Toxic Epidermal Necrolysis and Stevens-Johnson Syndrome

Definition and Epidemiology

Toxic Epidermal Necrolysis (TEN) and Stevens-Johnson Syndrome (SJS) are severe, life-threatening mucocutaneous reactions characterized by widespread epidermal detachment and mucosal erosions, typically triggered by medications or infections. SJS involves <10% body surface area (BSA), SJS-TEN overlap 10-30% BSA, and TEN >30% BSA.

- Prevalence Incidence of SJS is 1-6 per million person-years; TEN is rarer at 0.4-1.2 per million. Mortality is 10-20% for SJS and 30-50% for TEN.
- Risk Factors Recent medication exposure (e.g., allopurinol, sulfonamides), HIV infection, HLA-B*1502 allele (carbamazepine in Asians), active malignancy.
- Rare Demographics Pediatric cases (often Mycoplasma-related), post-transplant patients, autoimmune disease (e.g., SLE).

Pathophysiology

- Mechanisms SJS/TEN results from a cytotoxic T-cell (CD8+) mediated immune response targeting keratinocytes, triggered by drugs or infections. Granulysin and Fas-ligand induce apoptosis, leading to epidermal necrosis and detachment.
- Effects Widespread keratinocyte death causes full-thickness epidermal loss, resembling burns, with significant fluid loss, thermoregulatory failure, and infection risk. Mucosal involvement (oral, ocular, genital) causes erosions and scarring.
- Molecular Pathways Drug metabolites (e.g., allopurinol's oxypurinol) bind HLA-B alleles, activating T-cells via TCR signaling. IL-15 and TNF-α amplify inflammation. Annexin A1 dysregulation exacerbates keratinocyte death.
- Key Pathway Drug/infection antigen → HLA-TCR interaction → Cytokine release (granulysin, TNF-α) → Epidermal apoptosis → Detachment and mucosal erosion.

Causes

Category	Common Triggers	Rare Triggers	Notes
Medications	Allopurinol, carbamazepine, sulfonamides	Checkpoint inhibitors, NSAIDs	80-90% of cases; onset 1-4 weeks post-exposure
Infectious	Mycoplasma pneumoniae, HSV	Hepatitis A, Yersinia	Mycoplasma common in pediatric SJS
Genetic	HLA-B*1502 (carbamazepine), HLA-B*5801 (allopurinol)	HLA-A*3101 (lamotrigine)	Genetic screening reduces risk in high-risk populations
Autoimmune	SLE, graft-versus-host disease	Sjögren's syndrome	Autoimmune diseases may mimic or exacerbate SJS
Neoplastic	None	Lymphoma, paraneoplastic	Sarcoid-like reactions mimic SJS
Idiopathic	Unknown	Post-vaccination (rare)	<5% of cases; often multifactorial

Clinical Presentation

Symptoms

- Fever, malaise, prodromal flu-like symptoms (1-3 days)
- Painful rash progressing to blisters and skin sloughing
- Mucosal pain (oral, ocular, genital erosions)
- Rare Hemorrhagic crusting, dysphagia, vision loss

Exam

- Nikolsky sign (skin detachment with lateral pressure)
- Erythematous macules, targetoid lesions, bullae
- **Mucosal erosions (90%):** stomatitis, conjunctivitis, urethritis
- Rare Subungual hemorrhage, palmoplantar desquamation

Red Flags

>30% BSA detachment, respiratory distress (airway involvement), sepsis signs

Labs and Studies

Labs

- CBC Eosinophilia (20%), lymphopenia (sepsis risk)
- CMP Hypoalbuminemia (fluid loss), elevated Cr (AKI), transaminitis

- ESR/CRP Elevated, non-specific
- Advanced Cytokine panel (IL-15, granulysin), HLA typing (post-recovery)

Imaging

- CXR Rule out pneumonia (Mycoplasma), ARDS (sepsis)
- CT Chest If tracheobronchial involvement suspected
- Advanced Skin MRI (research, differentiates SJS from erythema multiforme)

Other

- Skin Biopsy Full-thickness epidermal necrosis, lymphocytic infiltrate
- SCORTEN Score Predicts mortality (age, HR, BSA, Cr, HCO3-, glucose, malignancy)
- Cultures Blood, skin, mucosal (rule out secondary infection)
- Advanced Direct immunofluorescence (negative in SJS/TEN, rules out pemphigus)
- Ocular Exam Slit-lamp for corneal erosions, synechiae

Diagnosis

Criteria

Prodromal fever, painful rash, mucosal involvement + skin biopsy showing epidermal necrosis + >1% BSA detachment (SJS <10%, TEN >30%).

Differential

Erythema multiforme major (EMM), drug reaction with eosinophilia and systemic symptoms (DRESS), pemphigus vulgaris, staphylococcal scalded skin syndrome (SSSS).

Flowsheet

- Step 1 History/Exam Recent drug exposure (1-4 weeks), fever, Nikolsky sign, mucosal erosions
- Step 2 Labs SCORTEN, CMP, CBC; rule out infection (cultures, Mycoplasma PCR)
- Step 3 Biopsy Confirm full-thickness necrosis; exclude EMM (subepidermal split)
- Step 4 Imaging CXR (pneumonia), ophthalmology consult (ocular involvement)
- Step 5 Score SCORTEN ≥3 or >30% BSA → Burn ICU transfer

Treatment

General Principles

Stop offending drug, provide supportive care, prevent infection, and modulate immune response.

