Dermatologic Emergencies: Diagnosing And Managing Life-Threatening Rashes

March 15, 2001: You see a patient for “fatigue.” This 52-year-old man was recently discharged from the hospital on ticlopidine and methylprednisolone. When you enter the room, he is fully clothed in a suit and tie—another violation of the ED’s “get naked” policy (which is more honored in breach than observance). He looks okay—he’s certainly well-dressed, and through his coat, his lungs sound clear. Looks like another “viral syndrome.”

February 25, 2002: You receive an ominous-looking certified letter. The complaint is lengthy but you understand the gist. A patient you had seen almost a year ago died two days after his visit from an intracerebral bleed. The plaintiff’s lawyers cite a triage note that documented complaints of “fatigue and rash”; your record did not mention a rash. The attached pathology report listed the cause of death as “medication-induced TTP.”

While most rashes seen in the ED are benign, some indicate a serious or even life-threatening medical illness. This issue of Emergency Medicine Practice provides a systematic approach to managing dangerous dermatologic complaints.

State Of The Literature

Guidelines and evidence-based literature regarding dermatologic emergencies are sparse. An extensive search using MEDLINE, the Cochrane Collaboration, and www.guidelines.gov (the National Guideline Clearinghouse) yielded no guidelines on life-threatening rashes. While specific guidelines exist for “mycotic infections” or “psoriasis,” the only relevant guideline yielded no guidelines on life-threatening rashes. While specific guidelines exist for “mycotic infections” or “psoriasis,” the only relevant guideline regards cutaneous adverse drug reactions.1

The classification of various skin diseases has changed over time, further confounding the literature. Many of the earlier studies on Stevens-Johnson syndrome and toxic epidermal necrolysis erroneously grouped

CME Objectives

Upon completing this article, you should be able to:

1. describe indicators that a rash may have a potentially life-threatening cause;
2. list aspects of the history and physical examination that may help identify life-threatening rashes;
3. discuss the differential diagnosis for maculopapular, petechial/purpuric, diffuse erythematous, and vesiculo-bullous rashes, emphasizing life-threatening causes of each; and
4. describe the proper disposition for patients with life-threatening rashes.

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See “Physician CME Information” on back page.
these conditions as variants of erythema multiforme.

**Epidemiology**

Dermatologic complaints account for approximately 5% of all ED visits. However, there are limited epidemiologic data that analyze the types of rashes seen in EDs. One pediatric ED reported that 31% of the cases primarily involved the skin. Most cases were classified as contusions, lacerations, and burns; non-traumatic causes included viral exanthems, bacterial infections, and contact dermatitis. In one survey, the most common skin complaints diagnosed by internists were dermatitis (16% of all diagnoses), bacterial skin infections (14%), fungal infections (5%), and acne vulgaris (5%). The emergency physician is more likely to encounter the life-threatening rashes, such as meningococcemia, toxic epidermal necrolysis, or toxic shock syndrome.

“A thick skin is a gift from God.”
—Konrad Adenauer (1876-1976), German statesman

**Pathophysiology**

The skin is comprised of three layers: the epidermis, the dermis, and the subcutaneous layer. The epidermis contains basal cells and keratinocytes, which form a protective barrier. Melanocytes produce the pigment that filters ultraviolet radiation. The dermis is comprised of connective tissues—collagen, elastin, and reticular fibers—which provide strength and elasticity to the skin. The subcutaneous layer contains mostly fat cells and connective tissue. Sweat glands, hair follicles, nerves, capillaries, and veins are dispersed within these three layers.

When these capillaries leak blood into the skin, petechiae appear. Leakage results from perivascular inflammation and/or thrombocytopenia. Petechiae are often first seen in dependent areas such as the ankles and wrists. If the petechiae are greater than 0.5 cm in size, they become purpura. In vasculitis, the purpura can become palpable.

The dermal-epidermal junction deserves special mention. It is the site of immunoglobulin and complement deposition and is the origin of blisters in diseases such as pemphigus and Stevens-Johnson syndrome. Immunofluorescence assays performed at the dermal-epidermal junction can help diagnose vesiculo-bullous skin disease.

**Differential Diagnosis And Terminology**

Common terminology is essential to describe cutaneous lesion, categorize rashes, and facilitate communication among clinicians. These descriptive terms are also crucial in developing a differential diagnosis.

A lesion is a general term for a single, small area of skin disease. A rash is the result of a more extensive process and generally involves many lesions. Table 1 lists some common terminologies for primary skin lesions, while Table 2 addresses secondary skin lesions. Disease evolution or various external factors such as scratching, healing, medications, and infections transform primary lesions into secondary lesions.

Pattern recognition is the key to the correct diagnosis of an unknown rash. Peter Lynch developed a taxonomy in which an unknown rash is classified based on its major

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**Table 1. Common Skin Lesions.**

<table>
<thead>
<tr>
<th>Lesion type</th>
<th>Description</th>
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<tbody>
<tr>
<td>Macule</td>
<td>Circumscribed area of change in normal skin color with no skin elevation</td>
</tr>
<tr>
<td>Papule</td>
<td>Solid, raised lesion up to 0.5 cm in diameter; variable color</td>
</tr>
<tr>
<td>Nodule</td>
<td>Similar to papule but located deeper in the dermis and subcutaneous tissue; more than 0.5 cm in diameter</td>
</tr>
<tr>
<td>Plaque</td>
<td>Circumscribed elevation of skin more than 0.5 cm in diameter; often a confluence of papules</td>
</tr>
<tr>
<td>Pustule</td>
<td>Circumscribed area of skin containing purulent fluid</td>
</tr>
<tr>
<td>Vesicle</td>
<td>Circumscribed, elevated, fluid-filled lesion up to 0.5 cm in diameter</td>
</tr>
<tr>
<td>Bulla</td>
<td>Circumscribed, elevated, fluid-filled lesion greater than 0.5 cm in diameter</td>
</tr>
<tr>
<td>Petechiae</td>
<td>Small red or brown macules up to 0.5 cm in diameter that do not blanch with pressure</td>
</tr>
<tr>
<td>Purpura</td>
<td>Circumscribed petechiae more than 0.5 cm in diameter</td>
</tr>
<tr>
<td>Scales</td>
<td>Excess dead epidermal cells produced by abnormal keratinization; scaling in sheets is desquamation</td>
</tr>
</tbody>
</table>

**Table 2. Secondary Skin Lesions.**

<table>
<thead>
<tr>
<th>Lesion type</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erosion</td>
<td>Focal loss of epidermis; heals without scarring</td>
</tr>
<tr>
<td>Ulcer</td>
<td>Focal loss of epidermis and dermis; heals with scar</td>
</tr>
<tr>
<td>Excoriation</td>
<td>Linear or angular erosions due to scratching</td>
</tr>
<tr>
<td>Crust</td>
<td>A collection of dried serum and cellular debris</td>
</tr>
<tr>
<td>Lichenification</td>
<td>Area of thickened epidermis that results from habitual rubbing</td>
</tr>
<tr>
<td>Atrophy</td>
<td>A depression in the skin resulting from thinning of the epidermis or dermis</td>
</tr>
<tr>
<td>Scales</td>
<td>Shedding of excess dead epidermal cells that are produced by keratinization and shedding</td>
</tr>
</tbody>
</table>
morphology, which has since been adopted by many clinicians.4,5 The Clinical Pathway on page 13, “Evaluating The Unknown Rash,” presents a modified Lynch algorithm using six major morphological groups and lists the differential diagnoses of potentially life-threatening rashes according to the clusters.

**Prehospital Care**

As a general rule, prehospital care providers should always use standard precautions and assume all bodily fluids or weeping lesions are infectious. In a patient with a fever and a petechial/purpuric rash (i.e., suspected meningococcemia or viral hemorrhagic fever), respiratory and contact isolation are advised, including a properly fitting mask for both the healthcare provider and the patient. The ambulance should be well-ventilated in order to eliminate potentially infectious airborne droplets.6 All equipment contaminated with blood or bodily fluids should be wiped down with a disinfectant solution, such as bleach diluted with water. These same protocols are used to disinfect a hospital room occupied by a patient with meningococcemia. If the patient is hypotensive, medics should give IV normal saline while en route to the hospital.

**Emergency Department Evaluation**

**Triage/Initial Nursing Interventions**

The triage nurse should rapidly identify those patients with a rash who appear seriously ill or likely to decompensate. High-risk patients include those with abnormal vital signs, altered mental status, or potential airway compromise. A petechial rash should also prompt early physician involvement, especially when accompanied by fever or confusion. In some hospitals, patients with fever and a rash are placed in respiratory isolation, especially if the patient is immunocompromised. The triage nurse should ensure early isolation of patients with lesions compatible with chickenpox or meningococcemia.

All toxic-appearing patients with a rash require IV access, an ECG, and pulse oximetry monitoring. Oxygenation, perfusion, and a bedside blood sugar must be assessed in all patients with altered mental status.

**Red Flags**

Look for the following “red flags” when evaluating a patient with an unknown rash, as these may indicate serious illness. (See Table 3.)

*Fever* suggests that an infectious or inflammatory process may be present. Infants and the elderly are more

<table>
<thead>
<tr>
<th>History or physical findings</th>
<th>Significance</th>
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<tbody>
<tr>
<td>Fever</td>
<td>Viral exanthem, septicemia, Rocky Mountain spotted fever, toxic shock syndrome, erythema multiforme, Kawasaki disease, Stevens-Johnson syndrome, toxic epidermal necrolysis</td>
</tr>
<tr>
<td>Age: Very young</td>
<td>Meningococcemia, Kawasaki disease, viral exanthem</td>
</tr>
<tr>
<td>Age: Elderly</td>
<td>Meningitis, pemphigus vulgaris, sepsis, meningococcemia, toxic epidermal necrolysis, Stevens-Johnson syndrome, hypersensitivity syndrome, toxic shock syndrome</td>
</tr>
<tr>
<td>Toxic-appearing</td>
<td>Necrotizing fasciitis, meningococcemia, toxic epidermal necrolysis, Stevens-Johnson syndrome, hypersensitivity syndrome, toxic shock syndrome, Rocky Mountain spotted fever</td>
</tr>
<tr>
<td>Immunocompromised</td>
<td>Meningococcemia, herpes zoster, septicemia, necrotizing fasciitis, (asplenia, alcoholic, debilitated)</td>
</tr>
<tr>
<td>Adenopathy</td>
<td>Drug reaction, hypersensitivity syndrome, viral illness</td>
</tr>
<tr>
<td>Diffuse erythroderma</td>
<td>Staphylococcal scalded skin syndrome, toxic shock syndrome, streptococcal toxic shock syndrome, necrotizing fasciitis</td>
</tr>
<tr>
<td>Petechiae/purpura</td>
<td>Meningococcemia, necrotizing fasciitis, vasculitis, disseminated intravascular coaugulopathy, Rocky Mountain spotted fever</td>
</tr>
<tr>
<td>Mucosal/oral lesions</td>
<td>Erythema multiforme major, toxic epidermal necrolysis, Stevens-Johnson syndrome, pemphigus vulgaris</td>
</tr>
<tr>
<td>Hypotension</td>
<td>Toxic shock syndrome, meningococcemia, Rocky Mountain spotted fever, toxic epidermal necrolysis, Stevens-Johnson syndrome</td>
</tr>
<tr>
<td>Severe localized pain/tenderness in extremity</td>
<td>Necrotizing fasciitis, cellulitis</td>
</tr>
<tr>
<td>Recent new drug use (1-4 weeks)</td>
<td>Cutaneous drug reaction, photosensitivity, erythema multiforme, toxic epidermal necrolysis, Stevens-Johnson syndrome, hypersensitivity syndrome</td>
</tr>
<tr>
<td>Arthralgias</td>
<td>Rocky Mountain spotted fever, drug reaction, viral illness</td>
</tr>
</tbody>
</table>
prone to infections due to a decrease in their immune status. While most patients with rash and fever have a benign viral exanthem, fever will also accompany lethal conditions such as Rocky Mountain spotted fever and meningococcemia. Other causes of fever include malignancy and certain medications.

