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Derm emergencies—detecting early signs of trouble

Life-threatening dermatologic conditions do not always present with classic findings. This review—and the accompanying images—will help you recognize and respond to them without delay.

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PRACTICE RECOMMENDATIONS

› *Consider starting a course of systemic corticosteroids for a patient with erythroderma, fever, and multiorgan involvement when you strongly suspect a drug reaction is the cause—and have ruled out infection.* (C)

› *Suspect Stevens–Johnson syndrome/toxic epidermal necrolysis (SJS/TEN) in a patient with widespread and rapidly progressive desquamation, fever, hypotension, and end-organ involvement.* (C)

› *In assessing the severity of skin pain, consider the location; involvement of the eyes, perineum, and hands are associated with greater morbidity.* (C)

Strength of recommendation (SOR)

(A) Good-quality patient-oriented evidence
(B) Inconsistent or limited-quality patient-oriented evidence
(C) Consensus, usual practice, opinion, disease-oriented evidence, case series

The usual approach to dermatologic conditions—honed pattern recognition, a deliberate differential diagnosis, and empiric treatment with longer follow-up—runs counter to the response that dermatologic red flags require. Because patients with signs and symptoms associated with dermatologic emergencies have the potential for rapid clinical deterioration, urgent action is paramount.

With this in mind, we've focused on 4 red flags—erythroderma, desquamation, skin pain, and petechiae/purpura—as a starting point, rather than presenting a list of dermatologic emergencies and discussing each diagnosis in turn. The text, tables, and images on the pages that follow will increase your awareness of dermatologic presentations that require an immediate response and help you differentiate between signs and symptoms of serious skin disorders and benign findings that might be described as red flag mimics (**TABLE 1**).

Erythroderma: Red skin that's life-threatening

From an etymological perspective, "erythroderma" simply means red skin. Clinically, however, it is defined as extensive erythema, typically covering ≥90% of the skin surface (**FIGURE 1**). True erythroderma can be life-threatening and must always be considered a dermatologic emergency.[1,2]

Diligent monitoring of the speed of progression and the presence of fever, systemic symptoms, and multiorgan dysfunction is essential. In a case review of 56 children who presented to an emergency department with fever and erythroderma, 45% progressed to shock.[3] Some common causes of erythroderma are psoriasis; contact, atopic, and seborrheic dermatitis; pityriasis rubra pilaris; cutaneous T-cell lymphoma; drug reaction; and toxic shock syndrome (TSS).[4]

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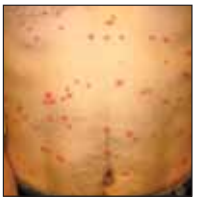


Derm emergency or red flag mimic? You decide

Peter A. Lio, MD

See page 67

TABLE 1

Conditions that mimic dermatologic emergencies

Red skin	
Diagnosis	*Key discriminating features*
Allergic contact dermatitis	Itchy, rather than painful
Red man syndrome	History of vancomycin infusion
Stasis dermatitis	Location (lower extremities), pruritus
Sunburn	History, sun-exposed areas
Desquamation	
Diagnosis	*Key discriminating features*
Bullous impetigo	Localized; no systemic manifestations
Postinfectious desquamation	Subungual location common; occurs during convalescent phase of illness
Petechiae and purpura	
Diagnosis	*Key discriminating features*
Local trauma	History and location
Pigmented purpuric dermatosis	History and healthy appearance
Viral exanthema	Healthy appearance

Is it a drug reaction? Erythroderma, fever, and evidence of multiorgan involvement in a patient taking any medication—not just a new one—prompts consideration of a drug reaction. Antiepileptics, dapsone, and sulfonamides are the most frequent offenders.[5]

