate taken orally is the most effective treatment for severe disabling psoriasis, especially severe psoriatic arthritis or widespread erythrodermic or pustular psoriasis unresponsive to topical agents or psoralen plus ultraviolet A (PUVA) light therapy. Methotrexate seems to interfere with the rapid proliferation of epidermal cells. Hematologic, renal, and hepatic function should be monitored. Dosage regimens vary, so only physicians experienced in its use for psoriasis should undertake methotrexate therapy.

Systemic retinoids (eg, acitretin, isotretinoin) may be effective for severe and recalcitrant cases of psoriasis vulgaris, pustular psoriasis (in which isotretinoin may be preferred), and hyperkeratotic palmoplantar psoriasis. Because of the teratogenic potential and long-term retention of acitretin in the body, women who use it must not be pregnant and should be warned against becoming pregnant for at least 2 yr after treatment ends. Pregnancy restrictions also apply to isotretinoin, but the agent is not retained in the body beyond 1 mo. Long-term treatment may cause diffuse idiopathic skeletal hyperostosis (DISH—see p. 342).

Immunosuppressants can be used for severe psoriasis. Cyclosporine is a commonly used immunosuppressant. It should be limited to courses of several months (rarely, up to 1 yr) and alternated with other therapies. Its effect on the kidneys and potential long-term effects on the immune system preclude more liberal use. Other immunosuppressants (eg, hydroxyurea, 6-thioguanine, mycophenolate mofetil) have narrow safety margins and are reserved for severe, recalcitrant psoriasis.

Immunomodulatory agents (biologics—see p. 1086) include tumor necrosis factor (TNF)-α inhibitors (etanercept, adalimumab, infliximab) and the T-cell modulator alefacept. TNF-α inhibitors lead to clearing of psoriasis, but their safety profile is still under study. Efalizumab is no longer available in the US due to increased risk of progressive multifocal

leukoencephalopathy.

Phototherapy: UV light therapy is typically used in patients with extensive psoriasis. The mechanism of action is unknown, although UVB light reduces DNA synthesis and can induce mild systemic immunosuppression. In PUVA, oral methoxypsoralen, a photosensitizer, is followed by exposure to long-wave UVA light (330 to 360 nm). PUVA has an antiproliferative effect and also helps to normalize keratinocyte differentiation. Doses of light are started low and increased as tolerated. Severe burns can result if the dose of drug or UVA is too high. Although the treatment is less messy than topical treatment and may produce remissions lasting several months, repeated treatments may increase the incidence of UV-induced skin cancer and melanoma. Less UV light is required when used with oral retinoids (the so-called re-PUVA regimen). Narrow-band UVB light (311 to 312 nm) used without psoralens is similar in effectiveness to PUVA. Excimer laser therapy is a type of phototherapy using extremely pure wavelengths.

Choice of therapy: Choice of specific agents and combinations requires close cooperation with the patient, always keeping in mind the untoward effects of the treatments. There is no single ideal combination or sequence of agents, but treatment should be kept as simple as possible. Monotherapy is preferred, but combination therapy is the norm. Rotational therapy refers to the substitution of one therapy for another after 1 to 2 yr to reduce the adverse effects caused by chronic use and to circumvent disease resistance. Sequential therapy refers to initial use of potent agents (eg, cyclosporine) to quickly gain control followed by use of agents with a better safety profile.

Mild plaque psoriasis can be treated with emollients, keratolytics, tar, topical corticosteroids, vitamin D_3 analogs, or anthralin alone or in combination. Exposure to sunlight is beneficial, but sunburn can induce exacerbations.

Moderate to severe plaque psoriasis should be treated with topical agents and either phototherapy or systemic agents. Immunosuppressants are used for quick, short-term control (eg, in allowing a break from other modalities) and for the most severe disease. Immunomodulatory agents (biologics) are used for moderate to severe disease unresponsive to other agents.

Scalp plaques are notoriously difficult to treat because they resist systemic therapy, and because hair blocks application of topical agents and scale removal and shields skin from UV light. A suspension of 10% salicylic acid in mineral oil may be rubbed into the scalp at bedtime manually or with a toothbrush, covered with a shower cap (to enhance penetration and avoid messiness), and washed out the next morning with a tar (or other) shampoo. More cosmetically acceptable corticosteroid solutions can be applied to the scalp during the day. These treatments are continued until the desired clinical response is achieved. Resistant skin or scalp patches may respond to local superficial intralesional injection of triamcinolone acetonide suspension diluted with saline to 2.5 or 5 mg/mL, depending on the size and severity of the lesion. Injections may cause local atrophy, which is usually reversible.

Special treatment needs for subtypes are described in Table 78-1.

For psoriatic arthritis, treatment with systemic therapy is important to prevent joint destruction; methotrexate or a TNF-α inhibitor may be effective.

Parapsoriasis

Parapsoriasis describes a poorly understood and poorly distinguished group of diseases that share clinical features. There are 2 general forms: a small-plaque type, which is usually benign, and a large-plaque type, which is a precursor of cutaneous T-cell lymphoma (CTCL). It is extremely rare for small-plaque parapsoriasis to transform into CTCL.

The plaques are usually asymptomatic; their typical appearance is thin, scaling, dull pink patches and plaques with a slightly atrophic or wrinkled appearance. Small-plaque parapsoriasis is defined by lesions < 5 cm in diameter, whereas large-plaque parapsoriasis has lesions > 6 cm in diameter. Sometimes digitate plaques develop along the dermatomes, especially on the flanks and abdomen, in small-plaque parapsoriasis.

Treatment of small-plaque parapsoriasis is unnecessary but can include emollients, topical tar preparations or corticosteroids, phototherapy, or a combination. Treatment of large-plaque parapsoriasis is phototherapy or topical corticosteroids.

Course for both types is unpredictable; periodic clinical follow-up and biopsies give the best indication of risk of developing CTCL.

Pityriasis Rosea

Pityriasis rosea (PR) is an inflammatory disease characterized by diffuse, scaling papules or plaques. Treatment is usually unnecessary.

PR most commonly occurs between ages 10 and 35. It affects women more often and peaks in incidence in cooler months in temperate climates. The cause may be viral infection (some research has implicated human herpesviruses 6 and 7). Drugs may cause a PR-like reaction.

Symptoms and Signs

The condition classically begins with a single, primary, 2- to 10-cm herald patch that appears on the trunk or proximal limbs (see Plate 42). A general centripetal eruption of 0.5- to 2-cm rose- or fawn-colored oval papules and plaques follows within 7 to 14 days. The lesions have a scaly, slightly raised border (collarette) and resemble ringworm (tinea corporis). Most patients itch, occasionally severely. Papules may dominate with little or no scaling in blacks, children, and pregnant women. The rose or fawn color is not as evident in blacks; blacks also more commonly have inverse PR (lesions in the axillae or groin that spread centrifugally). Classically, lesions orient along skin lines, giving PR a Christmas tree-like distribution when multiple lesions appear on the back. A prodrome of malaise and headache precedes the lesions in a minority of patients.

Diagnosis

• Clinical evaluation

Diagnosis is based on clinical appearance and distribution. Differential diagnosis includes tinea corporis, tinea versicolor, drug eruptions, psoriasis, parapsoriasis, pityriasis lichenoides chronica, lichen planus, and secondary syphilis. Serologic testing for syphilis is indicated when the palms or soles are affected, when a herald patch is not seen, or when lesions occur in an unusual sequence or distribution.

Treatment

• Antipruritic therapy

No specific treatment is necessary because the eruption usually remits within 5 wk and recurrence is rare. Artificial or natural sunlight may hasten resolution. Antipruritic therapy such as topical corticosteroids, oral antihistamines, or topical measures may be used as needed.

Pityriasis Rubra Pilaris

Pityriasis rubra pilaris is a rare chronic disorder that causes hyperkeratotic yellowing of the palms and soles and red follicular papules that merge to form red-orange scaling plaques and confluent areas of erythema with islands of normal skin between lesions.

The cause of pityriasis rubra pilaris is unknown.

The 2 most common forms of the disorder are

• Juvenile classic (characterized by autosomal dominant inheritance and childhood onset)

• Adult classic (characterized by no apparent inheritance and adult onset)

Atypical forms exist in both age groups. Sunlight can trigger a flare.

Diagnosis is by clinical appearance and may be supported by biopsy. Differential diagnosis includes seborrheic dermatitis (in children) and psoriasis when disease occurs on the scalp, elbows, and knees.

Treatment is exceedingly difficult and empiric. The disorder may be ameliorated but almost never cured; classic forms of the disorder resolve slowly over 3 yr, whereas non-classic forms persist. Scaling may be reduced with emollients or 12% lactic acid under occlusive dressing, followed by topical corticosteroids. Oral vitamin A may be effective. Oral retinoids or methotrexate is an option when a patient is resistant to topical treatment.

Pityriasis Lichenoides

Pityriasis lichenoides is a clonal T-cell disorder that may develop in response to foreign antigens (eg, infections or drugs) and may be associated with cutaneous T-cell lymphoma.

Pityriasis lichenoides has acute and chronic forms existing in a clinical continuum. The acute form typically appears in children and young adults, with crops of asymptomatic chickenpox-like lesions that typically resolve within weeks to months. Antibiotics (eg, tetracycline, erythromycin) or phototherapy may help.

The chronic form initially manifests as flatter, reddish brown, scaling papules that may take months or longer to resolve. No treatment has proved effective.

Lichen Planus

Lichen planus (LP) is a recurrent, pruritic, inflammatory eruption characterized by small, discrete, polygonal, flat-topped, violaceous papules that may coalesce into rough scaly patches, often accompanied by oral lesions. Diagnosis is usually clinical and supported by skin biopsy. Treatment generally requires topical or intralesional corticosteroids. Severe cases may require phototherapy or systemic immunosuppressants.

Etiology

LP is thought to be caused by a T cell-mediated autoimmune reaction against basal epithelial keratinocytes in people with genetic predisposition. Drugs (especially β-blockers, NSAIDs, ACE inhibitors, sulfonylureas, gold, antimalarial drugs, penicillamine, and thiazides) can cause LP; drug-induced LP (sometimes called lichenoid drug eruption) may be indistinguishable from nondrug-induced LP or may have a pattern that is more eczematous. Associations with hepatitis C-induced liver insufficiency, primary biliary cirrhosis, and other forms of hepatitis have been reported.

Symptoms and Signs

Typical lesions are pruritic, purple, polygonal, flat-topped papules and plaques (see Plate 39). Lesions initially are 2 to 4 mm in diameter, with angular borders, a violaceous color, and a distinct sheen in cross-lighting. They are usually symmetrically distributed, most commonly on the flexor surfaces of the wrists, legs, trunk, glans penis, and oral and vaginal mucosae but can be widespread. The face is rarely involved. Onset may be abrupt or gradual. Children are affected infrequently. During the acute phase, new papules may appear at sites of minor skin injury (Koebner phenomenon), such as a superficial scratch. Lesions may coalesce or change over time, becoming hyperpigmented, atrophic, hyperkeratotic (hypertrophic LP), or vesiculobullous. Although pruritic, lesions are rarely excoriated or crusted. If the scalp is affected, patchy scarring alopecia (lichen planopilaris) may occur.

The oral mucosa is involved in about 50% of cases; oral lesions may occur without cutaneous lesions and usually persist for life. Reticulated, lacy, bluish-white, linear lesions (Wickham's striae) are a hallmark

of oral LP, especially on the buccal mucosae. Tongue margins and gingival mucosae in edentulous areas may also be affected. An erosive form of LP may occur in which the patient develops shallow, often painful, recurrent oral ulcers, which, if long-standing, rarely become cancerous. Chronic exacerbations and remissions are common. Vulvar and vaginal mucosae are often involved. Up to 50% of women with oral mucosal findings have undiagnosed vulvar LP. In men, genital involvement is common, especially of the glans penis.

Nails are involved in up to 10% of cases. Findings vary in intensity with nail bed discoloration, longitudinal ridging and lateral thinning, and complete loss of the nail matrix and nail, with scarring of the proximal nail fold onto the nail bed (pterygium formation).

Diagnosis

• Clinical evaluation

• Biopsy

Although diagnosis is suggested by appearance of the lesions, similar lesions may result from any of the papulosquamous disorders, lupus erythematosus, and secondary syphilis, among others. Oral or vaginal LP may resemble leukoplakia, and the oral lesions must also be distinguished from candidiasis, carcinoma, aphthous ulcers, pemphigus, cicatricial pemphigoid, and chronic erythema multiforme. Typically, biopsy is done.

If LP is diagnosed, some clinicians do laboratory testing for liver dysfunction, including hepatitis B and C infections.

Prognosis

Many cases resolve without intervention, presumably because the inciting agent is no longer present. Recurrence after years may be due to reexposure to the trigger or some change in the triggering mechanism. Sometimes treatment of a previously occult infection, such as a dental abscess, results in resolution.

Vulvovaginal LP may be chronic and refractory to therapy, causing decreased quality of life.

Treatment

• Topical treatments

• Systemic treatments

• Sometimes light therapy

Asymptomatic LP does not require treatment. Drugs suspected of triggering LP should be stopped.

Few controlled studies have evaluated treatments. Options differ by location and extent of disease. Most cases of LP on the trunk or extremities can be treated with local drugs. Topical corticosteroids are first-line treatment for most cases of localized disease. High-potency ointments or creams (eg, clobetasol, fluocinonide) may be used on the thicker lesions on the extremities; lower-potency drugs (eg, triamcinolone, desonide) may be used on the face, groin, and axillae. As always, courses should be limited to reduce risk of corticosteroid atrophy. Potency may be enhanced with use of polyethylene wrapping or flurandrenolide tape. Intralesional corticosteroids (triamcinolone acetonide solution diluted with saline to 5 to 10 mg/mL) can be used every 4 wk for hyperkeratotic plaques and those resistant to other therapies.

Topical therapy is impractical for generalized LP; oral drugs or phototherapy is used. Oral corticosteroids (eg, prednisone 20 mg once/day for 2 to 6 wk followed by a taper) may be used for severe cases. The disease may rebound when therapy ceases; however, long-term systemic corticosteroids should not be

used.

Oral retinoids (eg, acitretin 30 mg once/day for 8 wk) are indicated for otherwise recalcitrant cases. Griseofulvin 250 mg po bid given for 3 to 6 mo may be effective. Cyclosporine (1.25 to 2.5 mg/kg bid) can be used when corticosteroids or retinoids fail. Light therapy using psoralen plus ultraviolet A (PUVA) or narrow-band UVB is an alternative to oral therapies, especially if they have failed or are contraindicated for medical reasons.

Treatment of oral LP differs slightly. Viscous lidocaine may help relieve symptoms of erosive ulcers. Tacrolimus 0.1% ointment applied twice daily may induce lasting remission, although it has not been fully evaluated. Other treatment options include topical (in an adhesive base), intralesional, and systemic corticosteroids. Erosive oral LP may respond to oral dapsone or cyclosporine. Cyclosporine rinses also may be helpful.

Dapsone, hydroxychloroquine, azathioprine, systemic cyclosporine, and topical tretinoin may also be useful. As with any disease with so many therapies, individual drugs have not been uniformly successful.

Lichen Sclerosus

Lichen sclerosus is an inflammatory dermatosis of unknown cause, possibly autoimmune, that usually affects the anogenital area.

The earliest signs are skin fragility, bruising, and sometimes blistering. Lesions typically cause mild to severe itching. When lichen sclerosus manifests in children, the appearance may be confused with sexual abuse. With time, the involved tissue becomes atrophic, thinned, hypopigmented (there may be flecks of postinflammatory hyperpigmentation), fissured, and scaly. Hyperkeratotic and fibrotic forms exist. Severe and longstanding cases cause scarring and distortion of normal anogenital architecture. In women, this distortion can even lead to total absorption of the labia minora and fusion over the clitoris. In men, phimosis or fusion of the foreskin to the coronal sulcus can occur.

Diagnosis can usually be based on appearance, especially in advanced cases; however, biopsy should be done on any anogenital dermatosis that does not resolve with mild conventional therapy (eg, topical hydrocortisone, antifungal drug). It is especially important to biopsy any area that becomes thickened or ulcerated, because lichen sclerosus is a precursor of squamous cell carcinoma.

Treatment

• Topical corticosteroids

Treatment consists of potent topical corticosteroids (drugs that otherwise should be used with extreme caution in this area). The disease is generally intractable, so long-term follow-up, especially to monitor for squamous cell carcinoma and sexual function and for psychologic support, is indicated.

Chapter 79. Hypersensitivity and Inflammatory Disorders

Introduction

The immune system plays a significant role in a large number of skin disorders, including dermatitis, sunlight reactions, and bullous diseases. Although all of these disorders involve some level of inflammation, certain skin disorders are primarily characterized by their inflammatory component or as a hypersensitivity reaction, be it to a drug, infection, or cancer.

Acute Febrile Neutrophilic Dermatosis

(Sweet's Syndrome)

Acute febrile neutrophilic dermatosis is characterized by tender, indurated, dark-red papules and plaques with prominent edema in the upper dermis and dense infiltrate of neutrophils. Cause is not known. It frequently occurs with underlying cancer, especially hematologic cancers.

Etiology

Acute febrile neutrophilic dermatosis may occur with various disorders, including

• Acute respiratory illness

• GI infection

• Cancer

• Drug exposure

• Inflammatory or autoimmune disorders

• Pregnancy

About 25% of patients have an underlying cancer, 75% of which are hematologic cancers, especially myelodysplastic syndromes and acute myeloid leukemia. When not due to cancer, acute febrile neutrophilic dermatosis affects mostly women ages 30 to 50, with a female: male ratio of 3:1. In contrast, men who develop the condition tend to be older (60 to 90).

The cause is unknown; however, type 1 helper T-cell cytokines, including IL-2 and interferon-γ, are predominant and may play a role in lesion formation.

Symptoms and Signs

Patients are febrile, with an elevated neutrophil count, and have tender, dark-red plaques or papules, most often on the face, neck, and upper extremities, especially the dorsum of hands. Oral lesions can also occur. Rarely, bullous and pustular lesions are present. The lesions often develop in crops. Each crop is preceded by fever and persists for days to weeks.

Extracutaneous manifestations can involve the eyes (eg, conjunctivitis, episcleritis, iridocyclitis), joints (eg, arthralgia, myalgia, arthritis), and internal organs (eg, neutrophilic alveolitis; sterile osteomyelitis; psychiatric or neurologic changes; transient kidney, liver, and pancreatic insufficiency).

Diagnosis

• Clinical evaluation

• Skin biopsy

Diagnosis is suggested by the appearance of the lesions and is supported by the presence of associated conditions. Differential diagnosis includes erythema multiforme, erythema elevation diutinum, acute cutaneous lupus erythematosus, pyoderma gangrenosum, and erythema nodosum. If diagnosis is unclear, skin biopsy should be done. The histopathologic pattern is that of edema in the upper dermis with a dense infiltrate of neutrophils in the dermis. Vasculitis may be present but is secondary.

Treatment

• Corticosteroids

Treatment involves systemic corticosteroids, chiefly prednisone 0.5 to 1.5 mg/kg po once/day tapered over 3 wk. Antipyretics are also recommended. In difficult cases, dapsone 100 to 200 mg po once/day, indomethacin 150 mg po once/day for 1 wk and 100 mg po once/day for 2 additional wk, or K iodide 900 mg po once/day or 300 mg po tid can be given.

Drug Eruptions and Reactions

Drugs can cause multiple skin eruptions and reactions. The most serious of these are discussed elsewhere in THE MANUAL and include Stevens-Johnson syndrome and toxic epidermal necrolysis, hypersensitivity syndrome, serum sickness, exfoliative dermatitis, angioedema and anaphylaxis, and drug-induced vasculitis. Drugs can also be implicated in hair loss, lichen planus, erythema nodosum, pigmentation changes, SLE, photosensitivity reactions, pemphigus, and pemphigoid. Other drug reactions are classified by lesion type (see Table 79-1).

[**Table 79-1.** Types of Drug Reactions and Typical Causative Agents]

Symptoms and Signs

Symptoms and signs vary based on the cause and the specific reaction (see Table 79-1).

Diagnosis

• Clinical evaluation and drug exposure history

• Sometimes skin biopsy

A detailed history is often required for diagnosis, including recent use of OTC drugs. Because the reaction may not occur until several days or even weeks after first exposure to the drug, it is important to consider all new drugs and not only the one that has been most recently started. No laboratory tests reliably aid diagnosis, although biopsy of affected skin is often suggestive. Sensitivity can be definitively established only by rechallenge with the drug, which may be hazardous and unethical in patients who have had severe reactions.

Treatment

• Discontinuation of offending drug

• Sometimes antihistamines and corticosteroids

Most drug reactions resolve when drugs are stopped and require no further therapy. Whenever possible, chemically unrelated compounds should be substituted for suspect drugs. If no substitute drug is available and if the reaction is a mild one, it might be necessary to continue the treatment under careful watch despite the reaction. Pruritus can be controlled with antihistamines and topical corticosteroids. For IgE-mediated reactions (eg, urticaria), desensitization (see p. 1124) can be considered when there is critical need for a drug.

When progression from urticaria to anaphylaxis is a concern, treatment is with aqueous epinephrine (1:1000) 0.2 mL sc or IM and with the slower-acting but more persistent soluble hydrocortisone 100 mg IV, which may be followed by an oral corticosteroid for a short period (see also p. 1121).

Erythema Multiforme

Erythema multiforme (EM) is an inflammatory reaction, characterized by target or iris skin lesions. Oral mucosa may be involved. Diagnosis is clinical. Lesions spontaneously resolve but frequently recur. Erythema multiforme can occur as reaction to a drug or an infectious agent such as herpes simplex virus or mycoplasma. Suppressive antiviral therapy may be indicated for patients with frequent or symptomatic recurrence due to herpes simplex virus.

For years, EM was thought to represent the milder end of a spectrum of drug hypersensitivity disorders that included Stevens-Johnson syndrome and toxic epidermal necrolysis. Recent evidence suggests that EM is different from these other disorders.

Etiology

The majority of cases are caused by herpes simplex virus (HSV) infection (HSV-1 more so than HSV-2), although it is unclear whether EM lesions represent a specific or nonspecific reaction to the virus. Current thinking holds that EM is caused by a T-cell-mediated cytolytic reaction to HSV DNA fragments present in keratinocytes. A genetic disposition is presumed given that EM is such a rare clinical manifestation of HSV infection, and several HLA subtypes have been linked with the predisposition to develop lesions. Less commonly, cases are caused by drugs, vaccines, other viral diseases (especially hepatitis C), or possibly SLE. EM that occurs in patients with SLE is sometimes referred to as Rowell's syndrome.

Symptoms and Signs

EM manifests as the sudden onset of asymptomatic, erythematous macules, papules, wheals, vesicles, bullae, or a combination on the distal extremities (including palms and soles) and face. The classic lesion is annular, with a violaceous center and pink halo separated by a pale ring (target or iris lesion). Distribution is symmetric and centripetal; spread to the trunk is common. Some patients have itching. Oral lesions include target lesions on the lips and vesicles and erosions on the palate and gingivae.

Diagnosis

• Clinical evaluation

Diagnosis is by clinical appearance; biopsy is rarely necessary. Differential diagnosis includes essential urticaria, vasculitis, bullous pemphigoid, pemphigus, linear IgA dermatosis, acute febrile neutrophilic dermatosis, and dermatitis herpetiformis; oral lesions must be distinguished from aphthous stomatitis, pemphigus, herpetic stomatitis, and hand-foot-and-mouth disease. Patients with widely disseminated purpuric macules and blisters and prominent involvement of the trunk and face are likely to have Stevens-Johnson syndrome rather than EM.

Treatment

• Supportive care

• Sometimes prophylactic antivirals

EM spontaneously resolves, so treatment is usually unnecessary. Topical corticosteroids and anesthetics may ameliorate symptoms and reassure patients. Recurrences are common, and empiric oral maintenance therapy with acyclovir 400 mg po q 12 h, famciclovir 250 mg po q 12 h, or valacyclovir 1000 mg po q 24 h can be attempted if symptoms recur more than 5 times/yr and HSV association is suspected or if recurrent EM is consistently preceded by herpes flares.

Panniculitis

Panniculitis describes inflammation of the subcutaneous fat that can result from multiple causes. Diagnosis is by clinical evaluation and biopsy. Treatment depends on the cause.

Etiology

There are multiple causes of panniculitis, including

• Infections (the most common)

• Physical factors (eg, cold, trauma)

• Proliferative disorders

• Connective tissue disorders (eg, SLE, systemic sclerosis)

Idiopathic panniculitis is sometimes referred to as Weber-Christian disease.

Symptoms and Signs

Panniculitis is characterized by tender and erythematous subcutaneous nodules located over the extremities and sometimes over the posterior thorax, abdominal area, breasts, face, or buttocks. Rarely, nodules can involve the mesentery, lungs, scrotum, and cranium. Signs of systemic inflammation can accompany panniculitis. In Weber-Christian disease, systemic involvement can result in fever as well as signs of organ dysfunction, including hepatic, pancreatic, and bone marrow insufficiency, which is potentially fatal.

Diagnosis

• Clinical evaluation

• Excisional biopsy

Diagnosis is by usually by clinical appearance and can be confirmed by excisional biopsy.

Treatment

• Supportive care

• Anti-inflammatory drugs

• Immunosuppressants

There is no specific definitive treatment for panniculitis. A variety of strategies have been used with modest results, including NSAIDs, antimalarials, dapsone, and thalidomide. Corticosteroids (1 to 2 mg/kg po or IV once/day) and other immunosuppressive or chemotherapeutic drugs have been used to treat patients with progressive symptoms or signs of systemic involvement. Surgical abdominal panniculectomy has been used with varying levels of success in morbidly obese patients but should be reserved for patients with serious disease that does not respond to other measures.

Erythema Nodosum

Erythema nodosum (EN) is a specific form of panniculitis (see p. 687) characterized by tender, red or violet, palpable, subcutaneous nodules on the shins and occasionally other locations. It often occurs with an underlying systemic disease, notably streptococcal infections, sarcoidosis, inflammatory bowel disease, and TB. Diagnosis is by clinical evaluation and biopsy. Treatment depends on the cause.

Etiology

EN primarily affects people in their 20s and 30s but can occur at any age; women are more often affected. Etiology is unknown, but an immunologic reaction is suspected because EN is frequently accompanied by other disorders; the most common are

- Streptococcal infection (especially in children)
- Sarcoidosis
- Inflammatory bowel disease
- TB

Other possible triggers include

- Other bacterial infections (eg, *Yersinia*, *Salmonella*, mycoplasma, chlamydia, leprosy, lymphogranuloma venereum)
- Fungal infections (eg, coccidioidomycosis, blastomycosis, histoplasmosis)
- Rickettsial infections
- Viral infections (eg, Epstein-Barr, hepatitis B)
- Use of drugs (eg, sulfonamides, iodides, bromides, oral contraceptives)
- Hematologic and solid cancers
- Pregnancy

Up to one third of cases of EN are idiopathic.

Symptoms and Signs

EN is a subset of panniculitis that manifests as erythematous, tender plaques or nodules, primarily in the pretibial region (see
Plate 34), accompanied by fever, malaise, and arthralgia.

Diagnosis

- Clinical evaluation
- Excisional biopsy

Diagnosis is usually by clinical appearance and can be confirmed by excisional biopsy of a nodule when necessary. A diagnosis of EN should prompt evaluation for causes. Evaluation might include biopsy, skin testing (PPD or anergy panel), antinuclear antibodies, CBC, chest x-ray, and antistreptolysin O titer or pharyngeal culture. ESR is often high.

Treatment

- Supportive care
- Anti-inflammatory drugs
- Corticosteroids

EN almost always resolves spontaneously. Treatment includes bed rest, elevation, cool compresses, and NSAIDs. K iodide 300 to 500 mg po tid can be given to decrease inflammation. Systemic corticosteroids are effective but are an intervention of last resort as they can worsen an occult infection. If an underlying disorder is identified, it should be treated.

Granuloma Annulare

Granuloma annulare is a benign, chronic, idiopathic condition characterized by papules or nodules that spread peripherally to form a ring around normal or slightly depressed skin.

Etiology

Etiology is unclear but proposed mechanisms include cell-mediated immunity (type IV), immune complex vasculitis, and an abnormality of tissue monocytes. Granuloma annulare is not associated with systemic disorders, except that the incidence of abnormal glucose metabolism is increased among adults with many lesions. In some cases, exposure to sunlight, insect bites, TB skin testing, BCG vaccination, trauma, *Borrelia* infection, and viral infections have induced disease flares. The condition is twice as prevalent among women.

Symptoms and Signs

Lesions are erythematous, yellowish tan, bluish, or the color of the surrounding skin; one or more lesions may occur, most often on dorsal feet, legs, hands, or fingers. They are usually asymptomatic but may occasionally be tender. The lesions often expand or join to form rings. The center of each ring may be a slightly depressed, pale or light brown. In some cases, lesions may become generalized and widespread.

Diagnosis

Diagnosis is usually clinical but can be confirmed by skin biopsy.

