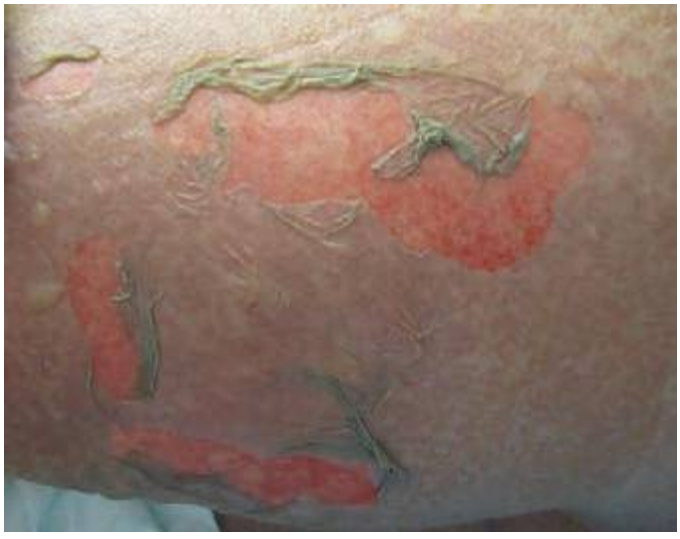

FIGURE 74-9 Toxic epidermal necrolysis. *(Photo credit: Lindy Peta Fox, MD, and Jubin Ryu, MD, PhD.)*

lesions; some believe that this clinical entity is the syndrome originally described by Stevens and Johnson.

Patients with SJS, SJS/TEN, or TEN initially present with acute onset of painful skin lesions, fever >39°C (102.2°F), sore throat, and conjunctivitis resulting from mucosal lesions. Intestinal and pulmonary involvement is associated with a poor prognosis, as are a greater extent of epidermal detachment and older age. About 10% and 30% of SJS- and TEN-affected persons die from their disease, respectively. Drugs that most commonly cause SJS or TEN are sulfonamides, nevirapine (1 in 1000 risk of SJS or TEN), allopurinol, lamotrigine, aromatic anticonvulsants, and NSAIDs, specifically oxicam. Frozen-section skin biopsy may aid in rapid diagnosis. At this time, SJS and TEN have no proven effective treatment. The best results come from early diagnosis, immediate discontinuation of any suspected drug, supportive therapy, and paying close attention to ocular complications and infection. Systemic glucocorticoid therapy (prednisone 1–2 mg/kg) may be useful early in the evolution of the disease, but long-term systemic glucocorticoid use has been associated with higher mortality. Cyclosporine may be a possible therapy for SJS/TEN. After initial enthusiasm for the use of intravenous immunoglobulin (IVIG) in the treatment of SJS/TEN, some recent data questions whether IVIG benefits these patients. Randomized studies to more definitively assess the potential benefit of systemic glucocorticoids and IVIG are lacking and difficult to perform but are necessary.

Overlap Hypersensitivity Syndromes An important emerging concept in the clinical approach to severe drug eruptions is the presence of overlap syndromes, most notably DIHS with TEN-like features, DIHS with pustular eruption (AGEP-like), and AGEP with TEN-like features. In several case series of AGEP, 50% of cases had TEN-like or DRESS-like features, and 20% of cases had mucosal involvement resembling SJS/TEN. In one study, up to 20% of all severe drug eruptions had overlap features, suggesting that AGEP, DIHS, and SJS/TEN represent a clinical spectrum with common pathophysiologic mechanisms. Designation of a single diagnosis based on cutaneous and extracutaneous involvement may not always be possible in cases of hypersensitivity.

MANAGEMENT OF A PATIENT WITH A DRUG ERUPTION

There are four main questions to answer regarding an eruption:

1. Is it a drug reaction?
2. Is it a severe eruption or the onset of a form that may become severe?
3. Which drug(s) is (are) suspected, and which drug(s) should be withdrawn?
4. What is recommended for future use of drugs?

TABLE 74-2 CLINICAL AND LABORATORY FINDINGS ASSOCIATED WITH MORE SERIOUS DRUG-INDUCED CUTANEOUS CLINICAL FINDINGS

Cutaneous
Generalized erythema
Facial edema
Skin pain
Palpable purpura
Target lesions
Skin necrosis
Blisters or epidermal detachment
Positive Nikolsky's sign
Mucous membrane erosions
Urticaria
Swelling of tongue
General
High fever (temperature >40°C [>104°F])
Enlarged lymph nodes
Arthralgias or arthritis
Shortness of breath, wheezing, hypotension
Laboratory Results
Eosinophil count >1000/μL
Lymphocytosis with atypical lymphocytes
Abnormal liver or kidney function tests

Source: Adapted from JC Roujeau, RS Stern: N Engl J Med 331:1272, 1994.

EARLY DIAGNOSIS OF SEVERE ERUPTIONS

Rapid recognition of adverse drug reactions that may become serious or life threatening is paramount. Table 74-2 lists clinical and laboratory features that, if present, suggest that the reaction may be serious. Table 74-3 provides key features of the most serious adverse cutaneous reactions. Intensity of symptoms and rapid progression of signs should raise the suspicion of a severe eruption. Any doubt should lead to prompt consultation with a dermatologist and/or referral of the patient to a specialized center.

CONFIRMATION OF DRUG REACTION

The probability of drug etiology varies with the pattern of the reaction. Only fixed drug eruptions are always drug-induced. Morbilliform eruptions are usually viral in children and drug-induced in adults. Among severe reactions, drugs account for 10–20% of anaphylaxis and vasculitis and between 70–90% of AGEP, DIHS, SJS, or TEN. Skin biopsy helps in characterizing the reaction but does not indicate drug causality. Blood counts and liver and renal function tests are important for evaluating organ involvement. The association of mild elevation of liver enzymes and high eosinophil count is frequent but not specific for a drug reaction. Blood tests that could identify an alternative cause, antihistone antibody tests (to rule out drug-induced lupus), and serology or polymerase chain reaction for infections may be of great importance to determine a cause.

WHAT DRUG(S) TO SUSPECT AND WITHDRAW

Most cases of drug eruptions occur during the first course of treatment with a new medication. A notable exception is IgE-mediated urticaria and anaphylaxis that need presensitization and develop a few minutes to a few hours after rechallenge. Characteristic times of onset to drug reaction are as follows: 4–14 days for morbilliform eruptions, 2–4 days for AGEP, 5–28 days for SJS/TEN, and 14–48 days for DIHS. A drug chart, compiling information of all current and past medications/supplements and the timing of administration relative to the rash, is a key diagnostic tool to identifying the inciting drug. Medications introduced for the first time in the relevant time frame are prime suspects. Two other important elements to suspect causality at this stage are (1) previous experience with the drug in the population and (2) alternative etiologic candidates.