Dermatologic Drug Reactions and Common Skin Conditions

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INTRODUCTION

1. Skin is an essential part of the body. Although it is not commonly thought of as such, skin is an organ. In fact, it is the human body’s largest organ, with an average surface area of about 1.8 m². The organ system that includes the skin is known as the integumentary system.

2. The human skin consists of an outer epidermis and an inner dermis. The epidermis primarily provides protection from the environment and performs a critical barrier function—keeping in water and other vital substances and keeping out foreign elements. The dermis is a connective tissue layer that primarily provides resiliency and support for various skin structures and appendages such as sweat glands, sebaceous glands, hair, and nails.

3. Because the skin surface is such a visible part of the body, changes that are slow or subtle often go unnoticed. Slowly enlarging and evolving moles or dry skin conditions can go undetected even though such changes can be life threatening in some cases (e.g., malignancy). Health professionals who have direct contact with patients should be able to distinguish between common self-treatable skin lesions and common skin lesions that must be seen and treated professionally, such as melanoma and squamous cell carcinoma.

4. Skin infections and infestations are not covered in this chapter but are discussed in Chapter 88. Acne, psoriasis, and atopic dermatitis are discussed in Chapters 77 to 79.

STRUCTURE AND FUNCTIONS OF THE SKIN

The integumentary system comprises the epidermis and dermis. The epidermis, which is derived from ectoderm, is further divided into four layers: stratum basale (basal layer), stratum spinosum (prickle cell layer), stratum granulosum (granular layer), and stratum corneum (horny layer). The stratum corneum is the outermost layer of skin and primarily is responsible for the barrier function. The epidermis is thick on the palms and soles and thin on other parts of the body, with some variations. For example, the palms and soles contain sweat glands but lack sebaceous glands, which are found almost everywhere else in the skin, with the highest concentration on the face and trunk areas. Sebaceous glands and small hair follicles together form pilosebaceous units, which originate in the dermis and have follicular ducts extending through the epidermis to the skin surface. Sebaceous glands produce sebum,
Skin cells are called keratinocytes. They produce keratin, a protein network that gives epithelial cells resilience to mechanical stress. Keratinocytes begin at the stratum basale as box-shaped basal cells. As the cells mature, they migrate toward the skin surface, elongating and flattening as they divide and differentiate, ending as corneocytes in the stratum corneum. Corneocytes are flattened keratinocytes containing keratin tonofilaments (filaments composed of keratin and keratohyalin granules). They are often termed dead because they do not contain nuclei and are not capable of mitosis. Each cell covers a much larger surface area as a corneocyte compared with its basal origin. Overlapping corneocytes provide for the skin barrier. \(^1\) (Note that abnormal keratinocyte activity accounts for some skin diseases. For example, psoriasis is associated with increased keratinocyte cell turnover, and acne is partially caused by increased keratin production.\(^2\))

Melanocytes are pigment-producing cells in the stratum basale. They produce melanin, a yellow–brown/black pigment. Melanin granules are spread out into a protective layer in the stratum corneum, reducing ultraviolet (UV) penetration into the skin. UV radiation causes human skin to increase both melanin production and keratinocyte proliferation as a protective effort.\(^3\)

The skin surface is normally covered with a hydrophilic film composed of sweat, oils (sebaceous lipids and free fatty acids), corneocytes, protein decomposition products, and transdermal water. Some of these are natural moisturizing factors that help the skin retain water. Thus, the hydrophilic film is a permeability barrier that keeps the skin supple.\(^1\)

Because of the presence of lactic acid and various amino acids from sweat, free fatty acids from sebum, and amino acids from shedding corneocytes, human skin is normally acidic, generally with a pH of 5.5 to 6. Bacteria thrive in an alkaline environment. As a result, the skin also functions as a protective acid mantle against invasion by pathogenic bacteria and fungi.\(^1\)

The dermis, which is derived from mesoderm, is a much thicker layer that contains nerve endings and blood vessels. It is made up of collagen and elastin, which provide support for various skin structures and appendages. Eccrine (sweat) glands, hair follicles, sebaceous glands, and arrector pili muscles originate in the dermis. Subcutaneous tissue (adipose tissue with nerves and blood vessels) lies beneath the dermis.\(^1\)

Skin is also involved in regulating body temperature, preventing dehydration, acting as a sense organ, and playing a role in vitamin D production and absorption.