*Petechiae or purpura* can be seen in some benign conditions; however, their presence should “raise the antennae” of the emergency physician.

*Lesions of the oral or genital mucosa*, as seen in Stevens-Johnson syndrome, may suggest that a severe systemic process is present, usually due to drugs or an infectious process.

*Altered mental status* or confusion should alert the emergency physician to the possibility of sepsis, hypoperfusion, and central nervous system involvement, as seen in meningococcemia.

Most rashes are not significantly painful, nor are they exquisitely tender to the touch. Patients who have pain out of proportion to tenderness of an extremity may have necrotizing fasciitis. (Necrotizing fasciitis is discussed in further detail in the January 2001 issue of *Emergency Medicine Practice*, “Skin And Soft-Tissue Infections: The Common, The Rare, And The Deadly.”)

**History**

Gathering data about the character and progression of the rash, along with other key elements of the patient history, is essential to detect life-threatening rashes. The following key questions should be a part of every patient history:

1. **When did the rash appear, and how quickly did it progress?** The most lethal rashes often progress rapidly. Acute urticaria with anaphylaxis can start within minutes after contact with the inciting agent. (See the April 2000 issue of *Emergency Medicine Practice*, “Allergic Emergencies And Anaphylaxis: How To Avoid Getting Stung.”) The petechial rash of Rocky Mountain spotted fever generally occurs four days after exposure but will then spread swiftly. In meningococcemia, the rash can progress over hours. A non-allergic drug-induced rash can take days or weeks to evolve.

2. **Did the rash change over time?** Certain rashes change their morphology over time. For example, the lesion of anthrax begins as a pruritic papule that then forms an ulcer over 24-48 hours, finally becoming a black eschar after seven days. (See the July 2002 issue of *Emergency Medicine Practice*, “Bioterrorism And The Emergency Physician: On The Front Lines.”)

3. **What was the progression of the rash? Where did the rash start?** Vasculitic rashes generally spread in a peripheral-to-central pattern, whereas viral rashes (e.g., varicella) start centrally and spread peripherally. A localized rash that does not progress may mean a contact dermatitis depending on the situation (e.g., dermatitis on both hands after wearing latex gloves).

4. **Is the lesion pruritic?** Itching is probably a primitive form of pain, mediated by histamine released by mast cells. Other mediators of itch include opioid peptides, prostaglandins, and tachykinins. Diffuse pruritus without a rash can be seen in biliary cirrhosis or certain cancers, especially lymphomas. Pruritus with a diffuse rash may be from an acute allergic reaction or other inciting agents, such as dermatitis herpetiformis from gluten sensitivity. Scabies and poison ivy, in particular, usually present with a profound itch, although the most common reason for pruritus is xerosis (dry skin).

5. **Has there been any recent travel?** Travel to certain geographical regions may expose the patient to organisms not typically seen in your ED. For example, a petechial rash in someone who has been to a wooded area may be Rocky Mountain spotted fever or ehrlichiosis. Lyme disease is endemic in the Northeast, mid-Atlantic, north Central, and far West regions of the United States. Consider typhus if there is a history of flea bites, travel to the southwestern United States, and a maculopapular rash that spreads from the trunk to the extremities. Hemorrhagic fevers present with a maculopapular rash and recent travel; dengue fever is endemic to parts of the Caribbean, while Ebola is found in sub-Saharan Africa.

6. **What is the patient’s past medical history?** A person’s medical history may predispose him or her to certain dermatologic findings. For example, patients with an artificial heart valve, cardiac valvular lesions, or IV drug use may have endocarditis. Certain cutaneous conditions tend to recur in the same patient, such as herpes zoster associated with HIV or recurrent erythema multiforme following herpes simplex or mycoplasma infections.

   Inquire about the patient’s immune status. An asplenic or immunocompromised patient is susceptible to encapsulated organisms such as meningococccemia. HIV disease and chemotherapy predispose to thrombotic thrombocytopenic purpura, while those who are diabetic, debilitated, or alcoholic are vulnerable to necrotizing fasciitis.

7. **What is the patient’s occupation?** Daycare workers, college students, and military personnel are susceptible to outbreaks of meningococccemia, while postal workers or healthcare professionals may be exposed to anthrax. Consider tularemia in a game trapper who presents with regional adenopathy, an ulcerated lesion, and flu symptoms.

8. **What medications is the patient taking?** Cutaneous drug reactions occur in about 2%-3% of hospitalized patients and 1% of outpatients. While most reactions are benign maculopapular or fixed eruptions, life-threatening presentations may occur. Such potentially lethal conditions include Stevens-Johnson syndrome and toxic epidermal necrolysis. Immediate life-threatening drug reactions include anaphylaxis and angioedema, both of which can
compromise the airway.13

Determine whether the patient used any creams or medications that may have altered the morphology of the rash. Diphenhydramine or topical corticosteroids may decrease the erythema or urticaria of a histamine-mediated rash.

Physical Examination
Perform the physical examination in a systematic fashion from head to toe, paying special attention to abnormal vital signs. When evaluating a rash, the “get naked” policy should be enforced (for the patient). Patients often remain blissfully unaware of a rash on their back, buttocks, perineum, or soles. Look carefully for involvement of the mucous membranes (mouth, lips, conjunctiva, anus, and vagina). Adequate exposure and good lighting are important when looking at a rash; natural light or white light is recommended. Touch the rash (with gloved hands, as lesions of secondary syphilis are contagious and no one knows how far scabies can jump). Press on lesions to see whether they blanch to better diagnose petechiae. Rub erythematous skin to see if it sloughs. This result, known as Nikolsky’s sign, signifies a potentially life-threatening diagnosis such as toxic epidermal necrolysis.

The goal of the physical examination is not necessarily an instant diagnosis. In many cases, it is enough to detect toxicity and categorize the rash so that it can be identified with the aid of books or a consultant.

General Appearance And Vital Signs
Before closely examining the rash, assess the general appearance of the patient. Abnormal vital signs or evidence of toxicity should prompt interventions and accelerate the evaluation.

Head-To-Toe Examination
• **Head:** Look at the patient’s scalp, conjunctiva, and oral mucosa. Oral ulcers or blisters imply a serious systemic reaction, as seen, for example, in Stevens-Johnson syndrome or pemphigus vulgaris. The presence of oral thrush suggests HIV-related disease (although it can be seen in patients with uncontrolled diabetes and those who have recently completed a course of antibiotics). Conjunctival injection is found in Kawasaki disease and viral syndromes. When endocarditis is a possibility, a funduscopic exam may reveal Roth’s spots, which appear as white-centered retinal hemorrhages.

• **Neck:** In the ill-appearing patient, check for nuchal rigidity and other meningeal signs. In potential cases of anaphylaxis, look for signs of airway compromise, such as stridor, drooling, or laryngeal swelling.

• **Lymph nodes:** Adenopathy is a nonspecific finding seen with drug reactions such as serum sickness and hypersensitivity syndrome. Adenopathy may be associated with infections, including viral, bacterial, rickettsial, and spirochetal disease. Mononucleosis is a common cause of generalized adenopathy. The acute retroviral syndrome that occurs with the initial

Pearls And Pitfalls In Patients With Rashes

1. In Rocky Mountain spotted fever (RMSF), don’t just give just any broad-spectrum antibiotic. Give doxycycline (or, if it is contraindicated, as in pregnancy, chloramphenicol). Other regimens will not work. If you cannot quickly distinguish RMSF from meningococcemia, treat for both.

2. If a drug is suspected as the cause for a severe cutaneous drug reaction, stop it immediately. Withdrawal of the offending drug reduces the risk of death by about 30% a day. Do not start a chemically related drug.

3. Consider infections as a cause for a “drug allergy.” Viral exanthems are by far more common than true drug allergies, especially in the pediatric population. The “ampicillin rash” is a classic example. This prevents the patient having an extensive list of “drug allergies.”

4. Remember to give antibiotic prophylaxis to contacts of patients with meningococcemia. These include close contacts (school mates, dorm mates, household members) and certain medical personnel (those in contact with respiratory droplets). Contact the local health department to assist in notification.

5. For patients with meningococcemia, a skin biopsy and Gram’s stain of the cutaneous lesion are much more sensitive than CSF analysis. While CSF analysis is the gold standard for meningitis, for meningococcemia, it’s blood cultures.

6. EM minor and major usually occur secondary to infection. Drugs commonly cause toxic epidermal necrolysis and Stevens-Johnson syndrome.

7. Toxic shock syndrome (caused by *Staphylococcus* or *Streptococcus*) presents with high fever, rash, hypotension, and mucous membrane involvement. Streptococcal toxic shock has a higher morbidity and mortality and is associated with bacteremia in 60% of cases.

8. About 80% of streptococcal toxic shock syndrome cases are associated with a soft-tissue or skin infection.
infection of HIV presents as a “mono-like” illness with diffuse rash and generalized lymphadenopathy.

Look for regional lymphadenopathy as well. Patients with Kawasaki disease usually demonstrate cervical lymphadenopathy, with at least one lymph node measuring 1.5 cm or more in diameter. Post-auricular nodes accompany adenovirus infection. In addition to the cervical nodes, evaluate for adenopathy proximal to an extremity lesion. The axillary nodes are often swollen in cutaneous anthrax of the upper extremity.

• **Lung:** Observe for signs of bronchial constriction and edema, such as tachypnea, wheezing, and retractions that may accompany acute allergic reactions or early sepsis.

• **Cardiovascular:** While most heart murmurs are either functional or benign, they may be associated with endocarditis—especially in the setting of IV drug abuse.

• **Abdominal:** Palpate for hepatosplenomegaly, which can occur with drug hypersensitivity or viral illness. Non-surgical diffuse abdominal pain may occur with allergic angioedema, while dull right upper quadrant pain suggests a hepatitis-related rash. Look for a laparotomy scar. If present, ask the patient, “Are you sure you still have your spleen?”

• **Trunk and chest:** Most viral exanthems start on the trunk and then spread to the extremities (centrifugal spread). These rashes are fine, macular papular erythematous eruptions that usually become confluent. Drug allergies usually begin on the trunk as discrete macules/papules, which spare the face, and then spread to the extremities. Bullous lesions in a dermatomal pattern are likely to be herpes zoster. Fine, scaling, faint pink papules in a “Christmas tree” pattern in the trunk may be pityriasis rosea, especially if accompanied by a “herald patch.” This oval lesion marks the first appearance of pityriasis rosea and is usually found on the trunk. It measures 1-2 cm in diameter and has central pink area, sometimes lined with small scales, surrounded by a darker peripheral zone.