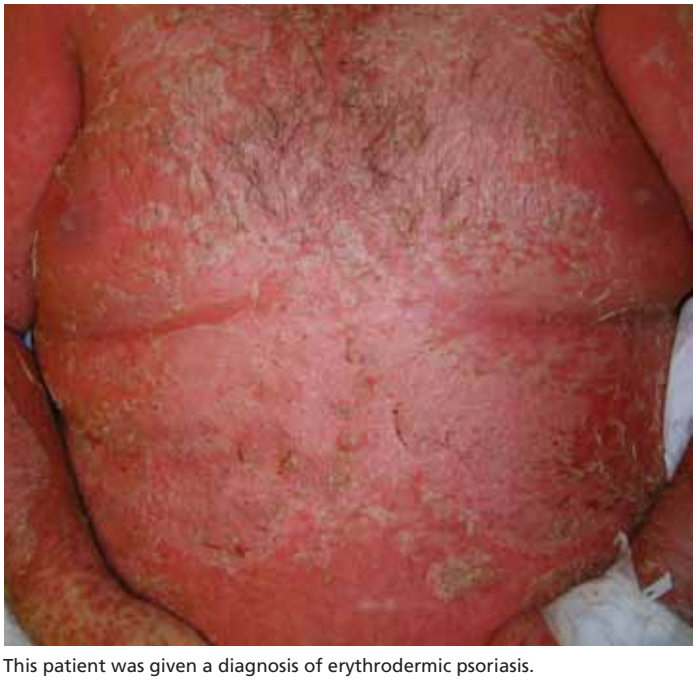
DRESS syndrome (drug reaction with eosinophilia and systemic symptoms) is characterized by fever, lymphadenopathy, elevated liver enzymes, and leukocytosis with eosinophilia, as well as erythroderma. The rash may be urticarial or morbilliform in appearance; petechiae, purpura, and blisters may be present, as well.

Because fever, leukocytosis, and transaminitis are also suggestive of an infectious etiology, DRESS syndrome is frequently overlooked. As a result, its true incidence is unknown. Estimates range from about one in 1000 to one in 10,000 drug exposures.[6]

In addition to discontinuing the medication, treatment for DRESS calls for systemic corticosteroids—which may actually be harmful when infection, rather than a drug reaction, is the cause. Thus, it is necessary to maintain a high index of suspicion and to thoroughly review the medication history of any patient who presents with erythroderma and systemic symptoms.