### Age-Related Changes and Other Skin-Related Considerations

Age-related changes in the structure and functions of the epidermis and dermis are important.

In general, pediatric skin contains more water and is thinner, allowing for enhanced topical drug absorption in both the rate and amount of drug absorbed. This increases the potential for drug toxicities. Increased topical absorption and toxicity have been reported with the use of rubbing alcohol, boric acid powders, and hexachlorophene emulsions and soaps in infants and young children. Even drugs that are not normally used topically may be systemically absorbed. For example, a theophylline gel (17 mg spread over an area 2 cm in diameter) applied to the abdomens of premature infants produced therapeutic serum theophylline concentrations.\(^3\)

Well-hydrated, unbroken skin provides maximal protection against microbial invaders. Aged skin tends to be drier, thinner, and more friable, which increases susceptibility to external insults.

In addition, the healing time after skin injury may be prolonged in aged skin. UV radiation is associated with accelerated skin aging and skin cancers (e.g., malignant melanoma, basal cell carcinoma). Skin should be constantly protected from UV damage by the use of sunscreens that block both UVA and UVB, with a sun protection factor (SPF) of at least 15, preferably 30 or higher. Sunscreens should be applied 20 minutes before sun exposure and reapplied after sweating or swimming.

It should not be surprising that skin health is related to overall health. Exercise and adequate sleep along with maintaining a healthy, well-balanced diet are key factors. Ample daily fluid intake and regular use of moisturizers are important for skin hydration. Malnourishment can cause a patient to become immunocompromised, which may adversely affect the ability of the skin to act as a barrier. Nutritional deficiencies can cause skin problems, including dry skin. Specific food allergies can cause skin reactions (e.g., rashes, hives). Patients with atopic dermatitis often have multiple food sensitivities and allergies, resulting in hives and skin rashes and/or systemic manifestations. For skin cleansing, soapless cleansers may be preferable to soap because they may cause less skin irritation. Repeated and frequent exposure to soap or other cleansers that cause cumulative irritation (e.g., with surfactants and emulsifiers) can result in irritant contact dermatitis.

### PATIENT ASSESSMENT

When patients present with dermatologic disorders, a standard approach to assessment should be used. This is especially important for pharmacists who must decide whether to recommend nonprescription therapies or refer patients to medical practitioners, and to nurse practitioners and physician assistants, who must evaluate symptoms and decide whether a supervising physician or dermatologist should be involved.

**Patient History: Questions to Ask**

With all skin conditions, including possible drug-induced reactions, a comprehensive patient history is important. These include questioning and physically assessing the patient to obtain the following information:

1. **Signs and Symptoms**
   a. **Onset.** When did the lesions first appear? It is important to distinguish between an acute and a chronic condition.
   b. **Progression.** Are the lesions improving or worsening or spreading? If lesions are worsening, how quickly are the lesions becoming more severe or widespread?
   c. **Timeframe.** Did the occurrence of skin lesions correlate temporally with the use of any medications? This may help to distinguish between a drug-induced condition and a disease-related condition.
   d. **Location(s) and description of the lesions.** Specific details about where the lesions occur and what they look like will help to identify the type of skin condition. For example, plaque psoriasis is usually diagnosed in this manner and not through laboratory means. However, for conditions such as skin cancers, a skin biopsy may be needed to establish a definitive histopathologic diagnosis.
   e. **Presenting symptoms.** Is there pruritus? Are the lesions painful? Pruritus is a common symptom for various skin conditions (e.g., atopic dermatitis, allergic and irritant contact dermatitis, psoriasis, bullous pemphigoid, lichen planus, pityriasis rosea) as well as systemic conditions...
be categorized as macules (eFig. 23-1), papules (eFig. 23-2), nodules (eFig. 23-3), blisters (eFig. 23-4), or plaque and lichenification (eFig. 23-5).

