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1 ABSTRACT

2 Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are life-threatening
3 conditions with high morbidity and mortality. Supportive care management of SJS/TEN is highly
4 variable. A systematic review of the literature was performed by dermatologists,
5 ophthalmologists, intensivists and gynecologists with expertise in SJS/TEN to generate
6 statements for supportive care guideline development. Members of the Society of Dermatology
7 Hospitalists (SDH) with expertise in SJS/TEN were invited to participate in a modified, online
8 Delphi-consensus. 9-point Likert scale questionnaires regarding 135 statements were
9 administered. The RAND/UCLA appropriateness method was employed to evaluate and select
10 proposed statements for guideline inclusion; statements with median ratings of 6.5-9 and
11 disagreement index ≤ 1 were included in the guideline. For the final round, the guidelines were
12 appraised by all the participants. An evidence-based discussion and recommendations for
13 hospital setting and care team, wound care, ocular care, oral care, urogenital care, pain
14 management, infection surveillance, fluid and electrolyte management, nutrition and stress ulcer
15 prophylaxis, airway management, and anticoagulation in adult patients with SJS/TEN are
16 included.

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24 **CAPSULE SUMMARY**

- 25 • Supportive care management of SJS/TEN in practice is highly varied.
- 26 • The Society of Dermatology Hospitalists presents evidence-based practice guidelines for
- 27 hospital setting and care team, wound care, ocular care, oral care, urogenital care, pain
- 28 management, infection surveillance, fluid and electrolyte management, nutrition and stress
- 29 ulcer prophylaxis, airway management, and anticoagulation for adult patients with SJS/TEN.

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47 **BACKGROUND**

48 Stevens-Johnson syndrome/toxic epidermal necrosis (SJS/TEN) spectrum disease (i.e., SJS, SJS-
49 TEN overlap, and TEN) is a rare, severe cutaneous reaction affecting 1.6 to 9.2 patients per
50 million annually in the United States.¹⁻⁶ With mortality rates between 15% and 49%,⁷⁻⁹ early
51 intervention with intensive supportive care is critical, yet the care implemented in practice is
52 highly variable.¹⁰ Standardized SJS/TEN management guidelines are a pressing unmet clinical
53 and research priority.

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55 **METHODS**

56 Eleven topics were developed within the scope of the guidelines (**Table 1**). For each topic,
57 PubMed, EMBASE, CINAHL, the Cochrane Library, and clinicaltrials.gov were searched for
58 meta-analyses, clinical trials, open studies, case series, and case reports through November 2018.
59 Articles not written in English were excluded. The search terms and strategies are detailed in
60 **eAppendix1**. The authors identified additional references from manuscript citations, performed
61 detailed evaluation, summarized the literature, and provided level of evidence and strength of
62 recommendations, as indicated in **eAppendix2**. Prior guidelines on SJS/TEN were also
63 evaluated.¹¹⁻¹⁶

64 Experts in SJS/TEN from the Society of Dermatology Hospitalists (SDH) were invited to
65 participate in the modified Delphi process (**eAppendix3**) and to evaluate the level of
66 appropriateness of 135 statements regarding supportive care of patients with SJS/TEN.

67 Using the RAND/UCLA appropriateness method,¹⁷ each statement was evaluated by the 1-to-9
68 appropriateness rating scale and by the level of disagreement, as measured by a disagreement
69 index (DI). A median appropriateness value of $1 \leq \text{median} < 3.5$ was considered “inappropriate;”

70 3.5 ≤ median < 6.5 “uncertain;” and 6.5 ≤ median ≤ 9.0 “appropriate.” Descriptive statistics were
71 calculated for each item during each round and presented with a histogram (**eAppendix4**). R
72 version 3.6.1 (R Core Team 2019, Vienna, Austria) was used to perform all analyses.

73

74 **RESULTS**

75 The SDH supportive care practice guidelines for the management of SJS/TEN in adults are
76 presented in **Table 2**.

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78 **DISCUSSION**

79 **Hospital setting and care team**

80 Specialized care with a multidisciplinary approach is essential to the evaluation and treatment of
81 patients with SJS/TEN.^{11,13,14,16} Dermatologists should directly participate in patient
82 management, with input from other specialists with expertise in management of the
83 complications of complex epidermal loss, such as fluid management, wound care, and
84 mechanical ventilation.¹⁸⁻²⁰ Several small uncontrolled studies have shown decreased mortality
85 with early transfers to burn units or intensive care units (ICU).²¹⁻²⁸ The SDH expert panel
86 recommends care take place in a medical or burn ICU setting, with staff trained in the care of
87 patients with SJS/TEN. A private room with temperature and humidity control and at least 1:1
88 nursing care is recommended.

