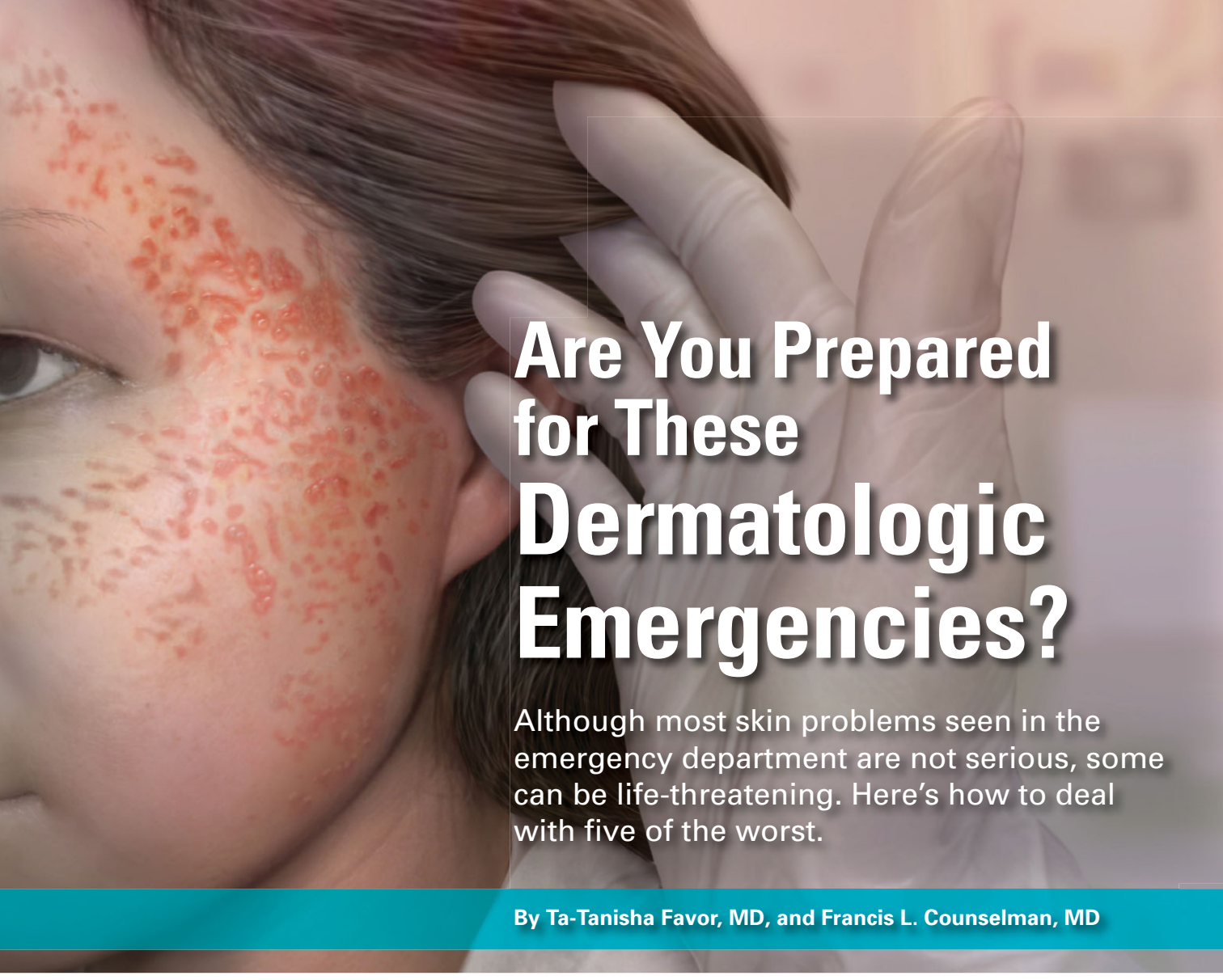

Are You Prepared for These Dermatologic Emergencies?

Although most skin problems seen in the emergency department are not serious, some can be life-threatening. Here's how to deal with five of the worst.

By Ta-Tanisha Favor, MD, and Francis L. Counselman, MD

By the way, doc, what about this rash?" is a familiar patient question in the emergency department. Although skin problems are common in this setting, they are usually secondary complaints, not primary ones. Dermatologic disorders can range from simple infections (such as cellulitis) to drug eruptions (such as those caused by sulfonamides) to manifestations of systemic disease (such as Janeway lesions with endocarditis). While most skin problems are not life-threatening, emergency physicians need to be able to recognize those that are and treat them appropriately. This article reviews the pathophysiology, clinical presentation, management, and complications of five dermatologic emergencies.