However, some skin conditions may cause more than one type of lesion. For example, patients with acne vulgaris may present with macules, papules, nodules, or a combination of these. Another example is psoriasis—the most common type is plaque psoriasis noted by discrete, well-defined plaques; however, there are other types of psoriasis such as guttate or erythrodermic with

**Lesion Assessment**

As discussed briefly in the following section, the appearance of skin lesions can give some clues as to their causes. Lesions may
**Section**: Organ-Specific Function Tests and Drug-Induced Diseases

**eFIGURE 23-2** Papules are small, solid, elevated lesions that are usually less than 1 cm in diameter. The major portion of a papule projects above the plane of the surrounding skin. A. Papules may result, for example, from metabolic deposits in the dermis (a), from localized dermal cellular infiltrates (b), and from localized hyperplasia of cellular elements in the dermis and epidermis (c). Papules with scaling are referred to as papulosquamous lesions, as in psoriasis (see Chap. 78). B. Clinical examples of papules. The examples are two well-defined and dome-shaped papules of firm consistency and brownish color, which are dermal melanocytic nevi. C. Multiple, well-defined and coalescing papules of varying size are seen. Their violaceous color, glistening surface, and flat tops are characteristic of lichen planus. (Reprinted with permission from Stewart MI, Bernhard JD, Cropley TG, Fitzpatrick TB. The structure of skin lesions and fundamentals of diagnosis. In: Freedberg IM, Eisen AZ, Wolff K, et al., eds. Fitzpatrick’s Dermatology in General Medicine, 6th ed. New York: McGraw-Hill, 2003:18.)

**eFIGURE 23-3** Nodules are palpable, solid, round, or ellipsoidal lesions. Depth of involvement or substantive palpability, rather than diameter, differentiates a nodule from a papule. A. Nodules may extend into the dermis or subcutaneous tissue (a) or be located in the epidermis (b). B. A well-defined, firm nodule with a smooth and glistening surface through which telangiectasia (dilated capillaries) can be seen; there is central crusting indicating tissue breakdown and thus incipient ulceration (nodular basal cell carcinoma). C. Multiple nodules of varying size can be seen (melanoma metastases). (Reprinted with permission from Stewart MI, Bernhard JD, Cropley TG, Fitzpatrick TB. The structure of skin lesions and fundamentals of diagnosis. In: Freedberg IM, Eisen AZ, Wolff K, et al., eds. Fitzpatrick’s Dermatology in General Medicine, 6th ed. New York: McGraw-Hill, 2003:18.)
eFIGURE 23-4 Vesicles and bullae are the technical terms for blisters. Whereas vesicles are circumscribed lesions that contain fluids, bullae are vesicles that are larger than 0.5 cm in diameter. A. Whereas subcorneal vesicles (a) result from fluid accumulation just below the stratum corneum, spongiotic vesicles (b) result from intercellular edema. B. Multiple translucent subcorneal vesicles are extremely fragile, collapse easily, and thus lead to crusting (arrows). These lesions are staphylococcal impetigo. (Reprinted with permission from Stewart MI, Bernhard JD, Cropley TG, Fitzpatrick TB. The structure of skin lesions and fundamentals of diagnosis. In: Freedberg IM, Eisen AZ, Wolff K, et al., eds. Fitzpatrick’s Dermatology in General Medicine, 6th ed. New York: McGraw-Hill, 2003:18.)

eFIGURE 23-5 A. Plaque is a mesa-like elevation that occupies a relatively large surface area relative to its height above the skin surface. B. Well-defined, reddish, scaling plaques can coalesce to cover large areas of the back and buttocks, with some regression in the center as is common in psoriasis (see Chap. 78). C. Lichenification, a thickening of the skin and accentuation of skin, can result from repeated rubbing. It develops frequently in patients with atopy and occurs in eczematous dermatitis and other conditions associated with pruritus. Lesions of lichenification are not as well defined as most plaques and often show signs of scratching, such as excoriations and crusts. (Reprinted with permission from Stewart MI, Bernhard JD, Cropley TG, Fitzpatrick TB. The structure of skin lesions and fundamentals of diagnosis. In: Freedberg IM, Eisen AZ, Wolff K, et al., eds. Fitzpatrick’s Dermatology in General Medicine, 6th ed. New York: McGraw-Hill, 2003:18, and Garg Amit, Levin Nikki A, Bernhard Jeffrey D. Structure of Skin Lesions and Fundamentals of Clinical Diagnosis. In: Wolff K, Goldsmith LA, Katz SI, Gilchrest B, Paller AS, Leffell DJ, eds. Fitzpatrick’s Dermatology in General Medicine, 7th ed. http://www.accessmedicine.com/content.aspx?aID=2965385).
Drug-induced skin reactions can be irritant or allergic in origin. Irritant reactions are localized. Examples include chemical vaginitis, such as those resulting from vaginal douches, spermicides, and imidazoles; and vesication, produced by drug extravasation, as with agents such as anthracyclines.