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90 **Wound care**

91 Wound care for SJS/TEN generally follows current practices in burn management, as strong
92 evidence specific to SJS/TEN is lacking.²⁹ Percentage body surface area (BSA) of detachable

93 epidermis is integral to patient prognosis and disease progression.³⁰ Unlike burn guidelines,
94 which recommend surgical or high-velocity saline debridement of detached epidermis,^{12,31,32} the
95 dermatologic SDH expert panel favors a conservative approach to preserve detached epidermis
96 as a biologic dressing, reflecting the different underlying mechanisms involved with SJS/TEN
97 and burn injury.³³ Anti-shear strategies, such as limiting dressing changes, using an air-fluidized
98 bed, and selecting non-adherent dressings, are recommended.^{11,16,34} Lysis and careful drainage of
99 large or painful bullae may be performed for comfort only. Gentle cleansing, consisting of sterile
100 water or dilute chlorhexidine with dressing changes, is advised.³⁵ Application of an emollient
101 such as petrolatum jelly to the skin enhances barrier function, reduces transcutaneous water loss
102 and encourages re-epithelialization.^{11,36} Alternatively, modern non-adherent, silver-impregnated
103 primary dressings are recommended for their antibacterial properties, reduced requirement for
104 dressing changes, and improved patient comfort.^{29,37-41} Secondary absorptive dressings should be
105 used to control exudate.

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107 **Ocular care**

108 Ocular involvement may precede or follow cutaneous disease and occurs in 50-90% of
109 patients.^{27,42-48} Acute ocular findings range from conjunctival hyperemia to loss of the entire
110 ocular surface and eyelid margin epithelium.^{45,49,50} The severity of ocular involvement disease
111 has not been reliably correlated with the severity of skin disease or SCORTEN.^{48,49,51,52}
112 The SDH expert panel recommends ophthalmic evaluation of all patients with suspected
113 SJS/TEN, even if there is no apparent ocular involvement. Examination should occur during the
114 initial assessment, daily until findings have stabilized, and then the frequency is determined on
115 an individual basis. The entire ocular surface and eyelid margins should be examined with eyelid

116 eversion, eye rotation and fluorescein staining. Resting eyelid position should be assessed so
117 lagophthalmos can be promptly addressed. Saline may be used to remove loose debris and
118 appropriate tools used to lyse adhesions during daily exams. Grading of ocular findings may aid
119 in medical and surgical decision making (e.g. eAppendix5).⁴⁶

120 Amniotic membrane transplantation (AMT) has shown to mitigate long-term ocular
121 complications in multiple studies.^{51,53-59} AMT should be offered to patients with significant
122 conjunctival, corneal or eyelid margin epithelial defects. If AMT is indicated and not available, a
123 hospital transfer should be considered. Amniotic membrane should cover the entire affected
124 surface including eyelid margins and may need to be replaced over time.

125 Limited data address the use of topical therapies, including lubricants, anti-inflammatory agents
126 and anti-microbial agents.^{15,49,60} For patients without acute ocular involvement, preservative-free
127 artificial tears (AT) should be considered (e.g. AT 4 x/day). Any degree of ocular involvement
128 should prompt high-frequency AT (e.g. AT every 1-2 hours). Topical corticosteroids are used to
129 ameliorate ocular inflammation and may improve visual outcomes.^{15,46,59,62} For any degree of
130 ocular inflammation, a topical corticosteroid drop should be applied to the ocular surface (e.g.
131 prednisolone acetate 1%, 2-6 x/day), and a corticosteroid ointment should be applied to the
132 eyelids (e.g. fluorometholone 0.1%, 2-6 x/d). There is limited evidence to guide the use of
133 prophylactic topical antibiotics; however, for patients with ocular epithelial defects, a broad-
134 spectrum topical antibiotic (e.g. Moxifloxacin 0.5%, 3 x/day) should be used. If an ocular
135 infection is suspected, appropriate cultures should be obtained.

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139 **Oral care**

140 Oral involvement occurs in 93 to 100 % of patients with SJS/TEN, resulting in pain, impaired
141 oral intake, and poor oral hygiene.^{43,63} Long-term complications include sicca syndrome in up to
142 40% of patients and scarring.⁶⁴⁻⁶⁶

143 All patients with SJS/TEN should have an oral cavity exam on initial presentation and daily
144 thereafter. The use of topical therapies for treating oral involvement in acute SJS/TEN has been
145 adapted from studies in patients with autoimmune blistering diseases involving the oral mucosa,
146 chemotherapy-induced mucositis, and oral graft-versus-host disease (GvHD).⁶⁷⁻⁷¹ To provide
147 short-term pain relief and facilitate oral intake, a mouthwash containing a topical anesthetic
148 agent such as lidocaine is recommended.⁶³ Topical coating agents have been recommended to
149 reduce pain and facilitate healing by covering mucosal ulcerations, such as hydroxypropyl
150 methylcellulose film-forming agents (e.g., Zilactin®), Gelclair®, and Amphojel®.⁶⁸