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STEVENS-JOHNSON SYNDROME

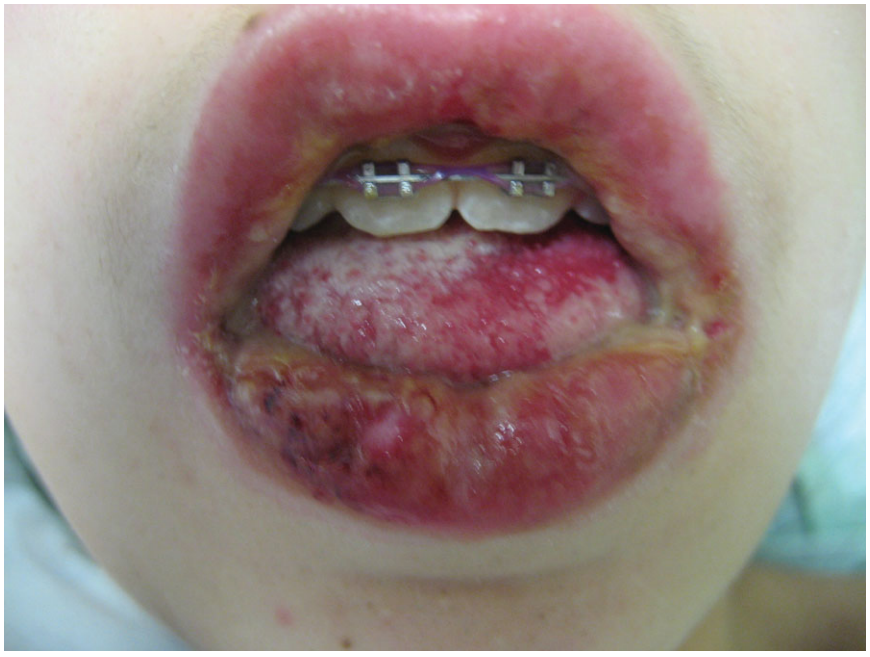
Stevens-Johnson syndrome (SJS) is a hypersensitivity reaction involving both the skin and mucous membranes, resulting in blistering and skin necrosis. It is a severe form of erythema multiforme. Although SJS is a rare condition, it can lead to a potentially life-threatening event.

Pathophysiology. Identifiable causes of SJS include infection (both viral and bacterial) and drug reactions (most common); it may also be idiopathic. Medications often implicated include sulfonamides, quinolones, anticonvulsants, nonsteroidal anti-inflammatory drugs, antimalarials, and allopurinol. The exact mechanism of action is unknown, but the syndrome is most likely due to an immune complex reaction.

Clinical presentation. The syndrome begins with several days of flu-like symptoms, followed by the development of skin lesions. These lesions are usually red or purplish and can be macular or papular,

but they are usually bullous. Detachment of skin may occur, but it usually involves less than 10% of the body surface area. The hallmark of SJS is involvement of the mucous membranes in the mouth, eyes, and genital areas (see image). In this severe form of erythema multiforme, systemic involvement is common with diarrhea, pneumonia, and hematuria.

Management. While in the emergency department, the first and most important element of treatment is to discontinue drugs that may be causing SJS. A study conducted by Garcia-Doval suggests that early discontinuation of the offending agent can reduce the mortality rate by 30%. Otherwise, treatment is supportive and symptomatic. Fluid status and electrolyte replacement must be addressed early, along with pain control and wound care. A burn specialist should also be consulted early, and denuded areas should be treated as burns and covered with compresses of saline or Burow solution. Underlying diseases and secondary infection must be identified and treated. Prophylactic treatment with antibiotics is not indicated, because this leads to the emergence of resistant organisms and increases mortality.



>Hypersensitivity reaction. Stevens-Johnson syndrome with mucous membrane involvement.

Complications. Common complications include esophageal strictures, tracheobronchial shedding with resultant respiratory failure, secondary infection with sepsis, and renal failure. There is an overall 5% mortality rate associated with SJS.

TOXIC EPIDERMAL NECROLYSIS

Toxic epidermal necrolysis (TEN), also known as Lyell syndrome, is a life-threatening dermatologic condition associated with large areas of detachment of the epidermis from the dermal layer of the skin. This syndrome and SJS share many predisposing and clinical similarities and are considered by some experts to be the same process. The major difference is that SJS usually involves less than 10% of the body surface area, while TEN usually involves more than 30%.