• **Genital:** Look in the mucosal areas of the anus and scrotum or vulva for target lesions and bullous lesions characteristic of erythema multiforme or Stevens-Johnson syndrome.

Tinea cruris and erythrasma are also found in the genitocrural area. Both conditions present with a finely wrinkled, scaly rash that is reddish-brown in color. When erythrasma is viewed under a Wood’s lamp, it fluoresces a bright coral red. Diffuse tender erythema around the scrotal and perineal areas (especially if associated with subcutaneous air) may represent Fournier’s gangrene. (See the November 2000 issue of *Emergency Medicine Practice,* “Male Genitourinary Emergencies: Preserving Fertility And Providing Relief.”)

• **Extremities:** Palpable purpura and petechiae usually present in the extremities, especially around the ankles and wrists. The petechial rash of Rocky Mountain spotted fever spreads from the wrists and ankles toward the body (centripetal spread). Pain out of proportion to tenderness is found with necrotizing fasciitis; in this case, the affected limb may become tense with shiny erythema. (See the January 2001 issue of *Emergency Medicine Practice,* “Skin And Soft-Tissue Infections: The Common, The Rare, And The Deadly.”) Sparse hemorrhagic pustules about the hands and feet imply gonococcemia.

• **Joints:** Arthralgias are thought to be the result of antibody-antigen deposits in joints and may be a sign of serum sickness. Arthralgias with a rash are seen in Rocky Mountain spotted fever, drug reactions, and bacterial and viral illnesses. Disseminated gonococcal infection may present with frank arthritis and a meager hemorrhagic-pustular rash.

• **Palms and soles:** Involvement of the palms and soles usually signifies inflammation of the small vessels and can be drug-induced or pathogen-induced. The classic target lesions of erythema multiforme are often found on the palms and soles. The “nickel and dime” lesions of secondary syphilis are similarly prominent in these areas. In secondary syphilis, these symmetric lesions begin as faint papulosquamous macules that darken over time. In toxic epidermal necrolysis, Kawasaki disease, scarlet fever, and toxic shock syndrome, there is late desquamation of the hands and feet. However, since desquamation usually occurs 7-10 days after the acute illness, this finding is usually not helpful in the ED.

• **Nails and fingers:** These areas provide important clues to the diagnosis of endocarditis. Splinter hemorrhages are found under the nails, while Osler’s nodes are pea-sized subcutaneous nodules in the pulp of the fingers or toes. Janeway lesions are nontender erythematous, hemorrhagic macules on the palmar aspect of the fingers.

“I’m tired of all this nonsense about beauty being only skin-deep….What do you want—an adorable pancreas?”

—Jean Kerr

**The Skin Examination**

First, the clinician should get an overall view of the rash, and then the primary lesion can be closely examined. A magnifying glass may be helpful when looking at a single lesion. The lesion should be palpated with a gloved finger to assess its texture and to see if the lesion blanches. If it is unclear whether a lesion blanches, use a finger to assess its texture and to see if the lesion blanches. The following four major skin signs should be noted during the evaluation of any skin lesion or rash:14

1. **Type of lesion:** This description should be for the representative lesion, as described in Table 1. Note if there are any secondary changes or if there are scaling, crusts, or fissures, as described in Table 2. Determine the color of the lesion and assess for
erythema, desquamation, and tenderness.

2. Shape of the individual lesion: Is the lesion round, oval, annular (ringed-shaped as in anthrax), iris-shaped (as in erythema multiforme), umbilicated (molluscum), or irregular (petechial)?

3. Arrangement of multiple lesions: Are the lesions isolated, grouped (linear, annular, serpiginous), or disseminated (scattered discrete lesions, or diffuse involvement as in viral exanthem or drug allergy)? Linear patterns not in a dermatomal distribution usually signify contact dermatitis (e.g., poison ivy) and, when located in the finger web spaces, scabies. A scattered, diffuse macular rash suggests a drug allergy.

4. Pattern of the rash: Pattern is the functional/physiologic arrangement of the lesion, such as sun-exposed area, flexor/extensor surface, or hair-bearing areas. Also, note if the distribution is symmetrical or unilateral. Bilateral symmetry usually signifies a systemic internal event, whereas isolated lesions indicate a local process such as contact dermatitis. A rash in a sun-exposed distribution is compatible with a photosensitive drug reaction (e.g., tetracycline).

General Diagnostic Testing

Blood Tests

There are few studies that provide an evidence-based approach to laboratory testing in patients with a rash. Furthermore, with the exception of secondary syphilis, blood tests will almost never supply the etiology of a rash in the ED. In patients who are not toxic or febrile, laboratory testing is driven by clinical suspicion. If the rash appears benign, then laboratory studies are generally unnecessary.

This said, toxic-appearing patients with an unexplained rash and fever may benefit from a complete blood count with differential, along with a platelet count, chemistry panel, liver function tests, and blood cultures. The platelet count may implicate thrombocytopenia as a cause of petechiae. In the patient with unstable vital signs or who appears dehydrated, a chemistry panel will detect acidosis as well as renal or electrolyte abnormalities. Patients with Stevens-Johnson syndrome or toxic epidermal necrolysis, in particular, may have electrolyte abnormalities from fluid losses through the disrupted skin. Liver function tests may tell the clinician if there is hepatitis, which is occasionally seen with some drug hypersensitivity reactions.

Serology is occasionally useful. A Venerable Disease Research Laboratory (VDRL) or fluorescent treponemal antibodies (FTA) test for syphilis can be diagnostic in a person with papulosquamous lesions suggestive of the disease. If Lyme disease is suspected, then an IgM antibody to Lyme or rising IgG titers may be sent for confirmation. However, the sensitivity and specificity are not perfect, and a positive test does not discriminate between previous and current infection. Serologic testing for Lyme disease is recommended only when the physician believes the patient has a 20% or greater chance of harboring active disease.

Scrapings

In certain cases, aspirates or scrapings of pustular fluid may be obtained for Gram’s stain (useful in suspected cases of anthrax or gonococcemia). When evaluating an unknown ulceration, Tzanck smears are 74% sensitive to herpes infections. Potassium hydroxide preparations to look for hyphae are sometimes useful in the diagnosis of yeast infections.

Punch Biopsies

Punch biopsies are relatively simple to do. A circular cutting instrument called a trephine is pushed vertically into the skin with rotational movements until the instrument sinks into subcutaneous tissue. The operator then lifts the specimen with a toothless forceps, and the base is cut with iris scissors. Specimens can then be sent in a sterile container for Gram’s staining or other tests (e.g., immunofluorescence).

Emergency physicians familiar with the technique can use punch biopsies to identify a variety of lesions. For example, a febrile patient with a petechial/purpuric rash may have either meningococcemia or Rocky Mountain spotted fever. A Gram’s stain of a punch biopsy specimen may identify the organism and streamline antibiotic selection. The sensitivity for punch biopsy in meningococcemia is approximately 72%.

Diagnostic Decision Making

After the initial stabilization, history, and physical examination, formulate a differential diagnosis using the modified Lynch algorithm presented in the Clinical Pathway on page 13, “Evaluating The Unknown Rash.” The unknown lesion is classified into one of six major categories, as described in the Pathway. In the sample case mentioned at the beginning of this paper, our patient (a 52-year-old man on ticlopidine and methyldopa) presented with a petechial rash and underlying erythema. Following the Lynch algorithm, the lesion would be classified first as solid, meaning not vesicular or bullous. Going down the algorithm, the lesion would then be assessed as having erythema, then as petechial/purpuric. The differential diagnosis to entertain would include vasculitis, thrombotic thrombocytopenic purpura, meningococcemia, Rocky Mountain spotted fever, and endocarditis. A history of taking ticlopidine and methyldopa moves thrombotic thrombocytopenic purpura to the top of the list. A platelet count in the ED would have been diagnostic—and possibly life-saving.

Maculopapular Rashes

Maculopapular rashes are the most common types of rash and have the broadest differential diagnosis. They are usually seen with viral illnesses, bacterial infections, drug reactions, and other immune-related syndromes.

It is probably easiest to categorize maculopapular
Cutaneous Drug Reactions

Etiology
Cutaneous drug reactions commonly present as a maculopapular rash. The most commonly involved drugs are sulfonamides, penicillins, anticonvulsants, and nonsteroidal-anti-inflammatory drugs.12

Epidemiology
Cutaneous allergic reactions to drugs are reported in about 1%-3% of hospitalized patients and 1% of outpatients.1,8 Fortunately, most drug reactions are not serious, though life-threatening reactions can occur. The most severe reactions include the hypersensitivity syndrome, Stevens-Johnson syndrome (SJS), and toxic epidermal necrolysis (TEN).

Pathophysiology
Cutaneous drug reactions can be immunologic or non-immunologic. Non-immunologic causes account for more than 75% of cutaneous drug reactions.12

Clinical Presentation
Most cutaneous drug eruptions are morbilliform (meaning it looks like measles) or exanthematous. The rash is comprised of brightly erythematous macules and papules, mostly on the trunk and extremities, discrete in some areas and confluent in others.14 A morbilliform rash often erupts in patients with mononucleosis who take ampicillin. This type of rash is self-limited and usually resolves without permanent sequelae after the offending agent is discontinued.

A drug hypersensitivity syndrome is a severe, idiosyncratic systemic reaction. The patient has a severe exanthematous rash that may exfoliate, often combined with fever, hepatitis, nephritis, carditis, facial swelling, and/or lymphadenopathy. The hypersensitivity syndrome usually develops 2-6 weeks after a drug is started, vs. 1-3 weeks as seen in TEN or SJS. Drugs commonly implicated are phenytoin, carbamazepine, phenobarbital, sulfonamides, allopurinol, and dapsone. The incidence may be higher in blacks and in people who have slow N-acetylation of sulfonamides.23 Drugs with a long half-life are more likely to result in a fatal outcome than reactions from drugs with a short half-life.24

Diagnosis
The diagnosis is essentially clinical. While a skin biopsy does not help identify the offending agent, it can assist the consultant in defining the reaction pattern.8,14,22 (See Table 5, Table 6, and Table 7 on page 9.)

Treatment
The first step in managing a suspected cutaneous drug reaction is removing the drug. In one retrospective study, withdrawal of the offending drug reduced the risk of death by about 30% per day.24 If possible, all drug therapy should be stopped in a patient who develops an unexplained syndrome of blisters or substantial epidermal erosions accompanied by fever. The need for drug withdrawal is less clear in patients who present with a minor maculopapular eruption with or without pruritus. Routine use of corticosteroids is not indicated.25,26 Oral antihistamines (diphenhydramine 25-50 mg PO q6h prn) may alleviate pruritus. Alternatives include hydroxyzine, cetrizine, or loratadine, which have the advantage of less sedation. An evidence-based review on the efficacy of antihistamines in relieving pruritus showed no
Table 5. Red Flags That A Cutaneous Drug Reaction May Be Serious.