Allergic reactions depend on inducing an immune response from the host; thus, the reaction may be systemic rather than limited to skin manifestations.

Allergic drug reactions can be classified as exanthematous, urticarial, blistering, or pustular eruptions (eFig. 23-6). Skin reactions accompanied by fever are generally more serious systemic disorders. These may be life threatening in some cases, although afebrile skin reactions are not always minor (e.g., urticaria, angioedema).

Maculopapular skin reaction is an afebrile exanthematous eruption that is considered the most commonly encountered allergic skin reaction. Signs and symptoms of a maculopapular skin rash include erythematous macules and papules that may be pruritic. No fever, blisters, or pustules are present. The lesions usually begin within 7 to 10 days after starting the offending medication and generally resolve within 7 to 14 days after drug discontinuation. However, in a previously sensitized patient, the onset may be earlier (within 2–3 days). The lesions may spread and become confluent. Usual drug culprits include penicillins, cephalosporins, sulfonamides, and some anticonvulsant medications.

Drug hypersensitivity syndrome is an exanthematous eruption accompanied by fever, lymphadenopathy, and multiorgan involvement (including the kidneys, liver, lung, bone marrow, heart, and brain). Signs and symptoms usually begin 1 to 4 weeks after starting the offending drug, and the reaction may be fatal if not promptly treated.

This condition is also known as drug reaction with eosinophilia and systemic symptoms. It is commonly referred to by the acronym DRESS.

Usual drug culprits include allopurinol, sulfonamides, some anticonvulsants (barbiturates, phenytoin, carbamazepine, lamotrigine), and dapsone. For patients taking allopurinol, several factors increase the risk of serious skin reactions: renal impairment, hypertension, and use of thiadiazide diuretics or excessive allopurinol doses (i.e., not dose adjusted for renal impairment).  

Urticaria and angioedema are simple eruptions that are caused by drugs in about 5% to 10% of cases. Other causes include foods (likely the most significant offenders) and physical factors such as cold or pressure, infections, and exposure to latex. The condition may also be idiopathic.

Urticaria has been called the cutaneous manifestation of anaphylaxis. It is an IgE-related (type 1) allergic reaction that may be the first symptom of an emerging anaphylactic reaction. It is characterized by hives, extremely pruritic red raised wheals; angioedema; and mucous membrane swelling. These symptoms typically occur within minutes (anaphylactic) to hours (anaphylactoid) (eFig. 23-7). Individual lesions typically last less than 24 hours, but new lesions may continually develop. Offending drugs include penicillins and related antibiotics, aspirin, sulfonamides, x-ray contrast media, opiates, and others. Latex allergy is linked to the natural rubber latex (NRL) proteins, which bind with human IgE and result in contact urticaria, asthma, and anaphylaxis.  

Aside from latex gloves and medical products, other sources of NRL proteins include rubber insoles of shoes, balloons, inflatable mattresses, and poinsettia plants.

Serum sickness–like reactions are complex urticarial eruptions presenting with fever, rash (usually urticarial), and arthralgias, usually within 1 to 3 weeks after starting the offending drug. This is not a true serum sickness, and the patient does not have immune complex formation, vasculitis, or renal lesions.  

Fixed drug eruptions are simple eruptions presenting as pruritic, red, raised lesions that may blister. Symptoms can include burning or stinging. Lesions may evolve into plaques. These so-called “fixed” drug eruptions recur in the same area each time the offending drug is given. Lesions appear within minutes to days and

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disappear within days, leaving hyperpigmented skin for months (eFig. 23-8). Usual drug culprits include tetracyclines, barbiturates, sulfonamides, codeine, phenolphthalein, acetaminophen, and NSAIDs.

Stevens-Johnson's syndrome (SJS) and toxic epidermal necrolysis (TEN) are complex blistering eruptions that, together with erythema multiforme (EM), are known as acute bullous disorders. They are histologically similar and have been considered part of an "EM spectrum of diseases." EM may be considered a dermatologic disorder not associated with a drug reaction, whereas SJS and TEN are immune complex or cell-mediated allergic responses to offending agents, including drugs. Because of their histologic similarity, SJS and TEN have been considered either distinct disorders or progressions of the same disorder based on the percentage of skin area involved, and these two entities are often discussed together.