Treatment

• Sometimes corticosteroids, anti-inflammatory drugs, or psoralen plus ultraviolet A (PUVA) therapy

Usually no treatment is necessary; spontaneous resolution is common. For patients with more widespread or bothersome lesions, quicker resolution may be promoted by the use of high-strength topical corticosteroids under occlusive dressings every night, flurandrenolide-impregnated tape, and intralesional corticosteroids. PUVA therapy is also effective and practical for patients with widespread disease. Recent reports have suggested that tumor necrosis factor-α inhibitors (eg, infliximab, adalimumab), 595-nm pulsed dye laser, and fractional photothermolysis are useful in managing disseminated and recalcitrant lesions.

Pyoderma Gangrenosum

Pyoderma gangrenosum is a chronic progressive skin necrosis of unknown etiology often associated with systemic illness.

Etiology

Etiology is unknown, but pyoderma gangrenosum can be associated with vasculitis, gammopathies, RA, leukemia, lymphoma, hepatitis C virus infection, SLE, sarcoidosis, polyarthritis, and especially inflammatory bowel disease and is thought to be caused by an abnormal immune response.

Pathophysiology

Pathophysiology is poorly understood but may involve problems with neutrophil chemotaxis. Ulcerations of pyoderma gangrenosum may occur after trauma or injury to the skin in 30% of patients; this process is termed pathergy.

Symptoms and Signs

Pyoderma gangrenosum begins as an inflamed erythematous papule, pustule, or nodule. The lesion, which may resemble a furuncle or an arthropod bite at this stage, then ulcerates and expands rapidly, developing a swollen necrotic base and a raised dusky to violaceous border. An undermined border is common, if not pathognomonic. Systemic symptoms such as fever, malaise, and arthralgias are common. The ulcers coalesce to form larger ulcers, often with cribriform or sieve-like scarring.

Diagnosis

Diagnosis is clinical. Biopsies of lesions are not often diagnostic but may be supportive; 40% of biopsies from a leading edge show vasculitis with neutrophils and fibrin in superficial vessels.

Treatment

• Corticosteroids

• Sometimes other anti-inflammatory drugs or immunosuppressants

• Avoidance of surgical debridement

Prednisone 60 to 80 mg po once/day is still the mainstay of treatment, although cyclosporine 3 mg/kg po once/day is also quite effective. Dapsone, clofazimine, thalidomide, tumor necrosis factor-α inhibitors (eg, infliximab), and mycophenolate mofetil have also been used successfully. Surgical treatments are avoided because of the risk of wound extension.

Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis

Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are severe cutaneous hypersensitivity reactions. Drugs, especially sulfa drugs, antiepileptics, and antibiotics, are the most common causes. Macules rapidly spread and coalesce, leading to epidermal blistering, necrosis, and sloughing. Diagnosis is usually obvious by appearance of initial lesions and clinical syndrome. Treatment is supportive care; corticosteroids, cyclophosphamide, and other drugs may be tried. Prognosis depends on how early the disorders are diagnosed and treated. Mortality can be as high as 7.5% in children and 20 to 25% in adults.

SJS and TEN are clinically similar except for their distribution. By one commonly accepted definition, changes affect < 10% of body surface area in SJS and > 30% of body surface area in TEN; involvement of 15 to 30% of body surface area is considered SJS-TEN overlap.

The disorders affect between 1 and 5 people/million. Incidence, severity, or both of these disorders may be higher in bone-marrow transplant recipients, in *Pneumocystis jirovecii*-infected HIV patients, in patients with SLE, and in patients with other chronic rheumatologic diseases.

Etiology

Drugs precipitate over 50% of SJS cases and up to 95% of TEN cases. The most common drug causes include

• Sulfa drugs (eg, cotrimoxazole, sulfasalazine)

• Other antibiotics (eg, aminopenicillins, fluoroquinolones, cephalosporins)

• Antiepileptics (eg, phenytoin, carbamazepine, phenobarbital, valproate, lamotrigine)

• Miscellaneous individual drugs (eg, piroxicam, allopurinol, chlormezanone)

Cases that are not caused by drugs are attributed to

• Infection (mostly with *Mycoplasma pneumoniae*)

• Vaccination

• Graft-vs-host disease

Rarely, a cause cannot be identified.

Pathophysiology

Exact mechanism is unknown; however, one theory holds that altered drug metabolism in some patients causes formation of reactive metabolites that bind to and alter cell proteins, triggering a T-cell-mediated cytotoxic reaction to drug antigens in keratinocytes.

Another possible mechanism involves interactions between Fas (a cell-surface receptor that induces apoptosis) and its ligand, particularly a soluble form of Fas ligand released from mononuclear cells. Recent findings suggest that granulysin released from cytotoxic T cells and natural killer cells might play a role in keratinocyte death.

Symptoms and Signs

Within 1 to 3 wk after the start of the offending drug, patients develop a prodrome of malaise, fever, headache, cough, and conjunctivitis. Macules, often in a target configuration, then appear suddenly, usually on the face, neck, and upper trunk. These macules simultaneously appear elsewhere on the body, coalesce into large flaccid bullae, and slough over a period of 1 to 3 days. Nails and eyebrows may be lost along with epithelium.

In severe cases of TEN, large sheets of epithelium slide off the entire body at pressure points (Nikolsky's sign), exposing weepy, painful, and erythematous skin. Painful oral crusts and erosions, keratoconjunctivitis, and genital problems (eg, phimosis, vaginal synechiae) accompany skin sloughing in up to 90% of cases. Bronchial epithelium may also slough, causing cough, dyspnea, pneumonia, pulmonary edema, and hypoxemia. Glomerulonephritis and hepatitis may develop.

Diagnosis

• Clinical evaluation

• Often skin biopsy

Diagnosis is often obvious from appearance of lesions and rapid progression of symptoms. Histologic examination of sloughed skin shows necrotic epithelium, a distinguishing feature.

Differential diagnosis in SJS and early TEN includes erythema multiforme, viral exanthems, and drug rash; and, in later stages of TEN, paraneoplastic pemphigus, toxic shock syndrome, exfoliative erythroderma, and thermal burn. In children, TEN is less common and must be distinguished from staphylococcal scalded skin syndrome.

Prognosis

Severe TEN is similar to extensive burns; patients are acutely ill, may be unable to eat or open their eyes, and suffer massive fluid and electrolyte losses. They are at high risk of infection, multiorgan failure, and death. With early therapy, survival rates approach 90%. The severity-of-illness score for TEN (see Table 79-2) systematically scores 7 independent risk factors within the first 24 h of presentation to the hospital to determine the mortality rate for a particular patient.

Treatment

• Supportive care

• Possibly immune modulator treatment

• Possibly plasmapheresis

Treatment is most successful when SJS or TEN is recognized early and treated in an inpatient dermatologic or ICU setting; treatment in a burn unit may be needed for severe disease. Ophthalmology consultation is mandatory for patients with ocular involvement. Drugs should be stopped immediately. Patients

[**Table 79-2.** Severity-of-Illness Score for Toxic Epidermal Necrolysis (Scorten)]

are isolated to minimize exposure to infection and are given fluids, electrolytes, blood products, and nutritional supplements as needed. Skin care includes prompt treatment of secondary bacterial infections. Prophylactic antibiotics are controversial.

Drug treatment of STS and TEN is controversial. High-dose systemic corticosteroids (eg, methylprednisolone 80 to 200 mg IV or prednisone 80 mg po once/day for 7 to 10 days or until progression stops) or cyclophosphamide (300 mg IV q 24 h for 7 days or until significant improvement) can be given to inhibit T-cell-mediated cytolysis. Cyclosporine (3 to 5 mg/kg po once/day) inhibits CD8 cells and has been shown to decrease the duration of active disease by 2 to 3 days in some instances. However, corticosteroids are controversial and are thought by some to increase mortality. Plasmapheresis can remove reactive drug metabolites or antibodies. Early high-dose IV immune globulin (IVIG) 2.7 g/kg over 3 days blocks antibodies and Fas ligand. Despite some remarkable results using high-dose IVIG for TEN, clinical trials involving small cohorts have reported conflicting results.

Chapter 80. Sweating Disorders

Introduction

There are two types of sweat glands: apocrine and eccrine.

Apocrine glands are clustered in the axillae, areolae, genitals, and anus; modified apocrine glands are found in the external auditory meatus. Apocrine glands become active at puberty; their excretions are oily and viscid and are presumed to play a role in sexual olfactory messages. The most common disorders of apocrine glands are bromhidrosis and hidradenitis suppurativa (see p. 698).

Eccrine glands are sympathetically innervated, distributed over the entire body, and active from birth. Their secretions are watery and serve to cool the body in hot environments or during activity. Disorders of eccrine glands include hyperhidrosis, hypohidrosis, and miliaria.

Bromhidrosis

Bromhidrosis is excessive or abnormal body odor caused by decomposition by bacteria and yeasts of apocrine secretions and cellular debris.

Apocrine secretions are lipid-rich, sterile, and odorless but become odoriferous when decomposed. Eccrine bromhidrosis is not as fragrant because eccrine sweat is nearly 100% water. The cause of apocrine bromhidrosis is poor hygiene of skin and clothing.

In some people, a few days of washing with an antiseptic soap, which may be combined with use of antibacterial creams containing clindamycin or erythromycin, may be necessary. Shaving the hair in the armpits may also help control odor.

Hyperhidrosis

Hyperhidrosis is excessive sweating, which can be focal or diffuse and has multiple causes. Sweating of the axillae, palms, and soles is most often due to stress; diffuse sweating is usually idiopathic but should raise suspicions for cancer, infection, and endocrine disease. Diagnosis is obvious, but tests for underlying causes may be indicated. Treatment is topical aluminum chloride, tap water iontophoresis, botulinum toxin, and, in extreme cases, surgery.

Etiology

Hyperhidrosis can be focal or generalized.

Focal sweating: Emotional causes are common, causing sweating on the palms, soles, axillae, and forehead at times of anxiety, excitement, anger, or fear. It may be due to a generalized stress-increased sympathetic outflow. Although such sweating is a normal response, patients with hyperhidrosis sweat excessively and under conditions that do not cause sweating in most people.

Gustatory sweating occurs around the lips and mouth when ingesting foods and beverages that are spicy or hot in temperature. There is no known cause in most cases, but gustatory sweating can be increased in diabetic neuropathy, facial herpes zoster, cervical sympathetic ganglion invasion, CNS injury or disease, or parotid gland injury. In the case of parotid gland injury, surgery, infection, or trauma may disrupt parotid gland innervation and lead to regrowth of parotid parasympathetic fibers into sympathetic fibers innervating local sweat glands in skin where the injury took place, usually over the parotid gland. This condition is called Frey's syndrome.

Other causes of focal sweating include pretibial myxedema (shins), hypertrophic osteoarthropathy (palms), and blue rubber bleb nevus syndrome and glomus tumor (over lesions). Compensatory sweating is intense sweating after sympathectomy.

Generalized sweating: Generalized sweating involves most of the body. Although most cases are

idiopathic, numerous conditions can be involved (see Table 80-1).

Symptoms and Signs

Sweating is often present during examination and sometimes is extreme. Clothing can be soaked, and palms or soles may become macerated and fissured. Hyperhidrosis can cause emotional distress to patients and may lead to social withdrawal. Palmar or plantar skin may appear pale.

Diagnosis

• History and examination

• Iodine and starch test

• Tests to identify a cause

Hyperhidrosis is diagnosed by history and examination but can be confirmed with the iodine and starch test (apply iodine solution to the affected area, let dry, dust on corn starch: areas of sweating appear dark). Testing is necessary only to confirm foci of sweating (as in Frey's syndrome or to locate the

[**Table 80-1.** Some Causes of Generalized Sweating]

area needing surgical or botulinum toxin treatment) or in a semiquantitative way when following the course of treatment.

Tests to identify a cause of hyperhidrosis are guided by a review of symptoms and might include CBC to detect leukemia, serum glucose to detect diabetes, and thyroid-stimulating hormone to screen for thyroid dysfunction.

Treatment

• Aluminum chloride hexahydrate solution

• Tap water iontophoresis

• Botulinum toxin type A

• Surgery

Initial treatment of focal and generalized sweating is similar.

Aluminum chloride hexahydrate 6 to 20% solution in absolute ethyl alcohol is indicated for topical treatment of axillary, palmar, and plantar sweating; these preparations require a prescription. The solution blocks sweat ducts and is most effective when applied nightly and covered tightly with a thin polyvinylidene or polyethylene film; it should be washed off in the morning. Sometimes an anticholinergic drug is taken before applying to prevent sweat from washing the aluminum chloride away. Initially, several applications weekly are needed to achieve control, then a maintenance schedule of once or twice weekly is followed. If treatment under occlusion is irritating, it should be tried without occlusion. This solution should not be applied to inflamed, broken, wet, or recently shaved skin. High-concentration, water-based aluminum chloride solutions may provide adequate relief in milder cases. Topical alternatives to aluminum chloride, including glutaraldehyde, formaldehyde, and tannic acid, are effective but can cause contact dermatitis and skin discoloration. A solution of methenamine also may help.

Tap water iontophoresis, in which salt ions are introduced into the skin using electric current, is an option for patients unresponsive to topical treatments. The affected areas (typically palms or soles) are placed in 2 tap water basins each containing an electrode across which a 15- to 25-mA current is applied for 10 to 20 min. This routine is done daily for 1 wk and then repeated weekly or bimonthly. Treatments may be

made more effective with topical or oral anticholinergic drugs. Although the treatments are usually effective, the technique is time-consuming and somewhat cumbersome, and some patients tire of the routine.

Botulinum toxin type A is a neurotoxin that decreases the release of acetylcholine from sympathetic nerves serving eccrine glands. Injected directly into the axillae, palms, or forehead, botulinum toxin inhibits sweating for about 5 mo depending on dose. Complications include local muscle weakness and headache. Injections are effective but painful and expensive.

Surgery is indicated if more conservative treatments fail. Patients with axillary sweating can be treated with surgical excision of axillary sweat glands either through open dissection or by liposuction (the latter seems to have lower morbidity). Patients with palmar sweating can be treated with endoscopic transthoracic sympathectomy. The potential morbidity of surgery must be considered, especially in sympathectomy. Potential complications include phantom sweating, compensatory sweating, gustatory sweating, neuralgia, and Horner's syndrome.

Hypohidrosis

Hypohidrosis is inadequate sweating.

Hypohidrosis due to skin abnormalities is rarely clinically significant. It is most commonly focal and caused by local skin injury (eg, from trauma, radiation, infection [eg, leprosy], or inflammation) or by atrophy of glands from connective tissue disease (eg, systemic sclerosis, SLE, Sjogren's syndrome). Hypohidrosis may be caused by drugs, especially those with anticholinergic properties. It is also caused by diabetic neuropathy and a variety of congenital syndromes. Heatstroke causes inadequate sweating but is a CNS rather than a skin disorder (see p. 3265). A rare presentation is fever of unknown origin.

Diagnosis is by clinical observation of decreased sweating or by heat intolerance. Treatment is by cooling measures (eg, air-conditioning, wet garments).

Miliaria

In miliaria, sweat flow is obstructed and trapped within the skin, causing papular lesions.

Miliaria most often occurs in warm humid weather but may occur in cool weather in an overdressed patient. Lesions vary depending on the depth of tissue at which the sweat duct is obstructed.

- **Miliaria crystallina** is ductal obstruction in the uppermost epidermis, with retention of sweat subcorneally. It causes clear droplike vesicles that rupture with light pressure.

- **Miliaria rubra** (prickly heat) is ductal obstruction in the mid-epidermis with retention of sweat in the epidermis and dermis. It causes irritated, pruritic papules (prickling).

- **Miliaria pustulosa** is similar to miliaria rubra but manifests as pustules rather than papules.

- **Miliaria profunda** is ductal obstruction at the entrance of the duct into the dermal papillae at the dermo-epidermal junction, with retention of sweat in the dermis. It causes papules that are larger and more deeply seated than those of miliaria pustulosa. Papules are frequently painful.

Diagnosis is by clinical appearance in the context of hot environment.

Treatment is cooling and drying of the involved areas and avoidance of conditions that may induce sweating; an air-conditioned environment is ideal. Once the rash develops, corticosteroid creams or lotions are used, sometimes with a bit of menthol added.

Chapter 81. Bacterial Skin Infections

Introduction

Bacterial skin infections may be uncomplicated or complicated. Uncomplicated infections usually respond promptly to systemic antibiotics and local wound care. A skin infection is considered complicated when it meets 2 of the following 5 criteria:

- Involves a preexisting wound or ulceration of the skin
- Involves the deeper soft tissues
- Requires surgical intervention
- Is caused or exacerbated by underlying comorbid disease states (eg diabetes, systemic immunosuppression)
- Is unresponsive to conventional antibiotic therapy or is recurrent

All uncomplicated skin infections have the potential to become complicated. Complicated skin and soft-tissue infections may require multidrug therapy and the assistance of other consultants (eg, surgeons, infectious disease specialists), particularly in light of resistance in many strains of bacteria and the rapid loss of efficacy among more potent antibiotics. Recurrent skin infections should raise suspicion of colonization (eg, staphylococcal nasal carriage), resistant strains of bacteria (eg, methicillin-resistant *Staphylococcus aureus* [MRSA]), cancer, poorly controlled diabetes, or other reasons for immunocompromise (eg, HIV, hepatitis, advanced age, congenital susceptibility). Bacteria are involved in the pathophysiology of acne, but acne is not primarily considered a bacterial skin infection.

Cellulitis

Cellulitis is acute bacterial infection of the skin and subcutaneous tissue most often caused by streptococci or staphylococci. Symptoms and signs are pain, rapidly spreading erythema, and edema; fever may occur, and regional lymph nodes may enlarge. Diagnosis is by appearance; cultures are sometimes helpful but awaiting culture results should not delay empiric therapy. Treatment is with antibiotics. Prognosis is excellent with timely treatment.

Etiology

- *Streptococcus pyogenes*
- *Staphylococcus aureus*

Cellulitis is most often caused by group A β-hemolytic streptococci (eg, *Streptococcus pyogenes*) or *Staphylococcus aureus*. Streptococci cause diffuse, rapidly spreading infection because enzymes produced by the organism (streptokinase, DNase, hyaluronidase) break down cellular components that would otherwise contain and localize the inflammation. Staphylococcal cellulitis is typically more localized and usually occurs in open wounds or cutaneous abscesses.

Recently, methicillin-resistant *S. aureus* (MRSA) has become more common in the community (community-associated MRSA [CA-MRSA]). Historically, MRSA was typically confined to patients who were exposed to the organism in a hospital or nursing facility. MRSA infection should now be considered in patients with community-acquired cellulitis, particularly in those with cellulitis that is recurrent or unresponsive to monotherapy.

Less common causes are group B streptococci (eg, *Streptococcus agalactiae*) in older patients with diabetes; gram-negative bacilli (eg, *Haemophilus influenzae*) in children; and *Pseudomonas aeruginosa* in patients with diabetes or neutropenia, hot tub or spa users, and hospitalized patients. Animal bites may

result in cellulitis; *Pasteurella multocida* is the cause in cat bites, and *Capnocytophaga* sp is responsible in dog bites. Immersion injuries in fresh water may result in cellulitis caused by *Aeromonas hydrophila*; in warm salt water, by *Vibrio vulnificus*.

Risk factors include skin abnormalities (eg, trauma, ulceration, fungal infection, other skin barrier compromise due to preexisting skin disease), which are common in patients with chronic venous insufficiency or lymphedema. Scars from saphenous vein removal for cardiac or vascular surgery are common sites for recurrent cellulitis, especially if tinea pedis is present. Frequently, no predisposing condition or site of entry is evident.

Symptoms and Signs

Infection is most common in the lower extremities. Cellulitis is typically unilateral; stasis dermatitis closely mimics cellulitis but is usually bilateral. The major findings are local erythema and tenderness, frequently with lymphangitis and regional lymphadenopathy. The skin is hot, red, and edematous (see Plate 31), often with surface appearance resembling the skin of an orange (peau d'orange). The borders are usually indistinct, except in erysipelas (a type of cellulitis with sharply demarcated margins—see p. 696). Petechiae are common; large areas of ecchymosis are rare. Vesicles and bullae may develop and rupture, occasionally with necrosis of the involved skin. Cellulitis may mimic deep venous thrombosis but can often be differentiated by one or more features (see Table 81-1). Fever, chills, tachycardia, headache, hypotension, and delirium may precede cutaneous findings by several hours, but many patients do not appear ill. Leukocytosis is common.

[**Table 81-1.** Differentiating Cellulitis and Deep Venous Thrombosis]

Diagnosis

• Examination

• Blood and sometimes tissue cultures for immunocompromised patients

Diagnosis is by examination. Skin and (when present) wound cultures are generally not indicated because they rarely identify the infecting organism. Blood cultures are useful in immunocompromised patients to detect or rule out bacteremia. Culture of involved tissue may be required in immunocompromised patients if they are not responding to empiric therapy or if blood cultures do not isolate an organism.

Prognosis

Most cellulitis resolves quickly with antibiotic therapy. Local abscesses occasionally form, requiring incision and drainage. Serious but rare complications include severe necrotizing subcutaneous infection (see p. 700) and bacteremia with metastatic foci of infection.

Recurrences in the same area are common, sometimes causing serious damage to the lymphatics, chronic lymphatic obstruction, and lymphedema.

Treatment

• Antibiotics

Treatment is with antibiotics. For most patients, empiric treatment effective against both group A streptococci and *S. aureus* is used. Oral therapy is usually adequate with dicloxacillin 250 mg or cephalexin 500 mg qid for mild infections. Levofloxacin 500 mg po once/day or moxifloxacin 400 mg once/day works well for patients who are unlikely to adhere to multiple daily dosing schedules. For more serious infections, oxacillin or nafcillin 1 g IV q 6 h is given. Use of initial empiric therapy against MRSA is not typically advised unless there is compelling clinical evidence (eg, contact with a documented case or outbreak; culture-documented prevalence of > 10% or 15% in a practice area). For penicillin-allergic patients or those with suspected or confirmed MRSA infection, vancomycin 1 g IV q 12 h is the drug of

choice (see also p. 1230). Linezolid is another option for the treatment of MRSA at a dose of 600 mg IV or po q 12 h for 10 to 14 days. Teicoplanin has a mechanism of action similar to vancomycin. It is commonly used outside the US to treat MRSA; the usual dose is 6 mg/kg IV q 12 h for 2 doses, followed by 6 mg/kg (or 3 mg/kg) IV or IM once/day. Immobilization and elevation of the affected area help reduce edema; cool, wet dressings relieve local discomfort.

Cellulitis in a patient with neutropenia requires empiric antipseudomonal antibiotics (eg, tobramycin 1.5 mg/kg IV q 8 h and piperacillin 3 g IV q 4 h) until blood culture results are available. Penicillin is the drug of choice for cellulitis caused by *P. multocida*; an aminoglycoside (eg, gentamicin) is effective against *A. hydrophila*, and tetracycline is preferred for *V. vulnificus* infections.

Recurrent leg cellulitis is prevented by treating concomitant tinea pedis, which often eliminates the source of bacteria residing in the inflamed, macerated tissue. If such therapy is unsuccessful or not indicated, recurrent cellulitis can sometimes be prevented by benzathine penicillin 1.2 million units IM monthly or penicillin V or erythromycin 250 mg po qid for 1 wk/mo. If these regimens prove unsuccessful, tissue culture may be required.

Erysipelas

Erysipelas is a type of superficial cellulitis (see p. 694) with dermal lymphatic involvement.

Erysipelas should not be confused with erysipeloid, a skin infection caused by *Erysipelothrix* (see p. 1241). Erysipelas is characterized clinically by shiny, raised, indurated, and tender plaque-like lesions with distinct margins (see Plate 33). There is also a bullous form of erysipelas. Erysipelas is most often caused by group A (or rarely group C or G) β-hemolytic streptococci and occurs most frequently on the legs and face. However, other causes have been reported, including *Staphylococcus aureus* (including methicillin-resistant *S. aureus* [MRSA]), *Klebsiella pneumoniae*, *Haemophilus influenzae*, *Escherichia coli*, *S. warneri*, *Streptococcus pneumoniae*, *S. pyogenes*, and *Moraxella* sp. Erysipelas of the face must be differentiated from herpes zoster, angioedema, and contact dermatitis. It is commonly accompanied by high fever, chills, and malaise; MRSA is more common in facial erysipelas than in lower-extremity erysipelas. Erysipelas may be recurrent and may result in chronic lymphedema.

Diagnosis

Diagnosis is by characteristic appearance; blood culture is done in toxic-appearing patients. Diffuse inflammatory carcinoma of the breast may also be mistaken for erysipelas.

Treatment

• Usually penicillin for lower-extremity erysipelas

• Initially vancomycin for facial erysipelas

Treatment of choice for lower-extremity erysipelas is penicillin V 500 mg po qid for ≥ 2 wk. In severe cases, penicillin G 1.2 million units IV q 6 h is indicated, which can be replaced by oral therapy after 36 to 48 h. Dicloxacillin 500 mg po qid for 10 days can be used for infections with staphylococci. Erythromycin 500 mg po qid for 10 days may be used in penicillin-allergic patients; however, there is growing macrolide resistance in streptococci. In infections resistant to these antibiotics, cloxacillin or nafcillin can be used. In Europe, pristinamycin and roxithromycin have been shown to be good choices for erysipelas. If facial erysipelas is present or if MRSA is otherwise suspected, empiric therapy should be initiated with vancomycin 1 g IV q 12 h (which is active against MRSA). Cold packs and analgesics may relieve local discomfort. Fungal foot infections may be an entry site for infection and may require antifungal treatment to prevent recurrence.

Cutaneous Abscess

A cutaneous abscess is a localized collection of pus in the skin and may occur on any skin

surface. Symptoms and signs are pain and a tender, firm or fluctuant swelling. Diagnosis is usually obvious by examination. Treatment is incision and drainage.

Bacteria causing cutaneous abscesses are typically indigenous to the skin of the involved area. For abscesses on the trunk, extremities, axillae, or head and neck, the most common organisms are *Staphylococcus aureus* and streptococci. In recent years, methicillin-resistant *S. aureus* (MRSA) has become a more common cause.

Abscesses in the perineal (ie, inguinal, vaginal, buttock, perirectal) region contain organisms found in the stool, commonly anaerobes or a combination of aerobes and anaerobes. Carbuncles and furuncles are follicle-based cutaneous abscesses with characteristic features (see p. 697).

Cutaneous abscesses tend to form in patients with bacterial overgrowth, antecedent trauma (particularly when a foreign body is present), or immunologic or circulatory compromise.

Symptoms and Signs

Cutaneous abscesses are painful, tender, indurated, and sometimes erythematous. They vary in size, typically 1 to 3 cm in length, but sometimes much larger. Initially the swelling is firm; later, as the abscess "points," the overlying skin becomes thin and feels fluctuant. The abscess may then spontaneously drain. Local cellulitis, lymphangitis, regional lymphadenopathy, fever, and leukocytosis are variable accompanying features.

Diagnosis

• Examination

• Gram stain and culture to identify MRSA

Diagnosis is usually obvious by examination. Gram stain and culture are recommended, primarily to identify MRSA.

Conditions resembling simple cutaneous abscesses include hidradenitis suppurativa (see p. 698) and ruptured epidermal cysts. Epidermal cysts (often incorrectly referred to as sebaceous cysts) rarely become infected; however, rupture releases keratin into the dermis, causing an exuberant inflammatory reaction sometimes clinically resembling infection. Culture of these ruptured cysts seldom reveals any bacteria. Perineal abscesses may represent cutaneous emergence of a deeper perirectal abscess or drainage from Crohn's disease via a fistulous tract. These other conditions are usually recognizable by history and rectal examination.

Treatment

• Incision and drainage

• Sometimes antibiotics

Some small abscesses resolve without treatment, coming to a point and draining. Warm compresses help accelerate the process. Incision and drainage are indicated when significant pain, tenderness, and swelling are present; it is unnecessary to await fluctuance. Under sterile conditions, local anesthesia is administered as either a lidocaine injection or a freezing spray.

Patients with large, extremely painful abscesses may benefit from IV sedation and analgesia during drainage. A single puncture with the tip of a scalpel is often sufficient to open the abscess. After the pus drains, the cavity should be bluntly probed with a gloved finger or curette to clear loculations, and then irrigated with 0.9% saline solution. Some clinicians pack the cavity loosely with a gauze wick that is removed 24 to 48 h later. Local heat and elevation may hasten resolution of inflammation.

Antibiotics are unnecessary unless the patient has signs of systemic infection, cellulitis, multiple

abscesses, immunocompromise, or a facial abscess in the area drained by the cavernous sinus. In these cases, empiric therapy should be started with a drug active against MRSA (eg, trimethoprim/sulfamethoxazole, clindamycin; for severe infection, vancomycin) pending results of bacterial culture.

Folliculitis

Folliculitis is a bacterial infection of hair follicles.