Clinical findings
Cutaneous
- Confluent erythema
- Facial edema or central facial involvement
- Skin pain
- Palpable purpura
- Skin necrosis
- Blisters or epidermal detachment
- Positive Nikolsky’s sign
- Mucous membrane erosions
- Urticaria
- Swelling of the tongue

General
- High fever (>40°C)
- Enlarged lymph nodes
- Arthralgias or arthritis
- Shortness of breath, wheezing, hypotension

Laboratory results
- Eosinophil count >1000/mm³
- Lymphocytosis with atypical lymphocytes
- Abnormal liver function tests

Table 6. Guidelines For The Assessment Of A Possible Adverse Drug Reaction.

1. Alternative causes should be excluded, especially infection. Many infections (especially viral) are difficult to distinguish clinically from adverse drug reactions.
2. The interval between introduction of a drug and the onset of a reaction should be examined (e.g., 1-3 weeks for TEN/SJS, 2-6 weeks for hypersensitivity syndrome).
3. Any improvement after drug withdrawal should be noted.
4. The caregiver should determine whether similar reactions have been associated with the same compound.
5. Any reaction on re-administration of a drug should be noted.


Table 7. Drugs Commonly Implicated In Cutaneous Allergic Reactions.

- Aminopenicillins
- Sulfonamides
- Cephalosporins
- Allopurinol
- Phenobarbital
- NSAIDs
- Quinolones
- Phenytoin
- Valproic acid
- ACE inhibitors
- Thiazide diuretics
- Beta-blockers
- Oral contraceptives
- Phenothiazines
- Corticosteroids


Distinguishing Between Erythema Multiforme, Stevens-Johnson Syndrome, And Toxic Epidermal Necrolysis

Erythema multiforme (EM) is the archetypal maculopapular rash of the extremities. The rash typically begins as a macular eruption that then progresses to a papule with a dusky center—the classic “target” lesion.

In the past, EM major and minor, Stevens-Johnson syndrome (SJS), and toxic epidermal necrolysis (TEN) were all believed to be part of the same clinical spectrum. Now, EM minor and major are considered distinct from SJS and TEN.

Seven factors distinguish EM minor and major from SJS and TEN. They are: 1) the etiology; 2) the underlying pathology; 3) the degree of mucosal involvement (mouth, conjunctiva, rectum, vagina, respiratory tract); 4) the presence or absence of a “classic rash”; 5) the degree of epidermal detachment; 6) the degree of multisystem involvement; and 7) the morbidity and mortality.28,29 (See Table 8 on page 10.)

Unlike SJS and TEN, EM minor and major are not characterized by epidermal detachment. EM minor presents with the “classic rash” and has no mucosal involvement. EM major also presents with the “classic rash” but has only one mucous membrane involved. Neither SJS nor TEN demonstrate the classic target lesions, but both are characterized by mucous membrane involvement and epidermal detachment. (Because SJS and TEN produce widespread purpuric macules and mucosal erosions, along with epidermal detachment, they are discussed in more detail in the section on vesiculo-bullous rashes.) EM minor and major usually occur after an infection (when a cause can be identified), whereas SJS and TEN usually occur after drug exposure. In one retrospective study of 76 cases, the authors reported that cases could be classified as either EM or SJS/TEN based on the inciting cause.30 SJS and TEN have greater morbidity and mortality than EM minor and major.

Erythema Multiforme Etiology

EM is a common acute inflammatory disease that is usually self-limited. Many factors have been implicated in the etiology, including infectious agents, drugs, and malignancy. (See Table 9 on page 10.) However, in up to 50% of cases no etiologic agent can be identified. In children, EM commonly follows a herpes simplex or mycoplasma infection. A recurrent form of EM may
Pathophysiology
The pathogenesis of EM is not clearly understood but is most likely caused by an immune complex-mediated hypersensitivity reaction.31

Epidemiology
The true incidence of EM is not known. It occurs in all age groups but is more common in those 20-40 years old.

Morbidity And Mortality
Death from EM is rare. However, if patients have ocular involvement, disabling and permanent visual sequelae may occur. Scarring of the skin is unusual except in hyper-pigmented patients.

Clinical Presentation
Most patients with EM present to the ED with a chief complaint of rash. They often have a prodrome of malaise, fever, and arthralgias. Target lesions are the hallmark of EM minor and major. (See Figure 1.) Dusky red macules and papules appear suddenly on the palms, soles, and extensor surfaces of the extremities, especially the knees and elbows. They are usually symmetrical and evolve over 24-48 hours. As the maculopapular lesions enlarge, the central area becomes cyanotic, appearing as annular papules or plaques with dusky centers. Vesicles and bullae may form in the center of the lesion. Plaques may also develop without the classic target lesions. These lesions are uniform in size (averaging 1-2 cm in diameter), non-pruritic, and may remain unchanged for up to two weeks.

Lesions develop in crops for up to 2-4 weeks and heal without scarring in 1-2 weeks. The entire episode lasts for one month. In EM minor, mucous membrane involvement is absent; bullae and systemic symptoms do not develop. EM minor becomes EM major if a single mucous membrane is involved; erosions may occur on the lips, in the oral cavity, or on the

Table 8. Classification Of Erythema Multiforme, Stevens-Johnson Syndrome, And Toxic Epidermal Necrolysis.

<table>
<thead>
<tr>
<th>Entity</th>
<th>Most common etiologic agent/rash</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erythema multiforme minor</td>
<td>Infectious/classic target lesion without mucous membrane involvement (no epidermal detachment)</td>
</tr>
<tr>
<td>Erythema multiforme major</td>
<td>Infectious/classic target lesions with mucous membrane involvement (no epidermal detachment)</td>
</tr>
<tr>
<td>Stevens-Johnson syndrome</td>
<td>Drug induced/widespread purpuric macules and mucosal erosions with 10% epidermal detachment, plus Nikolsky’s sign</td>
</tr>
<tr>
<td>SJS/TEN transition</td>
<td>Drug induced/widespread purpuric macules and mucosal erosions with 10%-30% epidermal detachment, plus Nikolsky’s sign</td>
</tr>
<tr>
<td>Toxic epidermal necrolysis</td>
<td>Drug induced/widespread purpuric macules and mucosal erosions with more than 30% epidermal detachment, plus Nikolsky’s sign</td>
</tr>
</tbody>
</table>


Table 9. Etiologies Of Erythema Multiforme.

<table>
<thead>
<tr>
<th>Idiopathic (50% of cases)</th>
<th>Infectious</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Herpes simplex virus</td>
<td>- Epstein-Barr virus</td>
</tr>
<tr>
<td>- Adenovirus</td>
<td>- Coxsackievirus</td>
</tr>
<tr>
<td>- Vaccinia virus</td>
<td>- Mycoplasma</td>
</tr>
<tr>
<td>- Chlamydia</td>
<td>- Salmonella typhi</td>
</tr>
<tr>
<td>Medications</td>
<td>- Penicillin</td>
</tr>
<tr>
<td>- Sulfonamides</td>
<td>- Phenytoin</td>
</tr>
<tr>
<td>- Barbiturates</td>
<td>- Phenylbutazone</td>
</tr>
</tbody>
</table>

Figure 1. Erythema multiforme.

conjunctiva. Up to 10% of patients with EM major have ocular involvement.32

**Diagnosis**
The diagnosis of EM is clinical. The diagnosis is most ensured when classic target lesions are present. If the patient does not have target lesions, another diagnosis should be considered. Similarly, if the patient looks toxic, has systemic complaints, or has abnormal vital signs, consider an alternative diagnosis.

**Management**
EM minor and major generally resolve without treatment in 2-3 weeks. Any underlying infection should be treated. While many physicians treat EM with prednisone, supporting data remain weak to nonexistent, involving just a handful of patients. A prospective study of 16 children with EM major treated with steroids showed a significant reduction in the period of fever and reduction in the period of the eruption.33 Another prospective study of three patients with EM minor showed a rapid response to steroid therapy.34 However, other larger studies suggest minimal to no benefit from treatment with steroids.35,36 Based on a review of the literature, there is no strong evidence that steroids are beneficial in EM minor or major.

**Disposition**
Essentially all patients diagnosed with EM minor or major can be safely discharged home. Follow-up with the primary medical doctor or dermatologist is helpful. Patients must return to the ED if there is rapid progression of the rash or new systemic symptoms. Follow-up with an ophthalmologist is essential in cases of ocular involvement.

"You know what happens to scar tissue.
It’s the strongest part of your skin.”—Michael R. Mantell

**Vesiculo-Bullous Rashes**
Vesicles and bullae appear in many disorders. Some of these disorders are benign—such as poison ivy or a mild case of varicella zoster—whereas others are potentially life-threatening, such as SJS, TEN, and pemphigus vulgaris (PV).

**Stevens-Johnson Syndrome And Toxic Epidermal Necrolysis**

**Etiology**
SJS and TEN are related to the use of certain medications. Anticonvulsants, sulfonamides, other antibiotics, and non-steroidal anti-inflammatory drugs (NSAIDs) are the main offenders.22 (See Table 10.) In one retrospective study, sulfonamides were found to be the etiology in 30 cases, NSAIDs in 29 cases, anticonvulsants in seven cases, and allopurinol in three.37 Fewer than 5% of patients with TEN report no drug use.38

**Pathophysiology**
The pathophysiology of SJS and TEN is not completely understood. Some studies suggest it is the result of an altered metabolism and immune-mediated response.39,40

**Epidemiology**
The incidence of TEN varies from 0.4-1.2 cases per million per year.38 TEN occurs in all age groups but is more common in adults over 40. SJS commonly occurs in children and young adults. While HIV patients are predisposed to TEN, HIV is not considered to be a causative factor.41

**Morbidity And Mortality**
The leading causes of death in TEN are sepsis from *Staphylococcus aureus* or *Pseudomonas aeruginosa* and fluid/electrolyte abnormalities.38,42 The severity of complications is proportional to the extent of skin necrosis. Massive transepidermal fluid losses can produce significant electrolyte imbalance; prerenal azotemia is common. Bacterial colonization of the skin and decreased immune responsiveness leads to sepsis.

The mortality rate is 5%-10% for SJS and 23%-30% for TEN.42 The mortality rate is higher still in elderly patients—51% in one retrospective study of 77 elderly patients with TEN.43 Variables associated with a poor prognosis include increased age, extent of disease, extent of disease at time of transfer to a burn center, azotemia, multiple medication use, thrombocytopenia, and neutropenia.38,44 Ophthalmologic sequelae such as keratitis and corneal ulcerations, corneal scarring, and blindness occur in 40%-50% of patients.45

**Clinical Presentation**
In both SJS and TEN, patients present with a chief complaint of a rash. Some experience prodromal symptoms similar to a viral illness such as myalgias, fever, cough, or sore throat. If a new drug is the cause, the prodrome usually begins within days of ingestion. Skin lesions then develop suddenly, after 1-2 weeks of prodromal symptoms.