SJS and TEN are rare, severe, and life-threatening conditions with an acute onset (within 7–14 days of drug exposure). Patients present with generalized tender or painful bullous formation with accompanying systemic signs and symptoms, including fever, headache, and respiratory symptoms, that rapidly deteriorate. Lesions show rapid confluence and spread, resulting in extensive epidermal detachment and sloughing. This may result in marked loss of fluids; drop in blood pressure; electrolyte imbalances; and secondary infections, including *Staphylococcus epidermidis* and *methicillin-resistant Staphylococcus aureus* (MRSA). Usual drug culprits include sulfonamides, penicillins, some anticonvulsants (hydantoins, carbamazepine, barbiturates, lamotrigine), NSAIDs, and allopurinol. In children, a pooled analysis using data from two multicenter international case–control studies confirmed the following drug risk factors for SJS and TEN: antiinfective sulfonamides, phenobarbital, carbamazepine, and lamotrigine. In addition, acetaminophen use is suspected to increase the risk. However, cases in children only represented 10% of the population in both studies because the incidence of SJS and TEN increases with age.

*Acneiform drug reactions* are simple pustular eruptions caused by medications that induce acne (whiteheads or blackheads). The onset is usually about 1 to 3 weeks. Common drug culprits include corticosteroids, androgenic hormones, some
anticonvulsants, isoniazid, and lithium. Topical acne treatments can be used to manage symptoms if the offending drug cannot be discontinued or replaced.

**Acute generalized exanthematous pustulosis (AGEP)** is a complex pustular eruption characterized by acute onset (within days after starting the offending drug), fever, diffuse erythema, and many pustules. About 50% of patients have other cutaneous lesions, and 25% may have mucosal erosions. Generalized desquamation occurs 2 weeks later. Usual drug culprits include β-lactam antibiotics, macrolides, and calcium channel blockers.

**Other Drug-Induced Skin Reactions**

**Hyperpigmentation** of the skin (eFig. 23-8) may be related to increased melanin (e.g., hydantoins), direct deposition (e.g., silver, mercury, tetracyclines, antimalarials), or other mechanisms (some cytotoxic drugs, such as 5-fluorouracil, may cause banding on nails or tracking along veins).

**Photosensitivity** reactions (eFig. 23-9) may be phototoxic or photoallergic. Drugs that induce phototoxic reactions absorb UVA light, resulting in skin damage. Severity tends to be proportional to the drug dose. Usual drug culprits include amiodarone, tetracyclines, sulfonamides, psoralens, and coal tar.

Drug-induced photoallergic reactions result from UVA transformation of medications into allergens. In this syndrome, skin damage may occasionally spread beyond sun-exposed skin. These reactions require sensitization to the offending drug and are not dose related. Usual drug culprits include sulfonamides, sulfonyleureas, thiazides, NSAIDs, chloroquine, and carbamazepine.

**Management and Prevention of a Drug-Induced Skin Reaction** The first rule of thumb in managing skin reactions is to remember that not all are drug induced. In clinical practice, a diagnosis of drug-induced skin reaction is often a diagnosis of exclusion (i.e., the diagnosis is reached after other possible diagnoses have been ruled out). Potential foods and other causes have to be thoroughly investigated, and a detailed patient interview is important, as discussed earlier. Consistent with the assessment for any adverse drug reaction, the likelihood of a drug-induced skin reaction should be categorized as probable, possible, or not probable (unlikely). It may not be possible to categorize a drug-induced skin reaction as definite because this requires rechallenge with the potentially offending agent, and this should not be done with most reactions. Reactions are often unpredictable adverse drug reactions unrelated to the normal pharmacologic effects of the drug. Fortunately, unpredictable adverse drug reactions (e.g., allergic, idiosyncratic, carcinogenic) usually affect only a small percentage of patients.

If a drug-induced skin reaction is suspected, the most important treatment in nearly all cases is discontinuing the suspected drug as quickly as possible and avoiding the use of potential cross-sensitizers. In most instances, that is the only specific treatment required. In severe cases, a short course of systemic corticosteroids may be needed. In a few instances, it may be possible to continue the offending drug and “treat through” the reaction (e.g., ampicillin-associated maculopapular skin rash).

The next step is to control symptoms associated with the drug reaction (e.g., pruritus). Furthermore, any signs or symptoms of a systemic or generalized reaction may require additional supportive therapies specific to the severity and type of signs and symptoms seen. For high fevers, an antipyretic such as acetaminophen is more appropriate than aspirin or an NSAID because these may exacerbate skin lesions for some reactions. Depending on the type of skin reaction, the affected skin condition may take days to weeks or months to resolve.