Pathophysiology. About 95% of patients with TEN have a history of medication use, compared to 80% of those with SJS. Offending medications are the same as for SJS. Although these medications are thought to initiate an immune-related cytotoxic reaction, there is an overexpression of tumor necrosis factor-alpha in the epidermis, promoting apoptosis in patients suffering from TEN. This may account for the more generalized reaction.

Clinical presentation. Toxic epidermal necrolysis is defined as detachment of skin involving more than 30% of the body surface area. Patients usually present with a 7- to 10-day history of arthralgia, malaise, and fever. Mucosal lesions precede cutaneous involvement, with erythema of the eyes, nose, and mouth. Within hours, the erythematous areas become confluent and painful, followed by a bullous eruption. At this point, the patient may exhibit the Nikolsky sign—lateral pressure causing desquamation of the underlying skin, leaving a denuded area (see image on page 20). *continued*

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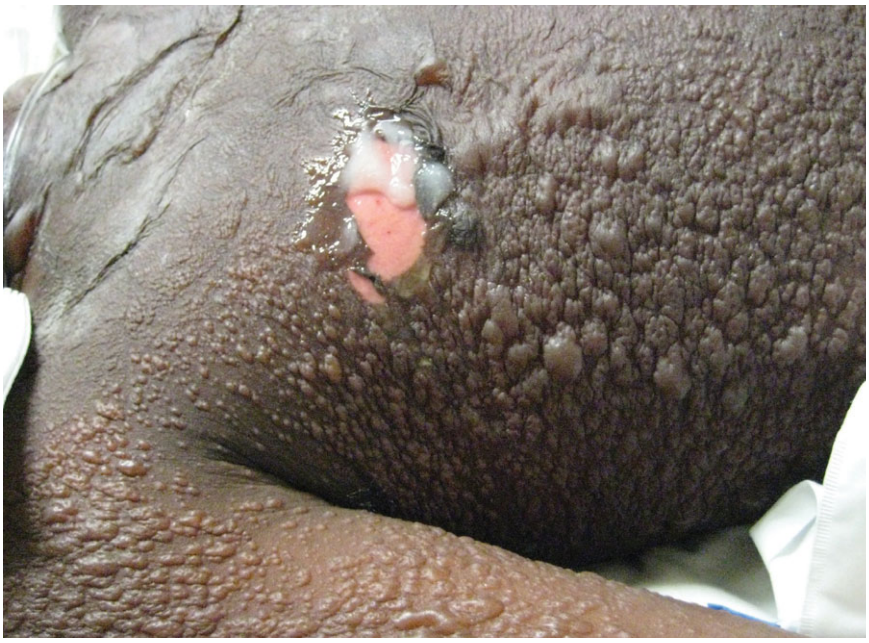
A study suggests that early discontinuation of the offending agent in Stevens-Johnson syndrome can reduce the mortality rate by 30%.



> Nikolsky sign. Skin detachment is observed in toxic epidermal necrolysis.

Management. When a patient presents with signs of TEN, clinicians should have a high index of suspicion and stop the offending drug immediately. Attention should be focused on respiratory status, because some patients may require intubation secondary to pulmonary edema or severe mucosal sloughing. Lesions should be treated like burns, and the patient's hemodynamic stability should be ensured with aggressive IV fluid replacement, monitoring and replacement of electrolytes, and transfer to a burn unit or ICU for further management. Antibiotics should be used only for an established infection, such as pneumonia, or signs of sepsis. The use of steroids is controversial. High-dose intravenous immunoglobulin has been used in the treatment of TEN, but controlled trials with meaningful numbers are lacking.

>>FAST TRACK<<

Some patients with toxic epidermal necrolysis may require intubation secondary to pulmonary edema or severe mucosal sloughing.

Complications. There is a 40% mortality associated with TEN, and the syndrome may take one to three weeks before complete resolution. Other serious sequelae relate to the mucous membranes. In all cases of SJS and TEN, early ophthalmologic consultation is advised. Synechiae, corneal ulcers, meibomian gland dysfunction, panophthalmitis, and blindness are all potential complications. Other sequelae include slow healing of the vaginal, urethral, and anal mucosae that may persist for months, potentially resulting in strictures. Further complications include loss of nails, esophageal strictures, pneumonia, and pigmentation abnormalities.

STAPHYLOCOCCAL SCALDED SKIN SYNDROME

Also known as Ritter disease, staphylococcal scalded skin syndrome (SSSS) is caused by a particular strain of *Staphylococcus aureus*, which releases an exotoxin that leads to blistering of the epidermal layer of the skin. This disorder is typically seen in children and rarely in adults.