Folliculitis is usually caused by *Staphylococcus aureus* but occasionally *Pseudomonas aeruginosa* (hot tub folliculitis) or other organisms. Hot tub folliculitis occurs because of inadequate treatment of water with chlorine or bromine.

Symptoms of folliculitis are mild pain, pruritus, or irritation. Signs of folliculitis are a superficial pustule or inflammatory nodule surrounding a hair follicle. Infected hairs easily fall out or are removed, but new papules tend to develop. Growth of stiff hairs into the skin may cause chronic low-grade irritation or inflammation that may mimic infectious folliculitis (pseudofolliculitis barbae—see p. 731).

Treatment

Because most folliculitis is caused by *S. aureus*, clindamycin 1% lotion or gel may be applied topically bid for 7 to 10 days. Alternatively, benzoyl peroxide 5% wash may be used when showering for 5 to 7 days. Extensive cutaneous involvement may warrant systemic therapy (eg, cephalexin 250 to 500 mg po tid to qid for 10 days). If these measures do not result in a cure, or folliculitis recurs, pustules are Gram stained and cultured to rule out gram-negative or methicillin-resistant *S. aureus* (MRSA) etiology, and nares are cultured to rule out nasal staphylococcal carriage. Potassium hydroxide wet mount should be done on a plucked hair to rule out fungal folliculitis.

Treatment for MRSA usually requires 2 oral antibiotics, and the choice of therapeutic drugs should be based on culture and sensitivity reports.

Hot tub folliculitis usually resolves without treatment. However, adequate chlorination of the hot tub is necessary to prevent recurrences and to protect others from infection.

Furuncles and Carbuncles

Furuncles are skin abscesses caused by staphylococcal infection, which involve a hair follicle and surrounding tissue. Carbuncles are clusters of furuncles connected subcutaneously, causing deeper suppuration and scarring. They are smaller and more superficial than subcutaneous abscesses (see p. 696). Diagnosis is by appearance. Treatment is warm compresses and often oral antistaphylococcal antibiotics.

Both furuncles and carbuncles may affect healthy young people but are more common in the obese, the immunocompromised (including those with neutrophil defects), the elderly, and possibly those with diabetes. Clustered cases may occur among those living in crowded quarters with relatively poor hygiene or among contacts of patients infected with virulent strains. Predisposing factors include bacterial colonization of skin or nares, hot and humid climates, and occlusion or abnormal follicular anatomy (eg, comedones in acne). Methicillin-resistant *Staphylococcus aureus* (MRSA) is a common cause.

Furuncles are common on the neck, breasts, face, and buttocks. They are uncomfortable and may be painful when closely attached to underlying structures (eg, on the nose, ear, or fingers). Appearance is a nodule or pustule that discharges necrotic tissue and sanguineous pus. Carbuncles may be accompanied by fever and prostration.

Diagnosis

Diagnosis is by examination. Material for culture should be obtained.

Treatment

• Drainage

• Often antibiotics effective against MRSA

Abscesses are incised and drained. Intermittent hot compresses are used to facilitate drainage. Antibiotics, when used, should be effective against MRSA, pending culture and sensitivity test results. In afebrile patients, treatment of a single lesion < 5 mm requires no antibiotics. If a single lesion is ≥ 5 mm, an oral antibiotic is given for 5 to 10 days; choices include trimethoprim/sulfamethoxazole (TMP/SMX) 160/800 mg to 320/1600 mg bid, clindamycin 300 to 600 mg q 6 to 8 h, and doxycycline or minocycline 100 mg q 12 h. Patients with fever, multiple abscesses, or carbuncles are given 10 days of TMP/SMX 160/800 mg to 320/1600 mg bid plus rifampin 300 mg bid. Systemic antibiotics are also needed for

• Lesions < 5 mm that do not resolve with drainage

• Evidence of expanding cellulitis

• Immunocompromised patients

• Patients at risk of endocarditis

Furuncles frequently recur and can be prevented by applying liquid soap containing either chlorhexidine gluconate with isopropyl alcohol or 2 to 3% chloroxylenol and by giving maintenance antibiotics over 1 to 2 mo. Patients with recurrent furunculosis should be treated for predisposing factors such as obesity, diabetes, occupational or industrial exposure to inciting factors, and nasal carriage of *S. aureus* or MRSA colonization.

Erythrasma

Erythrasma is an intertriginous infection with *Corynebacterium minutissimum* that is most common among patients with diabetes and among people living in the tropics.

Erythrasma resembles tinea or intertrigo. It is most common in the foot, where it manifests as superficial scaling, fissuring, and maceration most commonly confined to the 3rd and 4th web spaces. Erythrasma is also common in the groin, where it manifests as irregular but sharply marginated pink or brown patches with fine scaling. Erythrasma may also involve the axillae, submammary or abdominal folds, and perineum, particularly in obese middle-aged women and in patients with diabetes.

Erythrasma fluoresces a characteristic coral-red color under Wood's light. Absence of hyphae in skin scrapings also distinguishes erythrasma from tinea.

Treatment is erythromycin or tetracycline 250 mg po qid for 14 days. Topical erythromycin or clindamycin is also effective. Recurrence is common.

Hidradenitis Suppurativa

Hidradenitis suppurativa is a chronic, scarring inflammation of apocrine glands of the axillae, groin, and around the nipples and anus.

Blockage of apocrine ducts has been suggested as the cause, leading to subsequent inflammation, bacterial overgrowth, and scarring. *Staphylococcus aureus* is almost always implicated in acute cases, but gram-negative organisms such as *Proteus* may predominate in chronic cases.

Swollen, tender masses resembling cutaneous abscesses develop. Pain, fluctuance, discharge, and sinus tract formation are characteristic in chronic cases. In chronic axillary cases, coalescence of inflamed nodules causes palpable cordlike fibrotic bands. The condition may become disabling because of pain and foul odor.

Diagnosis

Diagnosis is by examination. Bacterial cultures may be helpful if there appears to be a concomitant cellulitis or loculated abscess.

Treatment

Treatment of acute cases consists of high-dose oral tetracycline (500 mg bid), doxycycline (100 to 200 mg once/day), minocycline (100 mg once/day), or erythromycin (250 to 500 mg qid) until the lesions resolve. Topical clindamycin applied bid may be equally effective. Incision and drainage are necessary for an abscess or fluctuance of the affected area but alone do not resolve the problem (unlike in cutaneous abscesses). Isotretinoin 1 mg/kg po bid has also been effective in some patients, but recurrences are common. Intralesional corticosteroid injections (eg, triamcinolone 1 to 10% suspension intradermally) may help with inflammation and pain. Surgical excision and repair or grafting of the affected areas is often necessary if the disease persists. Ablative laser therapy (CO_2 or erbium:YAG) is an alternate surgical treatment. Several studies report success in treating hidradenitis suppurativa with etanercept or infliximab, injectable tumor necrosis factor-α inhibitors. Although not the gold standard, this option may be useful when all other treatment modalities have failed.

Impetigo and Ecthyma

Impetigo is a superficial skin infection with crusting or bullae caused by streptococci, staphylococci, or both. Ecthyma is an ulcerative form of impetigo.

No predisposing lesion is identified in most patients, but impetigo may follow any type of break in the skin. General risk factors seem to be moist environment, poor hygiene, and chronic nasal carriage of staphylococci. Impetigo may be bullous or nonbullous. *Staphylococcus aureus* is the predominant cause of nonbullous impetigo and the cause of all bullous impetigo. Bullae are caused by exfoliative toxin produced by staphylococci. Methicillin-resistant *S. aureus* (MRSA) has been isolated in about 20% of recent cases of impetigo.

Symptoms and Signs

Nonbullous impetigo typically manifests as clusters of vesicles or pustules that rupture and develop a honey-colored crust (exudate from the lesion base) over the lesions (see Plate 35). Bullous impetigo is similar except that vesicles typically enlarge rapidly to form bullae. The bullae burst and expose larger bases, which become covered with honey-colored varnish or crust. Ecthyma is characterized by small, purulent, shallow, punched-out ulcers with thick, brown-black crusts and surrounding erythema.

Impetigo and ecthyma cause mild pain or discomfort. Pruritus is common; scratching may spread infection, inoculating adjacent and nonadjacent skin.

Diagnosis

• Clinical evaluation

Diagnosis is by characteristic appearance. Cultures of lesions are indicated only when the patient does not respond to empiric therapy. Patients with recurrent impetigo should have nasal culture. Persistent infections should be cultured to identify MRSA.

Treatment

• Topical mupirocin or retapamulin

• Sometimes oral antibiotics

The affected area should be washed gently with soap and water several times a day to remove any crusts. Treatment for localized disease is topical mupirocin antibiotic ointment tid for 7 days or retapamulin ointment bid for 5 days. Oral antibiotics (eg, dicloxacillin or cephalexin 250 to 500 mg qid, 12.5 mg/kg qid for children, for 10 days) may be needed in patients with extensive or resistant lesions. Use of initial empiric therapy against MRSA is not typically advised unless there is compelling clinical evidence (eg, contact with a documented case or outbreak; high culture-documented prevalence in a practice area). Treatment of MRSA should be directed by culture and sensitivity test results; typically, clindamycin, rifampin, and trimethoprim/sulfamethoxazole are effective against most strains of community-associated MRSA.

Other therapy includes restoring a normal cutaneous barrier in patients with underlying atopic dermatitis or extensive xerosis using topical emollients and corticosteroids if warranted. Chronic staphylococcal nasal carriers are given topical antibiotics (mupirocin) for 1 wk each of 3 consecutive months.

Prompt recovery usually follows timely treatment. Delay can cause cellulitis, lymphangitis, furunculosis, and hyperpigmentation or hypopigmentation with or without scarring. Children aged 2 to 4 yr are at risk of acute glomerulonephritis if nephritogenic strains of group A streptococci are involved; nephritis seems to be more common in the southern US than in other regions.

Lymphadenitis

(See also Lymphangitis, below.)

Lymphadenitis is an acute infection of one or more lymph nodes.

Lymphadenitis is a feature of many bacterial, viral, fungal, and protozoal infections. Focal lymphadenitis is prominent in streptococcal infection, TB or nontuberculous mycobacterial infection, tularemia, plague, cat-scratch disease, primary syphilis, lymphogranuloma venereum, chancroid, and genital herpes simplex. Multifocal lymphadenitis is common in infectious mononucleosis, cytomegalovirus infection, toxoplasmosis, brucellosis, secondary syphilis, and disseminated histoplasmosis.

Symptoms and Signs

Lymphadenitis typically causes pain, tenderness, and lymph node enlargement. Pain and tenderness typically distinguish lymphadenitis from lymphadenopathy. With some infections, the overlying skin is inflamed, occasionally with cellulitis. Abscesses may form, and penetration to the skin produces draining sinuses. Fever is common.

Diagnosis

The underlying disorder is usually suggested by history and examination. If not, aspiration and culture or excisional biopsy is indicated.

Treatment

• Treatment of cause

Treatment is directed at the cause and is usually empiric. Options include IV antibiotics, antifungals, and antiparasitics depending upon etiology or clinical suspicion. Many patients with lymphadenitis may respond to outpatient therapy with oral antibiotics. However, many also go on to form abscesses, which require surgical drainage; an extensive procedure is done with accompanying IV antibiotics. In children, IV antibiotics are commonly needed. Hot, wet compresses may relieve some pain. Lymphadenitis usually resolves with timely treatment, although residual, persistent, nontender lymphadenopathy is common.

Lymphangitis

(See also Lymphadenitis, above.)

Lymphangitis is acute bacterial infection (usually streptococcal) of peripheral lymphatic channels.

Bacteria enter the lymphatic channels from an abrasion, wound, or coexisting infection (usually cellulitis). Patients with underlying lymphedema are at particular risk. Red, irregular, warm, tender streaks develop on an extremity and extend proximally from a peripheral lesion toward regional lymph nodes, which are typically enlarged and tender. Systemic manifestations (eg, fever, shaking chills, tachycardia, headache) may occur and may be more severe than cutaneous findings suggest. Leukocytosis is common. Bacteremia may occur. Rarely, cellulitis with suppuration, necrosis, and ulceration develops along the involved lymph channels as a consequence of primary lymphangitis.

Diagnosis is clinical. Isolation of the responsible organism is usually unnecessary. Most cases respond rapidly to antistreptococcal antibiotics (see Cellulitis on p. 694).

Necrotizing Subcutaneous Infection

(Necrotizing Fasciitis)

Necrotizing subcutaneous infection (NSI) is typically caused by a mixture of aerobic and anaerobic organisms that cause necrosis of subcutaneous tissue, usually including the fascia. This infection most commonly affects the extremities and perineum. Affected tissues become red, hot, and swollen, resembling severe cellulitis (see p. 694). Without timely treatment, the area becomes gangrenous. Patients are acutely ill. Diagnosis is by history and examination and is supported by evidence of overwhelming infection. Treatment involves antibiotics and surgical debridement. Prognosis is poor without early, aggressive treatment.

Etiology

NSI typically results from infection with group A streptococci (eg, *Streptococcus pyogenes*) or a mixture of aerobic and anaerobic bacteria (eg, *Bacteroides* sp). These organisms typically extend to subcutaneous tissue from a contiguous ulcer, an infection, or after trauma. Streptococci can arrive from a remote site of infection via the bloodstream. Perineal involvement (also called Fournier's gangrene) is usually a complication of recent surgery, perirectal abscess, periurethral gland infection, or retroperitoneal infection from perforated abdominal viscera. Patients with diabetes are at particular risk of NSI.

Pathophysiology

NSI causes tissue ischemia by widespread occlusion of small subcutaneous vessels. Vessel occlusion results in skin infarction and necrosis, which facilitates the growth of obligate anaerobes (eg, *Bacteroides*) while promoting anaerobic metabolism by facultative organisms (eg, *Escherichia coli*), resulting in gangrene. Anaerobic metabolism produces hydrogen and nitrogen, relatively insoluble gases that may accumulate in subcutaneous tissues.

Symptoms and Signs

The primary symptom is intense pain. However, in areas denervated by peripheral neuropathy, pain may be minimal or absent. Affected tissue is red, hot, and swollen and rapidly becomes discolored. Bullae, crepitus (from soft-tissue gas), and gangrene may develop. Subcutaneous tissues (including adjacent fascia) necrose, with widespread undermining of surrounding tissue. Muscles are spared initially. Patients are acutely ill, with high fever, tachycardia, altered mental status ranging from confusion to obtundation, and hypotension. Patients may be bacteremic or septic and may require aggressive hemodynamic support.

Diagnosis

• Clinical examination

• Blood and wound cultures

Diagnosis, made by history and examination, is supported by leukocytosis, soft-tissue gas on x-ray, positive blood cultures, and deteriorating metabolic and hemodynamic status.

NSI must be differentiated from clostridial soft-tissue infections, in which cellulitis, myositis, and myonecrosis often occur (see p. 1295). Such infections are anaerobic. Anaerobic cellulitis produces lots of gas but little pain, edema, or change in skin; it very seldom travels into the muscle. Anaerobic myonecrosis has pronounced skin changes, pain, and edema and usually penetrates into muscle.

Prognosis

Mortality rate is about 30%. Old age, underlying medical problems, delayed diagnosis and therapy, and insufficient surgical debridement worsen prognosis.

Treatment

• Surgical debridement

• Antibiotics

• Amputation if necessary

Treatment of early NSI is primarily surgical. IV antibiotics are adjuncts, usually including 2 or more drugs, but regimens vary depending on results of Gram stain and culture (eg, penicillin G 4 million units q 4 h combined with clindamycin 600 to 900 mg q 8 h or ceftriaxone 2 g q 12 h). Evidence of bullae, ecchymosis, fluctuance, crepitus, and systemic spread of infection requires immediate surgical exploration and debridement. The initial incision should be extended until an instrument or finger can no longer separate the skin and subcutaneous tissue from the deep fascia. The most common error is insufficient surgical intervention; repeat operation every 1 to 2 days, with further incision and debridement as needed, should be carried out routinely. Amputation of an extremity may be necessary.

IV fluids may be needed in large volumes before and after surgery. Antibiotic choices should be reviewed based on Gram stain and culture of tissues obtained during surgery. Hyperbaric O_2 therapy as adjuvant therapy may also be of benefit; however, the evidence is inconclusive.

Staphylococcal Scalded Skin Syndrome

Staphylococcal scalded skin syndrome (SSSS) is an acute epidermolysis caused by a staphylococcal toxin. Infants and children are most susceptible. Symptoms are widespread bullae with epidermal sloughing. Diagnosis is by examination and sometimes biopsy. Treatment is antistaphylococcal antibiotics and local care. Prognosis is excellent with timely treatment.

SSSS almost always affects children < 6 yr (especially infants); it rarely occurs in older patients unless they have renal failure or are immunocompromised. Epidemics may occur in nurseries, presumably transmitted by the hands of personnel who are in contact with an infected infant or who are nasal carriers of *Staphylococcus aureus*. Sporadic cases also occur.

SSSS is caused by group II coagulase-positive staphylococci, usually phage type 71, which elaborate exfoliatin (also called epidermolysin), a toxin that splits the upper part of the epidermis just beneath the granular cell layer (see also p. 1228). The primary infection often begins during the first few days of life in the umbilical stump or diaper area; in older children, the face is the typical site. Toxin produced in these areas enters the circulation and affects the entire skin.

[
Table 81-2. Differentiating Staphylococcal Scalded Skin Syndrome (SSSS) and Toxic Epidermal Necrolysis (TEN)]

Symptoms and Signs

The initial lesion is usually superficial and crusted. Within 24 h, the surrounding skin becomes painful and scarlet, changes that quickly spread to other areas. The skin may be exquisitely tender and have a wrinkled tissue paper-like consistency. Large, flaccid blisters arise on the erythematous skin and quickly break to produce erosions. Intact blisters extend laterally with gentle pressure (Nikolsky's sign). The epidermis may peel easily, often in large sheets (see Plate 45). Widespread desquamation occurs within 36 to 72 h, and patients become very ill with systemic manifestations (eg, malaise, chills, fever). Desquamated areas appear scalded. Loss of the protective skin barrier can lead to sepsis and to fluid and electrolyte imbalance.

Diagnosis

• Biopsy

• Cultures may be useful in adults

Diagnosis is suspected clinically, but confirmation usually requires biopsy (frozen section may give earlier results). Specimens show noninflammatory superficial splitting of the epidermis. In children, skin cultures are seldom positive; in adults, they are frequently positive. Cultures should be taken from the nose, conjunctiva, throat, and nasopharynx.

Differential diagnosis: Differential diagnosis includes drug hypersensitivity, viral exanthemas, scarlet fever, thermal burns, genetic bullous diseases (eg, some types of epidermolysis bullosa), acquired bullous diseases (eg, pemphigus vulgaris, bullous pemphigoid), and toxic epidermal necrolysis (see p. 689 and Table 81-2). Stevens-Johnson syndrome is characterized by mucosal involvement, which is absent in SSSS.

Treatment

• Antibiotics

• Corticosteroids not recommended

• Gel dressings for weeping lesions

With prompt diagnosis and therapy, death rarely occurs; the stratum corneum is quickly replaced, and healing usually occurs within 5 to 7 days after start of treatment.

Penicillinase-resistant antistaphylococcal antibiotics given IV must be started immediately. Nafcillin 12.5 to 25 mg/kg IV q 6 h for neonates > 2 kg and 25 to 50 mg/kg for older children is given until improvement is noted, followed by oral cloxacillin 12.5 mg/kg q 6 h (for infants and children weighing ≤ 20 kg) and 250 to 500 mg q 6 h (for older children). Corticosteroids are contraindicated. Topical therapy and patient handling must be minimized.

If disease is widespread and lesions are weeping, the skin should be treated as for burns (see p. 3245). Hydrolyzed polymer gel dressings may be very useful, and the number of dressing changes should be minimized.

Steps to detect carriers and prevent or treat nursery epidemics are discussed elsewhere (see p. 2828).

Chapter 82. Fungal Skin Infections

Introduction

Fungal skin infections are caused by yeasts (*Candida* sp) or dermatophytes (*Epidermophyton*, *Microsporum*, and *Trichophyton* spp).

Candidiasis

Candidiasis (moniliasis) is skin infection with *Candida* sp, most commonly *Candida albicans*. Infections can occur anywhere and are most common in skinfolds and web spaces and on the genitals, cuticles, and oral mucosa. Symptoms and signs vary by site. Diagnosis is by clinical appearance and potassium hydroxide wet mount of skin scrapings. Treatment is with drying agents and antifungals.

Most candidal infections are of the skin and mucous membranes, but invasive candidiasis is common in immunosuppressed patients and can be life threatening. Systemic candidiasis is discussed in Ch. 142.

Etiology

Candida is a group of about 150 yeast species. *C. albicans* is responsible for about 70 to 80% of all candidal infections. Other significant species include *C. glabrata*, *C. tropicalis*, *C. krusei*, and *C. dubliniensis*.

Candida is a ubiquitous yeast that resides harmlessly on skin and mucous membranes until dampness, heat, and impaired local and systemic defenses provide a fertile environment for it to grow. Risk factors for candidiasis include

- Hot weather
- Restrictive clothing
- Poor hygiene
- Infrequent diaper or undergarment changes in children and elderly patients
- Altered flora from antibiotic therapy
- Inflammatory diseases (eg, psoriasis) that occur in skinfolds
- Immunosuppression resulting from corticosteroids and immunosuppressive drugs, pregnancy, diabetes, other endocrinopathies (eg, Cushing's disease, hypoadrenalism, hypothyroidism), blood dyscrasias, or T-cell defects

Candidiasis occurs most commonly in intertriginous areas such as the axillae, groin, and gluteal folds (eg, diaper rash—see Plate 30), in digital web spaces, in the glans penis, and beneath the breasts. Vulvovaginal candidiasis is common in women (see p. 2544). Candidal nail infections and paronychia may develop after improperly done manicures and in kitchen workers and others whose hands are continually exposed to water (see p. 734). In obese people, candidal infections may occur beneath the pannus (abdominal fold). Oropharyngeal candidiasis (see Plate 32) is a common sign of local or systemic immunosuppression.

Chronic mucocutaneous candidiasis typically affects the nails, skin, and oropharynx. Patients have cutaneous anergy to *Candida*, absent proliferative responses to *Candida* antigen (but normal proliferative responses to mitogens), and an intact antibody response to *Candida* and other antigens. Chronic mucocutaneous candidiasis may occur as an autosomal recessive illness associated with

hypoparathyroidism and Addison's disease (*Candida*-endocrinopathy syndrome).

Symptoms and Signs

Intertriginous infections manifest as pruritic, well-demarcated, erythematous patches of varying size and shape; erythema may be difficult to detect in darker-skinned patients. Primary patches may have adjacent satellite papules and pustules. Perianal candidiasis produces white maceration and pruritus ani. Vulvovaginal candidiasis causes pruritus and discharge (see p. 2544).

Candidal infection is a frequent cause of chronic paronychia, which manifests as painful red periungual swelling. Subungual infections are characterized by distal separation of one or several fingernails (onycholysis), with white or yellow discoloration of the subungual area (see p. 735).

Oropharyngeal candidiasis causes white plaques on oral mucous membranes that may bleed when scraped.

Perleche is candidiasis at the corners of the mouth, which causes cracks and tiny fissures. It may stem from chronic lip licking, thumb sucking, ill-fitting dentures, or other conditions that make the corners of the mouth moist enough that yeast can grow.

Chronic mucocutaneous candidiasis is characterized by red, pustular, crusted, and thickened plaques resembling psoriasis, especially on the nose and forehead, and is invariably associated with chronic oral candidiasis.

Diagnosis

• Clinical appearance

• Potassium hydroxide wet mounts

Diagnosis is based on clinical appearance and identification of yeast and pseudohyphae in potassium hydroxide wet mounts of scrapings from a lesion. Positive culture is usually meaningless because *Candida* is omnipresent.

Treatment

• Sometimes drying agents

• Topical or oral antifungals

Intertriginous infection is treated with drying agents as needed (eg, Burow's solution for oozing lesions, gentian violet for toe web spaces) and topical antifungals (see Table 82-1). Powdered formulations are ideal for dry lesions (eg, miconazole powder bid for 2 to 3 wk). Fluconazole 150 mg po once/wk for 2 to 4 wk is indicated for extensive intertriginous candidiasis; topical antifungal agents may be used at the same time.

Candidal diaper rash is treated with more frequent change of diapers, avoidance of disposable diapers with plastic coverings, and an imidazole cream bid. Oral nystatin is an option for infants with coexisting oropharyngeal candidiasis; 1 mL of suspension (100,000 units/mL) is placed in each buccal pouch qid.

Candidal paronychia is treated by protecting the area from wetness and giving topical or oral antifungals. These infections are often resistant to treatment.

Oral candidiasis is treated with fluconazole 200 mg po on the first day, then 100 mg po once/day for 2 to 3 wk thereafter.

Chronic mucocutaneous candidiasis requires long-term oral antifungal treatment with ketoconazole 400 mg once/day or itraconazole 200 mg once/day.

[Table 82-1. Options for Treatment of Superficial Fungal Infections*]

Dermatophytoses

Dermatophytoses are fungal infections of keratin in the skin and nails (nail infection is called tinea unguium—see p. 734). Symptoms and signs vary by site of infection. Diagnosis is by clinical appearance and by examination of skin scrapings on potassium hydroxide wet mount. Treatment varies by site but always involves topical or oral antifungal drugs.

Dermatophytes are molds that require keratin for nutrition and must live on stratum corneum, hair, or nails to survive. Human infections are caused by *Epidermophyton*, *Microsporum*, and *Trichophyton* spp. These infections differ from candidiasis in that they are rarely if ever invasive. Transmission is person-to-person, animal-to-person, and rarely, soil-to-person. The organism may persist indefinitely. Most people do not develop clinical infection; those who do may have impaired T-cell responses from an alteration in local defenses (eg, from trauma with vascular compromise) or from primary (hereditary) or secondary (eg, diabetes, HIV) immunosuppression.

Symptoms and Signs

Symptoms and signs vary by site (skin, hair, nails). Organism virulence and host susceptibility and hypersensitivity determine severity. Most often, there is little or no inflammation; asymptomatic or mildly itching lesions with a scaling, slightly raised border remit and recur intermittently. Occasionally, inflammation is more severe and manifests as sudden vesicular or bullous disease (usually of the foot) or as an inflamed boggy lesion of the scalp (kerion).

Diagnosis

• Clinical appearance

• Potassium hydroxide wet mount

Diagnosis is based on clinical appearance and site of infection and confirmed by skin scrapings and demonstration of hyphae on potassium hydroxide (KOH) wet mount. Identification of specific organisms by culture is unnecessary except for scalp infection (where an animal source may be identified and treated) and nail infection (which may be caused by a nondermatophyte). Culture may also be useful when overlying inflammation and bacterial infection are severe and/or accompanied by alopecia.

Differential diagnosis includes

• Folliculitis decalvans

• Bacterial pyodermas

• Entities that cause scarring alopecia, such as discoid lupus, lichen planopilaris, and pseudopelade

Treatment

• Topical or oral antifungals

• Sometimes corticosteroids

Topical antifungals are generally adequate (see Table 82-1). In general, OTC terbinafine is best; econazole or ciclopirox may be better if candidal infection cannot be excluded. Oral antifungals are used for most nail and scalp infections, resistant skin infections, and patients unwilling or unable to adhere to prolonged topical regimens; doses and duration differ by site of infection.

Corticosteroid creams can be used to help relieve itching and pain for the first few days. Low-dose

hydrocortisone can be applied separately, or more potent corticosteroids may be added to the antifungal cream. Oral corticosteroids are occasionally used for treatment of severe inflammatory lesions.

Tinea Barbae

(Barber's Itch)

Tinea barbae is a dermatophyte infection of the beard area most often caused by *Trichophyton mentagrophytes* or *T. verrucosum*.

Tinea barbae manifests as superficial annular lesions, but deeper infection similar to folliculitis may occur. It may also occur as an inflammatory kerion that can result in scarring hair loss. Diagnosis is by KOH wet mount, culture, or biopsy.

Treatment is micronized griseofulvin 500 mg to 1 g po once/day until 2 to 3 wk after clinical clearance. Terbinafine 250 mg po once/day and itraconazole 200 mg po once/day have also been used. If the lesions are severely inflamed, a short course of prednisone should be added (to lessen symptoms and perhaps reduce the chance of scarring), starting with 40 mg po once/day (for adults) and tapering the dose over 2 wk.

Tinea Capitis

(Scalp Ringworm)

Tinea capitis is a dermatophyte infection of the scalp.

Tinea capitis mainly affects children, is contagious, and can be epidemic. *T. tonsurans* is the most common cause in the US, followed by *Microsporum canis* and *M. audouinii*; other *Trichophyton* sp (eg, *T. schoenleinii*, *T. violaceum*) are common elsewhere.

Tinea capitis causes the gradual appearance of round patches of dry scale, alopecia, or both. *T. tonsurans* infection causes "black dot ringworm," in which hair shafts break at the scalp surface; *M. audouinii* infection causes "gray patch ringworm," in which hair shafts break above the surface, leaving short stubs. Tinea capitis less commonly manifests as diffuse scaling, like dandruff, or in a diffuse pustular pattern.

