SEVERE CUTANEOUS REACTIONS TO DRUGS


Take home points:
1. Stevens-Johnson syndrome and toxic epidermal necrolysis (TEN) are both acute life-threatening conditions. Look for erosions of mucous membranes, extensive detachment of the epidermis, and severe constitutional symptoms.
2. The most common medications associated with Stevens-Johnson syndrome and TEN are sulfa drugs, anticonvulsant agents, oxicam NSAIDs, allopurinol, and corticosteroids.
3. Treatment: discontinue all meds; treat like burn patient (fluids, nutritional support, pain control, consider antibiotics); avoid corticosteroids.

General Considerations:
- Adverse cutaneous reactions occur in 2-3% of hospitalized patients but most are not severe.
- Severe adverse drug reactions include Stevens-Johnson syndrome and toxic epidermal necrolysis (TEN) which are both acute life-threatening conditions.
- In these syndromes, look for erosions of mucous membranes, extensive detachment of the epidermis, and severe constitutional symptoms.
- TEN is usually caused by drugs, presents with very extensive skin detachment, and carries a poor prognosis (mortality 30-40%, usually due to sepsis).
- Stevens-Johnson syndrome can be caused by drugs or as a complication of infections and is milder than TEN.
- The most common medications associated with Stevens-Johnson syndrome and TEN are sulfa drugs, anticonvulsant agents, oxicam NSAIDs, allopurinol, and corticosteroids.

Indications that a drug-induced cutaneous eruption 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 tongue

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

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

*The outer layer of the epidermis separates readily from the basal layer with lateral pressure.
Summary and distinguishing features of severe, drug-induced adverse cutaneous reactions:

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Mucosal Lesions</th>
<th>Typical Skin Lesions</th>
<th>Frequent Signs and Symptoms</th>
<th>Percent Drug-Induced</th>
<th>Percent Fatal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stevens–Johnson syndrome</td>
<td>Erosions usually at ≥2 sites</td>
<td>Small blisters on dusky purpuric macules or atypical targets, rare areas of confluence, detachment of ≤10% of body-surface area</td>
<td>10–30% of cases involve fever, lesions of the respiratory tract* and gastrointestinal tract</td>
<td>50</td>
<td>&lt;5</td>
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<tr>
<td>Toxic epidermal necrolysis</td>
<td>Erosions usually at ≥2 sites</td>
<td>Individual lesions like those seen in Stevens–Johnson syndrome, confluent erythema, outer layer of epidermis separates readily from basal layer with lateral pressure, large sheets of necrotic epidermis, total detachment of &gt;30% of body-surface area</td>
<td>Nearly all cases involve fever, “acute skin failure,”** neutropenia, lesions of the respiratory tract* and gastrointestinal tract</td>
<td>&gt;80</td>
<td>30</td>
</tr>
<tr>
<td>Hypersensitivity syndrome</td>
<td>Infrequent</td>
<td>Severe exanthematous rash (may become purpuric), exfoliative dermatitis</td>
<td>30–50% of cases involve fever, lymphadenopathy, hepatitis,* nephritis,* cardiitis,* eosinophilia,* atypical lymphocytes</td>
<td>&gt;90</td>
<td>10</td>
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<tr>
<td>Small-vessel vasculitis</td>
<td>Infrequent</td>
<td>Palpable purpura, most often on the legs; nodules; ulcerations; urticaria</td>
<td>30–50% of cases involve the gastrointestinal tract,* neutritis,* fever, glomerulonephritis*</td>
<td>10</td>
<td>&lt;5</td>
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<tr>
<td>Serum sickness or reactions</td>
<td>Absent</td>
<td>Morbilliform lesions, sometimes with urticaria</td>
<td>Fever, arthralgias</td>
<td>&gt;90</td>
<td>&lt;5</td>
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<td>resembling serum sickness</td>
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<tr>
<td>Anticoagulant-induced necrosis</td>
<td>Infrequent</td>
<td>Erythema then purpura and necrosis, especially of fatty areas</td>
<td>Pain in affected areas</td>
<td>100</td>
<td>&gt;10</td>
</tr>
<tr>
<td>Angioedema</td>
<td>Often involved</td>
<td>Urticaria or swelling of central part of face</td>
<td>Respiratory distress,* cardiovascular collapse*</td>
<td>&gt;30†</td>
<td>1–6</td>
</tr>
</tbody>
</table>

*Potential cause of death.
†Systemic consequences of widespread injury to the skin, as seen with thermal burns.
‡Nikolsky’s sign.
§The figure refers to the percentage among hospitalized patients; a much smaller percentage of all cases are drug-induced.

Treatment of Stevens-Johnson syndrome and TEN:

- Treatment is supportive; there are no proven treatments for these syndromes.
- Discontinue all medications.
- Don’t give corticosteroids (higher morbidity and mortality).
- Treat like a burn patient with aggressive fluids, pain control, aseptic handling, nutritional support, and antibacterial treatment.