Skin lesions in SJS look like atypical target lesions or purpuric macules on the trunk. (This is in contrast to EM minor and major, where the majority of the distribution is...
on the face and extensor surfaces of the extremities.) Patients commonly develop oropharyngeal lesions causing an erosive stomatitis. A purulent conjunctivitis can lead to ocular erosions and blindness. SJS is a self-limited disease; new lesions may appear, but they usually resolve in one month.

In contrast to SJS, patients with TEN complain of skin tenderness, pruritus, and pain. Onset is more rapid with repeated ingestion of the inciting agent. Objective skin findings are characterized by a warm and tender erythema that first affects the face around the eyes, nose, and mouth. Erythema then extends to the shoulders and trunk and proximal extremities in a symmetric fashion. All areas become confluent over several hours to days. Small, irregularly confluent bullae form within the areas of erythema. Lateral pressure on normal skin adjacent to a bullous lesion dislodges the epidermis. (This is known as Nikolsky’s sign.) (See Figure 2.) Bullae form between the epidermis and dermis, leading to widespread sloughing of the epidermis in large sheets and resulting in sizeable areas of exposed dermis.

Mucous membrane involvement is characteristic of TEN. Stomatitis or conjunctivitis may precede the generalized erythematous rash by 24-48 hours. Most patients have erythema and sloughing of the lips and buccal mucosa. In about three-quarters of patients, the eyes are also affected, producing conjunctivitis or painful erosions. These lesions can form synechiae between the eyelids and the conjunctiva, causing blindness. Up to half of patients develop genital and anal lesions. Respiratory failure can also occur.

The appearance of dermatologic manifestations of TEN is variable and unpredictable, ranging from 24 hours to two weeks. Re-epithelialization begins after several days, and most of the skin surface is re-epithelialized in three weeks. Mucosal lesions may remain crusted for two or more weeks.

**Figure 2. A positive Nikolsky’s sign in toxic epidermal necrolysis.**


The clinically distinguishing features of SJS and TEN is the degree of epidermal detachment. SJS involves mucosal erosions and less than 10% of epidermal detachment. TEN is defined by more than 30% of epidermal detachment. (See Figure 3.) Between 10%-30% is considered the overlap zone of SJS and TEN.

**Diagnosis**

As with most rashes, the diagnosis SJS and TEN is clinical. However, it can be confirmed by biopsy, which will demonstrate detachment of the epidermis from the dermis. The visual appearance of TEN is very similar to that of staphylococcal scalded skin syndrome (SSSS). Biopsy distinguishes these conditions, as the split in SSSS is high in the epidermis below the stratum corneum. SSSS also tends to occur in infants and children less than five years of age and is rare in adults.

**Treatment**

Treatment for SJS and TEN is supportive. Management focuses on removal of the offending agent and replacement of fluid losses. Patients are treated in a manner similar to burn victims. They should have two IV lines in place and be placed on a monitor. IV fluid repletion with large volumes of colloids and crystalloids is essential, with special attention to electrolyte balance. Provide liberal doses of analgesics; oral symptoms can be relieved with viscous lidocaine. All drugs started within the past month should be discontinued. Avoid topical sulfadiazine due to possible cross-reactivity.

The role of corticosteroids in SJS and TEN is highly controversial. In one retrospective study of 32 children with SJS, systemic corticosteroid therapy did not affect the course of disease. One prospective study showed higher rates of morbidity and mortality in...
Clinical Pathway: Evaluating The Unknown Rash

Possible life-threatening rash

Solid

Fluid-filled

Erythematous

Non-erythematous
(see below for differential diagnosis)

Diffuse erythematous
(see below for differential diagnosis)

Vesiculo-bullous
(see below for differential diagnosis)

Pustular
(see below for differential diagnosis)

Maculopapular
(see below for differential diagnosis)

Petechial/purpuric
(see below for differential diagnosis)

Non-erythematous
(see below for differential diagnosis)

Clear

Maculopapular
(see below for differential diagnosis)

Petechial/purpuric
(see below for differential diagnosis)

Diffuse erythematous
(see below for differential diagnosis)

Vesiculo-bullous
(see below for differential diagnosis)

Pustular
(see below for differential diagnosis)

Non-erythematous
(see below for differential diagnosis)


Differential Diagnosis Of Rash By Morphology Types.

<table>
<thead>
<tr>
<th>Rash type</th>
<th>Differential diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maculopapular</td>
<td>Meningococcemia (early), Rocky Mountain spotted fever (early), toxic shock syndrome, erythema multiforme, cutaneous drug reactions, systemic lupus erythematosus, viral exanthems (rubeola, rubella, Epstein-Barr virus, adenovirus, enterovirus), Lyme disease</td>
</tr>
<tr>
<td>Petechial/purpuric</td>
<td>Meningococcemia, Rocky Mountain spotted fever, vasculitis, Henoch-Schönlein purpura, hypersensitivity drug reactions, necrotizing fasciitis, gonococccemia, enteroviral infection, rubella, Epstein-Barr virus, thrombocytopenia, systemic lupus erythematosus, idiopathic thrombocytopenic purpura, thrombotic thrombocytopenic purpura, endocarditis, purpura fulminans</td>
</tr>
<tr>
<td>Diffuse erythematous</td>
<td>Necrotizing fasciitis, toxic shock syndrome, streptococcal toxic shock syndrome, staphylococcal scalded skin syndrome, Kawasaki disease, erythema multiforme, hypersensitivity drug reactions, cellulitis, viral exanthems, enteroviral infection</td>
</tr>
<tr>
<td>Vesiculo-bullous</td>
<td>Erythema multiforme major, Stevens-Johnson syndrome, toxic epidermal necrolysis, pemphigus vulgaris, varicella zoster, herpes simplex virus, necrotizing fasciitis (late)</td>
</tr>
<tr>
<td>Pustular</td>
<td>Bacterial folliculitis, gonorrhea</td>
</tr>
<tr>
<td>Non-erythematous</td>
<td>Secondary syphilis, anthrax (ulcerated lesions)</td>
</tr>
</tbody>
</table>

This clinical pathway is intended to supplement, rather than substitute for, professional judgment and may be changed depending upon a patient’s individual needs. Failure to comply with this pathway does not represent a breach of the standard of care.

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Clinical Pathway: Evaluating The Maculopapular Rash

Maculopapular rash

Central

Sick contact?

Yes

Consider viral exanthem

No

Has the patient been using a new drug?

Yes

Possible cutaneous drug reaction

No

Consider:
- Lyme disease
- Arboviruses
- Pityriasis rosea

Peripheral

Sick contact?

Yes

Consider:
- Meningococcal disease
- Hand-foot-mouth disease

No

Has there been any travel, or local incidence of tick-borne disease?

Yes

Consider:
- Rocky Mountain spotted fever
- Ehrlichiosis

No

Consider:
- Erythema multiforme
- Secondary syphilis
- Anthrax

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Clinical Pathway: Evaluating The Petechial Rash

Petechial rash

If the patient is ill-appearing, consider empiric treatment for meningococcemia and Rocky Mountain spotted fever

Does the patient have any sick contacts?

Yes

Consider:
- Meningococcemia
- Rubella
- Epstein-Barr virus
- Enterovirus
- Hepatitis B
- Gonococcemia
- Rheumatic fever

No

Has there been any travel, or local incidence of tick-borne disease?

Yes

Consider:
- Rocky Mountain spotted fever
- Dengue fever
- Typhus
- Rat bite fever

No

Is there palpable purpura?

Yes

Consider vasculitis

No

Possible thrombocytopenia:
- Idiopathic thrombocytopenic purpura
- Thrombotic thrombocytopenic purpura

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patients treated with corticosteroids—66% survival in the group treated without corticosteroids vs. 33% in those treated with corticosteroids. Other trials suggest that steroids increase the risk of sepsis and delay epithelialization,44,45,47 although one prospective trial of 67 consecutive patients with SJS treated with steroids reported no fatalities or adverse affects.48 Based on a review of the literature, there does not appear to be a consensus on the use of steroids in the treatment of SJS and TEN. Since there is no evidence to support their use, and because steroids may increase morbidity and mortality, avoid using them.

Cyclosporin is occasionally used to treat SJS and TEN, based on very small case series.49,50 As with the burn patient, those with SJS or TEN require aseptic technique to avoid infection. Use of adhesive material, ointments, and creams should be avoided. Patients should be covered in a clean white sheet. Debridement of necrotic tissue may be necessary (usually after the patient is admitted). Prophylactic antibiotic therapy is no longer given for fear of cross-reactivity with the drug that initiated the TEN and because of the risk of selecting for resistant organisms.51

Disposition
Some patients diagnosed with SJS can be safely discharged from the ED if all of the following criteria are met: 1) the patient is non-toxic and has stable vital signs; 2) the patient is tolerating oral fluids; 3) the rash is not rapidly progressing; 4) the patient is not immunocompromised; and 5) close follow-up is ensured. All patients with ocular involvement should be evaluated by an ophthalmologist soon after discharge.

If these criteria are not met, patients with SJS should be admitted to the hospital for 24-hour observation, IV hydration, local skin care, and nutritional support. If there is any progression of lesions, transfer to a burn or intensive care unit should be considered.

All patients suspected of having TEN should be admitted to an intensive care unit. Depending on hospital resources, early transfer to a burn unit may be necessary. In one retrospective review, patients who were treated in a burn unit had lower rates of bacteremia, septicemia, and mortality if transfer was done early in the hospital course (less than seven days).52 An earlier study yielded similar results.51

Pemphigus Vulgaris

Etiology
Pemphigus vulgaris (PV) is a rare but potentially lethal blistering condition predominantly seen in the elderly. This autoimmune disease is characterized by erosions and blistering of epithelial surfaces of the oral mucosa and skin.

Epidemiology
The incidence of PV is estimated to be about 4500 cases a year with a mean age of onset in the sixth decade. Because of a genetic predisposition, patients with PV may report a family member who once had “bad blisters.”54 If not recognized and treated early, PV can lead to significant morbidity (due to pain and disfigurement) and mortality (due to loss of protective barrier and secondary infection). The natural course of PV is relentless and progressive over months to years.55 In some cases, patients may have a rapid progression with extensive involvement.56

Pathophysiology
PV is characterized by circulating IgG autoantibodies that bind to the surface of the keratinocytes. This results in the loss of cohesion between the epidermal cells (acantholysis), while cells in the basement membrane remain intact.57 Clinically, this means that blisters form within the epidermal layer of the skin.

Clinical Presentation
Initially, blisters localize to the oral mucosa weeks to months before the skin blisters appear. These oral lesions rupture and create painful erosions. Over several weeks, non-pruritic skin blisters erupt over the rest of the body, ranging in size from one to several centimeters in diameter. (See Figure 4.) These blisters may be localized, usually affecting the head and trunk first. If left untreated, they generalize over months.58 With pressure, the thin roof of the bullae may rupture or the fluid may dissect laterally into the mid-epidermal areas (a positive Nikolsky’s sign).

Ruptured blisters develop into painful erosions that may become secondarily infected. Prior to the availability of corticosteroids, mortality ranged from 50% to 90%; currently, the mortality is approximately 10%-20%. Most of the complications are due to infections.59 Some patients can develop extensive fluid, protein, and electrolyte loss in association with extensive blistering.