Pathophysiology. The strain of *S. aureus* responsible for causing SSSS has been shown to produce epidermolytic toxins. The two toxins identified—exfoliative toxin A (ETA) and erythrogenic toxin B (ETB)—are thought to cause loss of desmosome-mediated cell adhesion within the superficial epidermis. Exfoliative toxin A is the most commonly secreted toxin thought to bind to fillagrin, an intracellular protein that anchors desmosomes in the granular layer cells. This binding is thought to cause epidermal splitting, resulting from rupture of desmosomes by the proteolytic activity of the toxin. It is believed that predisposing factors must be present to facilitate this mechanism.

Healthy adults rarely get SSSS, because most of them probably produce an antibody against the ETA and ETB exotoxins, inhibiting their activity. Approximately 90% of adults over age 40 demonstrate antibodies, whereas only 30% of children between ages 2 months and 2 years have them. Risk factors for SSSS in adults include immunosuppression (for example, in AIDS) and renal failure.

Clinical presentation. Staphylococcal scalded skin syndrome typically occurs in children under age 5. The diagnosis is based on clinical, microbiological,

and histologic findings. Children typically present with a prodrome of pharyngitis and conjunctivitis, followed by the development of tender erythematous patches, malaise, and fever within a 48-hour period. Flaccid bullae eventually develop that are easily denuded, yielding the scalded skin appearance. Erythematous patches and bullae may occur in a variety of places, including the face, neck, extremities, and mucous membranes.

The disease occurs in three phases: initial (erythroderma), exfoliation, and desquamation. Obtaining skin and blood samples for cultures and immunoassays for the detection of the exotoxin-producing bacterium is important in establishing the diagnosis. Histologically, skin biopsies made at the edge of a lesion demonstrate subcorneal splitting along the granular cell layer, usually with no involvement of the dermal layer of skin. The disease course is generally 7 to 10 days.

Management. Initial management begins with intravenous fluid resuscitation and support of organ function. Blood cultures should be obtained and the source of infection identified and addressed. An early attempt to decrease the bacterial load by initiating parenteral antistaphylococcal antibiotics, such as flucloxacillin/dicloxacillin (beta-lactamase inhibitors) plus clindamycin, is recommended. In penicillin-allergic patients, consider vancomycin. Blisters should be left intact and eroded areas covered with petrolatum gauze to reduce further trauma. The use of corticosteroids is controversial and not recommended.

Complications. Mortality in childhood SSSS is approximately 4% and is associated with widespread skin involvement and sepsis. However, the mortality rate in adults is reported to be greater than 60%, mainly due to the underlying factors that predisposed the patient to the illness.

ANGIOEDEMA

Urticaria and angioedema are common cutaneous vascular reactions. Urticaria is characterized by pruritic, edematous, lightly erythematous wheals of varying sizes, frequently associated with central clearing. Angioedema is similar to urticaria except that it involves deeper skin layers, such as the dermis and subcutaneous tissue. Because life-threatening reactions are associated with angioedema, our focus will be on this condition.

Pathophysiology. There are five major forms of angioedema, with varying mechanisms of action. *Allergic angioedema*—a type 1 hypersensitivity reaction triggered by allergens, such as medications and foods—results in activation of mast cells leading to the release of histamine and other vasoactive mediators. This is the most common cause of angioedema. *Hereditary angioedema* results from a deficiency in the C1 esterase inhibitor (C1 INH) that regulates the activity of the complement component C1, the first step in the classic complement cascade. This autosomal dominant deficiency results in unregulated activity of vasoactive mediators, such as plasmin, bradykinin, and kallikrein, resulting in vasodilation, capillary leakage, and edema. Attacks are usually random. *Acquired angioedema* also results from C1 INH deficiency; however, it is thought to be an autoimmune condition and most commonly presents after age 40. Acquired C1 INH deficiency is also seen with lymphoproliferative disorders. *Angiotensin-converting enzyme (ACE) inhibitor–induced angioedema* results from elevated levels of bradykinin. The incidence of this form is highest during the first month of taking an ACE inhibitor; however, the reaction can occur at any time, even many years later. *Idiopathic angioedema* is a diagnosis of exclusion, after all the other forms have been ruled out.

Clinical presentation. A detailed history is important in identifying a causative agent for the reaction, including foods, medications, and family history. Because the reaction can occur months after a patient has taken an ACE inhibitor, it is easy to overlook. Angioedema may occur with or without urticaria. Patients may present with nonpitting swelling of the lips, tongue, and face, but swelling may also occur in other areas. Involvement of the larynx can become life-threatening and should be suspected if the patient complains of a lump in the throat or difficulty breathing. Gastrointestinal symptoms caused by visceral edema may result in varying degrees of intestinal obstruction. Typical symptoms of gastrointestinal tract involvement include anorexia, nausea, vomiting, and crampy abdominal pain.