Kerion: Dermatophyte infection occasionally leads to formation of a kerion, which is a large, boggy, inflammatory scalp mass (see Plate 48) caused by a severe inflammatory reaction to the dermatophyte. A kerion may have pustules and crusting and can be mistaken for an abscess. A kerion may result in scarring hair loss.

Diagnosis

• Clinical appearance

• KOH wet mount

• Sometimes Wood's light examination

Tinea capitis is diagnosed by clinical appearance and by KOH wet mount of plucked hairs or of hairs and scale obtained by scraping or brushing. Spore size and appearance inside (endothrix) or outside (ectothrix) the hair shaft distinguish organisms and can help guide treatment. Blue-green fluorescence during Wood's light examination is diagnostic for infection with *M. canis* and *M. audouinii* and can distinguish tinea from erythrasma.

Differential diagnosis of tinea capitis includes

• Seborrheic dermatitis

• Psoriasis

Treatment

• Oral antifungals

• Selenium sulfide shampoo

• Sometimes prednisone

Children are treated with micronized griseofulvin suspension 10 to 20 mg/kg po once/day (doses vary by several parameters, but maximum dose is generally 1 g/day) or, if > 2 yr, with ultramicronized griseofulvin 5 to 10 mg/kg (maximum 750 mg/day) po once/day or in 2 divided doses with meals or milk for 4 to 6 wk or until all signs of infection are gone. Terbinafine also may be used; children < 20 kg are given 62.5 mg once/day; those 20 to 40 kg, 125 mg once/day, and those > 40 kg, 250 mg once/day. An imidazole or ciclopirox cream should be applied to the scalp to prevent spread, especially to other children, until tinea capitis is cured; selenium sulfide 2.5% shampoo should also be used at least twice/wk. Children may attend school during treatment.

Adults are treated with terbinafine 250 mg po once/day for 2 to 4 wk, which is more effective for endothrix infections, or itraconazole 200 mg once/day for 2 to 4 wk or 200 mg bid given for 1 wk, followed by 3 wk without the drug (pulsed) for 2 to 3 mo.

For severely inflamed lesions and for kerion, a short course of prednisone should be added (to lessen symptoms and perhaps reduce the chance of scarring), starting with 40 mg po once/day (1 mg/kg for children) and tapering the dose over 2 wk.

Tinea Corporis

(Body Ringworm)

Tinea corporis is a dermatophyte infection of the face, trunk, and extremities.

Common causes are *T. mentagrophytes*, *T. rubrum*, and *M. canis*.

Tinea corporis causes pink-to-red annular patches and plaques with raised scaly borders that expand peripherally and tend to clear centrally (see
Plate 49). A variant form appears as nummular scaling patches studded with small papules or pustules.

Diagnosis

• Clinical evaluation

Differential diagnosis includes

• Pityriasis rosea

• Drug eruptions

• Nummular dermatitis

• Erythema multiforme

• Tinea versicolor

• Erythrasma

• Psoriasis

• Secondary syphilis

Treatment

• Topical or oral antifungals

Treatment of mild-to-moderate lesions is an imidazole, ciclopirox, naftifine, or terbinafine in cream, lotion, or gel. The drug should be rubbed in bid continuing at least 7 to 10 days after lesions disappear, typically at about 2 to 3 wk.

Extensive and resistant lesions occur in patients infected with *T. rubrum* and in people with debilitating systemic diseases. For such cases, the most effective therapy is oral itraconazole 200 mg once/day or terbinafine 250 mg once/day for 2 to 3 wk.

Tinea Cruris

(Jock Itch)

Tinea cruris is a dermatophyte infection of the groin.

Common organisms include *T. rubrum* or *T. mentagrophytes*. The primary risk factors are associated with a moist environment (ie, warm weather, wet and restrictive clothing, obesity causing constant apposition of skin folds). Men are affected more than women because of apposition of the scrotum and thigh.

Typically, a pruritic, ringed lesion extends from the crural fold over the adjacent upper inner thigh (see Plate 50). Infection may be bilateral. Lesions may be complicated by maceration, miliaria, secondary bacterial or candidal infection, and reactions to treatment. In addition, scratch dermatitis and lichenification can occur. Recurrence is common because fungi may repeatedly infect susceptible people. Flare-ups occur more often during summer.

Diagnosis

• Clinical evaluation

Differential diagnosis includes

• Contact dermatitis

• Psoriasis

• Erythrasma

• Candidiasis

Scrotal involvement is usually absent or slight; by contrast, the scrotum is often inflamed in candidal intertrigo or lichen simplex chronicus.

Treatment

• Topical antifungal cream or lotion

Antifungal choices include terbinafine, miconazole, clotrimazole, ketoconazole, econazole, naftifine, and ciclopirox applied bid for 10 to 14 days. Itraconazole 200 mg po once/day or terbinafine 250 mg po once/day for 3 to 6 wk may be needed in patients who have refractory, inflammatory, or widespread infections.

Tinea Pedis

(Athlete's Foot)

Tinea pedis is a dermatophyte infection of the feet.

Tinea pedis is the most common dermatophytosis because moisture from foot sweating facilitates fungal growth. Tinea pedis may occur as any of 4 clinical forms or in combination:

• Chronic hyperkeratotic

• Chronic intertriginous

• Acute ulcerative

• Vesiculobullous

Chronic hyperkeratotic tinea pedis due to *T. rubrum* causes a distinctive pattern of lesion, manifesting as scaling and thickening of the soles, which often extends beyond the plantar surface in a moccasin distribution. Differential diagnosis is sterile maceration (due to hyperhidrosis and occlusive footgear), contact dermatitis (due to type IV delayed hypersensitivity to various materials in shoes, particularly adhesive cement, thiuram compounds in footwear that contains rubber, and chromate tanning agents used in leather footwear), irritant dermatitis, and psoriasis.

Chronic intertriginous tinea pedis is characterized by scaling, erythema, and erosion of the interdigital and subdigital skin of the feet, most commonly affecting the lateral 3 toes.

Acute ulcerative tinea pedis (most often caused by *T. mentagrophytes* var. *interdigitale*) typically begins in the 3rd and 4th interdigital spaces and extends to the lateral dorsum and/or the plantar surface of the arch. These toe web lesions are usually macerated and have scaling borders (see Plate 51). Secondary bacterial infection, cellulitis, and lymphangitis are common complications.

Vesiculobullous tinea pedis, in which vesicles develop on the soles and coalesce into bullae, is the less common result of a flare of interdigital tinea pedis; risk factors are occlusive shoes and environmental heat and humidity.

Diagnosis

Diagnosis is usually obvious based on clinical examination and review of risk factors.

Treatment

• Moisture reduction and drying agents

• Topical and oral antifungals

The safest treatment is topical antifungals, but recurrence is common and treatment must often be prolonged. Alternatives that provide a more durable response include itraconazole 200 mg po once/day for 1 mo (or pulse therapy with 200 mg bid 1 wk/mo for 1 to 2 mo) and terbinafine 250 mg po once/day for 2 to 6 wk. Concomitant topical antifungal use may reduce recurrences.

Moisture reduction on the feet and in footwear is necessary for preventing recurrence. Permeable or open-toe footwear and sock changes are important especially during warm weather. Interdigital spaces should be manually dried after bathing. Drying agents are also recommended; options include antifungal powders (eg, miconazole), gentian violet, Burow's solution (5% aluminum sub-acetate) soaks bid, and 20 to 25% aluminum chloride hexahydrate powder once/day.

Dermatophytid Reaction

Dermatophytid is an inflammatory reaction to dermatophytosis at a cutaneous site distant from the primary infection.

Dermatophytid (identity or id) reactions are protean; they are not related to localized growth of the fungus but rather are an inflammatory reaction elsewhere on the body. Lesions are typically pruritic but may manifest as

• Vesicular eruptions on the hands and feet

• Follicular papules

• Erysipelas-like plaques

• Erythema nodosum

• Erythema annulare centrifugum

• Urticaria

Distribution may be extensive.

Diagnosis is by KOH wet mounts that are negative at the site of the id reaction and positive at the distant site of dermatophyte infection.

Treatment of the primary infection cures dermatophytid; pending cure, topical corticosteroids and/or antipruritics (eg, hydroxyzine 25 mg qid) can be used to relieve symptoms.

Intertrigo

Intertrigo is skinfold changes caused by moisture and infection.

Intertrigo develops when friction and trapped moisture in intertriginous areas cause skin maceration with formation of patches or plaques; bacterial, yeast, and dermatophyte infection is common. Typical locations are the inframammary, infrapannicular, interdigital, axillary, infragluteal, and genitocrural folds.

Diagnosis is based on clinical appearance; potassium hydroxide wet mounts and cultures can guide treatment.

If no bacteria or yeast are detected, drying agents (powders such as talc rather than cornstarch, which can support fungal growth, Burow's solution) to decrease moisture should be therapeutic. If bacteria or yeasts are present, topical antibacterial lotions or antifungal creams are given in addition to drying agents.

Tinea Versicolor

(Pityriasis Versicolor)

Tinea versicolor is skin infection with *Malassezia furfur* that manifests as multiple asymptomatic scaly patches varying in color from white to brown. Diagnosis is based on clinical appearance and skin scrapings. Treatment is topical antifungals.

Malassezia furfur is a dimorphic fungus that is normally a harmless component of normal skin flora but that in some people causes tinea versicolor. The high prevalence of tinea versi-color in young adults suggests a link to increased sebaceous secretions; other risk factors include heat and humidity and immunosuppression due to corticosteroids, pregnancy, undernutrition, diabetes, and other disorders.

Symptoms and Signs

Tinea versicolor usually is asymptomatic. Classically, it causes the appearance of multiple tan, brown, salmon, or white scaling lesions (see Plate 52) on the trunk, neck, abdomen, and occasionally face. The lesions coalesce. In whites, the condition is often diagnosed in summer months because the lesions, which do not tan, become more obvious against tanned skin.

Diagnosis

• Clinical appearance

• Potassium hydroxide wet mount

• Sometimes Wood's light examination

Diagnosis is based on clinical appearance and by identification of hyphae and budding cells ("spaghetti and meatballs") on potassium hydroxide wet mount. Wood's light examination reveals golden-white fluorescence.

Treatment

• Topical antifungals

• Sometimes oral antifungals

Treatment is any topical antifungal drug. Examples include selenium sulfide shampoo 2.5% (in 10-min applications daily for 1 wk or 24-h applications weekly for 1 mo); topical azoles (eg, ketoconazole 2% daily for 2 wk); and bathing with zinc pyrithione soap 2% or sulfur-salicylic shampoo 2% for 1 to 2 wk.

Oral treatment is indicated for patients with extensive disease and those with frequent recurrences. Two convenient regimens are a single 400-mg dose of fluconazole and ketoconazole 200 mg once/day for 1 to 5 days.

Hypopigmentation from tinea versicolor is reversible in months to years after the yeast has cleared. Recurrence is almost universal after treatment because the causative organism is a normal skin inhabitant. Fastidious hygiene, regular use of zinc pyrithione soap, or once-monthly use of topical antifungal therapy lowers the likelihood of recurrence.

Chapter 83. Parasitic Skin Infections

Introduction

Parasitic skin infections can cause severe itching and be distressing. Most skin parasites are insects or worms that burrow into the skin for part or all of their life cycle. Also, some systemic parasitic infections have cutaneous manifestations; these include certain nematodes (ancylostomiasis, dracunculosis, strongyloidiasis, toxocariasis—see p. 1342) and flukes (schistosomiasis—see p. 1358). Very rarely, patients have delusional parasitosis.

Cutaneous Larva Migrans

(Creeping Eruption)

Cutaneous larva migrans (CLM) is the skin manifestation of hookworm infestation.

CLM is caused by *Ancylostoma* sp, most commonly dog or cat hookworm *Ancylostoma braziliense*. Hookworm ova in dog or cat feces develop into infective larvae when left in warm moist ground or sand; transmission occurs when skin directly contacts contaminated soil or sand and larvae penetrate unprotected skin, usually of the feet, legs, buttocks, or back. CLM occurs worldwide but most commonly in tropical environments.

CLM causes intense pruritus; signs are erythema and papules at the site of entry, with a winding, threadlike subcutaneous trail of reddish-brown inflammation. Diagnosis is by history and clinical appearance.

Topical thiabendazole 15% liquid or cream (compounded) bid to tid for 5 days is extremely effective. Oral thiabendazole is not well tolerated and not usually used. Albendazole (400 mg po once/day for 7 days) and ivermectin can cure the infestation and are well tolerated.

CLM may be complicated by a self-limiting pulmonary reaction called Loffler's syndrome (patchy pulmonary infiltrates and peripheral blood eosinophilia).

Cutaneous Myiasis

Cutaneous myiasis is skin infestation by the larvae of certain fly species.

Myiasis involves the larvae of two-winged (dipterous) flies. Three types of cutaneous infestation exist, depending on the species involved:

• Furuncular

• Wound

• Migratory

Other organs sometimes are involved (eg, nasopharynx, GI tract, GU tract). Infestation usually occurs in tropical countries, so most cases in the US occur in people who have recently arrived from endemic areas.

Furuncular myiasis: Many of the common sources are known as bot flies. *Dermatobia hominis*, native to South and Central America, is the most common cause in travelers returning to the US. Other species include *Cordylobia anthropophaga* (in sub-Saharan Africa), and various *Cuterebra* sp (in tropical Africa). Many of the flies do not lay their eggs on humans but on other insects (eg, mosquitoes) or objects (eg, drying laundry) that may contact skin. Eggs on the skin hatch into larvae, which burrow into the skin and develop through successive stages (instars) into mature larvae; mature larvae may be 1 to 2 cm long, depending on the species. If the infestation is untreated, larvae eventually emerge from the skin and drop

to the ground to continue their life cycle.

Typical symptoms include itching, a sensation of movement, and sometimes lancinating pain. The initial lesion may resemble an arthropod bite or bacterial furuncle but may be distinguished by the presence of a central punctum with serosanguineous drainage; sometimes a small portion of the end of the larva is visible.

Because larvae require atmospheric O_2, occlusion of the skin opening may cause them to depart or at least come closer to the surface, facilitating manual removal. The numerous occlusal methods include use of petrolatum, nail polish, bacon, or a paste of tobacco. However, larvae that die during occlusion are difficult to remove and often trigger an intense inflammatory reaction. Other options for removal include manual expression (ie, squeezing) and extraction through a small incision. Ivermectin, oral (200 µg/kg, one dose) or topical, may kill the larvae or induce migration.

Wound myiasis: Open wounds, typically in the homeless, alcoholics, and other people in poor social circumstances, may be infested by fly larvae, most often from green or black blowflies. Unlike larvae of common houseflies, most agents of wound myiasis invade healthy as well as necrotic tissue. Treatment is usually with irrigation and manual debridement.

Migratory myiasis: The most common agents are *Gasterophilus intestinalis* and *Hypoderma* sp. These flies typically infest horses and cattle; people acquire them via contact with infested animals or, less often, via direct egg-laying on their skin. Larvae of these agents burrow under the skin, causing pruritic, advancing lesions, which may be mistaken for cutaneous larva migrans; however, fly larvae are much larger than nematodes, and the lesions created by fly larvae last longer. Treatment is similar to that of furuncular myiasis.

Delusional Parasitosis

In delusional parasitosis, patients mistakenly believe that they are infested with parasites.

Patients have an unshakable belief that they are infested with insects, worms, mites, lice, or other organisms. They often provide vivid descriptions of how the organisms enter their skin and move around their bodies, and bring samples of hair, skin, and debris such as dried scabs, dust, and lint on slides or in containers (the matchbox sign) to prove that the infestation is real. The condition is considered a hypochondriacal psychosis, but the cause is unknown.

Diagnosis is suspected by history. Work-up requires ruling out true infestations and other physiologic disease by physical examination and judicious testing, such as skin scrapings and CBC.

Treatment is with antipsychotic drugs (see p. 1562). Typically, the patient seeks confirmation that the drug treats the infestation itself, and any suggestion that the treatment is for something else is met with resistance and/or rejection. Thus, effective treatment often requires diplomacy and a delicate balance between offering proper treatment and respecting the patient's right to know.

Lice

(Pediculosis)

Lice can infect the scalp, body, pubis, and eyelashes. Head lice are transmitted by close contact; body lice, in cramped, crowded conditions; and pubic lice, by sexual contact. Symptoms, signs, diagnosis, and treatment differ by location of infestation.

Lice are wingless, blood-sucking insects that infest the head (*Pediculus humanus* var. *capitis*), body (*P. humanus* var. *corporis*), or pubis (*Phthirus pubis*). The 3 kinds of lice differ substantially in morphology and clinical features. Head lice and pubic lice live directly on the host; body lice live in garments. All types occur worldwide.

Head lice: Head lice are most common in girls aged 5 to 11 but can affect almost anyone; infestations

are rare in blacks. Head lice are easily transmitted from person to person with close contact (as occurs within households and classrooms) and may be ejected from hair by static electricity or wind; transmission by these routes (or by sharing of combs, brushes, and hats) is likely but unproven. There is no association between head lice and poor hygiene or low socioeconomic status.

Infestation typically involves the hair and scalp, but the eyebrows, eyelashes, and beard may be involved as well. Active infection usually involves ≤ 20 lice and causes severe pruritus. Examination is most often normal but may reveal scalp excoriations and posterior cervical adenopathy.

Diagnosis depends on demonstration of living lice. Lice are detected by a thorough combing-through of wet hair from the scalp with a fine-tooth detection comb; lice are usually found at the back of the head or behind the ears. Nits are ovoid, grayish white eggs fixed to the base of hair shafts (see Plate 38). Each adult female louse lays 3 to 5 eggs/day, so nits typically vastly outnumber lice and are not a measure of severity of infestation.

Treatment is outlined in Table 83-1. Drug resistance is common and should be managed with use of oral ivermectin and by attempting to rotate pediculicides. Termination of live (viable) nits is important in preventing reinfestation; live nits fluoresce on illumination with a Wood's lamp. Most pediculicides also kill nits. Dead nits remain after successful treatment and do not signify active infection; they do not have to be removed. Nits grow away from the scalp with time; the absence of nits less than one fourth of an inch from the scalp rules out current active infection. Hot air has been shown to kill > 88% of eggs but has been variably effective in killing hatched lice. Thirty minutes of hot air, slightly cooler than a blow drier, may be an effective adjunctive measure to treat head lice.

Controversy surrounds the need to clean the personal items of people with lice or nits and the need to exclude children with head lice or nits from school; there are no conclusive data supporting either approach.

Body lice: Body lice primarily live on bedding and clothing, not people, and are most frequently found in cramped, crowded conditions (eg, military barracks) and in people of low socioeconomic status. Transmission is by sharing of contaminated clothing and bedding. Body lice are important vectors of epidemic typhus, trench fever, and relapsing fever.

Body lice cause pruritus; signs are small red puncta caused by bites, usually associated with linear scratch marks, urticaria, or superficial bacterial infection. These findings are especially common on the shoulders, buttocks, and abdomen. Nits may be present on body hairs.

Diagnosis is by demonstration of lice and nits in clothing, especially at the seams.

Primary treatment is thorough cleaning or replacement of clothing and bedding, which is often difficult because affected people often have few resources and little control over their environment.

[**Table 83-1.** Treatment Options for Scabies and Lice]

Pubic lice: Pubic lice ("crabs") are sexually transmitted in adolescents and adults and may be transmitted to children by close parental contact. They may also be transmitted by fomites (towels, bedding, clothing). They most commonly infest pubic and perianal hairs but may spread to thighs, trunk, and facial hair (beard, mustache, and, in children, eyelashes).

Pubic lice cause pruritus. Physical signs are few, but some patients have excoriations and regional lymphadenopathy and/or lymphadenitis. Pale, bluish gray skin macules (maculae caeruleae) on the trunk, buttocks, and thighs are caused by anticoagulant activity of louse saliva while feeding; they are unusual but characteristic of infestation. Eyelash infestation manifests as eye itching, burning, and irritation.

Diagnosis is by demonstration of nits and/or living lice by close inspection (Wood's light) or microscopic analysis. A supporting sign of infestation is scattering of dark brown specks (louse excreta) on skin or undergarments.

Treatment is outlined in Table 83-1. Treatment of eyelid and eyelash infestation is often difficult and involves use of petrolatum, physostigmine ointment, oral ivermectin, or physical removal of lice with forceps. Sex partners should also be treated.

Scabies

Scabies is an infestation of the skin with the mite *Sarcoptes scabiei*. Scabies causes intensely pruritic lesions with erythematous papules and burrows in web spaces, wrists, waistline, and genitals. Diagnosis is based on examination and scrapings. Treatment is with topical scabicides or, rarely, oral ivermectin.

Etiology

Scabies is caused by the mite *Sarcoptes scabiei* var. *hominis*, an obligate human parasite that lives in burrowed tunnels in the stratum corneum. Scabies is easily transmitted from person to person through physical contact; animal and fomite transmission probably also occurs. The primary risk factor is crowded conditions (as in schools, shelters, barracks, and some households); there is no clear association with poor hygiene. For unknown reasons, crusted scabies is more common in immunosuppressed patients (eg, those with HIV infection, hematologic cancer, chronic corticosteroid or other immunosuppressant use), patients with severe physical disabilities or intellectual disability, and Australian Aborigines. Infestations occur worldwide. Patients in warm climates develop small erythematous papules with few burrows. Severity is related to the patient's immune status, not geography.

Symptoms and Signs

The primary symptom is intense pruritus, classically worse at night, although that timing is not specific to scabies.

Classic scabies: Erythematous papules initially appear in finger web spaces, flexor surfaces of the wrist and elbow, axillary folds, along the belt line, or on the lower buttocks. Papules can spread to any area of the body, including the breasts and penis. The face remains uninvolved in adults. Burrows are pathognomonic for disease, manifesting as fine, wavy, and slightly scaly lines several mm to 1 cm long. A tiny dark papule—the mite—is often visible at one end.

Signs of classic scabies may be atypical. In blacks and other people with dark skin, scabies can manifest as granulomatous nodules. In infants, the palms, soles, face, and scalp may be involved, especially in the posterior auricular folds. In elderly patients, scabies can cause intense pruritus with subtle skin findings, making it a challenge to diagnose. In immunocompromised patients, there may be widespread nonpruritic scaling (particularly on the palms and soles in adults and on the scalp in children).

Other forms: Crusted (Norwegian) scabies is due to an impaired host immune response, allowing mites to proliferate and number in the millions. Nodular scabies is more common in infants and young children and may be due to hypersensitivity to retained organisms. Bullous scabies occurs more commonly in children. When it occurs in the elderly, it can mimic bullous pemphigoid, resulting in a delay in diagnosis. Scalp scabies occurs in infants and immunocompromised people and can mimic dermatitis, particularly atopic or seborrheic dermatitis. Scabies incognito is a widespread atypical form resulting from application of topical corticosteroids.

Diagnosis

• Clinical evaluation

• Burrow scrapings

Diagnosis is suspected by physical findings, especially burrows, and confirmed by mites, ova, or fecal pellets on microscopic examination of burrow scrapings. Scrapings should be obtained by placing glycerol, mineral oil, or immersion oil over a burrow or papule (to prevent dispersion of mites and material

during scraping), which is then unroofed with the edge of a scalpel. The material is then placed on a slide and covered with a coverslip; potassium hydroxide should be avoided because it dissolves fecal pellets.

Treatment

• Topical permethrin or lindane

• Sometimes oral ivermectin

Primary treatment is topical or oral scabicides (see Table 83-1). Permethrin is the 1st-line topical drug.

Older children and adults should apply permethrin or lindane to the entire body from the neck down and wash it off after 8 to 14 h. Treatments should be repeated in 7 days.

For infants and young children, permethrin should be applied to the head and neck, avoiding periorbital and perioral regions. Special attention should be given to intertriginous areas, fingernails, toenails, and the umbilicus. Mittens on infants can keep permethrin out of the mouth. Lindane is not recommended in children < 2 yr and in patients with a seizure disorder because of potential neurotoxicity.

Precipitated sulfur 6 to 10% in petrolatum, applied for 24 h for 3 consecutive days, is safe and effective.

Ivermectin is indicated for patients who do not respond to topical treatment, are unable to adhere to topical regimens, or are immunocompromised with Norwegian scabies. Ivermectin has been used with success in epidemics involving close contacts, such as nursing homes.

Close contacts should also be treated, and personal items (eg, towels, clothing, bedding) should be washed or isolated for at least 3 days.

Pruritus can be treated with corticosteroid ointments and/or oral antihistamines (eg, hydroxyzine 25 mg po qid). Secondary infection should be considered in patients with weeping, yellow-crusted lesions and treated with the appropriate systemic or topical antistaphylococcal or antistreptococcal antibiotic.

Symptoms and lesions take up to 3 wk to resolve despite killing of the mites, making failed treatment due to resistance, poor penetration, incompletely applied therapy, reinfection, or nodular scabies difficult to recognize. Skin scrapings can be done periodically to check for persistent scabies.

Chapter 84. Viral Skin Diseases

Introduction

Many systemic viral infections cause skin lesions. Molluscum contagiosum and warts are the 2 most common primary viral skin diseases without systemic manifestations. Herpes simplex virus infection is discussed on p. 1417.

Molluscum Contagiosum

Molluscum contagiosum is clusters of smooth, waxy, or pearly umbilicated papules 1 to 5 mm in diameter caused by molluscum contagiosum virus, a poxvirus.

Molluscum contagiosum virus commonly causes a localized chronic infection. Transmission is by direct contact; spread occurs by autoinoculation and via fomites (eg, towels, bath sponges).

Symptoms and Signs

Molluscum contagiosum can appear anywhere on the skin except the palms and soles. Lesions consist of clusters of flesh-colored papules, which occur most commonly on the face, trunk, and extremities in children and on the pubis, penis, or vulva in adults. Lesions may grow to 10 to 15 mm in diameter, especially among patients with HIV infection and other immunocompromised patients. Lesions are usually not pruritic or painful and may be discovered only coincidentally during a physical examination. However, the lesions can become inflamed and itchy as the body fights off the virus.

Diagnosis

• Clinical evaluation

Diagnosis is based on clinical appearance; hematoxylin and eosin staining of expressed fluid demonstrates inclusion bodies but is necessary only when diagnosis is uncertain. Differential diagnosis includes folliculitis, milia, and warts (for lesions < 2 mm) and juvenile xanthogranuloma and Spitz nevus (for lesions > 2 mm).

Treatment

• Curettage, cryosurgery, laser therapy, or electrocautery

• Topical irritants (eg, trichloroacetic acid, cantharidin, tretinoin, tazarotene), imiquimod, or both

• Sometimes combination therapies

Most lesions spontaneously regress in 1 to 2 yr, but they can remain for 2 to 3 yr. Treatment is indicated for cosmetic reasons or for prevention of sexual spread. Options include curettage, cryosurgery, laser therapy, electrocautery, trichloroacetic acid (25 to 40% solution), cantharidin, tretinoin, tazarotene and imiquimod 5% cream. Especially in children, treatments that cause minimal pain (eg, tretinoin, imiquimod, tazarotene, cantharidin) are used first. Curettage or liquid nitrogen can be used after application of a topical anesthetic such as EMLA (eutectic mixture of local anesthetics) or 4% lidocaine cream. EMLA cream must be applied judiciously because it can cause systemic toxicity, especially in children. In adults, curettage is very effective but painful. Dermatologists often use combination therapy such as liquid nitrogen or cantharidin in the office and imiquimod cream at home. This form of therapy is typically successful, but resolution often takes 1 to 2 mo in some patients.

Nondermatologists should feel comfortable using imiquimod cream. The cream is applied at night, 1 drop to each molluscum lesion and rubbed in well, until the cream turns clear. The area is washed with soap and water. The cream can be applied 3 to 7 times/wk. Molluscum lesions within the orbital rim should not be treated, and those in the genital region can easily become irritated. Lesions should be treated until they develop a scant amount of redness; treatment is then withheld to avoid weeping and crusting.

Cantharidin is safe and effective but can cause blistering. Cantharidin is applied in 1 small drop directly to the molluscum lesion. Areas that patients (especially children) may rub are covered with a bandage because contact with the fingers should be avoided. Cantharidin should not be applied to the face or near the eyes because blistering is unpredictable. If cantharidin comes into contact with the cornea, it can scar the cornea. Cantharidin should be washed off with soap and water in 6 h. Parents should be warned about blistering if their children are prescribed this drug.

Warts

(Verrucae Vulgaris)

Warts are common, benign epidermal lesions caused by human papillomavirus infection. They can appear anywhere on the body in a variety of morphologies. Diagnosis is by examination. Warts are usually self limited but may be treated by excision, cautery, cryotherapy, liquid nitrogen, and topical or injected agents.

Warts are almost universal in the population; they affect all ages but are most common among children and are uncommon among the elderly.

