Chapter 5
Dermatologic Emergencies

Caroline LaRosa, Andrew Chen, and Amy Y.-Y. Chen

Stevens-Johnson Syndrome (SJS) and Toxic-Epidermal Necrolysis (TEN) [1, 2]

Key Points:

- Rare, severe, acute, most often drug-related, skin reactions characterized by significant epidermal and mucosal loss.
  - SJS < 10% body surface area (BSA)
  - SJS/TEN overlap 10–30% BSA
  - TEN >30% BSA

C. LaRosa
Dermatology Associates of Western Connecticut, Southbury, CT, USA

A. Chen
Division of Plastic Surgery, Department of Surgery, University of Connecticut School of Medicine, Farmington, CT, USA

A. Y.-Y. Chen (✉)
Central Connecticut Dermatology, Cromwell, CT, USA
e-mail: ayyen@alum.mit.edu

N. A. Vashi (ed.), *The Dermatology Handbook*,
https://doi.org/10.1007/978-3-030-15157-7_5

Signs and symptoms:

- Suspect in patients with fever, flu -like symptoms preceding severe mucocutaneous involvement typically occurs 7–10 days following initiation of inciting drug.
- Skin involvement classically starts on the face and trunk and rapidly spread over the course of a few days to their maximum extent. Skin lesions may be macular or targetoid, coalesce, and desquamate over time.
- + Nikolsky sign
- Erosions of any mucosal surface (eyes, nose, mouth, gastrointestinal tract, vagina, penis, urinary tract)
  - Oral mucosa and conjunctiva are most commonly affected.
  - If any concern of involvement, needs evaluation by appropriate specialist as soon as possible (ophthalmology, ENT, GYN, urology etc.)

Before you see the patient suspected of SJS/TEN:

1. Call pathology lab. Find out how and where to bring the frozen section specimen
2. Call pathology attending and inform his/her about a potential need for reading of a frozen section
3. If you work in a hospital system with a burn unit, you should touch base with the burn unit team regarding such a potential patient. If there is no burn unit in your hospital, medical or surgical intensive care unit will be your best option.

Diagnostic work up:

- Skin biopsy with frozen sections for rapid diagnosis.
  - Obtain two 4 mm perilesional punch biopsy specimens, one for frozen section and one for permanent section.
  - Histology shows full-thickness necrosis of keratinocytes, subepidermal split, and sparse or absent inflammatory infiltrate.
- Baseline CBC, LFTs, BMP, stat IgA level (for IVIG) and cultures.

Table 5.1 Potential causative agents

Medications/class commonly associated with SJS and TEN
Allopurinol
Aminopenicillins
Amithiozone
Antiretrovirals (especially non-nucleoside reverse transcriptase inhibitors)
Barbiturates
Carbamazepine
Chlormezanone
Phenytoin anticonvulsants
Lamotrigine
Phenylbutazone
Piroxicam
Sulfadiazine
Sulfadoxine
Sulfasalazine
Trimethoprim-sulfamethoxazole

Intervention:

- Identify and stop potential causative agents: medication (antibiotics, anticonvulsants or anti-inflammatories) or infection (Table 5.1)
- Correct fluid and electrolyte imbalances; watch for hypercatabolism, and acute respiratory distress syndrome
- Watch out for infection, bacteremia. Low threshold to reculture and treat any suspected infection
- Avoid manipulation of skin and use of adhesive dressings; erosions can be managed with xeroform dressings or vaseline embedded gauze or saline soaked gauze. Many burn units have their own specific wound dressing preference.

- Viscous lidocaine for oral erosions
- Pain management as per primary team
- IV/NG tube for nutrition
- Calculate SCORTEN Severity score for prognosis. One point for each item below (Table 5.2).
  - Age ≥ 40
  - HR ≥ 120 bpm
  - Malignancy
  - BSA detachment ≥ 10% at day 1
  - Serum BUN > 10 mmol/L
  - Serum bicarbonate level < 20 mmol/L,
  - Serum glucose level > 14 mmol/L
- IVIG is frequently used to manage more severe patients. Depending on your hospital, you may need hematology consult to obtain IVIG and nephrology consult if impaired renal function (for dosing). Anti-TNF agents (mostly infliximab and etanercept but also adalimumab) and cyclosporine have shown some efficacy in a few case studies. Role of systemic corticosteroids and other non-steroid immunosuppressive medications is controversial.
- Average time for epidermal regrowth ~ 3 weeks. The most common sequelae are ocular scarring and visual loss. Overall morbidity ~ 5% SJS and ~ 30% TEN.
- The most frequent causes of death are sepsis and multiorgan failure

Table 5.2 SCORTEN Severity score for prognosis

SCORTEN	Mortality rate (%)
0–1	3.2
2	12.1
3	35.8
4	58.3
≥5	90

Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) [3–5]

Key Points:

- Rare, idiosyncratic adverse drug reaction often related to reactivation of herpesviruses. Delayed onset, 2–6 weeks following drug ingestion.