Figure 4. Pemphigus vulgaris.
**Diagnosis**

The diagnosis of PV is made by biopsy of the skin adjacent to the blister. Light microscopy will show intraepidermal blister, acantholysis of the epidermal cell, and a slight eosinophilic infiltrate. Direct immunofluorescence demonstrates IgG on the surface of keratinocytes. Circulating autoantibodies can be found in 80%-90% of PV patients.60

For the emergency physician, the skin biopsy and immunofluorescence may not be practical. Therefore, the emergency physician must act based on the clinical scenario—for example, an elderly patient who complains of oral blisters for a few months and now has generalized vesicles on the body. In the case of SJS or TEN, bullous lesions progress faster, the patient will look more toxic, and he or she may have recently taken a suspect drug.

**Treatment**

A low daily dose of prednisone (1 mg/kg/d) is the initial treatment for cutaneous PV.54 Steroids are given until remission (defined as a state of no new blisters for one week). If new lesions appear after 1-2 weeks of treatment, the dose of prednisone is increased.61

In general, begin the first dose of prednisone (1 mg/kg PO or IV) in the ED after consultation with a dermatologist. (Alternatively, the dermatologist can begin steroids as indicated if close follow-up is ensured.) Most cases of PV can be treated at home as long as the patient is not toxic-appearing and has only a few blisters.54 A dermatologist should see the patient within days. The consultant can then perform an outpatient biopsy and adjust corticosteroids as indicated.

Patients with extensive blisters, erosions of the skin, or who are toxic-looking should be admitted. Once in the hospital, they can be monitored and treated for fluid or electrolyte imbalances and observed for potential infection. If there are overt signs of infection in the ED, start antibiotics immediately.

**Petechial/Purpuric Rashes**

Certain petechial eruptions are among the most rapidly fatal of the rashes. Prompt and accurate diagnosis and proper treatment may be life-saving, especially in patients with meningococcal disease or Rocky Mountain spotted fever.

**Etiology**

There are many causes of petechial rashes. It may be easier to separate petechial rashes into bacterial, viral, and non-infectious causes. (See Table 11.) While petechial rashes caused by bacteria are usually the most lethal, they are potentially treatable. Viral causes include Epstein-Barr virus, rubella, hepatitis B, and enteroviruses. Enteroviruses (e.g., echo 9 and coxsackie 9) more commonly occur in summer and fall seasons. Affected patients may have disseminated petechial rash and aseptic meningitis, mimicking meningococcal disease.9

**General Approach**

First, consider isolating the patient with a rapidly progressive petechial rash who looks ill and has a fever. In such cases, the examiner should wear a fitted respiratory mask until meningococcemia can be ruled out. As a rule, whenever confronted with a petechial rash, consider the worst-case scenario—that is, meningococcemia and Rocky Mountain spotted fever—as both of these diseases can be rapidly progressive and fatal if not treated aggressively. (See the Clinical Pathway on page 15, “Evaluating The Petechial Rash.”) It is prudent to rapidly (and empirically) treat the ill-appearing patient for these conditions, especially if the work-up will take several hours.

**History**

In a patient with petechiae, it is important to elicit any sick contacts (especially those with meningococcemia). Patients with viral infections may have upper respiratory illnesses, body aches, and fever. It is also important to elicit a travel history. Dengue fever should be suspected for those who have traveled to Central or South America (although recent outbreaks have erupted in Puerto Rico, Hawaii, and the South Pacific). The petechial/purpuric rash will appear in about 30%-50% of patients and will materialize a few days after initial symptoms of malaise, cough, and fever.62 Rocky Mountain spotted fever is associated with tick bites and is most often acquired in

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**Table 11. Causes Of Petechial/Purpuric Rashes.**

<table>
<thead>
<tr>
<th><strong>Bacterial</strong></th>
<th>• Meningococcal disease</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Rocky Mountain spotted fever</td>
</tr>
<tr>
<td></td>
<td>• Gonococcemia</td>
</tr>
<tr>
<td></td>
<td>• Pneumococcal sepsis</td>
</tr>
<tr>
<td></td>
<td>• Haemophilus influenzae sepsis</td>
</tr>
<tr>
<td></td>
<td>• Rat bite fevers (Spirillum minor and Streptobacillus moniliformis)</td>
</tr>
<tr>
<td></td>
<td>• Epidemic typhus</td>
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<tr>
<td><strong>Viral</strong></td>
<td>• Dengue</td>
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<tr>
<td></td>
<td>• Hemorrhagic fevers (Ebola, Lassa, etc.)</td>
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<tr>
<td></td>
<td>• Enteroviral infections</td>
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<tr>
<td></td>
<td>• Epstein-Barr virus</td>
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<td></td>
<td>• Rubella</td>
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<tr>
<td></td>
<td>• Hepatitis B</td>
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<tr>
<td><strong>Noninfectious</strong></td>
<td>• Coughing, sneezing, strangulation, Valsalva (mostly petechiae in face or above nipple line)</td>
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<tr>
<td></td>
<td>• Thrombocytopenia</td>
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<td></td>
<td>• Idiopathic thrombocytopenic purpura</td>
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<td>• Thrombotic thrombocytopenic purpura</td>
</tr>
<tr>
<td></td>
<td>• Vasculitis (Henoch-Schönlein purpura, hypersensitivity)</td>
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<tr>
<td></td>
<td>• Systemic lupus erythematosus</td>
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</table>

then progress to systemic invasion, ultimately leading to bacteremia, then sepsis and/or CNS invasion. Untreated, meningococcemia is invariably fatal. Even with prompt treatment, the mortality rate is about 10%-20%.67

There are about 3000 cases of meningococcal disease per year in the United States; about 50% of these involve meningitis.68 Most cases occur sporadically, but outbreaks arise in crowded environs such as dormitories or military settings.69 Most cases develop during the winter and spring months. Children from 6 months to 1 year of age are at highest risk, followed by adults under 20 years. Persons with complement deficiencies, protein C&S deficiency, or who are asplenic are at higher risk than the rest of the population.57

Clinical Presentation
The incubation period varies from two to 10 days, but the disease usually begins 3-4 days after exposure. Symptoms usually begin with an upper respiratory infection. The patient can have fever, chills, malaise, myalgias, headaches, nausea, and vomiting. A rash is seen in more than 70% of people with meningococcemia.70 Petechiae, which develop on the wrist and ankles, are the first sign of impending septicemia. At this stage, the rash may be mistaken for Rocky Mountain spotted fever. The petechiae then spread to the rest of the body, becoming confluent and eventually developing into purpuric macules. This process can be very rapid—with as little as 12 hours between onset of fever until death.67

In certain people, the rash of meningococcemia can also be described as faint pink macules or erythematous papules in addition to the classic petechiae and purpuric lesions.71 Some petechiae may appear “smudged,” and the purpura can appear “gun metal gray” in the center. Look for signs of meningeal irritation—neck soreness or stiffness, photophobia, and headaches.

The clinical manifestations of meningococcemia are those of septic shock, with acute renal failure, hypoxia, hypotension, multi-organ failure, and disseminated intravascular coagulopathy. This fulminating septicemia is termed Waterhouse-Friederichsen syndrome, accompanied by hemorrhagic destruction of the adrenal glands.

Early diagnosis and treatment are crucial. The diagnosis of meningococcemia must rest on clinical findings and is confirmed by positive cultures of the skin or blood. In meningococcal sepsis, a Gram’s stain of a skin biopsy specimen is significantly more sensitive (72%) than Gram’s-stained cerebrospinal fluid (22%). Also, a Gram’s-stained punch biopsy can be positive up to 45 hours after antibiotics, compared to 13 hours for blood cultures.19 Patients should only have a punch biopsy when blood cultures results are negative for suspected N. meningitidis and a definitive diagnosis needs to be made. This decision is usually in the hands of the consultant and not the emergency physician.

Meningococcus

Acute meningococcemia and meningococcal meningitis are caused by Neisseria meningitidis, an encapsulated gram-negative diplococcus.66 Most cases of meningococccemia begin with colonization of the nasopharynx and then progress to systemic invasion, ultimately leading to
cover the most common bacterial causes of purpuric disease: *N. meningitidis*, *H. influenzae*, and *S. pneumoniae*. Once a definitive diagnosis of *N. meningitidis* is made in the hospitalized patient, ceftriaxone can be continued or the patient can be switched to IV penicillin G (4 million units q4h). An alternative regimen is ampicillin (2 g q6h); for those who are penicillin-allergic, ceftriaxone (2 g q12h) or cefotaxime can be used. In cases of severe penicillin allergy, IV chloramphenicol 4 g/d is indicated. Supportive care involving IV fluids is crucial in patients with overt or incipient shock. Patients with suspected meningococcemia should be admitted to an isolation room.

Close contacts, such as daycare center personnel, household members, or ED personnel who have been in contact with the patient’s oral secretions should receive antibiotic prophylaxis. Others who should receive prophylaxis include those with prolonged contact (for at least 4 hours in the week before onset of illness). In the case of healthcare workers, prophylaxis is indicated for those involved with intubation, nasotracheal suctioning, or resuscitation efforts. (A housekeeper who inadvertently walks into an isolation room to change the garbage bag does not need prophylaxis.) The recommendation for prophylaxis is a single dose of ciprofloxacin 500 mg PO. An alternative is rifampin 600 mg q12h PO for two days or ceftriaxone 250 mg IM.

**Rocky Mountain Spotted Fever**

Rocky Mountain spotted fever (RMSF) is an acute infectious disease caused by *Rickettsia rickettsii*, an obligate intracellular coccobacillus. This organism is transmitted by the bites of several species of ticks, mostly *Dermacentor variabilis* (American dog tick) in the eastern United States and *Dermacentor andersoni* (Rocky Mountain wood tick) in the western United States. The term “Rocky Mountain” spotted fever is misleading because the majority of the cases occur in the eastern part of the United States (although the first cases were described in Idaho and Montana).

There are about 1000 cases of RMSF a year, most of which occur between April and September, when the ticks are most active. However, cases have been reported year-round. The mortality rate for the untreated exceeds 30%. Risk factors for mortality include delay in treatment and advanced age. It is thought that the tick must be attached for a prolonged period (hours) in order for the rickettsii to be released into the bloodstream; however, a tick bite is recalled in only 50% of patients. After the tick bite, the *R. rickettsii* organism disseminates into the bloodstream and invades the endothelium of blood vessels. The resulting vasculitis produces the characteristic rash of petechiae, hemorrhage, and edema.

**Clinical Presentation**

The rash typically appears on the fourth day after the bite (range, 1-15 days), erupting first on the wrist and ankles. Subsequently, the rash spreads centrally to the trunk and proximal extremities. The rash begins as reddish macules that Blanch with pressure, eventually becoming petechial and purpuric. (See Figure 5.) In approximately 10%-15% of the cases, a rash does not appear (producing “spotless” fever). In darker-skinned people, the rash may be difficult to see, which may contribute to the higher mortality rate in blacks (16%) as compared to whites (3%). Most patients with RMSF complain of fever, headaches, myalgias, and malaise. Pain in the calves and abdomen is common. In severe cases of RMSF, multiple organs can be involved. CNS involvement may range from headaches (very common) to coma and even seizures. Disseminated intravascular coagulopathy is a predictor for mortality. Third spacing of fluids and concomitant edema, hypoalbuminemia, and hypovolemia may occur secondary to increased capillary permeability. In severe cases, the syndrome of inappropriate secretion of antidiuretic hormone can produce hyponatremia.