Etiology

Warts are caused by human papillomavirus (HPV) infection; there are over 100 HPV subtypes. Trauma and maceration facilitate initial epidermal inoculation. Spread may then occur by autoinoculation. Local and systemic immune factors appear to influence spread; immunosuppressed patients (especially those with HIV infection or a renal transplant) are at particular risk of developing generalized lesions that are difficult to treat. Humoral immunity provides resistance to HPV infection; cellular immunity helps established infection to regress.

Symptoms and Signs

Warts are named by their clinical appearance and location; different forms are linked to different HPV types (for unusual manifestations, see Table 84-1).

Common warts: Common warts (verrucae vulgaris) are caused by HPV 1, 2, 4, 27, and 29. They are usually asymptomatic but sometimes cause mild pain, especially when they are located on a weight-bearing surface (eg, bottom of the feet). They are sharply demarcated, rough, round or irregular, firm, and light gray, yellow, brown, or gray-black nodules 2 to 10 mm in diameter. They appear most often on sites subject to trauma (eg, fingers, elbows, knees, face) but may spread elsewhere. Variants of unusual shape (eg, pedunculated or resembling a cauliflower) appear most frequently on the head and neck, especially the scalp and beard area.

Filiform warts: These warts are long, narrow, frondlike growths, usually located on the eyelids, face, neck, or lips. They are usually asymptomatic. This morphologically distinct variant of the common wart is benign and easy to treat.

Flat warts: Flat warts, caused by HPV 3, 10, 28, and 49, are smooth, flat-topped, yellow-brown papules, most often located on the face and along scratch marks; they are more common among children and young adults and develop by autoinoculation. They generally cause no symptoms but can be difficult to treat.

Palmar and plantar warts: These warts, caused by HPV 1, occur on the palms and soles; they are flattened by pressure and surrounded by cornified epithelium (see Plate 55). They are

[**Table 84-1.** Wart Variants]

often tender and can make walking and standing uncomfortable. They can be distinguished from corns and calluses by their tendency to pinpoint bleeding when the surface is pared away. Classically, warts hurt with side-to-side pressure, and calluses hurt with direct pressure; in reality, this is not a reliable sign.

Mosaic warts: Mosaic warts are plaques formed by the coalescence of myriad smaller, closely set plantar warts. As with other plantar warts, they are often tender.

Periungual warts: These warts appear as thickened, fissured cauliflower-like skin around the nail plate. Patients frequently lose the cuticle and are susceptible to paronychia. Periungual warts are more common among patients who bite their nails.

Genital warts: Genital warts (see p. 1470) manifest as discrete flat to broad-based smooth to velvety papules on the perineal, perirectal, labial, and penile areas. Infection with high-risk HPV types (most notably types 16 and 18) is the main cause of cervical cancer. These warts are usually asymptomatic.

Diagnosis

• Clinical evaluation

• Rarely biopsy

Diagnosis is based on clinical appearance; biopsy is rarely needed. A cardinal sign of warts is the absence of skin lines crossing their surface and the presence of pinpoint black dots (thrombosed capillaries) or bleeding when warts are shaved. Differential diagnosis includes corns (clavi), lichen planus, seborrheic keratosis, skin tags, and squamous cell carcinomas. DNA typing is available in some medical centers but is generally not needed.

Prognosis

Many warts regress spontaneously; others persist for years and recur at the same or different sites, even with treatment. Factors influencing recurrence appear to be related to the patient's overall immune status as well as local factors. Patients who subject themselves to local trauma (eg, athletes, mechanics, butchers) may have recalcitrant and recurrent HPV infection. Genital HPV infection has malignant potential, but malignant transformation is rare in HPV-induced skin warts, except among immunosuppressed patients.

Treatment

• Topical irritants (eg, salicylic acid, cantharidin, podophyllum resin)

• Destructive methods (eg, cryosurgery, electrocautery, curettage, excision, laser)

Treatment is aimed at eliciting an immune response to HPV. In most instances, this response is achieved by applying an irritant (eg, salicylic acid [SCA], trichloroacetic acid, 5-fluorouracil, podophyllum resin, tretinoin, cantharidin).

These compounds can be used in combination or with a destructive method (eg, cryosurgery, electrocautery, curettage, excision, laser). Direct antiviral effects can be achieved with bleomycin and interferon alfa-2b, but these treatments are reserved for the most recalcitrant warts. Topical imiquimod 5% cream induces skin cells to locally produce antiviral cytokines. Topical cidofovir, HPV vaccines, and contact immunotherapy (eg, squaric acid dibutyl ester and *Candida* allergen) have been used to treat warts. Oral treatments include cimetidine, isotretinoin, and oral zinc. In most instances, modalities should be combined to increase the likelihood of success.

Common warts: In immunocompetent patients, common warts usually spontaneously regress within 2 to 4 yr, but some linger for many years. Numerous treatments are available. Destructive methods include

• Electrocautery

• Cryosurgery with liquid nitrogen

• SCA preparations

Which method is used depends on the location and severity of involvement. For example, 17% liquid SCA can be used on the fingers, and 40% plaster SCA can be used on the soles.

The most common topical agent to be used is SCA. SCA is available in a liquid, plaster, or impregnated within tape. Patients apply SCA to their warts at night and leave on for 8 to 48 h depending on the site.

Cantharidin can be used alone or in combination (1%) with SCA (30%) and podophyllum (5%) in a collodion base. Cantharidin alone is removed with soap and water after 6 h; cantharidin with SCA or podophyllum is removed in 2 h. The longer these agents are left in contact with the skin, the more brisk the blistering response.

Cryosurgery is painful but extremely effective. Electrodesiccation with curettage, laser surgery, or both is effective and indicated for isolated lesions but may cause scarring. Recurrent or new warts occur in about 35% of patients within 1 yr, so methods that scar should be avoided as much as possible.

Filiform warts: Treatment is removal with scalpel, scissors, curettage, or liquid nitrogen. Liquid nitrogen should be applied so that up to 2 mm of skin surrounding the wart turns white. Damage to the skin occurs when the skin thaws, which usually takes 10 to 20 sec. Blisters can occur 24 to 48 h after treatment with liquid nitrogen. Care must be taken when treating cosmetically sensitive sites, such as the face and neck, because hypopigmentation frequently occurs after treatment with liquid nitrogen. Patients with darkly pigmented skin can develop permanent depigmentation.

Flat warts: Treatment is daily tretinoin (retinoic acid 0.05% cream). If peeling is not sufficient for wart removal, another irritant (eg, 5% benzoyl peroxide) or 5% SCA cream can be applied sequentially with tretinoin. Imiquimod 5% cream can be used alone or in combination with topical drugs or destructive measures. Topical 5-fluorouracil (1% or 5% cream) can also be used. Spontaneous resolution may follow unprovoked inflammation of the lesions; however, flat warts are frequently recalcitrant to treatment.

Plantar warts: Treatment is vigorous maceration with 40% SCA plaster kept in place for several days. The wart is debrided while damp and soft, then destroyed by freezing or using caustics (eg, 30 to 70% trichloroacetic acid). Other destructive treatments (eg, CO_2 laser, pulsed-dye laser, various acids) are often effective. Duct tape is effective when applied for 6-day intervals, followed by debridement of macerated tissue.

Periungual warts: Combination therapy with liquid nitrogen and imiquimod 5% cream, tretinoin, or SCA is effective.

Recalcitrant warts: Several methods whose long-term value and risks are not fully known are available for recalcitrant warts. Intralesional injection of small amounts of a 0.1% solution of bleomycin in saline often cures stubborn plantar and periungual warts. However, Raynaud's syndrome or vascular damage may develop in injected digits, especially when the drug is injected at the base of the digit, so caution is warranted. Interferon, especially interferon alfa, administered intralesionally (3 times/wk for 3 to 5 wk) or IM, has also cleared recalcitrant skin and genital warts. Extensive warts sometimes improve or clear with oral isotretinoin or acitretin. Cimetidine at doses up to 800 mg po tid has been used with success but is more effective when combined with another therapy.

Zoonotic Diseases

Two viral skin diseases are rarely transmitted from animals to humans.

Contagious ecthyma: Contagious ecthyma (contagious pustular dermatitis) is caused by orf virus, a poxvirus that infects ruminants (most often sheep and goats). Farmers, veterinarians, zoo caretakers, and others with direct animal contact are at risk. The cutaneous findings pass through 6 stages that together

last about 1 wk:

• Stage 1 (papular): A single red edematous papule on a finger (most commonly right index finder)

• Stage 2 (target): A larger nodule with a red center surrounded by a white ring with a red periphery

• Stage 3 (acute): A rapidly growing infected-looking tumor

• Stage 4 (regenerative): A nodule with black dots covered with a thin transparent crust

• Stage 5 (papillomatous): A nodule with a surface studded with small projections

• Stage 6 (regressive): A flattened nodule with a thick crust

Patients can develop regional adenopathy, lymphangitis, and fever.

Diagnosis is by history of contact; differential diagnosis is extensive depending upon the stage of the lesion. Acute lesions must be differentiated from milker's nodules, *Mycobacterium marinum* infection, and other bacterial infections; regressed lesions must be differentiated from cutaneous tumors, such as Bowen's disease or squamous cell carcinoma. Lesions spontaneously heal; no treatment is necessary.

Milker's nodules: These nodules are caused by paravaccinia virus, a parapoxvirus that causes udder lesions in cows. Infection requires direct contact and produces macules that progress to papules, vesicles, and nodules. This infection has 6 stages, which are similar to those of contagious ecthyma. Fever and lymphadenopathy are uncommon. Diagnosis is by history of contact and cutaneous findings. Differential diagnosis varies depending upon morphology but includes primary inoculation TB, sporotrichosis, anthrax, and tularemia. Lesions heal spontaneously; no treatment is necessary.

Chapter 85. Pigmentation Disorders

Introduction

Pigmentation disorders involve hypopigmentation, depigmentation, or hyperpigmentation. Areas may be focal or diffuse.

Focal hypopigmentation is most commonly a consequence of

- Injury
- Inflammatory dermatoses (eg, atopic dermatitis, psoriasis)
- Burns
- Chemical exposure

Focal hypopigmentation or depigmentation is also a feature of vitiligo (which may involve large areas of skin), leprosy, nutritional deficiencies (kwashiorkor), and genetic conditions (tuberous sclerosis, piebaldism, Waardenburg's syndrome).

Diffuse hypopigmentation is most often caused by

- Albinism
- Vitiligo

Focal hyperpigmentation typically occurs after inflammation of various causes, but it also may occur in patients with a systemic disorder or cancer.

Albinism

Albinism (officially called oculocutaneous albinism) is an inherited defect in melanin formation that causes diffuse hypopigmentation of the skin, hair, and eyes; deficiency of melanin (and hence pigmentary dilution) may be total or partial, but all areas of the skin are involved. Ocular involvement causes strabismus, nystagmus, and decreased vision. Diagnosis is usually obvious from the skin, but ocular evaluation is necessary. No treatment for the skin involvement is available other than protection from sunlight.

Pathophysiology

Oculocutaneous albinism (OCA) is a group of rare inherited disorders in which a normal number of melanocytes are present but melanin production is absent or greatly decreased. Cutaneous and ocular pathologies (ocular albinism) are both present. Ocular albinism involves abnormal optic tract CNS development manifested by foveal hypoplasia with decreased photoreceptors and misrouting of optic chiasmal fibers. Ocular albinism may occur without cutaneous abnormalities.

Most cases are autosomal recessive; autosomal dominant inheritance is rare. There are 4 main genetic forms:

- Type I is caused by absent (OCA1A; 40% of all OCA) or reduced (OCA1B) tyrosinase activity; tyrosinase catalyzes several steps in melanin synthesis.
- Type II (50% of all OCA) is caused by mutations in the P (pink-eyed) gene. The function of the P protein is not yet known. Tyrosinase activity is present.
- Type III occurs only in people with dark skin (skin types III to V). It is caused by mutations in a tyrosinase-related protein 1 gene whose product is important in eumelanin synthesis.

• Type IV is an extremely rare form in which the genetic defect is in a gene that codes a membrane transporter protein. Type IV is the most common form of OCA in Japan.

In a group of inherited diseases, a clinical phenotype of OCA occurs in conjunction with bleeding disorders. In the Hermansky-Pudlak syndrome, OCA-like findings occur with platelet abnormalities and a ceroid-lipofuscin lysosomal storage disease. This syndrome is rare except in people with family origin in Puerto Rico, where its incidence is 1 in 1800. In the Chediak-Higashi syndrome, OCA-like findings occur (hair is silvery gray), and a decrease in platelet-dense granules results in a bleeding diathesis. Patients have severe immunodeficiency due to abnormal lymphocyte lytic granules. Progressive neurologic degeneration occurs.

Symptoms and Signs

The different genetic forms have a variety of phenotypes.

Type I (OCA1A) is classic tyrosinase-negative albinism; skin and hair are milky white, and eyes are blue-gray. Pigmentary dilution in OCA1B ranges from obvious to subtle.

Type II has phenotypes with pigmentary dilution that ranges from minimal to moderate. Pigmented nevi and lentigines may develop if skin is exposed to the sun; some lentigines become large and dark. Eye color varies greatly.

In type III, skin is brown, hair is rufous (reddish), and eye color can be blue or brown.

In type IV, the phenotype is similar to that for type II.

Patients with ocular involvement may have decreased retinal pigmentation (see Plate 25), leading to photophobia. In addition, nystagmus, strabismus, reduced visual acuity, and loss of binocular vision likely result from defective routing of the optic fibers.

Diagnosis

• Clinical evaluation

Diagnosis of all types of OCA is based on examination of the skin. Early ocular examination may detect iris translucency, reduced retinal pigmentation, foveal hypoplasia, reduced visual acuity, and ocular movement disorders (strabismus and nystagmus).

Treatment

• Sun protection

• Sometimes surgical intervention for ocular movement disorders

There is no treatment for albinism. Patients are at high risk of sunburn and skin cancers (especially squamous cell carcinoma) and should avoid direct sunlight, use sunglasses with UV filtration, wear protective clothing, and use sunscreen with an SPF of ≥ 30 that protects against UVA and UVB wavelengths (see p. 673). Some surgical interventions may lessen ocular movement disorders.

Vitiligo

Vitiligo is a loss of skin melanocytes that causes areas of skin depigmentation of varying sizes. Cause is unknown, but the condition may be autoimmune; up to one third of patients have evidence of other autoimmune disease. Diagnosis is often obvious on examination. First-line treatment is topical corticosteroids. Calcineurin inhibitors (tacrolimus and pimecrolimus) and psoralens plus ultraviolet A are commonly used. For severe widespread pigment loss, depigmentation (bleaching) of residual patches of normal skin may be done with hydroquinone.

Vitiligo affects 0.5 to 2% of the population.

Etiology

Etiology is unclear, but melanocytes are lacking in affected areas. It is both familial (autosomal dominant, with incomplete penetrance and variable expression) and acquired. Proposed mechanisms include autoimmune destruction of melanocytes, reduced survival of melanocytes, and primary melanocyte defects. Occasionally, vitiligo occurs after a direct physical injury to the skin (eg, as a response to sunburn). This form of vitiligo is called the Koebner phenomenon. Patients may associate the onset of vitiligo with emotional stress.

Some patients have antibodies to melanin. Up to 30% have other autoimmune antibodies (to thyroglobulin, adrenal cells, and parietal cells) or clinical autoimmune endocrinopathies (Addison's disease, diabetes mellitus, pernicious anemia, and thyroid dysfunction), leading to speculation that vitiligo is an autoimmune disease. However, the relationship is unclear and may be coincidental. The strongest association is with hyperthyroidism (Graves' disease) and hypothyroidism (Hashimoto's thyroiditis).

Symptoms and Signs

Vitiligo is characterized by depigmented areas (see Plate 54), usually sharply demarcated and often symmetric. Depigmentation may be localized, involving 1 or 2 spots or entire body segments (segmental vitiligo); rarely, it may be generalized, involving most of the skin surface (universal vitiligo). However, vitiligo most commonly involves the face (especially around the orifices), digits, dorsal hands, flexor wrists, elbows, knees, shins, dorsal ankles, armpits, inguinal area, anogenital area, umbilicus, and nipples. Cosmetic disfigurement can be especially devastating in dark-skinned patients. Hair in vitiliginous areas is usually white.

Diagnosis

• Clinical evaluation

Depigmented skin is typically obvious on examination. Skin lesions are accentuated under Wood's light. Differential diagnosis includes postinflammatory hypopigmentation, morphea, leprosy, chemical leukoderma, and leukoderma due to melanoma. Additional testing for autoimmune endocrine disease is probably unnecessary unless symptoms or signs suggest a particular disorder.

Treatment

• Protection of affected areas from sunlight

• Topical corticosteroids

• Topical calcineurin inhibitors when face or groin involved

• Sometimes psoralen plus ultraviolet A (PUVA) therapy

Treatment is supportive and cosmetic. Physicians must be aware of individual and ethnic sensibilities regarding uniform skin coloring; the disease can be psychologically devastating. All depigmented areas are prone to severe sunburn and must be protected with clothing or sunscreen.

Small, scattered lesions may be camouflaged with makeup. First-line therapy for more extensive involvement is potent topical corticosteroids, which may cause hypopigmentation or atrophy in normal surrounding skin. Calcineurin inhibitors (tacrolimus and pimecrolimus) may be particularly useful for treating areas of the skin (such as the face and groin) where adverse effects of topical corticosteroid therapy most commonly occur. Oral and topical PUVA is often successful, although hundreds of treatment sessions may be necessary. Narrowband UVB is as effective as topical PUVA and has few adverse effects. Lasers may be useful, particularly for localized disease that does not respond to initial topical

therapy.

Surgery is reasonable only for patients with stable, limited disease when medical therapy has failed. Therapies include autologous micrografting, suction blister grafting, and tattooing; tattooing is especially useful for difficult-to-repigment areas such as the nipples, lips, and fingertips.

Depigmentation of unaffected skin to achieve homogeneous skin tone is possible with 20% monobenzyl ether of hydroquinone applied twice daily and is indicated only when most of the skin is involved and the patient is prepared for permanent pigment loss. This treatment can be extremely irritating, so a smaller test area should be treated before widespread use. Treatment for ≥ 1 yr may be required.

Hyperpigmentation

Hyperpigmentation has multiple causes and may be focal or diffuse. Most cases are due to an increase in melanin production and deposition.

Focal hyperpigmentation is most often postinflammatory in nature, occurring after injury (eg, cuts and burns) or other causes of inflammation (eg, acne, lupus). Focal linear hyperpigmentation is commonly due to phytophotodermatitis, which results from ultraviolet light combined with furocoumarins in limes, celery, and other plants.

Hyperpigmentation also has systemic and neoplastic causes.

Melasma (chloasma): Melasma consists of dark brown, sharply marginated, roughly symmetric patches of hyperpigmentation on the face (usually on the forehead, temples, and cheeks). It occurs primarily in pregnant women (melasma gravidarum, or the mask of pregnancy) and in women taking oral contraceptives. Ten percent of cases occur in nonpregnant women and dark-skinned men. Melasma is more prevalent and lasts longer in people with dark skin.

Because all cases are associated with sun exposure, the mechanism probably involves overproduction of melanin by hyperfunctional melanocytes. Other than sun exposure, aggravating factors include

• Autoimmune thyroid disorders

• Photosensitizing drugs

In women, melasma fades slowly and incompletely after childbirth or cessation of hormone use. In men, melasma rarely fades.

Treatment depends on whether the pigmentation is epidermal or dermal; epidermal pigmentation becomes accentuated with Wood's light or can be diagnosed with biopsy. Only epidermal pigmentation responds to treatment. First-line therapy includes a combination of hydroquinone 2 to 4%, tretinoin 0.05 to 1%, and a class V to VII topical corticosteroid. Hydroquinone 3 to 4% applied twice daily is often effective, but long courses are usually required; 2% hydroquinone is useful as maintenance. Hydroquinone should be tested behind one ear or on a small patch on the forearm for 1 wk before use on the face because it may cause irritation. Bleaching agents, such as 0.1% tretinoin and azelaic acid 15 to 20% cream, can be used in place of or with hydroquinone. Chemical peeling with glycolic acid or 30 to 50% trichloroacetic acid is an option for patients with severe melasma unresponsive to topical bleaching agents.

Lentigines: Lentigines (singular: lentigo) are flat, tan to brown oval spots. They are commonly due to chronic sun exposure (solar lentigines; sometimes called liver spots) and occur most frequently on the face and back of the hands. They typically first appear during middle age and increase in number with age. Although progression from lentigines to melanoma has not been established, lentigines are an independent risk factor for melanoma. They are treated with cryotherapy or laser; hydroquinone is not effective.

Nonsolar lentigines are sometimes associated with systemic disorders, such as Peutz-Jeghers syndrome (in which profuse lentigines of the lips occur), multiple lentigines syndrome (Leopard syndrome), or

xeroderma pigmentosum.

[
Table 85-1. Hyperpigmentation Effects of Some Drugs and Chemicals]

Diffuse hyperpigmentation due to systemic disorders: Common systemic causes include Addison's disease (see p. 792), hemochromatosis (see p. 1032), and primary biliary cirrhosis (see p. 244). Skin findings are nondiagnostic as to cause.

Drug-induced hyperpigmentation: Changes are usually diffuse but sometimes have drug-specific distribution patterns or hues (see Table 85-1). Mechanisms include

• Increased melanin in the epidermis (tends to be more brown)

• Melanin in the epidermis and high dermis (mostly brown with hints of gray or blue)

• Increased melanin in the dermis (tends to be more grayish or blue)

• Dermal deposition of the drug or metabolite (usually slate or bluish gray)

Focal hyperpigmentation frequently follows drug-induced lichen planus (also known as lichenoid drug reactions).

In fixed drug eruptions, red plaques or blisters form at the same site each time a drug is taken; residual postinflammatory hyperpigmentation usually persists. Typical lesions occur on the face (especially the lips), hands, feet, and genitals. Typical inciting drugs include sulfonamides, tetracycline, NSAIDs (especially phenazone derivatives), barbiturates, and carbamazepine.

Chapter 86. Hair Disorders

Introduction

Hair growth in both men and women is regulated by androgens. Testosterone stimulates hair growth in the pubic area and underarms. Dihydrotestosterone stimulates beard hair growth and scalp hair loss.

Hair disorders include alopecia, hypertrichosis, hirsutism, and pseudofolliculitis barbae. Although most hair disorders are not serious, they are often perceived as major cosmetic issues that demand treatment. Dandruff is not a hair disorder but rather a skin disorder (seborrheic dermatitis) of the scalp (see p. 671).

Alopecia

(Baldness)

Alopecia is defined as loss of hair. Hair loss is often a cause of great concern to the patient for cosmetic and psychologic reasons, but it can also be an important sign of systemic disease.

Pathophysiology

Growth cycle: Hair grows in cycles. Each cycle consists of a long growing phase (anagen), a brief transitional apoptotic phase (catagen), and a short resting phase (telogen). At the end of the resting phase, the hair falls out (exogen) and a new hair starts growing in the follicle, beginning the cycle again. Normally, about 100 scalp hairs reach the end of resting phase each day and fall out. When significantly more than 100 hairs/day go into resting phase, clinical hair loss (telogen effluvium) may occur. A disruption of the growing phase causing abnormal loss of anagen hairs is an anagen effluvium.

Classification: Alopecia can be classified as focal or diffuse and by the presence or absence of scarring.

Scarring alopecia is the result of active destruction of the hair follicle. The follicle is irreparably damaged and replaced by fibrotic tissue. Several hair disorders show a biphasic pattern in which nonscarring alopecia occurs early in the course of the disease, and then permanent hair loss occurs as the disease progresses. Scarring alopecias can be subdivided further into primary forms, where the target of inflammation is the follicle itself, and secondary forms, where the follicle is destroyed as a result of nonspecific inflammation (see Table 86-1).

Nonscarring alopecia results from processes that reduce or slow hair growth without irreparably damaging the hair follicle. Disorders that primarily affect the hair shaft also are considered nonscarring alopecia.

Etiology

The alopecias comprise a large group of disorders with multiple and varying etiologies (see Table 86-1).

The **most common cause** of alopecia is

• Androgenetic alopecia (male-pattern or female-pattern hair loss)

Androgenetic alopecia is an androgen-dependent hereditary disorder in which dihydrotestosterone plays a major role.

Other common causes of hair loss are

• Drugs (including chemotherapeutic agents)

• Infection

• Systemic illnesses (particularly those that cause high fever, systemic lupus, endocrine disorders, and nutritional deficiencies)

Less common causes are primary hair shaft abnormalities, autoimmune disease, heavy metal poisoning, and rare dermatologic conditions.

Evaluation

History: History of present illness should cover the onset and duration of hair loss, whether hair shedding is increased, and whether hair loss is generalized or localized. Associated symptoms such as pruritus and scaling should be noted. Patients should be asked about typical hair care practices, including use of braids, rollers, and hair dryers, and whether they routinely pull or twist their hair.

Review of systems should include recent exposures to noxious stimuli (eg, drugs, toxins, radiation) and stressors (eg, surgery, chronic illness, fever, psychologic stressors). Symptoms of possible causes should be sought, including fatigue and cold intolerance (hypothyroidism) and, in women, hirsutism, deepening of the voice, and increased libido (virilizing syndrome). Other features, including dramatic weight loss, dietary practices (including vegetarianism), and obsessive-compulsive behavior, should be noted. In women, a hormonal/gynecologic/obstetric history should be obtained.

Past medical history should note known possible causes of hair loss, including endocrine and skin disorders. Current and recent

[**Table 86-1.** Classification and Causes of Alopecia]

drug use should be reviewed for offending agents (see Table 86-1). A family history of hair loss should be recorded.

Physical examination: Examination of the scalp should note the distribution of hair loss, the presence and characteristics of any skin lesions, and whether there is scarring. Part widths should be measured. Abnormalities of the hair shafts should be noted.

A full skin examination should be done to evaluate hair loss elsewhere on the body (eg, eyebrows, eyelashes, arms, legs), rashes that may be associated with certain types of alopecia (eg, lichen planus, atopy, psoriasis, discoid lupus lesions, hidradenitis, signs of secondary syphilis or of other bacterial or fungal infections), and signs of virilization in women (eg, hirsutism, acne, deepening voice, clitoromegaly). Signs of potential underlying systemic disorders should be sought, and a thyroid examination should be done.

Red flags: The following findings are of particular concern:

• Virilization in women

• Signs of systemic illness or constellations of nonspecific findings possibly indicating poisoning

Interpretation of findings: Hair loss that begins at the temples or vertex and spreads to diffuse thinning or nearly complete hair loss is typical of male-pattern hair loss. Hair thinning in the frontal, parietal, and crown regions is typical of female-pattern hair loss (see Fig. 86-1).

Hair loss that occurs 2 to 4 wk after chemotherapy or radiation therapy (anagen effluvium) can typically be ascribed to those causes. Hair loss that occurs 3 to 4 mo after a major stressor (pregnancy, febrile illness, surgery, medication change, or severe psychologic stressor) suggests a diagnosis of telogen effluvium.

Other findings help suggest alternative diagnoses (see Table 86-2).

Other than hair loss, scalp symptoms (eg, itching, burning, tingling) are often absent and, when present, are not specific to any cause.

Signs of hair loss in patterns other than those described above are nondiagnostic and may require microscopic hair examination or scalp biopsy for definitive diagnosis.

Testing: Evaluation for causative disorders (eg, endocrinologic, autoimmune, toxic) should be done based on clinical suspicion.

Male-pattern or female-pattern hair loss generally requires no testing. When it occurs in young men with no family history, the physician should question the patient about use of anabolic steroids and other drugs. In addition to questions regarding drug and illicit drug use, women with significant hair loss and evidence of virilization should have testosterone and dehydroepiandrosterone sulfate (DHEAS) levels measured (see p. 730).

The **pull test** helps evaluate diffuse scalp hair loss. Gentle traction is exerted on a bunch of hairs (40 to 60) on at least 3 different areas of the scalp, and the number of extracted hairs is counted and examined microscopically. Normally, < 3 telogen-phase hairs should come out with each pull. If at least 3 hairs are obtained with each pull or if > 10 hairs total are obtained, the pull test is positive and suggestive of telogen effluvium.

The **pluck test** pulls individual hairs out abruptly ("by the roots"). The roots of the plucked hairs are examined microscopically to determine the phase of growth and thus help diagnose a defect of telogen or anagen or an occult systemic disease. Anagen hairs have sheaths attached to their roots; telogen hairs have tiny bulbs without sheaths at their roots. Normally, 85 to 90% of hairs are in the

[**Fig. 86-1.** Male-pattern and female-pattern hair loss.]

anagen phase; about 10 to 15% are in telogen phase; and < 1% are in catagen phase. Telogen effluvium shows an increased percentage of telogen-phase hairs on microscopic examination, whereas anagen effluvium shows a decrease in telogen-phase hairs and an increased number of broken hairs. Primary hair shaft abnormalities are usually obvious on microscopic examination of the hair shaft.