Signs and symptoms:

- Fever
- Skin eruption (most often maculopapular morbiliform exantham)
- Multiorgan involvement. Any visceral organs can potentially be involved. Needs complete review of systems.
  - Liver (60- > 80% of cases), kidneys (10–30% of cases) and lungs (5–25% of cases)
  - Autoimmune thyroiditis is a late complication. Needs follow up with PCP after discharge.
- Hypereosinophilia
- Facial edema
- No mucosal involvement
- Lymphadenopathy (most common cervical lymph node)

Diagnostic work up:

- Skin biopsy often done but shows no diagnostic feature
- Labs: CBC, CMP, UA, viral hepatitis panel, thyroid function test
  - Hematologic abnormalities including high eosinophil counts (may be transient, need for frequent monitoring) and presence of atypical lymphocytes
  - No standardized protocol for herpes virus testing
- Two diagnostic criteria (Tables 5.3A and 5.3B):

Intervention:

- Identify and stop culprit medication: aromatic anticonvulsant (phenytoin, phenobarbital, carbamazepine); other drugs: sulfanamides, minocyclines, dapsone, sulfasalazine, and allopurinol.

Table 5.3A RegiSCAR criteria

RegiSCAR criteria (three out of four * required for diagnosis)
Hospitalization*
Reaction suspected to be drug-related*
Acute rash*
Fever >38 C*
Enlarged lymph nodes at minimum of 2 sites*
Involvement of at least 1 internal organ*
Blood count abnormalities*
Lymphocytes above or below normal limits
Eosinophils above the laboratory limits
Platelets below the laboratory limits

*Necessary for making the diagnosis

Table 5.3B Japanese group's criteria for the diagnosis of DRESS/DIHS

Japanese group's criteria for diagnosis of DRESS/DIHS (needs 7/10 for diagnosis)
Maculopapular rash developing >3 weeks after starting suspected drug
Prolonged clinical symptoms 2 weeks after discontinuation of suspected drug
Fever >38 C
Liver abnormalities (alanine aminotransferase>100 U/L)
Leukocyte abnormalities
Leukocytosis (>11 × 109/L)
Atypical lymphocytosis (>5%)
Eosinophilia (>1.5 × 109/L)
Lymphadenopathy
Humans Herpes 6 reactivation

- No evidence-based guidelinesfor management
  - Supportive measures.
  - Systemic corticosteroids are the first-line therapy. Most patients respond to moderate or high dose steroids of 40–60 mg prednisone equivalent daily, with long gradual dose-reduction given over 10 weeks. Treatments with non-steroids immunosuppressants, plasma exchange and IVIG depends on specific organ involvement.
- Potentially fatal drug reaction with a mortality rate of 10%.

Necrotizing Fasciitis [6]

Key Points:
- Aggressive, rapidly progressive inflammatory infection of the fascia leading to extensive necrosis of subcutaneous tissue and fascia with relative sparing of the muscle.

Signs and symptoms:
- Most common initial cutaneous findings are pain, swelling, and erythema (may be confused with cellulitis and other skin and subcutaneous infections).
- Think of necrotizing fasciitis if rapid progression of cutaneous lesion, necrosis, dusky appearance or cyanosis of the tissue, and extreme local tenderness that is out-of-proportion to the exam.
- Fever, tachycardia, hypotension, altered mental state + other signs of sepsis

Diagnostic work up:
- Imaging: CT is 80% sensitive, while MRI is 100% sensitive with 86% specificity.
  - Gas may be identified in tissue (most often seen in gas gangrene caused by clostridia).
  - Asymmetric fascial thickening, fat stranding, and gas tracking along fascial planes are the most important imaging findings on CT and MRI scans.
- Two types of necrotizing fasciitis, distinguished based on bacterial morphology. Type I: polymicrobial bacterial with both aerobic and anaerobic bacteria. Type II: monomicrobial, most common Group A Streptococcus.