FIGURE 1

Erythema covering the chest and arms

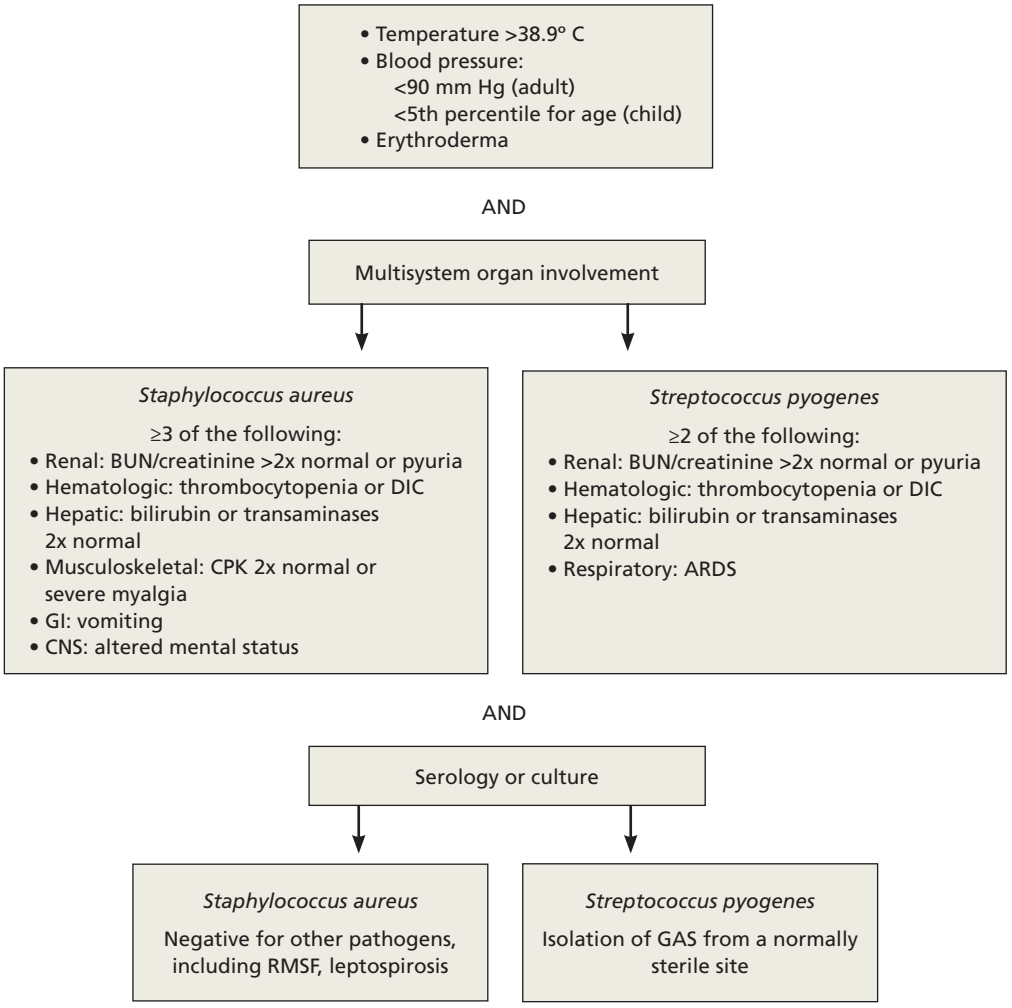


PHOTOS COURTESY OF: PETER A. LIO, MD, AND ALISA MCQUEEN, MD

This patient was given a diagnosis of erythrodermic psoriasis.

FIGURE 2

Diagnostic criteria for toxic shock syndrome



ARDS, acute respiratory distress syndrome; BUN, blood urea nitrogen; CNS, central nervous system; CPK, creatinine phosphokinase; DIC, disseminated intravascular coagulation; GAS, group A *Streptococcus*; GI, gastrointestinal; RMSF, Rocky Mountain spotted fever.

Adapted from: Pickering LK, et al, eds. *Red Book: 2009 Report of the Committee on Infectious Diseases.* 2009.[7]

Because fever, leukocytosis, and transaminitis are also suggestive of an infectious etiology, DRESS syndrome is frequently overlooked.

When to suspect toxic shock syndrome. Consider TSS in any patient with erythroderma and hypotension, as well as laboratory evidence of end-organ involvement (including transaminitis, elevated creatinine, anemia, thrombocytopenia, and elevated creatinine kinase). Diagnostic criteria are detailed in **FIGURE 2**.[7] Group A *Streptococcus* and *Staphylococcus aureus* are the classic infectious causes, but other bacteria have been implicated, as well. In most cases, the responsible bacterium is not known initially.

Because the toxins produced by these streptococcal and staphylococcal strains act as superantigens that fuel the immune response and worsen the shock, patients with a presumptive diagnosis of TSS should begin empiric treatment with an antimicrobial agent that inhibits toxin synthesis, such as clindamycin, immediately.[8,9]

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Desquamation/blistering: Act quickly when it's widespread

Although desquamation can be seen in benign skin conditions, widespread desquamation with or without bullae requires careful evaluation and a rapid response. Separation, either at the dermal-epidermal junction or intraepidermally, raises the specter of 2 emergent conditions: the Stevens–Johnson syndrome/toxic epidermal necrolysis (SJS/TEN) spectrum and staphylococcal scalded skin syndrome (SSSS). Mucosal involvement is another red flag, if the patient appears ill and the desquamation is progressing rapidly. Conjunctival involvement, in particular, is associated with greater morbidity, and a consult with an ophthalmologist is prudent.

Rapid progression is a hallmark of SJS/TEN. Desquamation that's widespread and rapidly progressive in a patient with fever, hypotension, and end-organ involvement is suggestive of SJS/TEN (**FIGURE 3**). Medications, including allopurinol, antimicrobials, and antiepileptics, are frequent culprits.[10,11]

Nonsteroidal anti-inflammatory drugs (NSAIDs) have also been linked to SJS/TEN.[10] Given their widespread use (1-2 per million users per week), however, the likelihood of NSAIDs leading to SJS/TEN is exceedingly low.[12]

Signs and symptoms of SJS/TEN may include target lesions with dusky centers, erythroderma, or significant pain without any visible skin abnormality, typically accompanied by fever and malaise. Widespread sloughing of the skin may be seen within several hours.[11]

Admission to an intensive care unit—preferably a burn unit—is suggested for aggressive fluid resuscitation and management of shock and end-organ dysfunction. Intravenous immunoglobulin G (IVIG) and steroids are often used, although there is little consensus as to the most effective treatment.[13] Mortality from TEN approaches 50%.[13]

SSSS can present at any age. Newborns often present with SSSS during their first week of life: Widespread erythema is quickly followed by fragile blisters, which may have already ruptured by the time the infant receives medical attention. Mucosal surfaces are not typically involved. Nikolsky's sign (separation of the upper epidermis with gentle pressure) is a classic finding.