Scalp biopsy is indicated when alopecia persists and diagnosis is in doubt. Biopsy may differentiate scarring from nonscarring forms. Specimens should be taken from areas of active inflammation, ideally at the border of a bald patch. Fungal and bacterial cultures may be useful; immunofluorescence studies may help identify lupus erythematosus, lichen planopilaris, and systemic sclerosis.

Daily hair counts can be done by the patient to quantify hair loss when the pull test is negative. Hairs lost in the first morning combing or during washing are collected in clear plastic bags daily for 14 days. The number of hairs in each bag is then recorded. Scalp hair counts of > 100/day are abnormal except after shampooing, when hair counts of up to 250 may be normal. Hairs may be brought in by the patient for microscopic examination.

Treatment

Androgenetic alopecia: Minoxidil (2% for women, 2% or 5% for men) prolongs the anagen growth phase and gradually enlarges miniaturized follicles (vellus hairs) into mature terminal hairs. Topical minoxidil 1 mL bid applied to the scalp is most effective for vertex alopecia in male-pattern or female-pattern hair loss. However, usually only 30 to 40% of patients experience significant hair growth, and minoxidil is generally not effective or indicated for other causes of hair loss except possibly alopecia areata. Hair regrowth can take 8 to 12 mo. Treatment is continued indefinitely because, once treatment is stopped, hair loss resumes. The most frequent adverse effects are mild scalp irritation, allergic contact dermatitis, and increased facial hair.

Finasteride inhibits the 5α-reductase enzyme, blocking conversion of testosterone to dihydrotestosterone, and is useful for male-pattern hair loss. Finasteride 1 mg po once/day can stop hair

loss and can stimulate hair

[Table 86-2. Interpreting Findings in Alopecia]

growth. Efficacy is usually evident within 6 to 8 mo of treatment. Adverse effects include decreased libido, erectile and ejaculatory dysfunction, hypersensitivity reactions, gynecomastia, and myopathy. There may be a decrease in prostate-specific antigen levels in older men, which should be taken into account when that test is used for cancer screening. Common practice is to continue treatment for as long as positive results persist. Once treatment is stopped, hair loss returns to previous levels. Finasteride is not indicated for women and is contraindicated in pregnant women because it has teratogenic effects in animals.

Hormonal modulators such as oral contraceptives or spironolactone may be useful for female-pattern hair loss associated with hyperandrogenemia.

Surgical options include follicle transplant, scalp flaps, and alopecia reduction. Few procedures have been subjected to scientific scrutiny, but patients who are self-conscious about their hair loss may consider them.

Hair loss due to other causes: Underlying disorders are treated.

Multiple treatment options for alopecia areata exist and include topical, intralesional, or, in severe cases, systemic corticosteroids, topical minoxidil, topical anthralin, topical immunotherapy (diphencyprone or squaric acid dibutylester), or psoralen plus ultraviolet A (PUVA).

Treatment for traction alopecia is elimination of physical traction or stress to the scalp.

Treatment for tinea capitis is topical or oral antifungals (see p. 707).

Trichotillomania is difficult to treat, but behavior modification, clomipramine, or an SSRI (eg, fluoxetine, fluvoxamine, paroxetine, sertraline, citalopram) may be of benefit.

Scarring alopecia as seen in central centrifugal scarring alopecia, dissecting cellulitis of the scalp, and acne keloidalis nuchae is best treated by a long-acting oral tetracycline in combination with a potent topical corticosteroid.

Lichen planopilaris and chronic cutaneous lupus lesions may be treated with oral antimalarials, corticosteroids, retinoids, or immunosuppressants.

Hair loss due to chemotherapy is temporary and is best treated with a wig; when hair regrows, it may be different in color and texture from the original hair. Hair loss due to telogen effluvium or anagen effluvium is usually temporary as well and abates after the precipitating agent is eliminated.

Key Points

• Androgenetic alopecia (male-pattern and female-pattern hair loss) is the most common type of hair loss.

• Concomitant virilization in women or scarring hair loss should prompt a thorough evaluation for the underlying disorder.

• Microscopic hair examination or scalp biopsy may be required for definitive diagnosis.

Alopecia Areata

Alopecia areata is sudden patchy hair loss in people with no obvious skin or systemic disorder.

The scalp and beard are most frequently affected, but any hairy area may be involved. Hair loss may affect most or all of the body (alopecia universalis). Alopecia areata is thought to be an autoimmune disorder affecting genetically susceptible people exposed to unclear environmental triggers, such as

infection or emotional stress. It occasionally coexists with autoimmune vitiligo or thyroiditis.

Diagnosis

• Examination

Diagnosis is by inspection. Alopecia areata typically manifests as discrete circular patches of hair loss characterized by short broken hairs at the margins, which resemble exclamation points. Nails are sometimes pitted or display trachyonychia, a roughness of the nail also seen in lichen planus. Differential diagnosis includes tinea capitis, trichotillomania, discoid lupus, and secondary syphilis. Measures of thyroid-stimulating hormone, vitamin B_{12}, and autoantibodies are indicated only when coexisting disease is suspected.

Treatment

• Corticosteroids

• Sometimes topical anthralin, minoxidil or both

Treatment is with corticosteroids. Triamcinolone acetonide suspension (in doses not to exceed 0.1 mL per injection site, eg, 10 mg/mL concentration to deliver 1 mg) can be injected intradermally if the lesions are small. Potent topical corticosteroids (such as betamethasone 0.05% bid) can be used; however, they often do not penetrate to the depth of the hair bulb where the inflammatory process is located. Oral corticosteroids are effective, but hair loss recurs after cessation of therapy and adverse effects limit use. Topical anthralin (0.5 to 1% for 10 to 20 min daily, then washed off, frequency titrated as tolerated up to 30 min bid) and/or minoxidil may be used. Induction of allergic contact dermatitis using diphencyprone or squaric acid dibutylester leads to hair growth due to unknown mechanisms, but this treatment is best reserved for patients with diffuse involvement who have not responded to other therapies.

Alopecia areata may spontaneously regress, become chronic, or spread diffusely. Risk factors for chronicity include extensive involvement, onset before adolescence, atopy, and involvement of the peripheral scalp (ophiasis).

Hirsutism

Hirsutism is the excessive growth of thick or dark hair in women in locations that are more typical of male hair patterns (eg, mustache, beard, central chest, shoulders, lower abdomen, back, inner thigh). The amount of hair growth that is considered excessive may differ depending on ethnic background and cultural interpretation. Men vary significantly in amount of body hair, some being quite hairy, but rarely present for medical evaluation.

Hypertrichosis is a separate condition. It is simply an increase in the amount of hair growth anywhere on the body. Hypertrichosis may be generalized or localized.

Pathophysiology

Hair growth depends on the balance between androgens (eg, testosterone, dehydroepiandrosterone sulfate [DHEAS], dihydrotestosterone [DHT]) and estrogens. Androgens promote thick, dark hair growth, whereas estrogens slow hair growth or modulate it toward finer, lighter hairs.

When caused by increased androgen activity, hirsutism is often accompanied by virilization, which may manifest as loss of menses, increased muscle mass, voice deepening, and clitoral hypertrophy.

Etiology

There are a number of causes of hirsutism (see Table 86-3). Overall, the most common causes are the following:

• Polycystic ovary syndrome

• Familial hirsutism

Androgen excess: Hirsutism typically results from abnormally high androgen activity as a result of increased central production of androgens (eg, from ovarian or adrenal disorders) or increased peripheral conversion of testosterone to DHT by 5α-reductase. Free androgen levels also can increase as a result of decreased production of sex hormone-binding globulin, which can occur in a variety of conditions, including hyperinsulinemia and liver disease. However, the severity of hirsutism does not correlate with the level of circulating

[**Table 86-3.** Some Causes of Hirsutism]

androgens because of individual differences in androgen sensitivity of the hair follicle.

No androgen excess: Hirsutism not associated with androgen excess may be physiologic (eg, postmenopausal, during pregnancy), the result of systemic nonandrogenic endocrine conditions, or a familial phenomenon, especially in people of Mediterranean or Middle Eastern ancestry.

Hypertrichosis involves nonandrogenic hair growth and is usually caused by a drug, systemic illness (see Table 86-4), or paraneoplastic syndrome. It also occurs as part of a rare familial disorder.

Evaluation

History: History of present illness should cover the extent and acuity of hair growth as well as the age of onset.

Review of systems should seek signs of virilization (eg, deepening of the voice, increased libido) and review menstrual and fertility history. Symptoms of causative disorders should be sought, including cold intolerance, fatigue, and weight gain (hypothyroidism); polyuria (diabetes); bingeing and purging (eating disorders); and weight loss and fevers (cancer).

Past medical history should specifically seek known causative disorders such as endocrine disorders, adrenal or ovarian pathology, and cancer.

Family history should inquire about excess hair growth in family members. Drug history should review all prescribed drugs and specifically query for the surreptitious use of anabolic steroids.

Physical examination: The presence of excess coarse and dark hair growth should be assessed at multiple sites, including the face, chest, lower abdomen, back, buttocks, and inner thigh. Signs of virilization should be sought, including clitoromegaly, acne, male-pattern hair loss, breast atrophy, and increased muscle mass.

General physical examination should note signs of potentially causative disorders.

The eyes should be examined for extraocular movements, and the visual fields should be assessed.

The breasts should be examined for galactorrhea.

The abdomen (including pelvic examination) should be examined for masses.

The skin should be examined for velvety, black pigmentation on the axillae and neck and under the breasts (acanthosis nigricans); acne; and striae.

The general habitus should be examined for fat distribution (particularly a round face and accumulation of fat at the base of the neck posteriorly).

[**Table 86-4.** Causes of Hypertrichosis]

Red flags: The following findings are of particular concern:

• Virilization

• Abrupt appearance of hirsutism

• Pelvic or abdominal mass

Interpretation of findings: Excess hair growth beginning after use of an anabolic steroid or other causative drug (see Tables 86-3 and 86-4) in an otherwise healthy female is likely due to that drug. Symptoms and signs sometimes point to a diagnosis (see Table 86-5).

Testing: Diagnostic testing in men with no other signs of illness is unnecessary.

Women should have laboratory measurement of serum hormone levels, including the following:

• Free and total testosterone

• DHEAS

• Follicle-stimulating hormone (FSH) and luteinizing hormone (LH)

• Androstenedione

• Thyroid-stimulating hormone

• Prolactin

High levels of testosterone accompanied by a normal level of DHEAS indicate that the ovaries, and not the adrenal glands, are producing the excess androgen. High levels of testosterone accompanied by moderate elevations in DHEAS suggest an adrenal origin for the hirsutism.

Often, in women with polycystic ovary syndrome, LH levels are elevated and FSH levels are depressed, which results in elevated LH/FSH ratios (> 3 is common).

Imaging: Pelvic ultrasonography, CT, or both should be done to rule out pelvic or adrenal cancer, particularly when a pelvic mass is appreciated, when the total testosterone level is > 200 ng/dL (> 100 ng/dL in postmenopausal women), or when the DHEAS level is > 7000 ng/dL (> 4000 ng/dL in postmenopausal women). However, the majority of patients with elevated DHEAS have adrenal hyperplasia rather than adrenal carcinoma.

Patients with signs of Cushing's syndrome or an adrenal mass on imaging studies should have 24-h urine cortisol levels measured.

Treatment

The underlying disorder should be treated, including stopping or changing causative drugs. Treatment for hirsutism itself is unnecessary if the patient does not find the excess hair cosmetically objectionable.

Nonandrogen-dependent excess hair growth, such as hypertrichosis, is treated primarily with physical hair removal methods. Patients with androgen-dependent hirsutism require a combination of hair removal and medical antiandrogen therapy.

Hair removal: There are several techniques. Depilatory techniques remove hair from the surface of the skin and include shaving and OTC depilatory creams, such as those containing barium sulfate and Ca thioglycolate.

Epilation involves removing intact hairs and the roots and can be achieved via mechanical means (eg, tweezing, plucking, waxing) or home epilating devices. Permanent epilation techniques, including electrolysis, thermolysis, and laser epilation, can result in more long-term hair removal but often require multiple treatments.

As an alternative to hair removal, hair bleaching is inexpensive and works well when hirsutism is not excessive. Bleaches lighten the color of the hair, rendering it less noticeable. There are several types of commercial

[Table 86-5. Some Symptoms and Signs for Diagnosis of Hirsutism]

hair-bleaching products, most of which use hydrogen peroxide as the active ingredient.

Topical eflornithine, applied twice daily, decreases hair growth and, with long-term use, may decrease the need to manually remove hair.

Hormonal treatment: Hirsutism resulting from androgen excess usually requires long-term therapy because the source of excess androgen rarely can be eliminated permanently. Hormonal treatments include

• Oral contraceptives

• Antiandrogenic drugs

• Sometimes other drugs

Oral contraceptives in standard doses often are the initial treatment for hirsutism caused by ovarian hyperandrogenism. Oral contraceptives reduce ovarian androgen secretion and increase sex hormone-binding globulin, thereby decreasing free testosterone levels.

Antiandrogenic therapy is also used and can include finasteride (5 mg po once/day), spironolactone (25 to 100 mg po bid), or flutamide (125 mg po once/day or bid). These drugs are contraindicated during pregnancy as they may cause feminization of a male fetus.

Insulin sensitizers such as metformin decrease insulin resistance, causing a decline in testosterone levels. However, they are less effective than other antiandrogenic drugs. Corticosteroids are used for adrenal suppression. Gonadotropin-releasing hormone agonists (eg, leuprolide acetate, nafarelin, triptorelin) can be used for severe forms of ovarian hyperandrogenism under the direction of a gynecologist or endocrinologist.

Key Points

• Hirsutism may be familial, and the degree of hair growth may vary with ethnicity.

• Polycystic ovary syndrome is the most frequent cause of hirsutism.

• Virilization suggests an androgenic disorder that requires further evaluation.

• Abrupt onset of hirsutism may indicate cancer.

Pseudofolliculitis Barbae

Pseudofolliculitis barbae (PFB) is irritation of the skin due to beard hairs that penetrate the skin before leaving the hair follicle or that leave the follicle and curve back into the skin, causing a foreign-body reaction.

PFB predominantly affects black men. It is most noticeable around the beard and neck. It causes small

papules and pustules that can be confused with bacterial folliculitis.

Diagnosis is by physical examination.

Treatment

Acute PFB can be treated with warm compresses and manual removal of ingrown hairs with a needle or tweezers. Topical hydrocortisone 1% or topical antibiotics can be used for mild inflammation. Oral tetracycline (250 to 500 mg qid) or oral erythromycin (250 to 500 mg qid, 333 mg tid, 500 mg bid) can be used for moderate to severe inflammation. Tretinoin (retinoic acid) liquid or cream or benzoyl peroxide cream may also be effective in mild or moderate cases but may irritate the skin. Topical eflornithine hydrochloride cream may help by slowing hair growth. Hairs should be allowed to grow out; grown hairs can then be cut to about 0.5 cm length. Depilatories are an alternative but may irritate the skin. Hair follicles can be permanently removed by electrolysis or laser treatment.

Chapter 87. Nail Disorders

Introduction

A variety of disorders can affect nails, including deformities, infections of the nail, paronychia, and ingrown toenails. Nail changes may occur in many systemic conditions and genetic syndromes.

Nails may also undergo changes due to local infection or trauma. For example, trauma to the finger may cause changes in the nail. The nail may develop a white coloration that starts at the nail bed and grows up with the nail. Sometimes, if a nail becomes separated from the nail bed, a new nail grows below the existing nail and replaces it when fully grown in.

Most nail infections are fungal (onychomycosis—see p. 734), but bacterial and viral infections can occur (eg, green-nail syndrome [*Pseudomonas*], herpetic whitlow [herpes simplex virus-1]). Paronychia is not actually an infection of the nail but rather of periungual tissues.

Common warts (verrucae vulgaris) result from papillomavirus infection and frequently infect the proximal nail fold and sometimes the subungual area. Onychophagia (nail-biting) can help to spread this infection. Warts involving these areas are especially difficult to treat. Freezing with liquid nitrogen may be effective.

Toenails require special attention in the elderly and in people with diabetes or peripheral vascular disease; a podiatrist can help avoid local breakdown and secondary infections.

Deformities

About 50% of nail deformities result from fungal infection. The remainder result from various causes, including trauma, psoriasis, lichen planus, and occasionally cancer. Diagnosis may be obvious on examination, but sometimes fungal scrapings and culture may be done. Deformities may resolve with treatment of the cause, but if not, manicurists may be able to hide nail deformities with appropriate trimming and polishes. Dystrophies are often considered together with deformities, but the two are slightly different; deformities are generally considered to be gross changes in nail shape, whereas dystrophies are changes in nail texture or composition (eg, onychomycosis).

Congenital deformities: In some congenital ectodermal dysplasias, patients have no nails (anonychia). In pachyonychia congenita, the nail beds are thickened, discolored, and hypercurved with a pincer nail deformity. Nail-patella syndrome (see p. 2910) causes triangular lunulae and partially absent thumb nails. Patients with Darier's disease can have nails with red and white streaks and a distal V-shaped nick.

Deformities associated with systemic problems: In Plummer-Vinson syndrome, 50% of patients have koilonychia (concave, spoon-shaped nails). Yellow nail syndrome (characterized by hard, hypercurved, transversely thickened, yellow nails with loss of the cuticle) occurs in patients with lymphedema of limbs, pleural effusion, and ascites. Half-and-half nails occur with renal failure; the proximal half of the nail is white, and the distal half is pink or pigmented. White nails occur with cirrhosis, although the distal third may remain pinker.

Deformities associated with dermatologic conditions: In psoriasis, nails may have a number of changes, including irregular pits, oil spots (localized areas of tan-brown discoloration), onycholysis, and thickening and crumbling of the nail plate. Lichen planus of the nail matrix causes scarring with early longitudinal ridging and splitting of the nail and later leads to pterygium formation. Pterygium of the nail is characterized by scarring from the proximal nail outward in a V formation, which leads ultimately to loss of the nail. Alopecia areata can be accompanied by regular pits that form a pattern.

Discoloration: Cancer chemotherapy drugs (especially the taxanes) can cause melanonychia (nail plate pigmentation), which can be diffuse or may occur in transverse bands. Some drugs cause characteristic changes in nail coloration. For example, quinacrine can cause nails to appear greenish yellow or white under ultraviolet light. Cyclophosphamide can cause the onychodermal bands (seal formed at the junction of the nail plate and distal nail bed at the free edge of the nail plate) to become slate-gray or bluish. With arsenic intoxication, the nails may turn diffusely brown. Tetracyclines, ketoconazole, phenothiazines,

sulfonamides, and phenindione can all cause brownish or blue discoloration. Gold therapy can turn nails light or dark brown. Tobacco use can result in yellow or brownish discoloration. In argyria, the nails may be diffusely blue-gray.

White transverse lines of the nails (Mees' lines) may occur with chemotherapy, acute arsenic intoxication, malignant tumors, MI, thallium and antimony intoxication, fluorosis, and even during etretinate therapy. They also develop with trauma to the finger, although traumatic white lines usually do not span the entire nail. The fungus *Trichophyton mentagrophytes* causes a chalky white discoloration of the nail plate.

Green-nail syndrome is caused by infection with *Pseudomonas*. It is generally a harmless infection, usually of 1 or 2 nails, and is noteworthy for its striking blue-green color. It often occurs in patients with onycholysis or chronic paronychia whose nails have been immersed in fresh water for a long period. Treatment is most effective with soaks of 1% acetic acid solution or alcohol diluted 1:4 with water. Patients should soak their affected nails twice a day for 10 min and should avoid trauma and excess moisture. Frequent clipping of the nail increases the response to treatment.

Melanonychia striata: Melanonychia striata are hyperpigmented bands that are longitudinal and extend from the proximal nail fold and cuticle to the free distal end of the nail plate. In dark-skinned people, these bands may be a normal physiologic variant requiring no treatment. Other causes include trauma; pregnancy; Addison's disease; post-inflammatory hyperpigmentation; and the use of certain drugs, including doxorubicin, 5-fluorouracil, zidovudine (AZT), and psoralens. Melanonychia striata can also occur in benign melanocytic nevi and malignant melanoma. Hutchinson's sign of the nail (melanin extending through the lunula, cuticle, and proximal nail fold) may signal a melanoma in the nail matrix. Rapid biopsy and treatment are essential.

Onychogryphosis: Onychogryphosis is a nail dystrophy in which the nail, most often on the big toe, becomes thickened and curved. It may be caused by ill-fitting shoes. It is common among the elderly. Treatment consists of trimming the deformed nails.

Onycholysis: Onycholysis is separation of the nail plate from the nail bed or complete nail plate loss. It can occur as a drug reaction in patients treated with tetracyclines (photo-onycholysis), doxorubicin, 5-fluorouracil, cardiovascular drugs (particularly practolol and captopril), cloxacillin and cephaloridine (rarely), trimethoprim/sulfamethoxazole, diflunisal, etretinate, indomethacin, isoniazid, and isotretinoin. Partial onycholysis may also result from infection with *Candida albicans* as a component of onychomycosis or from trauma. Partial onycholysis may occur in patients with psoriasis or thyrotoxicosis.

Onychotillomania: In this disorder, patients pick at and self-mutilate their nails, which can lead to parallel transverse grooves and ridges (washboard deformity or habit-tic nails). It most commonly manifests in patients who habitually push back the cuticle on one finger, causing dystrophy of the nail plate as it grows. Subungual hemorrhages can also develop in onychotillomania.

Pincer nail deformity: Pincer nail deformity is a transverse over-curvature of the nail plate. It can occur in patients with psoriasis, SLE, Kawasaki disease, cancer, end-stage renal disease, and some genetic syndromes. Patients often have pain at the borders of the nail where the nail plate curves into the tips of the fingers.

Subungual hematoma and nail bed trauma: Subungual hematoma occurs when blood becomes trapped between the nail plate and nail bed, usually as a result of trauma. Subungual hematoma causes significant pain and eventual separation of and temporary loss of the nail plate. When the cause is a crush injury, underlying fracture and nail bed damage are common. Nail bed damage may result in permanent nail deformity.

If the injury is acute, nail trephination (eg, creating a hole in the nail plate using a cautery device, 18-gauge needle, or red-hot paperclip) can help relieve pain by draining accumulated blood. It is not clear whether removing the nail and repairing any nail bed damage reduces risk of permanent nail deformity.

Trachyonychia: Trachyonychia (rough, opaque nails) may occur with alopecia areata, lichen planus, atopic dermatitis, and psoriasis. It is most common among children.

Tumors: Benign and malignant tumors can affect the nail unit, causing deformity. These tumors include benign myxoid cysts, pyogenic granulomas, glomus tumors, Bowen's disease, squamous cell carcinoma, and malignant melanoma. When cancer is suspected, expeditious biopsy followed by referral to a surgeon is strongly advised.

Onychomycosis

Onychomycosis is fungal infection of the nail plate, nail bed, or both. The nails typically are deformed and discolored white or yellow. Diagnosis is by appearance, wet mount, culture, PCR, or a combination. Treatment, when indicated, is with selective use of oral terbinafine or itraconazole.

About 10% (range 2 to 14%) of the population has onychomycosis. Risk factors include

- Tinea pedis
- Preexisting nail dystrophy (eg, in patients with psoriasis)
- Older age
- Male sex
- Exposure to someone with tinea pedis or onychomycosis (eg, a family member or through public bathing)
- Peripheral vascular disease or diabetes
- Immunocompromise

Toenails are 10 times more commonly infected than fingernails. About 60 to 80% of cases are caused by dermatophytes (eg, *Trichophyton rubrum*); dermatophyte infection of the nails is called tinea unguium. Many of the remaining cases are caused by nondermatophyte molds (eg, *Aspergillus*, *Scopulariopsis*, *Fusarium*). Immunocompromised patients and those with chronic mucocutaneous candidiasis may have candidal onychomycosis (which is more common on the fingers). Subclinical onychomycosis can also occur in patients with recurrent tinea pedis. Onychomycosis may predispose patients to lower extremity cellulitis.

Symptoms and Signs

Nails have asymptomatic patches of white or yellow discoloration and deformity. There are 3 characteristic manifestations:

- Distal subungual, in which the nails thicken and yellow, keratin and debris accumulate distally and underneath, and the nail separates from the nail bed (onycholysis)
- Proximal subungual, a form that starts proximally and is a marker of immunosuppression
- White superficial, in which a chalky white scale slowly spreads beneath the nail surface

Diagnosis

- Clinical evaluation
- Potassium hydroxide wet mount examination
- Culture

Onychomycosis is suspected by appearance; predictive clinical features include involvement of the 3rd or 5th toenail, involvement of the 1st and 5th toenails on the same foot, and unilateral nail deformity. Subclinical onychomycosis should be considered in patients with recurrent tinea pedis. Differentiation from psoriasis or lichen planus is important, because the therapies differ, so diagnosis is typically confirmed by microscopic examination and culture of scrapings. Scrapings are taken from the most proximal position that can be accessed on the affected nail and are examined for hyphae on potassium hydroxide wet mount and cultured. Obtaining an adequate sample of nail can be difficult because the distal subungual debris, which is easy to sample, often does not contain living fungus. Therefore, removing the distal portion of the nail with clippers before sampling or using a small curette to reach more proximally beneath the nail increases the yield. PCR can also be done on nail clippings if cultures are negative and the cost of finding a definitive diagnosis is warranted.

Treatment

• Sometimes oral terbinafine or itraconazole

Onychomycosis is not always treated because many cases are asymptomatic or mild and unlikely to cause complications, and the oral drugs that are the most effective treatments can potentially cause hepatotoxicity and serious drug interactions. Some proposed indications for treatment include the following:

• Previous ipsilateral cellulitis

• Diabetes or other risk factors for cellulitis

• Presence of bothersome symptoms

• Psychosocial impact

• Desire for cosmetic improvement (controversial)

Treatment is oral terbinafine or itraconazole. Terbinafine 250 mg once/day for 12 wk (6 wk for fingernail) or itraconazole 200 mg bid 1 wk/mo for 3 mo is used and achieves a cure rate of 60 to 75%, but the recurrence rate is estimated to be as high as 10 to 50%. It is not necessary to treat until all abnormal nail is gone because these drugs remain bound to the nail plate and continue to be effective after oral administration has ceased. The affected nail will not revert to normal; however, newly growing nail will appear normal. Topical antifungal nail lacquer containing ciclopirox 8% or amorolfine 5% (not available in the US) is rarely effective as primary treatment but can improve cure rate when used as an adjunct with oral drugs, particularly in resistant infections.

To limit relapse, the patient should trim nails short, dry feet after bathing, wear absorbent socks, and use antifungal foot powder. Old shoes may harbor a high density of spores and, if possible, should not be worn.

Paronychia

Paronychia is infection of the periungual tissues. Acute paronychia causes redness, warmth, and pain along the nail margin. Diagnosis is by inspection. Treatment is with antistaphylococcal antibiotics and drainage of any pus.

Paronychia is usually acute, but chronic cases occur. In acute paronychia, the causative organisms are usually *Staphylococcus aureus* or streptococci and, less commonly, *Pseudomonas* or *Proteus* spp. Organisms enter through a break in the epidermis resulting from a hangnail, trauma to a nail fold, loss of the cuticle, or chronic irritation (eg, resulting from water and detergents). Biting or sucking the fingers can also predispose people to developing the infection. In toes, infection often begins at an ingrown toenail (see p. 736).

In patients with diabetes and those with peripheral vascular disease, toe paronychia can threaten the

limb.

Symptoms and Signs

Paronychia develops along the nail margin (lateral and proximal nail folds), manifesting over hours to days with pain, warmth, redness, and swelling. Pus usually develops along the nail margin and sometimes beneath the nail. Infection can spread to the fingertip pulp, causing a felon. Rarely, infection penetrates deep into the finger, sometimes causing infectious flexor tenosynovitis.

Diagnosis

Diagnosis is by inspection. Several skin conditions can cause changes that mimic paronychia and should be considered, particularly when treatment is not effective initially. These conditions include squamous cell carcinoma, proximal onychomycosis, pyogenic granuloma, pyoderma gangrenosum, and herpetic whitlow.

Treatment

• Antistaphylococcal antibiotics

• Drainage of pus

Early treatment is warm compresses or soaks and an antistaphylococcal antibiotic (eg, dicloxacillin or cephalexin 250 mg po qid, clindamycin 300 mg po qid). In areas where methicillin-resistant *S. aureus* is common, antibiotics that are effective against this organism (eg, trimethoprim/sulfamethoxazole) should be chosen based on results of local sensitivity testing. In patients with diabetes and others with peripheral vascular disease, toe paronychia should be monitored for signs of cellulitis or more severe infection (eg, extension of edema or erythema, lymphadenopathy, fever).

Fluctuant swelling or visible pus should be drained with a Freer elevator, small hemostat, or #11 scalpel blade inserted between the nail and nail fold. Skin incision is unnecessary. A thin gauze wick should be inserted for 24 to 48 h to allow drainage.

Chronic Paronychia

Chronic paronychia is recurrent or persistent nail fold inflammation, typically of the fingers.