- Intervention:
- Surgical Emergency
  - Surgical debridement and IV antibiotics.
  - Hyperbaric oxygen may be used as adjunctive therapy.

Staphylococcal Scalded Skin Syndrome (SSSS) [7–10]

Key Points:

- Systemic toxic disease resulting from exfoliative toxin (ET) produced by infection with Staphylococcus aureus.
  - Toxin cleaves demoglein 1 in the superficial epidermis, creating blisters and denuding of the skin.
- More often occurs in children younger than 5. Occasionally occurs in adults (especially those with impaired immune status or renal dysfunction).

Signs and symptoms:

- Infection may begin as sore throat and purulent conjunctivitis (alternatively, in neonates, the umbilical cord is often the source of infection)
- Within 48 h of symptom onset, development of
  - Fever, malaise
  - Erythematous tender areas on the face, neck, axilla, and perineum develop. Flaccid bullae develop in erythematous areas
  - + Nikolsky sign
  - Mucosal membranes typically spared

Diagnostic work up:

- Skin biopsy: detached superficial epidermis with separation at the granular layer
- Culture from: blood, urine, nasopharynx, umbilicus, or any suspected focus of infection. Culture of intact blister are sterile.

Intervention:

- Management: ICU or burn unit
  - Supportive care including NG tube, IV fluids

  - Early initiation of IV antibiotics (penicillinase-resistant penicillins recommended, clarithromycin or cefuroxime if penicillin-allergic)
  - Pain management
    - Avoid NSAIDS due to risk of impaired renal function
  - IVIG or fresh frozen plasma useful in some cases
  - Silicone or none-stick dressings over denuded skin
  - Monitor for sepsis and pneumonia
- Prognosis: re-epithelialization of denuded skin in 6–12 days
  - No scarring
- Mortality is less than 10% in children, but between 40–63% in adults.

Filler Emergencies [11–15]

Key Points:

- Intravascular injection of filler can lead to devastating complications such as skin necrosis or blindness.
- Preparation of filler crash kit
- Danger Zones/Risk Factors
  - Deep injections – especially nasal radix and lateral nasal wall
  - Upper lip philtrum injection – vessel is superficial
  - Large volume bolus (greater than 0.1 cc)
  - Prior rhinoplasty
  - High pressure injection
  - Small, sharp needles

Signs and Symptoms:

- Arterial injection – immediate, severe, and disproportionate pain and color changes (white spots)
- Venous injection – less severe, dull, or delayed pain (in some cases, no pain)
- Filler blindness [11] – mechanism of action through retrograde flow; also possible vascular compression
  - Injection of supratrochlear, supraorbital, angular and dorsal nasal arteries (all branches of the external carotid artery) will result in retrograde flow of the filler – emboli into the ophthalmic artery [12]

  - Central retinal artery occlusion for more than 60–90 min causes irreversible blindness

Diagnostic work up: This is a clinical diagnosis

- Patients may exhibit:
  - Severe pain (or no pain)
  - Blanching
  - Mottled skin discoloration (livedo reticularis)
  - Blindness

Supplies for Filler Emergency Kit: Nitropaste, Hyaluronidase, Aspirin, oxygen
Others: timolol, acetazolamide, nitroglycerin, mannitol

Interventions:

- Use warm compress and massage filler out of entry site
  - 5–10 min, every 1–2 h
- Apply topical nitropaste to the area
  - Half inch of 2%
- Give oral baby aspirin
- Give supplemental oxygen
- Administer hyaluronidase for hyaluronic acid based fillers
  - Available forumlations: hylase (derived from bovine testicular hyaluronidase), vitrase (derived from ovine hyaluronidase), hylenex (recombinant human hyaluronidase)
  - For intravascular infarction, high doses of hyaluronidase (200–300 U) have been recommended – repeated daily for 2 days [13].
  - In acute ischemia, consensus recommendations to treat the entire ischemic area with hyaluronidase. Repeat until clinical resolution is achieved (hourly or daily) [14].
  - Doses up to 1500 U may be required for reversal of vascular compromise
- Recommended medical treatment for filler blindness [15]:
  - Digital massage: start immediately while preparing the treatment and to continue once the drugs have been administered.
    - Place patient in supine position with eyes closed