>>FAST TRACK<<

Risk factors for staphylococcal scalded skin syndrome in adults include immunosuppression and renal failure.

Management. Airway protection is the first priority. Life-threatening reactions can occur, particularly

with laryngeal edema. Physicians should be prepared to intubate early, particularly if laryngeal edema is a concern. If an offending agent is identified, such as an ACE inhibitor like captopril, the drug must be discontinued immediately. In the acute setting, intravenous antihistamines (such as diphenhydramine), corticosteroids, and epinephrine have been used for severe reactions with varying success. In patients with a known history of hereditary angioedema, the treatment of choice is C1 INH concentrate given intravenously. For acquired angioedema, C1 INH concentrate or fresh-frozen plasma given intravenously are the treatments of choice. Through a cascade of mechanisms, C1 INH concentrate prevents bradykinin release and subsequent symptoms. Fresh frozen plasma, which also contains C1 INH, is not recommended as therapy for hereditary angioedema if there is suspected laryngeal edema because of the potential for a paradoxical reaction such as exacerbation of the edema.

Complications. Laryngeal, nasal, and sinus edema may lead to respiratory compromise and death from suffocation. If undiagnosed, mortality from hereditary angioedema can be as high as 30% to 40%, primarily due to upper airway obstruction.

NECROTIZING FASCIITIS

Necrotizing fasciitis is a soft tissue infection that evolves rapidly to the superficial fascial layer and may develop into a potentially life-threatening event. It is more likely to occur in sites where skin integrity has been compromised, such as a surgical incision, needle puncture, insect bite, or site of motor vehicle trauma. However, it can also result from hematological spread.

Pathophysiology. Polymicrobial infections involving both aerobic and anaerobic bacteria are the most common cause of necrotizing fasciitis. Several common bacteria are involved in this disease process, including *S. aureus*, *Escherichia coli*, *Bacteroides*, and *Clostridium* species. Underlying comorbidities that affect the ability to mount a proper immune response (for example, diabetes mellitus, peripheral vascular disease, renal failure, and malignancy) predispose a patient to necrotizing fasciitis.

>>FAST TRACK<<

When selecting antibiotic therapy in necrotizing fasciitis, remember that certain populations are at risk for methicillin-resistant *Staphylococcus aureus*.

It is estimated that group A *Streptococcus*, as a single organism, causes up to 10% of cases of necrotizing fasciitis. This is typically seen in young, healthy patients, probably because this population does not have certain protective antibodies due to lack of previous exposure. Other less common pathogens implicated are *Haemophilus influenzae* type b, *Pseudomonas aeruginosa*, *Aeromonas hydrophila*, and *Vibrio vulnificus.*

Clinical presentation. Necrotizing fasciitis should be suspected if the patient's level of pain is out of proportion to skin findings. Patients may initially present with fever and an area of erythematous skin that may be mistaken for cellulitis. Clinical signs become more obvious as the disease progresses. Within 36 hours, the skin may transform from an erythematous area to a blue-gray discoloration. Violaceous bullae may be present. Or, a patient may present with altered mental status, fever, and septic shock. Be sure to thoroughly examine the patient's skin, especially the extremities, the most common site of infection.

Management. Intravenous fluid resuscitation, antibiotics, and extensive surgical debridement (fasciotomy) are the recommended treatments. The goal of surgery is to remove necrotic tissue, which may involve skin, fascia, and muscle. Once this is performed, hemostasis is usually improved. However, multiple debridements with surgical reexploration may be needed to ensure absolute removal of all necrotic tissue.

With regard to antibiotic therapy, a broad-spectrum approach with a beta-lactamase inhibitor and clindamycin is recommended until the results of the initial Gram stain or culture of aspirate are available. When selecting antibiotic therapy, remember that certain populations are at risk for methicillin-resistant *S. aureus*, such as military recruits, members of sports teams, or recently hospitalized patients. Immunocompromised patients may be at risk for *Pseudomonas*. Hyperbaric oxygen therapy may be considered as an adjunctive therapy, but its use remains controversial.

Complications. On occasion, debridement is not successful and amputation is necessary. Mortality rates range from 20% to 40%, with higher rates in patients whose immune responses are impaired.

EARLY RECOGNITION IS CRITICAL

Emergency physicians see many types of rashes and skin disorders in their daily practice. Because of the

severe and life-threatening nature of the five dermatologic disorders discussed here, it is critical that you be able to recognize them early and initiate treatment immediately. □

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