The diagnosis of RMSF is empiric and is initially based on clinical and epidemiologic findings. Serologic testing will be negative in the acute period. As a general rule, a patient with a history of possible tick exposure in an endemic area during the months of April to September who presents with fever, headaches, and a rash should be treated for RMSF. Unfortunately, this triad of fever, rash, and a history of tick bite is found in only 60%-70% of patients on initial examination. Serologic testing is confirmatory about two weeks after the tick bite but generally unnecessary. The Weil-Felix agglutination test is no longer used because of its low sensitivity and specificity.

**Treatment**

The recommended treatment for RMSF in adults is doxycycline 100 mg BID PO or IV for seven days or for two days after temperature has normalized.
While chloramphenicol is also active against the rickettsia, doxycycline is associated with fewer fatalities.\textsuperscript{84} In the past, doxycycline was not often used in children under 8 years because of the presumed risk of dental staining that occurs with tetracycline, a related drug. For this reason, some physicians prescribe chloramphenicol for young children in whom RMSF is suspected. However, a number of authorities strongly recommend doxycycline even in children under 8, arguing for its documented effectiveness, broad margin of safety, minimal risk of dental staining, and convenient dosing schedule.\textsuperscript{85} Evidence suggests that the short courses of doxycycline used to treat RMSF do not cause clinically significant staining of teeth.\textsuperscript{86} The recommended treatment for pregnant women is chloramphenicol 500 mg QID PO or IV for seven days or for two days after the temperature has normalized.\textsuperscript{87,88}

Patients who receive antirickettsial therapy within five days of symptom onset are significantly less likely to die than those who receive treatment after the fifth day (6.5\% vs 22.9\%; P < 0.03).\textsuperscript{81} The need for hospitalization depends on the severity of the illness. Long-term sequelae from severe illness due to RMSF include hearing loss, peripheral neuropathy, bladder and bowel incontinence, and cerebellar, vestibular, and motor dysfunction.\textsuperscript{89} Lifelong immunity appears to develop after infection.\textsuperscript{80}

**Henoch-Schönlein Purpura**

“Numerous smaller, and larger, dark red, or bluish, round patches are especially noticed on the legs and feet, while the upper portions of the body are free, or present but a few specks. They are not changed by pressure....The purpura in these cases was always combined with colic, tenderness of the colon, vomiting, intestinal hemorrhage, and, with one exception, with rheumatic pains, with swelling of the joints being less constant.”—Eduard Heinrich Henoch, Lectures on Diseases of Children: A Handbook for Physicians and Students, 1882

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**Ten Pitfalls To Avoid**

1. “I didn’t think Mr. Smith had Rocky Mountain spotted fever—he had no rash!”
    Well, he had “Rocky Mountain spotless fever.”
    Approximately 10\%-15\% of people diagnosed with RMSF have no rash. It can be fatal to presume otherwise. The index of suspicion should be high in individuals with fever, headache, myalgias, and possible tick exposure from April to September. Treat liberally and empirically with doxycycline.

2. “That elderly fellow kept returning to the ED with mouth sores and complained it was painful to eat. I referred him to his dentist.”
    Well, you neglected to check out the rest of his body for lesions or ask about personal or family history of bullous diseases. This patient had pemphigus vulgaris. Early treatment can significantly improve outcome.

3. “I thought that alcoholic, drug-abusing homeless person was seeking narcotics. He kept on saying he had severe pain in his leg, but I didn’t see any physical signs that anything was wrong. He was probably drunk.”
    Pain out of proportion to physical examination in a “toxic” person should raise suspicion for early necrotizing fasciitis. This patient was toxic with altered mental status—not drunk. History of alcohol abuse, diabetes, peripheral vascular disease, and a debilitated state are all risk factors for necrotizing fasciitis.

4. “I thought the patient might have had cellulitis of his face and chest. He had fever and lymphadenopathy, so I started him on IV penicillin G. He got worse, developing hepatitis and nephritis. Then his skin began to exfoliate for no reason.”
    There was a reason. You neglected to elicit that he had self-medicated with his girlfriend’s “antibiotic pill” for a sore throat. This pill turned out to be penicillin VK. Facial swelling and erythema without pain in a person with lymphadenopathy and a diffuse body erythema should raise suspicion for a hypersensitivity syndrome.

5. “I didn’t think about antibiotic prophylaxis for his dorm mates.”
    You did a splendid job in quickly diagnosing and treating the index case of meningococcemia, but you neglected to prophylax his roommates with ciprofloxacin or rifampin. Now two other students have contracted meningitis.

6. “I diagnosed the patient with Stevens-Johnson syndrome because he came in with denuded skin and lesions of the mouth, eyes, and rectum. I put silver sulfadiazene on the denuded areas, but he got worse.”
    Drugs are usually the inciting agent in SJS and TEN. This patient was started on sulfonamides the week he developed symptoms. You should have stopped the drug (and not given silver sulfadiazene) as soon as the diagnosis of SJS was considered.

7. “I thought the patient might have TEN because she had a really bad rash that was sloughing off and fever. It was 3:00 a.m. and I didn’t want to wake up the dermatologist, so I

Continued on page 21
Henoch-Schönlein purpura is a vasculitis that primarily affects children. It is a constellation of cutaneous purpura, arthritis, abdominal pain, gastrointestinal bleeding, and nephritis. Immunoglobulin A (IgA) plays an important role in the development of this syndrome.90 Patients present with palpable purpura on the legs and buttocks and often complain of joint pain. Abdominal pain is also common, and some children go on to develop intussusception. Nephritis occurs in 40% of patients, usually associated with gross or microscopic hematuria and frequently proteinuria.

Henoch-Schönlein purpura is an acute, self-limited disease of approximately one month’s duration. Corticosteroids are effective in treating the arthritis and abdominal pain.91,92 Consult a specialist if nephritis is suspected.

Diffuse Erythematous Rashes

The differential diagnosis for diffuse erythematous rashes is broad. Some of these diagnoses are not immediately life-threatening, such as a viral exanthema, staphylococcal scalded skin syndrome, and Kawasaki disease. Others are rapidly lethal, such as the toxic shock syndromes (TSS) and necrotizing fasciitis.

Staphylococcal Toxic Shock Syndrome and Streptococcal Toxic Shock Syndrome

For the purposes of this article, staphylococcal toxic shock syndrome (TSS) and streptococcal toxic shock syndrome (STSS) will be discussed together, since they are similar in etiology, clinical presentation, and treatment.

Etiology

TSS and STSS are exotoxin-mediated diseases with dramatic clinical presentations. First described by Todd et al in 1978, TSS is characterized by fever, rash, mucus membrane involvement, and hypotension. Initially, toxic just started the steroids in the ED. I admitted the patient to the floor and figured the dermatologist could see her in the morning.”

This emergency physician made two big mistakes: 1) He should have called the on-call dermatologist. 2) The patient should have been admitted to the ICU. Retrospective studies have shown that steroids may increase the rate of morbidity and mortality of patients with TEN. Steroids are generally not given for TEN and should only be given in consultation with a dermatologist. Patients with TEN should be treated like burn patients and admitted either to a burn unit or an ICU setting. The mortality rate from TEN is 25%-30%.

8. “The patient came in complaining of severe leg pain and malaise. He was febrile and hypotensive but responded to fluids and acetaminophen. I diagnosed him with cellulitis, started him on cefazolin, and admitted him to the floor. I had no idea he would deteriorate so quickly and require transfer to the ICU.”

This patient had streptococcal toxic shock syndrome. STSS often presents with pain out of proportion to physical exam findings. About 80% of patients with STSS have an associated soft-tissue infection, and 60% develop bacteremia. The emergency physician must have a high index of suspicion for STSS when patients present with a soft-tissue infection or injury, high fever, and hypotension. IV penicillin combined with clindamycin is the initial treatment of choice. Get a surgical consult if there is suspicion of a necrotizing infection.

9. “She was 68 years old and had a high fever and a red rash on her trunk. She said she had decreased energy and myalgias for the past few days with low-grade fever. She had a past medical history of hypertension. I thought she had a viral syndrome and sent her home with follow-up with her primary care physician the next day.”

This patient’s rash worsened, and when she went to her primary care physician the next day, the patient was found to have a high fever, hypotension, and upon admission to the hospital she had increased BUN/Cr, CPK, and bilirubin. The patient had a nosebleed approximately one week prior to presentation that required nasal packing. The emergency physician failed to obtain this history. She was admitted to the hospital with the diagnosis of staphyloccocal toxic shock syndrome.

10. “I suspected meningococcemia from the start. It takes time to get blood and urine cultures. I also needed to get a CT before I did the lumbar puncture. Plus, the nurses couldn’t find a vein to stick.”

This child arrested before antibiotics were ever given. When you suspect meningococcemia, set a timer. If the cultures, bloodwork, lumbar puncture, etc., are not done by 30 minutes, give the antibiotics anyway (the lesions can be biopsied and successfully Gram’s-stained the next day—and the cerebrospinal fluid will not be sterilized for hours). Can’t get a peripheral IV or a central line? If you can’t get access within a reasonable time, consider IM or intraosseous antibiotics for the first dose and give the IV dose as soon as a line is established. ▲
Pathophysiology

TSS is caused by colonization of toxin-producing strains of *S. aureus*. The systemic manifestations of the illness arise from a staphylococcal toxin and other mediators.

Unlike TSS, STSS is caused by a local tissue invasion of the infecting organism *S. pyogenes* (group A *Streptococcus*). Unlike TSS, a bacteremia ensues.94

Epidemiology

When TSS was first discovered, 85%-90% of the cases were in young, healthy women who used hyper-absorbent tampons, which resulted in vaginal colonization of toxin-producing strains of *S. aureus*.95 Increased patient and physician awareness, along with removal of these tampons from the market, has decreased the incidence of TSS in menstruating women. Currently, TSS occurs in all age groups but still occurs more commonly in women.96

Up to 45% of cases of TSS are non-menstrual.97 Non-menstrual cases of TSS occur with abscesses, bursitis, surgical wounds, indwelling foreign bodies such as nasal packing, and in post-partum patients.96-101

In STSS, most patients are 20-50 years old,78 and 80% of patients have an associated soft-tissue infection or minor skin trauma.94 In contrast to TSS, where blood cultures are usually sterile, more than 60% of patients with STSS develop bacteremia.102

Morbidity And Mortality

Even though most individuals who are susceptible to shock syndrome was thought to be associated only with staphylococcal infection, but it has since been found to be associated with streptococcal infection as well.93

STSS tend to be young and healthy, *the morbidity and mortality are higher in STSS than TSS*.103 Patients develop profound shock, renal failure, sepsis, and adult respiratory distress syndrome. The overall mortality is 30%, and mortality rates can reach 80% in the elderly.104-106 Between 1990 and 1994, 29 cases of STSS were reported in children up to 14 years of age, and five of these children died.107 The mortality rate for TSS is 2%-5%.108

Clinical Presentation

Patients report a prodrome of low-grade fever, malaise, myalgias, and vomiting.109 Symptoms may occur within 2-3 days of tampon use, soft-tissue infection, or within a week of other inciting factors.110

The onset of the major symptoms of TSS and STSS (high fever, rash, and hypotension) begins abruptly after the prodrome. Hypotension develops rapidly, leading to tissue ischemia and subsequent multisystem involvement. An endotoxin-induced vasculitis contributes to the systemic failure.