    - Apply firm pressure (enough to ensure that the eyeball is indented about 2–3 mm) on the eyeball through the closed eyelids
    - Apply firm pressure for 5–15 s and quickly release.
    - Repeat this cycle for at least 5 min.
- One drop of topical timolol 0.5% and/or an acetazolamide 500 mg tablet (after excluding allergy to sulfonamides)
- Sublingual pill of aspirin (325 mg) or one of nitroglycerin (0.6 mg).
- Intravenous mannitol infusion, 100 mL over 30 min, of mannitol 20%.
- If despite these measures the patient does not recover vision in the first 15–20 min, the patient must be referred to ophthalmology for anterior chamber paracentesis to decrease intraocular pressure, and possible retro-bulbar injection of hyaluronidase

References

1. Gonzalez-Herrada C, Rodriguez-Martin S, Cachafeiro L, Lerma V, Gonzalez O, Lorente JA, et al. Cyclosporine use in epidermal necrolysis is associated with an important mortality reduction: evidence from three different approaches. J Invest Dermatol. 2017;137(10):2092–100.
2. Monteiro D, Egipto P, Barbosa J, Horta R, Amarante J, Silva P, et al. Nine years of a single referral center management of Stevens-Johnson syndrome and toxic epidermal necrolysis (Lyell's syndrome). Cutan Ocul Toxicol. 2017;36(2):163–8.
3. Eshki M, Allanore L, Musette P, Milpied B, Grange A, Guillaume JC, et al. Twelve-year analysis of severe cases of drug reaction with eosinophilia and systemic symptoms: a cause of unpredictable multiorgan failure. Arch Dermatol. 2009;145(1):67–72.
4. Penchilaiya V, Kuppili PP, Preeti K, Bharadwaj B. DRESS syndrome: Addressing the drug hypersensitivity syndrome on combination of sodium valproate and olanzapine. Asian J Psychiatr. 2017;28:175–6.
5. Shiohara T, Iijima M, Ikezawa Z, Hashimoto K. The diagnosis of a DRESS syndrome has been sufficiently established on the

basis of typical clinical features and viral reactivations. Br J Dermatol. 2007;156(5):1083–4.
6. Kiat HJ, En Natalie YH, Fatimah L. Necrotizing fasciitis: how reliable are the cutaneous signs? J Emerg Trauma Shock. 2017;10(4):205–10.
7. Handler MZ, Schwartz RA. Staphylococcal scalded skin syndrome: diagnosis and management in children and adults. J Eur Acad Dermatol Venereol. 2014;28(11):1418–23.
8. Oranje AP, de Waard-van der Spek FB. Recent developments in the management of common childhood skin infections. J Infect. 2015;71 Suppl(1):S76–9.
9. Urata T, Kono M, Ishihara Y, Akiyama M. Adult staphylococcal scalded skin syndrome successfully treated with multimodal therapy including intravenous immunoglobulin. Acta Derm Venereol. 2018;98(1):136–7.
10. Valero-Portero S, Quesada-Dorigne L, Quesada Lopez JJ, Brea-Lamas AB, Cidras-Pidre M. Staphylococcal scalded skin syndrome in an extremely preterm newborn: management in a neonatal intensive care unit. Arch Dis Child Fetal Neonatal Ed. 2017;102(3):F224–F5.
11. Carruthers JD, Fagien S, Rohrich RJ, Weinkle S, Carruthers A. Blindness caused by cosmetic filler injection: a review of cause and therapy. Plast Reconstr Surg. 2014;134(6):1197–201.
12. Lazzeri D, Agostini T, Figus M, Nardi M, Pantaloni M, Lazzeri S. Blindness following cosmetic injections of the face. Plast Reconstr Surg. 2012;129(4):995–1012.
13. Cohen JL, Biesman BS, Dayan SH, DeLorenzi C, Lambros VS, Nestor MS, et al. Treatment of hyaluronic acid filler-induced impending necrosis with hyaluronidase: consensus recommendations. Aesthet Surg J. 2015;35(7):844–9.
14. Signorini M, Liew S, Sundaram H, De Boulle KL, Goodman GJ, Monheit G, et al. Global aesthetics consensus: avoidance and management of complications from hyaluronic acid fillers-evidence- and opinion-based review and consensus recommendations. Plast Reconstr Surg. 2016;137(6):961e–71e.
15. Urdiales-Galvez F, Delgado NE, Figueiredo V, Lajo-Plaza JV, Mira M, Moreno A, et al. Treatment of soft tissue filler complications: expert consensus recommendations. Aesthetic Plast Surg. 2018;42(2):498–510.