Infants with SSSS are frequently irritable, suggesting that the skin may be painful. Cultures from unruptured bullae will be negative as the blisters represent a cutaneous reaction to an infection, rather than a skin infection, but blood, urine, and nasopharynx cultures may be positive. Systemic treatment with nafcillin or oxacillin should be initiated, and supportive skin care provided.[14,15] Clindamycin or vancomycin should be used in parts of the country in which methicillin-resistant *Staphylococcus aureus* is prevalent. In very young infants, the outcome of SSSS is generally favorable. Not so with adults.

Because mature kidneys have a greater ability to excrete exfoliative toxins, SSSS primarily affects adults with significant comorbidities—and has a much poorer prognosis.[16] You may also see chronic autoimmune bullous diseases, such as bullous pemphigoid and pemphigus vulgaris, with widespread desquamation and blistering, in the adult population. Untreated, the secondary infection and electrolyte disturbances from fluid

FIGURE 3

Desquamation, full-thickness epidermal necrosis on the upper back

Erythroderma and widespread denudation on the upper back of a patient who was given a diagnosis of toxic epidermal necrolysis.

loss associated with pemphigus vulgaris can be fatal.

Desquamation is a late finding in Kawasaki disease. Desquamation is often cited as a potential skin finding in children with Kawasaki disease (KD) (**FIGURE 4**), but usually not until the convalescent stage.[17] (Desquamation may also appear during the recovery period of several other infections, including scarlet fever and TSS.) IVIG can prevent coronary aneurysm, the major complication of KD, but only if it is administered during the acute phase of the illness. Therefore, early diagnosis of KD (**TABLE 2**)[18]—before desquamation occurs—is critical.[19]

Skin pain is always a red flag

Widespread skin pain should always be taken seriously, as it is rarely associated with minor dermatoses.[20] Infectious cellulitis is the most likely diagnosis of a painful erythematous skin lesion. Patients with cellulitis do not usually have erythroderma, as the affected area tends to be very localized.

Cellulitis may be over- or undertreated. Once cellulitis has been diagnosed, the next thing to consider is severity. A recent retrospective study found that misclassification of skin and soft-tissue infections may result in both significant *overtreatment* of mild soft-tissue infections and dangerous *undertreatment* of severe infections, with consequent morbidity.[21]

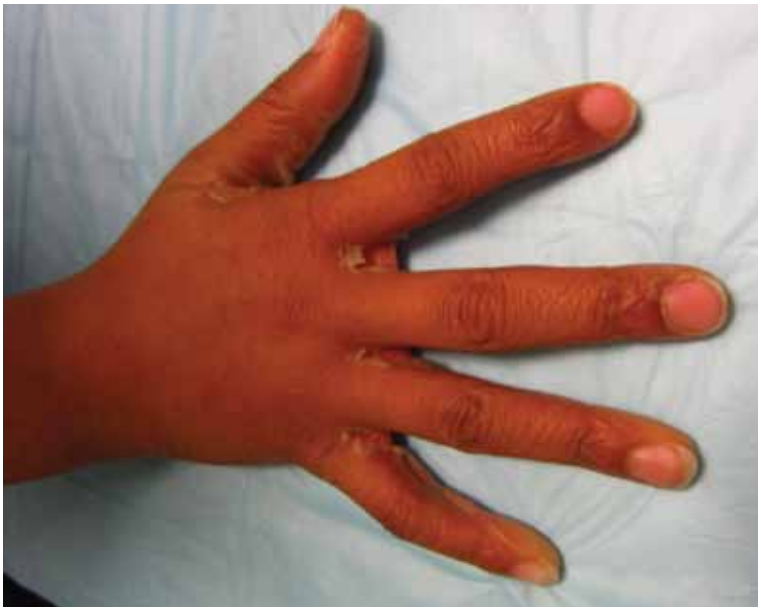
Location is a key consideration, as cellulitis in certain locations—including the eye, perineum, and hand—carries an increased risk of morbidity. Orbital cellulitis—which may be characterized by proptosis, ophthalmoplegia, and pain with extraocular movements—most often results from initial sinusitis, and can lead to vision loss, intracranial infection, and significant invasive disease. Prompt antimicrobial therapy and urgent ophthalmologic consultation are essential, as operative drainage may be required.[22,23]