Chronic paronychia occurs almost always in people whose hands are chronically wet (eg, dishwashers, bartenders, housekeepers), particularly if they are diabetic or immunocompromised. *Candida* is often present, but its role in etiology is unclear; fungal eradication does not always resolve the condition. The condition may be an irritant dermatitis with secondary fungal colonization.

The nail fold is painful and red as in acute paronychia, but there is almost never pus accumulation. Eventually, there is loss of the cuticle and separation of the nail fold from the nail plate. This forms a space that allows entry of irritants and microorganisms. The nail becomes distorted.

Diagnosis is clinical.

Treatment

• Keeping hands dry

• Topical corticosteroid or tacrolimus

Primary treatment is to keep the hands dry and to assist the cuticle in reforming to close the space between the nail fold and nail plate. Gloves or barrier creams are used if water contact is necessary. Topical drugs that may help include corticosteroids and, for their corticosteroid-sparing effects, immunosuppressants (eg, tacrolimus). Antifungal treatments are helpful only in reducing colonizing fungal

organisms. Thymol 3% in ethanol applied several times a day to the space left by loss of cuticle aids in keeping this space dry and free of microorganisms. If there is no response to therapy, squamous cell carcinoma should be considered and a biopsy should be done.

Ingrown Toenail

(Onychocryptosis)

An ingrown toenail is incurvation or impingement of a nail border into its adjacent nail fold, causing pain.

Causes include tight shoes, abnormal gait (eg, toe-walking), bulbous toe shape, excessive trimming of the nail plate, or congenital variations in nail contour (congenital pincer nail deformity). Sometimes an underlying osteochondroma is responsible, especially in the young. In the elderly, peripheral edema is a risk factor. Eventually, infection can occur along the nail margin (paronychia—see p. 735).

Symptoms and Signs

Pain occurs at the corner of the nail fold or, less commonly, along its entire lateral margin. Initially only mild discomfort may be present, especially when wearing certain shoes. In chronic cases, granulation tissue becomes visible, more often in the young.

Diagnosis

• Clinical evaluation

Redness, swelling, and pain suggest paronychia. In young patients (eg, < 20 yr) with ingrown toenails, x-rays should be considered to exclude underlying osteochondroma. In the elderly, apparent granulation tissue around the toe suggests the possibility of amelanotic melanoma, which is often overlooked; biopsy is necessary.

Treatment

• Usually nail excision and destruction of adjacent nail matrix

In mild cases, inserting cotton between the ingrown nail plate and painful fold (using a thin toothpick) may provide immediate relief and, if continued, correct the problem. If the shoes are too tight, a larger toe box is indicated. In most cases, however, particularly with paronychia, excision of the ingrown toenail after injecting a local anesthetic is the only effective treatment. If ingrown toenails recur, permanent destruction of the nearby lateral nail matrix by applying phenol or trichloroacetic acetic acid or by surgical excision is indicated. Phenol should not be used if there is arterial insufficiency.

Chapter 88. Pressure Ulcers

Introduction

(Pressure Sores; Bedsores; Decubitus Ulcers; Decubiti)

Pressure ulcers (PUs) are areas of necrosis and ulceration where tissues are compressed between bony prominences and hard surfaces; they result from pressure alone or pressure in combination with friction, shearing forces, or both. Risk factors include old age, impaired circulation, immobilization, undernutrition, and incontinence. Severity ranges from nonblanchable skin erythema to full-thickness skin loss with extensive soft-tissue necrosis. Diagnosis is clinical. Prognosis is excellent for early-stage ulcers; neglected and late-stage ulcers pose risk of serious infection and nutritional stress and are difficult to heal. Treatment includes pressure reduction, avoidance of friction and shearing forces, local care, and sometimes skin grafts or myocutaneous flaps.

Etiology

An estimated 1.3 to 3 million patients in the US have PUs; incidence is highest in older patients, especially those who are hospitalized or in long-term care facilities. Aging increases risk, in part because of reduced subcutaneous fat and decreased capillary blood flow. Immobility and comorbidities increase risk further.

Patients who are cognitively impaired, immobile, or both are at increased risk. Immobility—because of decreased spontaneous movement (eg, due to stroke, sedation, or severe illness) or inability to change position frequently because of weakness—is the most important factor. Other risk factors include urinary and fecal incontinence; poor nutritional status, including dehydration; diabetes; and cardiovascular disease. Clinical assessment is sufficient to identify patients at risk; several scales (eg, Norton, Braden —see
Fig. 88-1) are useful for predicting risk. The National Pressure Ulcer Advisory Panel has also issued guidelines for the prediction and prevention of PUs.

Pathophysiology

PUs develop when soft tissues are compressed between bony prominences and contact surfaces

[**Fig. 88-1.** Braden scale for predicting risk for pressure ulcers.]

[
Table 88-1. Pressure Ulcer Staging]

or when friction (eg, rubbing against clothing or bedding) or shearing forces (which develop when skin clings to surfaces) cause erosion, tissue ischemia, and infarction. PUs most frequently develop over the sacrum, ischial tuberosities, trochanters, malleoli, and heels, but they can develop elsewhere, including behind the ears when nasal cannulae are used for prolonged periods. Also, poorly fitting prosthetic devices can cause PUs to develop over bony prominences. Increased force and duration of pressure directly influence risk and severity, but PUs can develop in as little as 3 to 4 h in some settings (eg, trauma patients who are immobilized on rigid spine-immobilization boards). Ulcers worsen when skin is overly moist and macerated (eg, from perspiration or incontinence).

Other causes of skin ulcers: Chronic arterial and venous insufficiency can result in skin ulcers, particularly on the lower extremities. Although the underlying mechanism is vascular, the same forces that cause PUs can worsen these ulcers, and principles of treatment are similar.

Symptoms and Signs

Several staging systems exist; the most common classifies ulcers according to the depth of soft-tissue damage (see Table 88-1). PUs do not always present as Stage I and then progress to higher stages.

Sometimes the first sign of a PU is a deep, necrotic stage III or IV ulcer. In a rapidly developing PU, subcutaneous tissue can become necrotic before the epidermis erodes. A small ulcer might, like an iceberg, be quite large under the surface.

Stage I PUs manifest as nonblanchable erythema, usually over a bony prominence. Color changes may not be as visible in darkly pigmented skin. The lesion may also be warmer, cooler, firmer, softer, or more tender than adjacent or contralateral tissue. This stage is a misnomer in the sense that an actual ulcer (a defect of skin into the dermis) is not yet present. However, ulceration will occur if the course is not arrested and reversed.

Stage II PUs involve loss of epidermis with or without erosion (defect of epidermis) or true ulceration (partial-thickness loss of dermis); subcutaneous tissue is not exposed. The ulcers are shallow with a reddish base. Intact or partially ruptured blisters due to pressure are also stage II PUs. (NOTE: Non-pressure-related causes of erosion, ulceration, or blistering—eg, skin tears, tape burns, perineal dermatitis, maceration, excoriation—are excluded from stage II description.)

Stages III and IV PUs have deeper involvement of underlying tissue with more extensive destruction.

Ulcers covered with debris or eschar are by definition unstageable. However, stable, nonfluctuant heel lesions with dry eschar should not be debrided for the sake of staging. Bruising of an apparent stage II ulcer should raise the suspicion of a deeper-stage PU. PUs at any stage may be painful or pruritic but may not be noticed by patients with blunted awareness or sensation. Tenderness, erythema of surrounding skin, exudate, or foul odor suggests infection. Fever should raise suspicion of bacteremia or underlying osteomyelitis.

Complications

Nonhealing ulcers may be due to inadequate treatment but should raise suspicion of osteomyelitis or, rarely, squamous cell carcinoma within the ulcer (Marjolin's ulcer). Other complications of nonhealing PUs include sinus tracts, which can be superficial or connect the ulcer to deep adjacent structures (eg, to the bowel in sacral ulcers), and tissue calcification. In addition, PUs are a reservoir for hospital-acquired antibiotic-resistant organisms, which can slow healing and cause bacteremia and sepsis.

Diagnosis

• Clinical evaluation with continuous assessment

• Sometimes bone scan or MRI

Diagnosis is usually apparent clinically, but depth and extent can be difficult to determine. PUs are always colonized by bacteria, so wound surface cultures are uninterpretable. Underlying osteomyelitis is diagnosed with radionuclide bone scanning or gadolinium-enhanced MRI, but both techniques have poor sensitivity and specificity. Diagnosis may require bone biopsy and culture.

Continuous assessment is mandatory for effective management. Serial photographs can also document healing.

Prognosis

Prognosis for early-stage PUs is excellent with timely, appropriate treatment, but healing typically requires weeks. PUs often develop in patients with suboptimal care. If care cannot be improved, long-term outcome is poor, even if short-term wound healing is accomplished.

Treatment

• Pressure reduction

• Direct ulcer care

• Management of pain, infection, and undernutrition

• Sometimes adjunctive therapy or surgery

Treatment requires multiple simultaneous elements.

Reducing pressure: Reducing tissue pressure is accomplished through careful positioning of the patient, protective devices, and variation of support surfaces.

Frequent repositioning (and selection of the proper position) is most important. A written schedule should be used to direct and document repositioning. Bedbound patients should be turned a minimum of every 2 h, should be placed at a 30° angle to the mattress when on their side (ie, lateral decubitus) to avoid direct trochanteric pressure, and should be elevated as minimally as possible to avoid the shear forces on tissues that result from sliding down the bed. For repositioning patients, lifting devices (eg, a Stryker frame) or bed linen should be used instead of dragging the patient (which causes friction and shear forces). Patients placed in chairs should be repositioned every hour, and they should be encouraged to change position on their own every 15 min.

Protective padding includes pillows or foam wedges placed between knees, ankles, and heels when patients are on their side and pillows, foam, or heel protectors when patients are supine. Windows should be cut out of plaster casts at pressure sites in patients immobilized by fractures. Soft seat cushions should be provided for patients able to sit in a chair. Donut-shaped devices and sheepskins should be avoided as a treatment for PUs.

Support surfaces under bedbound patients can be changed to reduce pressure. A change from standard mattresses is indicated when patients are unable to reposition themselves and periodic repositioning care is unavailable.

Support surfaces are static or dynamic.

Static surfaces, which do not require electricity, include air, foam, gel, and water overlays and mattresses. Old-fashioned "egg crate" mattresses offer no advantage. In general, static surfaces increase surface support areas and decrease pressure and shear forces; they are indicated for high-risk patients without PUs and for patients with stage I PUs.

Dynamic surfaces require electricity. Alternating-air mattresses have air cells that are alternately inflated and deflated by a pump, thus shifting supportive pressure from site to site. Low-air-loss mattresses are giant air-permeable pillows that are continuously inflated with air; the air flow has a drying effect on tissues. These specialized mattresses are indicated for patients with stage I ulcers who develop hyperemia on static surfaces and for patients with stage III or IV ulcers. Air-fluidized (high-air-loss) mattresses contain silicone-coated beads that liquefy when air is pumped through the bed. Advantages include reduction of moisture on surfaces and cooling. They are indicated for patients with nonhealing stage III and IV ulcers or numerous truncal ulcers (see Table 88-2). Although specialized mattresses are designed to shift

[**Table 88-2.** Options for Support Surfaces]

pressure and reduce forces that lead to PUs, they are best thought of as an adjunct to comprehensive care.

Ulcer care: Appropriate ulcer care involves cleaning, debridement, and dressings.

Cleaning should be done initially and with each dressing change; ordinary soap and water (not hot) is usually best. Cleaning often involves irrigation with saline solution at pressures sufficient to remove bacteria without traumatizing tissue; commercial syringes, squeeze bottles, or electrically pressurized systems can be used. Alternatively, a 35-mL syringe and an 18-gauge IV catheter can be used. Irrigation should continue until no further debris can be loosened. Antiseptics (eg, iodine, hydrogen peroxide) and

antiseptic washes interfere with tissue healing and should be avoided. Rubbing of skin should be minimized, and moisturizer should be applied gently after each cleansing.

Debridement is necessary to remove dead tissue. Methods include

- Autolytic debridement: Synthetic occlusive dressings are used to facilitate digestion of dead tissues by enzymes normally present in wound fluids. Autolytic debridement may be used for small wounds with simple accumulation of tissue proteins and wounds that need to be sealed off anyway (eg, for protection from feces or urine). DuoDERM or Contreet (which is impregnated with silver and thus offers antimicrobial effects) are commonly applied. Infected wounds, however, should not be occluded.

- Mechanical debridement: Hydrotherapy (whirlpool baths), ultrasound, medical maggots, wound irrigation, or dextranomers (small carbohydrate-based beads that help absorb exudate and liquid debris) should be used to remove thick exudate or loose necrotic tissue. A scalpel or scissors can be used to remove eschar (except in heel ulcers, in which dry eschar in the absence of edema, erythema, fluctuance, or drainage can be safely left alone) or extensive areas of dead tissue. Modest amounts of eschar or tissue can be debrided at the patient's bedside, but extensive or deep areas should be debrided in the operating room. Urgent debridement is indicated in advancing cellulitis or sepsis. Debridement with wet-to-dry dressings should be done only for wounds with very loose exudate and only with great care because it is often painful and it may remove healthy tissue or overdry the wound.

- Enzymatic debridement (using collagenase, papain, fibrinolysin, or streptokinase/streptodornase): This method can be used for patients whose caretakers are not trained to do mechanical debridement or for patients unable to tolerate surgery. It is most effective after careful and judicious cross-hatching of the wound with a scalpel to improve penetration. Collagenase is especially effective as collagen comprises 75% of the dry weight of skin.

Dressings should be used for stage I ulcers that are subject to friction or incontinence and for all other ulcers (see
Table 88-3). Objectives are to keep the ulcer bed moist to retain tissue growth factors while allowing some evaporation and inflow of O_2, to keep surrounding skin

[**Table 88-3.** Options for Pressure Ulcer Dressings]

dry, to facilitate autolytic debridement, and to establish a barrier to infection. Transparent films (eg, OpSite, Tegaderm, Bioclusive) are sufficient for ulcers with limited exudate; they should not be used over cavities and must be changed every 3 to 7 days. Some experts recommend a small amount of triple antibiotic ointment under the dressing. Hydrogels (Clear-Site, Vigilon, FlexiGel), which are cross-linked polymer dressings that come in sheets or gels, are indicated for very shallow wounds, such as re-epithelializing wounds with minimal exudate.

Hydrocolloids (eg, RepliCare, DuoDERM, Restore, Tegasorb), which combine gelatin, pectin, and carboxymethylcellulose in the form of wafers, powders, and pastes, are indicated for light-to-moderate exudate; some have adhesive backings and others are typically covered with transparent films to ensure adherence to the ulcer and must be changed every 3 days. Alginates (polysaccharide seaweed derivatives containing alginic acid), which come as pads, ropes, and ribbons (AlgiSite, Sorbsan, Curasorb), are indicated for absorbing extensive exudate and for controlling bleeding after surgical debridement. Foam dressings (Allevyn, LYOfoam, Hydrasorb, Mepilex, Curafoam, Contreet) are useful as they can handle various levels of exudate and provide a moist environment for wound healing. Waterproof versions protect the skin from incontinence. Dressings with adhesive backings stay in place longer and need less frequent changing.

Pain management: Primary treatment of pain is treatment of the PU itself, but NSAIDs or acetaminophen is used for mild-to-moderate pain. Opioids should be avoided if possible because sedation promotes immobility. Opioids may be necessary during dressing changes and debridement. In cognitively impaired patients, changes in vital signs can be used as an indication of pain.

Infection management: PUs should be continually reassessed for bacterial infection using clinical signs

of erythema, warmth, increased drainage, fever, and elevated WBC count. Options for topical treatment include silver sulfadiazine, triple antibiotic, and metronidazole (the latter for anaerobic bacteria, which are often foul smelling). Systemic antibiotics should be administered for cellulitis, bacteremia, or osteomyelitis; usage should be guided by tissue culture or clinical suspicion and not by surface culture.

Nutrition: Undernutrition is common among patients with PUs and is a risk factor for nonhealing. Markers of undernutrition include albumin < 3.5 mg/dL or weight < 80% of ideal. Protein intake of 1.25 to 1.5 g/kg/day, sometimes requiring oral or parenteral supplementation (see p. 20), is desirable for optimal healing. Zinc supplementation supports wound healing, and replacement at a dose of 50 mg tid may be useful. Supplemental vitamin C 1 g/day may be provided. Providing a drink of water to patients at each repositioning may be useful to aid hydration.

Adjuncts: Multiple adjunctive treatments have been tried or are under investigation. Negative pressure therapy (for clean wounds) and the use of various topical recombinant growth factors (eg, nerve growth factor, platelet-derived growth factor-BB) and skin equivalents are showing promise in wound management; however, they do not ameliorate mechanical forces and tissue ischemia. Electrical stimulation, heat therapy, massage therapy, and hyperbaric O_2 therapy have not proven effective.

Surgery: Surgical debridement is necessary for any ulcer with devitalized tissue, except for stable, dry, nonfluctuant heel ulcers. Large defects, especially with exposure of musculoskeletal structures, require surgical closure. Skin grafts are useful for large, shallow defects. However, because grafts do not add to blood supply, measures must be taken to prevent pressure from developing to the point of ischemia and further breakdown. Myocutaneous flaps, because of their pressure-sharing bulk and rich vasculature, are the closures of choice over large bony prominences (eg, sacrum, ischia, trochanters).

Ischemic and venous ulcers: Wound care treatments also are useful for ischemic ulcers, but the underlying pathophysiology must be addressed (eg, better control of the inflammatory process in a rheumatoid ulcer or surgical stenting or bypass surgery to improve circulation in atherosclerosis). Pentoxifylline has been tried with minimal success. Some evidence supports the use of dalteparin for diabetic foot ulcers (5000 units sc once/day until healed); however, this finding has not been corroborated. Ischemic ulcers can become infected, often with anaerobic organisms, and the infection may spread, causing septicemia or osteomyelitis.

Venous ulcers are typically sterile at first but tend to lead to cellulitis. The same local care as for PUs can be used. In addition, treatment includes measures to reduce venous hypertension, such as using compression stockings or Unna boot bandages (applied at a pressure of 35 to 40 mm Hg) and elevating the leg above the heart. Pentoxifylline 800 mg po tid for up to 24 wk may be useful.

Prevention

Prevention requires

- Identification of high-risk patients
- Repositioning
- Conscientious skin care and hygiene
- Avoidance of oversedation

The mainstay of prevention is frequent repositioning. Pressure should not continue over any bony surface for > 2 h. Patients who cannot move themselves must be repositioned using pillows. Even when on low-pressure mattresses, patients must be turned. Pressure points should be checked for erythema or trauma at least once/day under adequate lighting. Patients and family members must be taught a routine of daily visual inspection and palpation of sites for potential ulcer formation.

Daily attention to hygiene and dryness is necessary to prevent maceration and secondary infection. Although sheepskin should not be used to redistribute pressure after ulceration has occurred, lying on a

sheepskin as a preventive measure helps keep the skin in good condition. Protective padding, pillows, or a sheepskin can be used to separate body surfaces. Bedding and clothing should be changed frequently; sheets should be soft, clean, and free from wrinkles and particulate matter. In hot weather, the skin should be sponge-bathed and thoroughly dried afterward. In incontinent patients, ulcers should be protected from contamination; synthetic dressings can help. Skin breakdown can be prevented with careful cleansing and drying (patting and not rubbing the skin) and using anticandidal creams and moisture barrier creams or skin protective wipes (eg, Skin-Prep). Use of adhesive tape should be minimized because it can irritate and even tear fragile skin.

Areas subject to friction may be powdered with plain talc. Use of cornstarch is discouraged because it may allow microbial growth.

Oversedation should be avoided, and activity should be encouraged. Adequate nutrition is important.

Chapter 89. Benign Tumors

Introduction

(See also Warts on p. 715 and Genital Warts on p. 1470)

Most skin tumors are benign. However, because skin cancers must be treated early, proper diagnosis of unusual skin growths should always be made definitively and without undue delay.

Dermatofibroma

(Fibrous Histiocytoma)

Dermatofibroma is a firm, red-to-brown, small papule or nodule composed of fibroblastic tissue. It usually occurs on the thighs or legs.

Dermatofibromas are common, more so in women, and typically appear when people are in their 20s. Their cause is unknown. Lesions are usually 0.5 to 1 cm in diameter and feel like a lentil embedded in the skin. Most are asymptomatic, but some itch or ulcerate following minor trauma. Diagnosis is clinical; lesions typically dimple when grasped between the fingers. They may regress spontaneously, but they can be excised if troublesome.

Epidermal Cysts

(Keratinous Cyst; Epidermal Inclusion Cyst; Sebaceous Cyst; Milia; Pilar Cyst [Wen]; Steatocystoma)

Epidermal cysts are slow-growing benign cysts containing material that is keratinous (keratinous or epidermal inclusion cyst, sebaceous cyst, milia), follicular (pilar cyst, or wen), or sebaceous (steatocystoma). They frequently occur on the scalp, ears, face, back, or scrotum.

On palpation, the cystic mass is firm, globular, movable, and nontender; cysts range from about 1 to 5 cm in diameter. This kind of cyst seldom causes discomfort unless it has ruptured internally, causing a rapidly enlarging, painful foreign body reaction and abscess. Keratinous cysts, the most common, often are surmounted with a punctum or pore; their contents are cheesy and often fetid (due to secondary bacterial colonization). Milia are minute superficial keratinous cysts noted on the face.

Treatment

Cysts may be left or removed. A small incision may be made to evacuate the contents, then the cyst wall itself should be removed with a curet or hemostat; otherwise, the lesion will recur. Surgical excision with complete removal of the cyst wall is also effective. Internally ruptured cysts should be incised and drained; a gauze drain is inserted and removed after 2 to 3 days. Antibiotics are not needed unless cellulitis is present. Milia may be evacuated with a #11 blade.

Keloids

Keloids are smooth overgrowths of fibroblastic tissue that arise in an area of injury (eg, lacerations, surgical scars, truncal acne) or, occasionally, spontaneously.

Keloids are more frequent in blacks. They tend to appear on the upper trunk, especially the upper back and mid chest, and on deltoid areas. Unlike hyperplastic scars, keloidal scar tissue always extends beyond the area of original injury.

Keloids are shiny, firm, smooth, usually ovoid but sometimes contracted or webbed, and slightly pink or hyperpigmented (see Plate 37). Diagnosis is clinical.

Treatment

Treatment is often ineffective. Monthly corticosteroid injections (eg, triamcinolone acetonide 5 to 40 mg/mL) into the lesion sometimes flatten the keloid. Surgical or laser excision may debulk lesions, but they usually recur larger than before. Excision is more successful if preceded and followed by a series of intralesional corticosteroid injections. Gel sheeting (applying a soft, semiocclusive dressing made of cross-linked polymethylsiloxane polymer, or silicone) or pressure garments are other adjuncts to prevent recurrence.

Keratoacanthoma

Keratoacanthoma is a round, firm, usually flesh-colored nodule with sharply sloping borders and a characteristic central crater containing keratinous material; it usually resolves spontaneously.

Etiology is unknown. Most consider these lesions to be well-differentiated squamous cell carcinomas with a tendency to involute.

Development is rapid. Usually the lesion reaches its full size, typically 1 to 3 cm but may be > 5 cm, within 1 or 2 mo. Common sites are sun-exposed areas, the face, the forearm, and the dorsum of the hand. Spontaneous involution may start within a few months. However, because this lesion cannot be relied upon to involute, biopsy or excision is recommended. Spontaneous involution may leave substantial scarring; surgery or intralesional injections with methotrexate or 5-fluorouracil usually yield better cosmetic results, and excision allows histologic confirmation of the diagnosis.

Lipomas

Lipomas are soft, movable, subcutaneous nodules of adipocytes (fat cells); overlying skin is normal.

A patient may have one or many lipomas. They occur more often in women than men, rarely grow to be > 7 to 8 cm in diameter, and appear most commonly on the trunk, nape, and forearms. They are rarely symptomatic, but they may be painful, especially in patients with familial variants presenting with multiple lesions.

Diagnosis

• Usually clinical

A lipoma is usually easily movable within the subcutis. Lipomas are generally soft, but some become firmer. Some superficial dimpling may occur, but frank inflammation is not normal.

A rapidly growing lesion should be biopsied, although lipomas rarely become malignant.

Treatment

Treatment is not usually required, but bothersome lipomas may be removed by excision or liposuction.

Moles

(Pigmented, Melanocytic, or Nevus Cell Nevi)

Moles are pigmented macules, papules, or nodules composed of clusters of melanocytes or nevus cells. Their main significance (other than cosmetic) is their potential for being or becoming malignant. Lesions with characteristics of concern (changing or highly irregular borders, color changes, pain, bleeding, ulceration, or itching) are biopsied.

Almost everyone has a few moles, which usually appear in childhood or adolescence. There are different types of moles (see
Table 89-1). During adolescence and pregnancy, more moles often appear, and existing ones may

enlarge or darken. Moles typically become more raised and less pigmented over the decades.

An individual mole is unlikely to become malignant (lifetime risk is about 1 in 3,000 to 10,000), but the single best predictor for risk of development of melanoma is the total number of moles. The presence of > 20 moles indicates a higher than average risk for melanoma; patients should be taught to self-monitor for warning signs and have skin surveillance as part of their primary care.

Diagnosis

• Biopsy

Because moles are extremely common and melanomas are uncommon, prophylactic removal is not justifiable. However, a mole should be biopsied and examined histologically if it has certain characteristics of concern:

• Changing or highly irregular borders

• Color changes

• Pain

• Bleeding

• Ulceration

• Itching

The biopsy specimen must be deep enough for accurate microscopic diagnosis and should contain the entire lesion if possible, especially if the concern for cancer is strong. However, wide primary excision should not be the initial procedure, even for highly abnormal-appearing lesions, because many such lesions are not melanomas. Incisional biopsy does not increase the likelihood of metastasis if the lesion is malignant, and it avoids extensive surgery for a benign lesion.

Treatment

• Sometimes excision

Moles can be removed by shaving or excision for cosmetic purposes, and all moles removed should be examined histologically. If hair growth is a concern for the patient, a hairy mole should be adequately excised rather than removed by shaving. Otherwise, hair regrowth will occur.

Atypical Moles

(Dysplastic Nevi)

Atypical moles (AM) are melanocytic nevi with irregular and ill-defined borders, variegated

[Table 89-1. Classification of Moles]

colors usually of brown and tan tones, and macular or papular components. Management is by monitoring and biopsy of highly atypical or changed lesions. Patients should reduce sun exposure and conduct regular self-examinations for new moles or changes in existing ones.

AM are nevi with a slightly different clinical and histologic appearance (disordered architecture and atypia of melanocytes). Patients with AM are at increased risk of melanoma; risk increases as the number of AM and as sun exposure increase. Some patients have only one or a few AM; others have many.

The propensity to develop AM may be inherited (autosomal dominant) or sporadic without apparent

familial association. Familial atypical mole-melanoma syndrome refers to the presence of multiple AM and melanoma in ≥ 2 1st-degree relatives. These patients are at markedly increased risk (25 times) for melanoma.

Symptoms and Signs

AM are often larger than other nevi (> 6 mm diameter) and primarily round (unlike many melanomas) but with indistinct borders and mild asymmetry. In contrast, melanomas have greater irregularity of color, not just tan and brown, but dark brown, black, red, and blue or whitish areas of depigmentation.

Diagnosis

• Regular physical examinations

• Biopsy

Although clinical findings suggest the diagnosis of AM (see Table 89-2), biopsy of the worst-appearing lesions should be done to establish the diagnosis and to determine the degree of atypia.

One or more atypical-appearing lesions should be biopsied. Patients with multiple AM and a personal or family history of melanoma should be examined regularly (eg, yearly for family history, more often for personal history, of melanoma).

Treatment

Atypical moles can be removed by excision or shaving.

Prevention

Patients with AM should avoid excessive sun exposure and use sunscreens. Also, they

[**Table 89-2.** Characteristics of Atypical vs Typical Moles]

should be taught self-examination to detect changes in existing moles and to recognize features of melanomas. Some experts recommend yearly photographs of the skin surface. Regular follow-up examinations may be combined with baseline and follow-up color photographs of most of the patient's body; this method is most useful in patients with many AM.

If patients have a family history of melanoma (whether developing from AM or de novo) or other skin cancers, 1st-degree relatives should be examined. Patients who are from melanoma-prone families (ie, ≥ 2 1st-degree relatives with cutaneous melanomas) have a high lifetime risk of developing melanomas. The entire skin (including the scalp) of members of an at-risk family should be examined.

Seborrheic Keratoses

Seborrheic keratoses are pigmented superficial epithelial lesions that are usually warty but may occur as smooth papules.

The cause is unknown. The lesions commonly occur in middle or old age and most often appear on the trunk or temples; in blacks and Asians, especially women, lesions that are 1 to 3 mm often occur on the cheekbones; this condition is termed dermatosis papulosa nigra.