For patients with life-threatening SJS or TEN, supportive measures such as maintenance of adequate blood pressure and fluid and electrolyte balance, use of broad-spectrum antibiotics and vancomycin for secondary infections, and IV immunoglobulin (IVIG) may all be appropriate. IVIG has been shown to halt disease progression and enhance recovery for SJS or TEN. The use of corticosteroids for SJS or TEN is somewhat controversial; although they may curb disease progression, they may also increase the risk of infection and thus contribute to increased mortality. If used, relatively high initial doses followed by rapid tapering as soon as disease progression halts is indicated. Refer to the Drug-Induced Skin Reactions case in the Pharmacotherapy Casebook to further explore management.

Patient education should be provided. Advice to the patient should include information about the suspected drug and potential drugs to avoid in the future and which drugs may be used. Potential cross-sensitizers should be identified. For patients with photosensitivity reactions, information should be provided about preventive measures such as the use of sunscreens and sun avoidance (eFig. 23-9). For patients with severe reactions (e.g., anaphylaxis), information about MedicAlert programs may be appropriate. Genetic predisposition has not been established for most drug-induced reactions, but for severe reactions such as SJS or TEN or hypersensitivity syndromes, the risk may be higher in first-degree relatives of affected patients.

**COMMON SKIN DISORDERS**

**Contact Dermatitis** Contact dermatitis is defined as an inflammation of the skin caused by irritants or allergic sensitizers. It describes and includes all skin reactions resulting from direct contact of the skin or mucous membranes with an exogenous agent, which may be a “foreign” molecule such as a drug or chemical, UV light, or temperature.

The skin or mucous membranes may react nonimmunologically or immunologically to an exogenous agent, resulting in either an irritant or allergic skin reaction as described earlier. However, the distinction between an allergic contact dermatitis (ACD) and irritant contact dermatitis (ICD) has become increasingly blurred: ICD is often a diagnosis of exclusion, as in cases when patch test results for ACD are negative.
Furthermore, an exogenous dermatitis can be superimposed on an endogenous skin eruption such as acne.\textsuperscript{14} Irritant effects may be considerably enhanced by occlusion. Contact dermatitis must also be distinguished from atopic dermatitis and other dermatologic conditions such as dyshidrotic dermatitis, lichen simplex dermatitis, acne rosacea, and other conditions. (See Chap. 79 for a discussion on atopic dermatitis.)

Contact dermatitis is a common skin problem for which 5.7 million physician visits are made per year.\textsuperscript{14} Almost any of the more than 85,000 chemicals in the world environment may be a skin irritant, and more than 3,700 substances have been identified as contact allergens.\textsuperscript{14} Although all age groups may be affected, ACD is rare in the first years of life (<10 years), but the rate of occurrence in older children may exceed that in adults.\textsuperscript{14}

The prevalences of ACD to individual allergens is similar in children and adults; allergens include nickel, fragrances, \textit{Toxicodendron} (formerly known as \textit{Rhus}), and rubber chemicals.\textsuperscript{14} There may be a slight female preponderance, presumably caused by exposure to specific contactants in jewelry and cosmetics.\textsuperscript{14}

The clinical presentation of contact dermatitis is that of an eczematous inflammation with erythema, vesicles, papules, crusting, fissuring, or scaling (\textit{eFigs. 23-10} and \textit{23-11}). The area may itch, burn, or sting and may be extremely pruritic. The severity may range from a mild, short-lived condition to a severe and persistent condition but is rarely life threatening.\textsuperscript{14} The gross and histologic appearances of ICD and ACD are often similar and may be difficult to distinguish.\textsuperscript{14} However, the rash or lesion for ICD is frequently localized, but for ACD, it may extend beyond the borders of the exposed area of contact, and the reaction may rarely become systemic (e.g., latex allergy).