When the perineum is involved, a careful exam must be performed to determine the limits of the affected area. Although Fournier's gangrene is uncommon, it is a life-threatening infection. In one small retrospective study, more than half of the patients presented with a perianal abscess.[24]

Similarly, the hand is vulnerable to sig-

FIGURE 4

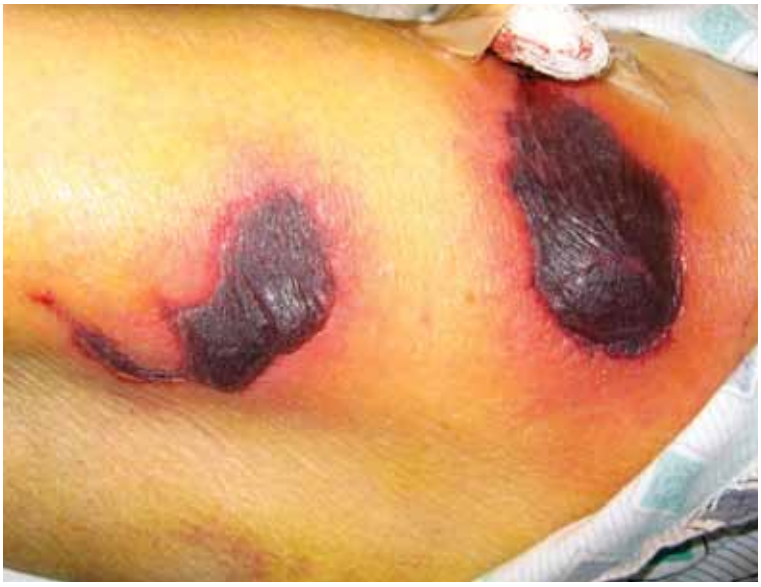
Desquamation on a young patient



Desquamation associated with Kawasaki disease (shown on the hand of a child) usually occurs during the convalescent stage.

FIGURE 5

Signs of a life-threatening condition



Hemorrhagic bullae with surrounding erythema on the lateral thigh of a patient with purpura fulminans from bacterial sepsis.

TABLE 2
Diagnostic criteria for Kawasaki disease

Fever for ≥5 days, and 4 out of 5 criteria (required):
1. Nonexudative bilateral conjunctivitis
2. Mucosal fissuring, injection, or strawberry tongue
3. Extremity erythema or edema
4. Polymorphous rash
5. Unilateral cervical lymphadenopathy (>1.5 cm diameter)
Supporting findings:
1. Thrombocytosis and other evidence of inflammation (elevated ESR, CRP)
2. Sterile pyuria
3. Transaminitis
4. Hyponatremia

CRP, C-reactive protein; ESR, erythrocyte sedimentation rate.

Source: Kawasaki Disease Research Committee. *Pediatr Int.* 2005.[18]

Desquamation with conjunctival involvement, in particular, is associated with greater morbidity, and a consultation with an ophthalmologist is prudent.

nificant infection, particularly if it is inoculated with bacteria from human mouth flora (the well-described "fight bite"). In a review of 100 cases of human fight bites, 18 patients ultimately required amputation.[25]

Early necrotizing fasciitis is often missed. Clinicians generally expect painful lesions to also have erythema, swelling, and increased warmth—the cardinal signs of inflammation. As a result, early necrotizing fasciitis, which initially presents with pain out of proportion to other dermatologic findings, may be overlooked. In fact, pain can precede significant skin findings by 24 to 48 hours; prior to that, only mild erythema or swelling (with minimal pain, in some cases) may be evident.[26,27]

The general pattern, however, is for a site with exquisite tenderness to evolve into a smooth, swollen area, then to develop dusky plaques and late-stage full thickness necrosis with hemorrhagic bullae.[26] At that point, necrosis can render the skin insensate. Case reviews have found necrotizing fasciitis to be protean, with only 3 findings—erythema, edema, and tenderness beyond the expected lesion borders—present in most patients.[27] Assiduous attention to skin pain in the presence of any other skin manifestation is the key to early diagnosis and rapid treatment.