Supportive Care

- Burn ICU Transfer For >10% BSA or SCORTEN ≥3; sterile environment
- Fluid Resuscitation Parkland formula (4 mL/kg/% BSA, half in first 8h), adjust for urine output
- Wound Care Non-adherent dressings (e.g., Vaseline gauze), avoid debridement
- Nutrition TPN or NG feeding (high protein, 1.5-2 g/kg/day)

Specific Therapies

- Stop Culprit Drug Immediate withdrawal (e.g., allopurinol, lamotrigine)
- IV Immunoglobulin (IVIG) 2-3 g/kg over 3-5 days, reduces mortality in TEN
- Cyclosporine 3-5 mg/kg/day IV/PO, inhibits T-cell activation (alternative to IVIG)
- Advanced Etanercept 50 mg SC weekly, anti-TNF (promising in trials), plasmapheresis (refractory)
- Ocular Care Erythromycin ointment, amniotic membrane transplant for severe erosions
- Infection Prophylaxis Silver sulfadiazine (avoid sulfa in sulfa-triggered cases), vancomycin for MRSA
- Rare Causes Mycoplasma-related (azithromycin 500 mg IV q24h), lymphoma (chemotherapy)

Monitoring

- Daily SCORTEN, CMP, CBC for organ dysfunction
- Wound cultures q48h, monitor for sepsis (fever, tachycardia)
- Ophthalmology follow-up q1-2 days for corneal protection

Complications

Acute

- Sepsis Leading cause of death (30-50% in TEN), often Pseudomonas or MRSA

- Multi-Organ Failure AKI, ARDS, hepatitis (SCORTEN ≥3)
- Ocular Damage Corneal scarring, synechiae, blindness

Long-Term

- Chronic Skin Changes Hypopigmentation, hypertrophic scars
- Mucosal Strictures Esophageal, urethral, vaginal stenosis
- Rare Post-inflammatory nail dystrophy, alopecia, sicca syndrome

Clinical Scenarios

Case 1 SJS from Lamotrigine

- Presentation 30 y/o F with fever, painful rash, and oral erosions 2 weeks after starting lamotrigine. Vitals BP 110/70, HR 100, SpO2 96%, RR 18. Exam 8% BSA detachment, Nikolsky sign, stomatitis.
- Labs/Studies Biopsy Epidermal necrosis. SCORTEN 1, eosinophilia. HLA-B*1502 negative.
- Interpretation SJS, lamotrigine-induced.
- Management Stop lamotrigine, IVIG 2 g/kg over 3 days, burn ICU transfer. Erythromycin ointment for eyes. Vancomycin prophylaxis. Rash stabilizes by day 5, discharge with dermatology follow-up.

Case 2 TEN with Mycoplasma (Rare)

- Presentation 15 y/o M with fever, cough, and extensive skin sloughing. Vitals BP 100/60, HR 120, SpO2 92%, RR 22. Exam 35% BSA detachment, conjunctival erosions.
- Labs/Studies Biopsy Necrosis, Mycoplasma PCR positive, CXR pneumonia. SCORTEN 3.
- Interpretation TEN, Mycoplasma-associated.
- Management Burn ICU, cyclosporine 4 mg/kg/day, azithromycin 500 mg IV q24h. TPN, amniotic membrane for eyes. Sepsis treated with piperacillin-tazobactam. Recovery by week 3.

Case 3 SJS-TEN Overlap in HIV

- Presentation: 40 y/o M with HIV (CD4 200) on cotrimoxazole presents with fever, rash, and genital erosions. Vitals BP 115/75, HR 110, SpO2 94%, RR 20. Exam 15% BSA detachment, urethritis.
- Labs/Studies: SCORTEN 2, Cr 1.8 mg/dL, blood cultures negative. Biopsy Confirms SJS-TEN.

- Interpretation: SJS-TEN overlap, cotrimoxazole-triggered, HIV-related.
- Management: Stop cotrimoxazole, etanercept 50 mg SC, burn ICU. Silver sulfadiazine, ID consult for ART adjustment. Erosions heal by week 2, discharge with ophthalmology follow-up.

Expert Tips

- Calculate SCORTEN on admission; score ≥3 warrants burn ICU transfer
- Avoid systemic steroids; they increase infection risk and delay healing
- Use IVIG or cyclosporine early (within 48h) to halt progression; etanercept for severe TEN
- Screen for HLA-B*1502 before carbamazepine in Asians; HLA-B*5801 for allopurinol
- Monitor ocular involvement daily; amniotic membranes prevent synechiae
- Pitfall Misdiagnosing as SSSS (children, superficial split); biopsy differentiates
- Advanced Trial anti-IL-15 therapies (research), genetic profiling for drug risk (CYP2C19)

Key Pearls

- SJS (<10% BSA) and TEN (>30% BSA) are drug-induced in 80-90% of cases; stop culprit immediately
- Nikolsky sign and mucosal erosions are diagnostic; biopsy confirms epidermal necrosis
- Burn ICU is critical for >10% BSA; fluid needs mirror burns (Parkland formula)
- IVIG or cyclosporine are mainstay therapies; avoid steroids
- Rare Mycoplasma-related SJS in children requires antibiotics and supportive care

References

UpToDate “Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis: Diagnosis and Management” (2025)

JAAD “SJS/TEN: Advances in Management” (2024)

Lancet “Toxic Epidermal Necrolysis: A Review” (2023)

NEJM “Mycoplasma-Associated SJS in Children” (2024)

J Allergy Clin Immunol “HLA and Drug-Induced SJS/TEN” (2023)

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