ICD is generally a multifactorial response involving contact with a substance that chemically abrades, irritates, or otherwise damages the skin; cellular damage in ICD occurs via T cells (activated by irritant or innate mechanisms) releasing proinflammatory cytokines.\textsuperscript{14} ACD is the clinical manifestation of contact hypersensitivity;\textsuperscript{15} skin allergens tend to be low-molecular-weight molecules (hapten) that become immunogenic after conjugation with skin proteins.
proteins, resulting in a complex series of interactions that involve antigen-presenting Langerhans or other dendritic cells or CD4+ and CD8+ T cells, including interleukin-17–producing T_{h}17 cells.15

Because ACD is immunologically mediated, the patient may have tolerated exposure to the offending agent for some time, making it more difficult to pinpoint the culprit. Furthermore, the reaction may continue to develop for some time after the offending agent is removed.

The first goal of therapy in the management of contact dermatitis involves identifying, withdrawal, and avoidance of the offending agent. A thorough history, including work history, must be carefully reviewed for potential contactants. Nonwork activities such as hobbies (e.g., painting, gardening, camping, fishing) may be additional potential sources of exposure. Patch testing is the gold standard for identifying a contact allergen,14 but it is impractical to test an unlimited number of allergens.

Standard panels of allergens have been designed and validated by collaborative research dermatologic societies; however, these may account for only 25% to 30% of the most relevant contact allergens.14 Many patients need additional testing. Customized patch tests may be needed, depending on the patient’s exposure history.14

The most common causes of occupational contact dermatitis are chromium (leather exposure); rubber and rubber additives (gloves); nickel (work tools and metal working); food ingredients, including intact proteins (for food processing workers); fertilizers and pesticides (for farmers); and handwashing (disinfectants, irritants in soaps).14

The most common cause of plant dermatitis is Toxicodendron (Rhus) dermatitis. This genus includes poison ivy, poison oak, and poison sumac. These plants contain the offender urushiol oil, one of several oleoresins that are sensitizers and irritants. Urushiol oil is also found in mango skin, cashew nut oil, ginkgo (female) leaves, Japanese lacquer, and Indian marking ink.14

Cosmetics and personal hygiene products, such as hair conditioners and shampoos, nail polishes and hardeners, mascaras, foundations, antiperspirants and deodorants, and toothpastes, may all contain potential causes of contact dermatitis. The most important classes are fragrances, preservatives, formulation excipients, glues, and sunblocks;14 fragrances are among the most common causes of contact dermatitis in the United States.14

The second goal of therapy in contact dermatitis is to provide symptomatic relief while decreasing skin lesions. The affected skin may require supportive treatment such as the use of cold compresses to soothe and cleanse the skin or topical corticosteroids to help resolve the inflammatory process. Compresses are applied to wet or oozing lesions, removed, remoistened, and reapplied every few minutes for a 20- to 30-minute period. Calamine lotion or Burow solution (aluminum acetate) may be soothing.

Topical corticosteroids are considered the mainstay of treatment, and patients with ACD respond better than those with ICD. Generally, higher potency corticosteroids are used initially, switching to medium- or lower-potency corticosteroids as the condition improves.14 Refer to the Topical Corticosteroid Potency Chart in Chapter 78 (Table 78-2) for specific examples.

Other treatments may be effective. Tacrolimus ointment has been shown to be effective for nickel-induced ACD in a small randomized placebo-controlled clinical trial.10 Oatmeal baths and oral first-generation antihistamines may provide relief for excessive itching. If the affected areas are already dry or hardened (e.g., lichenification), wet dressings applied as soaks (without removal for up to 20–30 minutes) will soften and hydrate the skin (these should not be used for acute exuding lesions because the skin area may become macerated, further damaging its barrier function).

The third goal of contact dermatitis therapy is to implement preventive measures. Prevention involves both primary and secondary measures.

Primary prevention may be done in the workplace by initiating surveillance programs and educating workers about proper skin care and chemical exposure.

Secondary prevention involves the use of moisturizers to prevent dryness and fissuring of the skin. The efficacy of barrier creams is controversial.15 The damaged skin may need to be protected against secondary infections, at least until the acute stage subsides. Debris, produced by oozing, scaling, or crusting, should not be allowed to accumulate. Rarely, some workers may have persistent dermatitis despite removal of offenders, and a small number of workers change jobs because of severe recalcitrant occupational contact dermatitis.14

A final goal of therapy is to provide patient and caregiver information and support, helping them to develop coping strategies for contact dermatitis, as required.

Diaper Dermatitis

Diaper dermatitis, more commonly known as diaper rash, is most often seen in infants, although the condition may also be seen in older adults who wear diapers for incontinence. It is an acute inflammatory dermatitis affecting the buttocks, genital, and perineum regions that are covered by a diaper. The rash is erythematous, and severe rashes may have vesicles or oozing erosions. The rash may be infected by Candida species and present with confluent red plaques, papules, and pustules.