Rash is a characteristic feature of TSS and usually develops 1-3 days after other major symptoms. The rash is a diffuse, non-pruritic, blanching, and macular erythoderm. It generally erupts on the trunk, where it remains most prominent, although scattered erythematous papules may coexist. If the patient is thrombocytopenic, purpura may develop. The initial rash may be subtle or even overlooked (especially in dark-skinned individuals) and generally resolves in 3-5 days. Half of patients develop a pruritic, diffuse, maculopapular eruption, usually on the hands and feet.99 If the patient survives the initial episode of TSS, full-thickness desquamation of the palms and soles occurs 5-12 days after the onset of rash.

Cost-Effective Strategies For Patients With Rashes

1. **Discharge appropriately.**

Patients with erythema multiforme minor and major, and even some with Stevens-Johnson syndrome, can be discharged home with timely follow-up.

**Caveat:** Certain patients requiring laboratory evaluation, including those who are ill-appearing (and especially if they have petechiae). In such patients, a CBC, with special attention to the platelet count, is useful. Order a VDRL for those with a papulosquamous rash, particularly if it involves the palms or soles.

2. **Limit laboratory studies.**

The diagnosis of most rashes is clinical. If the patient is not ill-appearing, most patients with rash will not require bloodwork. Confused about a rash? Get out a book or talk to a consultant instead of ordering gazillions of tests that will only further muddy the waters.

**3. Do a good physical examination.**

Nothing will provide as much “bang for the buck” as a superb physical examination. While the best way to examine a rash is to take a naked patient out into the afternoon sun, this is not always practical. At least make sure every patient is in a gown and touch the rash. Does the patient have palpable purpura or a positive Nikolsky’s sign? If there are “spots,” do they blanch? Always look in the mouth and at the eyes, as well as the palms and soles; if erythema multiforme or Stevens-Johnson syndrome is possible, look at the genitalia and rectum as well.▲
symptoms, as well as a fine desquamation of the face and trunk.

A key distinguishing factor of STSS, present in 85% of patients, is extreme localized pain at the site of infection that is out of proportion to physical findings. Desquamation is less common than in staphylococcal toxic shock syndrome.104

Diagnosis

The diagnosis of TSS and STSS is clinical and requires the presence of high fever, rash followed by desquamation, mucous membrane involvement, and the involvement of three or more organ systems. (See Table 12.) In patients less than 10 years of age, the diagnosis of Kawasaki disease should be considered.

In making the diagnosis of STSS, the clinician should search for a site of infection. Soft-tissue infection may progress to necrotizing fasciitis or myositis.94 One retrospective study of 20 patients with STSS found that 55% of patients had necrotizing fasciitis.104 Diagnosis of STSS requires isolation of group A Streptococcus from a normally sterile body site.

Treatment

Patients with TSS and STSS often require aggressive resuscitation. Some will need vasopressors, inotropic agents, and mechanical ventilation. In TSS, remove the source of staphylococcal colonization, such as vaginal tampons, nasal packing, or breast implants (involve a plastic surgeon with this last one). Antibiotic therapy with anti-staphylococcal coverage is recommended until a specific organism is identified (e.g., penicillin G or ampicillin, plus clindamycin, and possibly an aminoglycoside). Culture all potential sites of infection, and debride necrotic tissue.

Table 12. Toxic Shock Syndrome Case Definition.

Major criteria (all criteria must be present):
- Fever: Temperature >102°F
- Rash:
  - Erythroderma followed by desquamation
  - Mucous membrane: oral, conjunctival, and vaginal
- Hypotension: Systolic blood pressure < 90 mmHg

Multisystem manifestations (three or more):
- CNS: Altered mental status without focal neurologic symptoms
- Cardiovascular: distributive shock, heart failure, arrhythmias, AV blocks, non-specific ST changes
- Pulmonary: advanced respiratory distress syndrome, pulmonary edema
- Gastrointestinal: vomiting and diarrhea
- Hepatic: increased bilirubin, alkaline phosphatase, or transaminases
- Renal: azotemia
- Hematologic: thrombocytopenia, anemia, leukopenia
- Musculoskeletal: creatine phosphokinase more than two times upper limit normal
- Metabolic: hypocalcemia, hypophosphatemia


References

Evidence-based medicine requires a critical appraisal of the literature based upon study methodology and number of subjects. Not all references are equally robust. The findings of a large, prospective, randomized, and blinded trial should carry more weight than a case report.

To help the reader judge the strength of each reference, pertinent information about the study, such as the type of study and the number of patients in the study,
will be included in bold type following the reference, where available. In addition, the most informative references cited in the paper, as determined by the authors, will be noted by an asterisk (*) next to the number of the reference.


35. Ting HC, Adam BA. Erythema multiforme—response to


Physician CME Questions

33. When triaging patients with rashes, any of the following would qualify the patient as high-risk except:
   a. abnormal vital signs.
   b. altered mental status.
   c. a localized rash that does not progress.
   d. potential airway compromise.
   e. a petechial rash.

34. The most common cause of pruritus is:
   a. scabies.
   b. lymphomas.
   c. an acute allergic reaction.
   d. poison ivy.
   e. dry skin.

35. Recent travel can be associated with all of the following life-threatening rashes except:
   a. toxic epidermal necrolysis.
   b. Rocky Mountain spotted fever.
   c. Lyme disease.
   d. hemorrhagic fevers.

36. Oral ulcers or blisters can imply a serious systemic reaction, such as Stevens-Johnson syndrome or pemphigus vulgaris.
   a. True
   b. False

37. A patient who presents with a rash and fever:
   a. should receive a full, head-to-toe examination.
   b. only requires a skin examination.
   c. should receive acetaminophen for presumed viral syndrome.
   d. is considered low-risk unless he or she also has difficulty breathing.

38. When performing the skin examination, the emergency physician should evaluate:
   a. the type of lesion.
   b. the shape of the individual lesion.
   c. the arrangement of multiple lesions.
   d. the pattern of the rash.
   e. all of the above.

39. Patients who are not toxic or febrile and who have a rash that appears benign should receive:
   a. a CBC.
   b. a CBC, chemistry panel, and liver function tests.
   c. a Gram’s stain.
   d. a punch biopsy.
   e. none of the above.

40. Maculopapular rashes:
   a. are the most common types of rash.
   b. have the broadest differential diagnosis.
   c. are usually seen with viral illnesses, bacterial infection, drug reactions, and other immune-related syndromes.
   d. should prompt questions about sick contacts, travel, and new medications.
   e. all of the above.

41. Appropriate treatment of cutaneous drug reactions include all of the following except:
   a. removing the offending drug.
   b. a short course of steroids.
   c. diphenhydramine to alleviate pruritus.
   d. non-sedating antihistamines (instead of diphenhydramine if sedation would be a problem) to alleviate pruritus.

42. A target lesion is typically associated with:
   a. erythema multiforme.
   b. pemphigus vulgaris.
   c. Rocky Mountain spotted fever.
   d. toxic shock syndrome.

43. Which of the following would be the proper disposition of the patient with erythema multiforme?
   a. immediate admission to the ICU.
   b. discharge home with a two-week course of prednisone.
   c. discharge home with antihistamines and analgesia for symptomatic relief as needed.
   d. admission for a day of observation.

44. Diseases that produce diffuse erythematous rashes include all of the following except:
   a. staphylococcal scalded skin syndrome.
   b. toxic epidermal necrolysis.
   c. Kawasaki disease.
   d. the toxic shock syndromes.
   e. necrotizing fasciitis.

45. Antibiotic prophylaxis for all close contacts of patients with meningococcemia, including household members and medical personnel in contact with respiratory droplets, is mandatory.
   a. True
   b. False

46. Henoch-Schönlein purpura:
   a. rarely affects children.
   b. is a constellation of cutaneous purpura, arthritis, abdominal pain, gastrointestinal bleeding, and nephritis.
   c. requires hospital admission.
   d. treatment should include antibiotics and not corticosteroids.
47. Which of the following is/are a risk factor(s) associated with toxic shock syndrome?
   a. Soft-tissue infection
   b. Surgical wounds
   c. Indwelling foreign bodies such as nasal packing
   d. Use of hyper-absorbent tampons
   e. All of the above

48. All of the following are true of petechial/purpuric rashes except:
   a. They can be due to viral, bacterial, or non-infectious causes.
   b. They include some of the most rapidly lethal rashes.
   c. They are usually caused by toxic shock syndrome.
   d. They should be presumed to be caused by Rocky Mountain spotted fever or meningococcal disease until ruled out.

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**Class Of Evidence Definitions**

Each action in the clinical pathways section of Emergency Medicine Practice receives an alpha-numerical score based on the following definitions:

**Class I**
- Always acceptable, safe
- Definitely useful
- Proven in both efficacy and effectiveness

**Level of Evidence:**
- One or more large prospective studies are present (with rare exceptions)
- High-quality meta-analyses
- Study results consistently positive and compelling

**Indeterminate**
- Continuing area of research
- No recommendations until further research

**Class II**
- Safe, acceptable
- Probably useful

**Level of Evidence:**
- Generally higher levels of evidence
- Non-randomized or retrospective studies: historic, cohort, or case-control studies
- Less robust RCTs
- Results consistently positive

**Class III**
- May be acceptable
- Possibly useful
- Considered optional or alternative treatments

**Level of Evidence:**
- Generally lower or intermediate levels of evidence
- Case series, animal studies, consensus panels
- Occasionally positive results

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**Physician CME Information**

This CME enduring material is sponsored by Mount Sinai School of Medicine and has been planned and implemented in accordance with the Essentials and Standards of the Accreditation Council for Continuing Medical Education. Credit may be obtained by reading each issue and completing the printed post-tests administered in December and June or online single-issue post-tests administered at www.empractice.net.

**Target Audience:** This enduring material is designed for emergency medicine physicians.

**Needs Assessment:** The need for this educational activity was determined by a survey of medical staff, including the editorial board of this publication; review of morbidity and mortality data from the CDC; AHA, NCHS, and AACEP; and evaluation of prior activities for emergency physicians.

**Date of Original Release:** This issue of Emergency Medicine Practice was published September 1, 2002. This activity is eligible for CME credit through September 1, 2005. The latest review of this material was August 7, 2002.

**Discussion of Investigational Information:** As part of the newsletter, faculty may be presenting investigational information about pharmaceutical products that is outside Food and Drug Administration approved labeling. Information presented as part of this activity is intended solely as continuing medical education and is not intended to promote the off-label use of any pharmaceutical product. Disclosure of Off-Label Usage: This issue of Emergency Medicine Practice describes the use of doxycycline in young children with Rocky Mountain spotted fever. Although it is not approved for this use, clinical studies indicate it is safe and effective for this condition. (See text.)

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