Seborrheic keratoses vary in size and grow slowly. They may be round or oval and flesh-colored, brown, or black. They usually appear stuck on and may have a verrucous, velvety, waxy, scaling, or crusted surface (see Plate 44).

Diagnosis is clinical.

They are not premalignant and need no treatment unless they are irritated, itchy, or cosmetically bothersome. Lesions may be removed with little or no scarring by cryotherapy (which can cause hypopigmentation) or by electro-desiccation and curettage after local injection of lidocaine.

Skin Tags

Skin tags (acrochordons, soft fibromas) are common soft, small, flesh-colored or hyperpigmented, pedunculated lesions; there are usually multiple lesions, typically on the neck, axilla, and groin.

Skin tags are usually asymptomatic but may be irritating. Irritating or unsightly skin tags can be removed by freezing with liquid nitrogen, light electrodesiccation, or excision with a scalpel or scissors. The standard of care is to submit all skin tags individually for histologic examination, especially if there is any question of the diagnosis. However, for a patient with dozens of identical lesions, an individual lesion is unlikely to be anything other than a skin tag.

Vascular Lesions

Vascular lesions include acquired lesions (eg, pyogenic granuloma) and those that are present at birth or arise shortly after birth (vascular birthmarks). Vascular birthmarks include vascular tumors (eg, infantile hemangioma) and vascular malformations. Vascular malformations are congenital, life-long, localized defects in vascular morphogenesis and include capillary (eg, nevus flammeus), venous, arteriovenous (eg, cirsoid aneurysm), and lymphatic malformations. Vascular birthmarks usually involve only the skin and subcutaneous tissues and rarely affect the CNS.

Infantile Hemangioma

Infantile hemangiomas (IH) are raised, red or purplish, hyperplastic vascular lesions appearing in the first year of life. Most spontaneously involute; those obstructing vision, the airway, or other structures require treatment, usually with oral corticosteroids. Surgery is rarely recommended.

IH is the most common tumor of infancy, affecting 10 to 12% of infants by age 1 yr. IH is present at birth in 10 to 20% of those affected and almost always within the first several weeks of life; occasionally, deeper lesions may not be apparent until a few months after birth. Size and vascularity increase rapidly, usually peaking at about age 1 yr.

IH can be classified by general appearance (superficial, deep, or cavernous) or by other descriptive terms (eg, strawberry hemangioma). However, because all of these lesions share a common pathophysiology and natural history, the inclusive term infantile hemangioma is preferred.

Symptoms and Signs

Superficial lesions have a bright red appearance; deeper lesions have a bluish color. Lesions can bleed or ulcerate from minor trauma; ulcers may be painful. IH in certain locations can interfere with function. Lesions on the face or oropharynx may interfere with vision or obstruct the airway; those near the urethral meatus or anus may interfere with elimination. A periocular hemangioma in an infant is an emergency because even a few days of disrupted vision can result in permanent visual defects. Lumbosacral hemangiomas may be a sign of neurologic or GU anomalies.

Lesions slowly involute starting at 12 to 18 mo, decreasing in size and vascularity. Generally, IH involute by 10%/year of age (eg, 50% by age 5, 60% by age 6), with maximal involution by age 10. Involuted lesions commonly have a yellowish or telangiectatic color and a wrinkled or lax fibrofatty texture. Residual changes are almost always proportional to the lesion's maximal size and vascularity.

Diagnosis

Diagnosis is clinical; the extent can be evaluated by MRI if lesions appear to encroach on vital structures.

Treatment

• Sometimes laser therapy

• Sometimes intralesional or systemic corticosteroid therapy

• General wound care for ulcerated lesions

Treatment is controversial. Many physicians treat lesions early to prevent subsequent enlargement or to make them less noticeable; others do not treat unless a lesion causes (or risks) functional problems by its location. When treatment is elected, laser therapy or intralesional or systemic corticosteroids are chosen based on the location, extent, and rate of growth of the lesion. For systemic corticosteroid therapy, prednisone 1 to 3 mg/kg po bid or tid is given for ≥ 2 wk. If resolution starts, the prednisone should be decreased slowly; if not, the drug should be stopped.

Topical treatments and wound care are useful for ulcerated lesions and help prevent scarring, bleeding, and pain. Compresses, topical mupirocin or metronidazole, barrier dressings (polyurethane film dressing or petrolatum-impregnated gauze), or barrier creams may be used.

Unless complications are life threatening or vital organs are compromised, surgical excision or other destructive procedures should be avoided because they frequently cause more scarring than occurs with spontaneous involution. To help parents accept nonintervention, the physician can review the natural history (photographic examples are helpful), provide serial photography of the lesion to document involution, and listen sympathetically to parents' concerns.

Nevus Flammeus and Port-Wine Stain

Nevus flammeus and port-wine stains are capillary vascular malformations that are present at birth and appear as flat, pink, red, or purplish lesions.

Nevi flammei are flat pink marks that are very common on the nape, glabella, and eyelids. Lesions around the eyes disappear in a few months. Nape lesions may disappear in early childhood, only to recur in middle age.

Port-wine stains are flat, reddish to purple lesions appearing anywhere on the body. Lesions become darker and more palpable with time (often becoming quite hyperplastic by late middle age), but the lateral extent increases only in proportion to the growth of the patient. Port-wine stains of the trigeminal area may be a component of the Sturge-Weber syndrome (in which a similar vascular lesion appears on the underlying meninges and cerebral cortex and is associated with epilepsy).

Diagnosis is clinical.

Treatment with vascular lasers produces excellent results in many cases, especially if the lesion is treated as early in life as possible. The lesion can also be hidden with an opaque cosmetic cream prepared to match the patient's skin color.

Nevus Araneus

(Spider Nevus; Spider Angioma; Vascular Spider)

Nevus araneus is a bright red, faintly pulsatile vascular lesion consisting of a central arteriole with slender projections resembling spider legs (see Plate 26).

These lesions are acquired. One lesion or small numbers of lesions unrelated to internal disease may

occur in children or adults. Patients with cirrhosis develop many spider angiomas that may become quite prominent. Many women develop lesions during pregnancy or while taking oral contraceptives.

The lesions are asymptomatic and usually resolve spontaneously about 6 to 9 mo postpartum or after oral contraceptives are stopped. Lesions are not uncommon on the faces of children. Compression of the central vessel temporarily obliterates the lesion.

Diagnosis is clinical.

Treatment is not usually required. If resolution is not spontaneous or treatment is desired for cosmetic purposes, the central arteriole can be destroyed with fine-needle electrodesiccation; vascular laser treatment may also be done.

Pyogenic Granuloma

Pyogenic granuloma is a fleshy, moist or crusty, usually scarlet vascular nodule composed of proliferating capillaries in an edematous stroma.

The lesion, composed of vascular tissue, is neither of bacterial origin nor a true granuloma. It develops rapidly, often at the site of recent injury (although injury may not be recalled), typically grows no larger than 2 cm in diameter, and probably represents a vascular and fibrous response to injury. There is no sex or age predilection. The overlying epidermis is thin, and the lesion tends to be friable, bleeds easily, and does not blanch on pressure. The base may be pedunculated and surrounded by a collarette of epidermis.

During pregnancy, pyogenic granulomas may become large and exuberant (eg, gingival pregnancy tumors, or telangiectatic epulis).

Diagnosis involves biopsy and histologic examination. Histologic analysis is required for all removed tissue because these lesions occasionally resemble and must be differentiated from melanomas or other malignant tumors.

Treatment consists of removal by excision or curettage and electrodesiccation, but the lesions may recur.

Lymphatic Malformations

(Lymphangioma; Lymphangioma Circumscriptum; Cystic Hygroma; Cavernous Lymphangioma)

Lymphatic vascular malformations are elevated lesions composed of dilated lymphatic vessels.

Most lymphatic malformations are present at birth or develop within the first 2 yr. Lesions are usually yellowish tan but occasionally reddish or purple if small blood vessels are intermingled. Puncture of the lesion yields a colorless or blood-tinged fluid.

Diagnosis is made clinically and by MRI.

Treatment is usually not needed. If the lesion is excised, recurrence is common, even when removal of dermal and subcutaneous tissues is extensive.

Chapter 90. Cancers of the Skin

Introduction

Skin cancer is the most common type of cancer and usually develops in sun-exposed areas of skin. The incidence is highest among outdoor workers, sportsmen, and sunbathers and is inversely related to the amount of melanin skin pigmentation; fair-skinned people are most susceptible. Skin cancers may also develop years after therapeutic x-rays or exposure to carcinogens (eg, arsenic ingestion).

Over one million new cases of skin cancer are diagnosed in the US yearly. About 80% are basal cell carcinoma, 16% are squamous cell carcinoma, and 4% are melanoma. Paget's disease of the nipple or extramammary Paget's (usually near the anus), Kaposi's sarcoma, tumors of adnexa, and cutaneous T-cell lymphoma (mycosis fungoides—see p. 1024) make up the remaining, less common, forms of skin cancer.

Initially, skin cancers are often asymptomatic. The most frequent presentation is a papule or blind pimple that does not go away. Any lesion that appears to be enlarging should be biopsied—whether tenderness, mild inflammation, crusting, or occasional bleeding is present or not. If treated early, most skin cancers are curable.

Screening: Routine screening for skin cancer is by patient self-examination, physician examination, or both.

Prevention: Because many skin cancers seem to be related to ultraviolet (UV) exposure, a number of measures are recommended to limit exposure.

- Sun avoidance: Seeking shade, minimizing outdoor activities between 10 AM and 4 PM (when sun's rays are strongest), and avoiding sunbathing and the use of tanning beds
- Use of protective clothing: Long-sleeved shirt, pants, and broad-brimmed hat
- Use of sunscreen: At least sun protection factor (SPF) 30 with UVA protection, used as directed; should not be used to prolong sun exposure

Current evidence is inadequate to determine whether these measures reduce incidence or mortality of melanoma; in nonmelanoma skin cancers (basal cell and squamous cell carcinoma), sun protection does decrease the incidence of new cancers.

Basal Cell Carcinoma

(Rodent Ulcer)

Basal cell carcinoma is a superficial, slowly growing papule or nodule (see Plate 29) that derives from certain epidermal cells. Basal cell carcinomas arise from keratinocytes near the basal layer and can be referred to as basaloid keratinocytes. Metastasis is rare, but local growth can be highly destructive. Diagnosis is by biopsy. Treatment depends on the tumor's characteristics and may involve curettage and electrodesiccation, surgical excision, cryosurgery, topical chemotherapy, or, occasionally, radiation therapy.

Basal cell carcinoma is the most common type of skin cancer, with > 800,000 new cases yearly in the US. It is more common in fair-skinned people with a history of sun exposure and is very rare in blacks.

Symptoms and Signs

The clinical manifestations and biologic behavior of basal cell carcinomas are highly variable. They may appear as

- Small, shiny, firm, almost translucent nodules

- Ulcerated, crusted papules or nodules
- Flat, scarlike, indurated plaques
- Red, marginated, thin papules or plaques that are difficult to differentiate from psoriasis or localized dermatitis

Most commonly, the carcinoma begins as a shiny papule, enlarges slowly, and, after a few months or years, shows a shiny, pearly border with prominent engorged vessels (telangiectases) on the surface and a central dell or ulcer. Recurrent crusting or bleeding is not unusual. Commonly, the carcinomas may alternately crust and heal, which may unjustifiably decrease patients' and physicians' concern about the importance of the lesion.

Basal cell carcinomas rarely metastasize but may invade healthy tissues. Rarely, patients die because the carcinoma invades or impinges on underlying vital structures or orifices (eyes, ears, mouth, bone, dura mater).

Diagnosis

- Biopsy and histologic examination

Treatment

Treatment should be done by a specialist. The clinical appearance, size, site, and histologic subtype determine choice of treatment—curettage and electrodesiccation, surgical excision, cryosurgery, topical chemotherapy (imiquimod, 5-fluorouracil, and photodynamic therapy), or, occasionally, radiation therapy. Recurrent or incompletely treated cancers, large cancers, cancers at recurrence-prone sites, and morphea-like cancers with vague borders are often treated with Mohs microscopically controlled surgery, in which tissue borders are progressively excised until specimens are tumor-free (as determined by microscopic examination during surgery). Almost 25% of patients with a history of basal cell carcinoma develop a new basal cell cancer within 5 yr of the original carcinoma. Consequently, patients with a history of basal cell carcinoma should be seen annually for a skin examination.

Bowen's Disease

(Intraepidermal Squamous Cell Carcinoma)

Bowen's disease is a superficial squamous cell carcinoma in situ.

Bowen's disease is most common in sun-exposed areas but may arise at any location. Lesions can be solitary or multiple. They are red-brown and scaly or crusted, with little induration; they frequently resemble a localized thin plaque of psoriasis, dermatitis, or a dermatophyte infection. Diagnosis is by biopsy.

Treatment depends on the tumor's characteristics and may involve topical chemotherapy, curettage and electrodesiccation, surgical excision, or cryosurgery.

Squamous Cell Carcinoma

Squamous cell carcinoma is a malignant tumor of epidermal keratinocytes that invades the dermis; this cancer usually occurs in sun-exposed areas. Local destruction may be extensive, and metastases occur in advanced stages. Diagnosis is by biopsy. Treatment depends on the tumor's characteristics and may involve curettage and electrodesiccation, surgical excision, cryosurgery, or, occasionally, radiation therapy.

Squamous cell carcinoma, the 2nd most common type of skin cancer, may develop in normal tissue, in a preexisting actinic keratosis (see p. 674), in a patch of leukoplakia, or in a burn scar. The incidence in the

US is 200,000 to 300,000 cases annually, with 2000 deaths.

The clinical appearance is highly variable, but any nonhealing lesion on sun-exposed surfaces should be suspect. The tumor may begin as a red papule or plaque with a scaly or crusted surface and may become nodular, sometimes with a warty surface. In some cases, the bulk of the lesion may lie below the level of the surrounding skin. Eventually the tumor ulcerates and invades the underlying tissue.

Diagnosis

Biopsy is essential. Differential diagnosis includes many types of benign and malignant lesions, such as basal cell carcinoma, keratoacanthoma, actinic keratosis, verruca vulgaris, and seborrheic keratosis.

Prognosis

In general, the prognosis for small lesions removed early and adequately is excellent. Regional and distant metastases of squamous cell carcinomas on sun-exposed skin are uncommon but do occur, particularly with poorly differentiated tumors. However, about one third of lingual or mucosal cancers have metastasized before diagnosis (see p. 491).

Late-stage disease, which may require extensive surgery, is far more likely to metastasize. It spreads initially regionally to surrounding skin and lymph nodes and eventually to nearby organs. Cancers that occur near the ears, the vermilion, and in scars are more likely to metastasize. The overall 5-yr survival rate for metastatic disease is 34% despite therapy.

Treatment

Treatment is similar to that for basal cell carcinoma and includes curettage and electrodesiccation, surgical excision, cryosurgery, topical chemotherapy (imiquimod, 5-fluorouracil), and photodynamic therapy, or, occasionally, radiation therapy (see p. 749). Treatment and follow-up must be monitored closely because of the greater risk of metastasis. Squamous cell carcinoma on the lip or other mucocutaneous junction should be excised; at times, cure is difficult. Recurrences and large tumors should be treated aggressively with Mohs microscopically controlled surgery, or by a team approach with surgery and radiation therapy.

Metastatic disease is responsive to radiation therapy if metastases can be identified and are isolated. Widespread metastases do not respond well to chemotherapeutic regimens.

Melanoma

(Malignant Melanoma)

Malignant melanoma arises from melanocytes in a pigmented area (eg, skin, mucous membranes, eyes, or CNS). Metastasis is correlated with depth of dermal invasion. With spread, prognosis is poor. Diagnosis is by biopsy. Wide surgical excision is the rule for operable tumors. Metastatic disease requires chemotherapy but is difficult to cure.

About 60,000 new cases of melanoma occur yearly in the US, causing about 8400 deaths. Incidence has remained steady over the last 8 yr (it had previously been increasing at a faster rate than any other malignant tumor).

Melanomas occur mainly on the skin but also on the mucosa of the oral and genital regions and conjunctiva. Melanomas vary in size, shape, and color (usually pigmented) and in their propensity to invade and metastasize. Metastasis occurs via lymphatics and blood vessels. Local metastasis results in the formation of nearby satellite papules or nodules that may or may not be pigmented. Direct metastasis to skin or internal organs may occur, and occasionally, metastatic nodules or enlarged lymph nodes are discovered before the primary lesion is identified.

Etiology

Risk factors include

• Sun exposure

• Family and personal history

• Fair skin

• Increased numbers of melanocytic nevi

• Immunosuppression

• Occurrence of lentigo maligna

• Large congenital melanocytic nevus

• Dysplastic nevus syndrome

Patients with a personal history of melanoma have an increased risk of additional melanomas. People who have one or more 1st-degree relatives with a history of melanoma have an increased risk (up to 6 or 8 times) over those without a family history. Melanoma is rare in blacks.

About 40 to 50% of melanomas develop from pigmented moles (see also p. 744); almost all the rest arise from melanocytes in normal skin. Atypical moles (dysplastic nevi) may be precursors to melanoma (see p. 744). The very rare melanomas of childhood almost always arise from large pigmented moles (giant congenital nevi) present at birth. Although melanomas occur during pregnancy, pregnancy does not increase the likelihood that a mole will become a melanoma; moles frequently change in size and darken uniformly during pregnancy. However, the following signs of malignant transformation should be carefully sought:

• Change in size

• Irregular change in color, especially spread of red, white, and blue pigmentation to surrounding normal skin

• Change in surface characteristics, consistency, or shape

• Signs of inflammation in surrounding skin, with possible bleeding, ulceration, itching, or tenderness

Classification

There are 4 main types of melanoma.

Lentigo maligna melanoma: This type accounts for 5 to 15% of melanomas. It tends to arise in older patients. It arises from lentigo maligna (Hutchinson's freckle or malignant melanoma in situ). It appears on the face or other sun-exposed areas as an asymptomatic, flat, tan or brown, irregularly shaped macule or patch with darker brown or black spots scattered irregularly on its surface. In lentigo maligna, both normal and malignant melanocytes are confined to the epidermis. When malignant melanocytes invade the dermis, the lesion is called lentigo maligna melanoma, and the cancer may metastasize.

Superficial spreading melanoma: This type accounts for two thirds of melanomas. Typically asymptomatic, it occurs most commonly on women's legs and men's torsos. The lesion is usually a plaque with irregular, raised, indurated, tan or brown areas, which often have red, white, black, and blue spots or small, sometimes protuberant blue-black nodules (see Plate 40). Small notchlike indentations of the margins may be noted, along with enlargement or color change. Histologically, atypical melanocytes characteristically invade the dermis and epidermis.

Nodular melanoma: This type accounts for 10 to 15% of melanomas. It may occur anywhere on the body as a dark, protuberant papule or a plaque that varies from pearl to gray to black. Occasionally, a lesion contains little if any pigment or may look like a vascular tumor. Unless it ulcerates, nodular melanoma is asymptomatic, but patients usually seek advice because the lesion enlarges rapidly.

Acral-lentiginous melanoma: This type accounts for only 5 to 10% of melanomas, but it is the most common form of melanoma in blacks. It arises on palmar, plantar, and subungual skin and has a characteristic histologic picture similar to that of lentigo maligna melanoma.

Diagnosis

• Biopsy

The differential diagnosis includes basal cell and squamous cell carcinomas, seborrheic keratoses, atypical moles, blue nevi, dermatofibromas, moles, hematomas (especially on the hands or feet), venous lakes, pyogenic granulomas, and warts with focal thromboses. If doubt exists, biopsy should include the full depth of the dermis and extend slightly beyond the edges of the lesion. Biopsy should be excisional for small lesions and incisional for larger lesions. By doing step sections, the pathologist can determine the maximal thickness of the melanoma. Definitive radical surgery should not precede histologic diagnosis.

Pigmented lesions with the following features should be excised or biopsied:

• Recent enlargement

• Darkening

• Bleeding

• Ulceration

However, these features usually indicate that the melanoma has already invaded the skin deeply. Earlier diagnosis is possible if biopsy specimens can be obtained from lesions having variegated colors (eg, brown or black with shades of red, white, or blue), irregular elevations that are visible or palpable, and borders with angular indentations or notches. Polarized light and immersion contact dermoscopy, which is used to examine pigmented lesions, may be useful for distinguishing melanomas from benign lesions.

Staging: The staging of melanoma is based on clinical and pathologic criteria and closely corresponds to the traditional tumor-node-metastasis (TNM) classification system. The staging system classifies melanomas based on local, regional, or distant disease.

• Stage I and II: Localized primary melanoma

• Stage III: Metastasis to regional lymph nodes

• Stage IV: Distant metastatic disease

Stage strongly correlates with survival. A minimally invasive microstaging technique, the so-called sentinel lymph node biopsy (SLNB), is a major advance in the ability to stage cancers more accurately. Recommended staging studies depend on the Breslow depth (how deeply tumor cells have invaded) and histologic characteristics of the melanoma. Staging studies may include SLNB, laboratory tests (CBC, LDH, liver function tests), chest x-ray, CT, and PET and are done by a coordinated team that includes dermatologists, oncologists, general surgeons, plastic surgeons, and dermatopathologists.

Prognosis

Melanoma may spread rapidly, causing death within months of its recognition, yet the 5-yr cure rate of early, very superficial lesions is nearly 100%. Thus, cure depends on early diagnosis and early treatment.

For tumors of cutaneous origin (not CNS and subungual melanomas) that have not metastasized, the survival rate varies depending on the thickness of the tumor at the time of diagnosis (see Table 90-1). Mucosal melanomas (especially anorectal melanomas), which are more common in nonwhites, have a poor prognosis, although they often seem quite limited when discovered. Once melanoma has metastasized to the lymph nodes, 5-yr survival ranges from 25 to 70% depending on the degree of ulceration and number of nodes involved. Once melanoma has metastasized to distant sites, 5-yr survival is about 10%.

Degree of lymphocytic infiltration, which represents reaction by the patient's immunologic defense system, may correlate with the level of invasion and prognosis. Chances of cure are maximal when lymphocytic infiltration is limited to the most superficial lesions and decrease with deeper levels of tumor cell invasion, ulceration, and vascular or lymphatic invasion.

[**Table 90-1.** 5-yr Survival* for Malignant Melanoma Relative to Thickness and Ulceration]

Treatment

• Surgical excision

• Possibly adjuvant radiation therapy

• Possibly adjuvant interferon alfa

• Sometimes excision, imiquimod, and cryotherapy

Treatment is primarily by surgical excision. Although the width of margins is debated, most experts agree that a 1-cm lateral tumor-free margin is adequate for lesions < 1 mm thick. Thicker lesions may deserve larger margins, more radical surgery, and SLNB.

Lentigo maligna melanoma and lentigo maligna are usually treated with wide local excision and, if necessary, skin grafting. Intensive radiation therapy is much less effective. Treatment of lentigo maligna includes early excision (before the lesion is very large), imiquimod, and controlled cryotherapy. Most other treatment methods usually do not penetrate deeply enough into involved follicles, which must be removed.

Spreading or nodular melanomas are usually treated with wide local excision extending down to the fascia. Lymph node dissection may be recommended when nodes are involved. (See also the American Academy of Dermatology Association's Guidelines of Care for Primary Cutaneous Melanoma.)

Metastatic disease: Metastatic disease is generally inoperable, but in certain cases, localized and regional metastases can be excised. Chemotherapy with dacarbazine or temozolamide (oral dacarbazine analog) and aldesleukin can be used for the treatment of metastatic melanoma. Adjuvant therapy with recombinant biologic response modifiers (particularly interferon alfa) to suppress clinically inapparent micrometastases may also be used for inoperable metastatic melanoma. Brain metastases may be treated with palliative radiation, but the response is poor.

The following are under study:

• Infusion of lymphokine-activated killer cells or antibodies (for advanced-stage disease)

• Vaccine therapy

Kaposi's Sarcoma

(Multiple Idiopathic Hemorrhagic Sarcoma)

Kaposi's sarcoma (KS) is a multicentric vascular tumor caused by herpesvirus type 8. It can occur in classic, AIDS-associated, endemic, and iatrogenic forms. Diagnosis is by biopsy.

Treatment for indolent superficial lesions involves cryotherapy, electrocoagulation, excision, or electron beam radiation therapy. Radiation therapy is used for more extensive disease. In the AIDS-associated form, antiretrovirals provide the most improvement.

KS originates from endothelial cells in response to infection by human herpesvirus 8 (HHV-8). Immunosuppression (particularly by AIDS and drugs for organ transplant recipients) markedly increases the likelihood of KS in HHV-8-infected patients. The tumor cells have a spindle shape, resembling smooth muscle cells, fibroblasts, and myofibroblasts.

Classification

Classic KS: This form occurs most often in older (> 60 yr) men of Italian, Jewish, or Eastern European ancestry. The course is indolent, and the disease is usually confined to a small number of lesions on the skin of the lower extremities (see Plate 36); visceral involvement occurs in < 10%. This form is usually not fatal.

AIDS-associated (epidemic) KS: This form is the most common AIDS-associated cancer and is more aggressive than classic KS. Multiple cutaneous lesions are typically present, often involving the face and trunk. Mucosal, lymph node, and GI involvement is common. Sometimes KS is the first manifestation of AIDS.

Endemic KS: This form occurs in Africa independent of HIV infection. There are 2 main types:

- Prepubertal lymphadenopathic form: It predominantly affects children; primary tumors involve lymph nodes, with or without skin lesions. The course is usually fulminant and fatal.

- Adult form: This form resembles classic KS.

Iatrogenic (immunosuppressive) KS: This form typically develops several years after organ transplantation. The course is more or less fulminant, depending on the degree of immunosuppression.

Symptoms and Signs

Cutaneous lesions are asymptomatic purple, pink, or red macules that may coalesce into blue-violet to black plaques and nodules. Some edema may be present. Occasionally, nodules fungate or penetrate soft tissue and invade bone. Mucosal lesions appear as bluish to violaceous macules, plaques, and tumors. GI lesions can bleed, sometimes extensively, but usually are asymptomatic.

Diagnosis

- Biopsy

Diagnosis is confirmed by punch biopsy. Patients with AIDS or immunosuppression require evaluation for visceral spread by CT of the chest and abdomen. If CT is negative but pulmonary or GI symptoms are present, bronchoscopy or GI endoscopy should be considered.

Treatment

- Surgical excision, cryotherapy, or electrocoagulation for superficial lesions

- Local radiation therapy for multiple lesions or lymph node disease

- Antiretroviral therapy or sometimes IV interferon alfa for AIDS-associated KS

- Reduction of immunosuppressants for iatrogenic KS

Indolent lesions often require no treatment. One or a few superficial lesions can be removed by excision, cryotherapy, or electrocoagulation. Intralesional vinblastine or interferon alfa is also useful. Multiple

lesions and lymph node disease are treated locally with 10 to 20 Gy of radiation therapy.

AIDS-associated KS responds markedly to highly active antiretroviral therapy (HAART), probably because CD4+ count improves and HIV viral load decreases; however, there is some evidence that protease inhibitors in this regimen may block angiogenesis. AIDS patients with indolent disease and CD4+ counts > 150/µL and HIV RNA < 500 copies/mL can be treated with IV interferon alfa. Patients with more extensive or visceral disease can be given liposomal doxorubicin 20 mg/m^2 IV q 2 to 3 wk. If this regimen fails, patients may receive paclitaxel. Other agents being investigated as adjuncts include IL-12, desferrioxamine, and oral retinoids. Treatment of KS does not prolong life in most AIDS patients because infections dominate the clinical course.

Iatrogenic KS responds best to stopping immunosuppressants. In organ transplant patients, reduction of immunosuppressant dosage often results in reduction of KS lesions. If dosage reduction is not possible, conventional local and systemic therapies used in other forms of KS should be instituted. Sirolimus may also improve iatrogenic KS.

Treatment of endemic KS is challenging and typically palliative.

Paget's Disease of the Nipple

Paget's disease is a rare type of carcinoma that appears as a unilateral eczematous to psoriasiform plaque surrounding the nipple. It involves extension to the epidermis of an underlying ductal adenocarcinoma of the breast.

Paget's disease of the nipple should not be confused with the metabolic bone disease that is also called Paget's disease. In Paget's disease of the nipple, metastatic disease is often present at the time of the diagnosis.

Paget's disease of the nipple also occurs at other sites, most often in the groin or perianal area (extramammary Paget's disease). The bladder, anus, and rectum are the most common sites. Extramammary Paget's disease is a rare intraepithelial adenocarcinoma of apocrine gland-bearing sites.

Diagnosis

• Biopsy

The redness, oozing, and crusting closely resemble dermatitis; but physicians should suspect carcinoma because the lesion is sharply marginated, unilateral, and unresponsive to topical therapy. Biopsy shows typical histologic changes. Because this tumor is associated with underlying cancer, systemic evaluation is required.

Treatment

Treatment involves surgical removal of discovered tumors, including possible mastectomy for disease involving the nipple. Treatment may also involve ablation of overlying cutaneous involvement, either surgically or by CO_2 laser ablation.