Management of diaper dermatitis includes frequent diaper changes, air drying (removing the diaper for as long as practical), gentle cleansing (preferably with nonsoap cleansers and lukewarm water), and the use of barriers. Commercial diaper wipes containing fragrance or alcohol should be avoided. Zinc oxide has astringent and absorbent properties and provides an effective barrier. Petroleum also provides a water-impermeable barrier but has no absorbent ability and may trap moisture.

Patients with candidal (yeast) diaper rash should be treated with a topical antifungal agent which is then covered by a barrier product. Imidazoles are the treatment of choice for this type of diaper rash. After the rash subsides, the antifungal agent should be stopped and the barrier product continued to prevent recurrence.

In severe inflammatory diaper rashes, a very low-potency topical corticosteroid (hydrocortisone 0.5% to 1%) may be used for short periods of 1 to 2 weeks.

Skin Cancers

Actinic keratoses are precursors to the development of skin cancers. UV radiation (with UVA a greater risk than UVB) may induce abnormal keratinocyte changes. These present as actinic keratoses. These lesions can develop into squamous cell or basal cell carcinomas.

Actinic keratoses are most often found in elderly fair-skinned patients and on chronically sun-exposed areas, such as hands, forearms, head, and neck.

Skin cancers include squamous cell carcinoma, basal cell carcinoma, and malignant melanoma.

Squamous cell carcinoma (SCC) is a skin cancer most commonly seen in older patients (eFig. 23-12). Risk factors include fair complexion, prolonged sun exposure, UV radiation (including PUVA used for treatment of psoriasis), and long-term immunosuppression (including the use of biologic response modifiers for treatment of conditions such as psoriasis). Most SCCs present as firm, flesh-colored, or erythematous papules or plaques. Treatment is primarily via surgical excision.

Basal cell carcinoma (BCC) is a very common skin disorder (eFig. 23-13). BCC most commonly presents as a pigmented nodule on the head and neck. Treatment may vary based on histology and may involve surgical excision as well as the use of
topical agents such as imiquimod, or antineoplastic agents such as 5-fluorouracil.

Malignant melanoma, unless detected early and excised, often produces systemic metastases. Its incidence has increased over the past few decades, with an estimated one in 65 Americans developing melanoma during their lifetimes.17

A changing mole is often a harbinger of melanoma. These are detected by skin examination; dermatologists often have melanoma clinics for this purpose. Moles are examined for asymmetry, irregular borders, variegated colors, and size (eFig. 23-14). Full-body skin


examinations are important in screening for melanoma because it can occur anywhere on the skin.17 Other risk factors include prolonged sun exposure and the ability to tan, family history, and drug treatments such as PUVA (psoralen plus UVA) or biologic response modifiers used for psoriasis.

Suspicious pigmented lesions should be fully excised as soon as possible rather than biopsied; malignant melanomas are best diagnosed and microstaged with an excisional biopsy of the entire lesion.18 Delayed diagnosis of malignant melanoma directly affects patient survival adversely.17 Treatment may also include systemic antineoplastic therapy, such as temozolomide or dacarbazine for metastatic melanoma.

CONCLUSIONS

This chapter provided coverage about the skin and associated age-related changes, lesion assessment and recognition, drug-induced skin reactions, contact dermatitis, diaper dermatitis, and briefly discussed common skin cancers. Other common skin disorders are covered in the following three chapters, including acne (see Chap. 77), psoriasis (see Chap. 78), and atopic dermatitis (see Chap. 79). Skin and soft tissue infections (see Chap. 88) and parasitic diseases (see Chap. 93) are detailed later in this text.

ABBREVIATIONS

ACD allergic contact dermatitis
AGEP acute generalized exanthematous pustulosis
BCC basal cell carcinoma
EM erythema multiforme
ICD irritant contact dermatitis
IVIG IV immunoglobulin
MRSA methicillin-resistant Staphylococcus aureus
NRL natural rubber latex
NSAID nonsteroidal antiinflammatory agent
PUVA Psoralens + ultraviolet A light
SCC squamous cell carcinoma
SJS Stevens-Johnson syndrome
SPF a sun protection factor
TEN toxic epidermal necrolysis
UV ultraviolet
UVA ultraviolet A

REFERENCES