Petechiae/purpura may be severe or benign

Petechiae are flat, pinpoint, nonblanching spots caused by intradermal hemorrhage associated with a wide variety of conditions, ranging from benign (local trauma) to severe (eg, disseminated intravascular coagulation [DIC] and sepsis). Similarly, purpura—larger lesions that may be palpable—can accompany less severe diseases, such as Henoch-Schönlein purpura (HSP), or life-threatening conditions like sepsis and DIC (**FIGURE 5**). Here, as in many other dermatologic conditions, the key differentiating features are location (local vs diffuse), speed of progression, and signs and symptoms of systemic illness.

Localized petechiae are common with direct trauma, as well as barotrauma associated with coughing, vomiting, or even asphyxiation. Location is an important clue. Periorbital petechiae and petechiae on the chest above the nipple line suggest that the lesions were caused by the force of the barotrauma, rather than systemic disease.[28] A careful history and physical exam are needed to rule out serious underlying conditions, such as pneumonia, dehydration, and abdominal obstruction.

Petechiae out of proportion to the force applied may be an indication of an underlying bleeding diathesis, including thrombocytopenia, coagulation defects, and some fulminant infections. Idiopathic thrombocytopenic purpura (ITP) and HSP may present with more widespread petechiae/purpura, but without fever or systemic symptoms. ITP can develop spontaneously, after a viral infection or after a child's inoculation with the measles-mumps-rubella vaccine.[29] ITP typically presents as easy bruising and petechiae out of proportion to the condition that caused it. These patients, as a rule, will have a healthy appearance.

Treatment (with steroids, IVIG, or anti-D immunoglobulin) is generally not required for children with ITP unless they have bleeding that is mucosal or substantial, as sponta-

neous remission is expected. Adults, who are more likely to develop chronic ITP, may benefit from treatment.[30]

HSP occurs most commonly in children, who may have palpable purpura, typically in the lower extremities, as well as arthritis or arthralgia, abdominal pain, and renal involvement that can progress from microscopic hematuria or proteinuria to renal insufficiency.[31] Typically, children whose disease is in the acute phase do not appear to be sick, with an important exception: Those who develop hemorrhage and edema in the bowel wall, resulting in intussusception, have significant abdominal pain and are more likely to need surgical reduction.[32]

Diffuse petechiae in the absence of any trauma, accompanied by significant signs of systemic illness, may be an indication of fulminant infection, including meningococcemia, DIC, and Rocky Mountain spotted fever (RMSF). (Fever and diffuse petechiae can also be seen in viral exanthema, but patients usually look well and the rash often has both blanching and petechial components.[33])

When a returning traveler presents with a rash and systemic symptoms, it is important to take a thorough history and to consider infections endemic to the area visited. RMSF may initially be localized to the wrists and progress to widespread petechiae over hours to days. Because the cutaneous findings may not be as fulminant—and up to 10% of patients with RMSF have no rash at all[34]—attention to the noncutaneous features is important. Fever, headache, neurologic symptoms, joint complaints, and abdominal pain (or only a few of these manifestations) in the context of potential tick bite exposure should prompt consideration of RMSF.[35]

Keep in mind, too, that in cases of fulminant infections such as meningococcemia and DIC, the hallmark purpura fulminans may not be present initially.[36] Although the initial cutaneous findings may be subtle, however, such patients will appear quite ill, and their condition will deteriorate rapidly. Because prompt antibiotic therapy can save life and limb, a high index of suspicion should be maintained for any patient who presents with a rash in the setting of fever and hypotension or other evidence of shock. JFP

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Periorbital petechiae and petechiae on the chest above the nipple line suggest that barotrauma, and not systemic disease, is to blame.

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