151 Oral rinses increase clearance of debris, promote oral hygiene, and improve patient comfort.⁶⁸

152 Antiseptic oral agents are preferred by the SDH expert panel, with a recommendation to consider
153 diluted chlorhexidine.⁷² Ultrapotent topical corticosteroids (e.g., clobetasol gel or ointment
154 (0.05%) with or without adhesive bases such as carboximethyl or hydroxyethyl-cellulose, three
155 to four times a day) have been shown to be beneficial in the management of patients with erosive
156 diseases of the oral mucosa^{73, 69, 74-76} and are recommended by the expert panel. Dexamethasone
157 mouth rinse (0.1 mg/mL) or clobetasol propionate 0.05% in aqueous solution, are alternative
158 options. Evidence to support the use of other topical anti-inflammatory agents is lacking.⁷⁷

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162 Urogenital care

163 Urogenital involvement occurs in approximately 70% of women⁷⁸⁻⁸⁰ and men⁸⁰ with SJS/TEN,
164 resulting in erosions of the scrotum/labia, penis/vulva, dysuria, hematuria, urinary retention, and
165 long-term sequelae such as urethral stenosis and scarring, xerosis, phimosis, dyspareunia,
166 chronic pain, bleeding, sexual dysfunction, infertility, and anxiety.⁷⁸⁻⁸⁹

167 The urogenital tract of all patients with SJS/TEN should be examined upon initial assessment
168 and daily during hospitalization, ideally by a gynecologist, urologist, or urogynecology
169 specialist. The efficacy of treatment strategies has not been adequately studied. Emollients, such
170 as petrolatum, are commonly used to protect inflamed mucosa, reduce adhesion formation, and
171 facilitate healing.^{16,80,85} Ultrapotent topical corticosteroids applied to genital lesions during the
172 acute phase may be helpful.⁸⁵ If there is clinical suspicion for candidiasis in the setting of vaginal
173 steroid use, consider obtaining a KOH and fungal culture and initiating treatment with antifungal
174 medications.

175 Insertion of an intravaginal device as early as possible may prevent adhesions and stenosis in
176 those with visible disease.⁷⁹ Intravaginal devices should be used regularly until complete healing
177 of lesions and may remain in place for up to 24 hours before being replaced. In patients
178 uncomfortable with using an intravaginal device, medications can be applied twice daily with a
179 vaginal applicator. The role of intravaginal devices in patients without visible disease is
180 uncertain (median 5, DI 0.49).

181 Menstrual suppression may reduce the risk of vaginal adenosis and endometriosis and can be
182 considered in women with severe genital mucosal involvement.^{83,85} Topical estrogen has been
183 shown to promote healing in other vulvar dermatoses and burns and should be considered as
184 adjuvant therapy.⁹⁰⁻⁹⁴

185 Urinary catheters are recommended to decrease pain with urination, prevent urinary obstruction,
186 and monitor fluid balance.^{11,80} They should be removed as soon as complete healing occurs and
187 the patient passes a voiding trial. The SDH expert panel recommends topical lidocaine to
188 minimize pain with urinary catheter and vaginal device insertion.

189

190 **Pain management**

191 Mucocutaneous pain is a key feature of SJS/TEN, occurring in ~ 90% of patients and associated
192 with physical and psychological burden and prolonged hospital stay. It is exacerbated by
193 physical activity, procedures, and dressing changes.⁹⁵

194 Pain management should be individualized according to pain level and patient comorbidities.

195 Pain level should be evaluated every 4 hours using visual or numeric analog scales.⁹⁶

196 Wound care strategies that minimize dressing changes are associated with reduced pain.^{37,39,97}

197 Acetaminophen may be sufficient for treatment of mild pain. However, opioid therapy is

198 frequently indicated. Oral synthetic opiates are helpful to control moderate pain. Morphine or

199 fentanyl given enterally, by intravenous bolus, patient-controlled analgesia, or via infusion, may

200 be necessary for more severe pain.⁹⁸ Low-dose ketamine infusions may be considered as an

201 alternative or adjuvant therapy for pain in SJS/TEN.^{96,99,100} Gabapentin and pregabalin help

202 address neuropathic pain and may decrease opioid consumption in both the acute and healing

203 phases.¹⁰¹⁻¹⁰⁴ Non-steroidal anti-inflammatory drugs should generally be avoided due to their

204 potential for renal and gastric injury.

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208 Infection surveillance

209 Infections have been reported in up to 85% of patients with SJS/TEN,¹⁰⁵ and sepsis is the most
210 common cause of death.¹⁰⁶⁻¹⁰⁹ Exposed dermis facilitates bacterial colonization, leading to
211 increased infection risk and impaired re-epithelialization.¹¹
212 The skin should be monitored frequently for signs of infection, such as increasing skin pain.¹¹
213 Confusion, hypotension, reduced urinary output, and reduced oxygen saturation may indicate
214 systemic infection.^{106,110} In patients in whom infection is suspected, bacterial swabs should be
215 obtained. Slow-healing sites with erosions or vesicles may indicate HSV super-infection,
216 particularly in genital and oral sites; viral swabs should be obtained in such cases.¹¹ The SDH
217 expert panel did not favor routine performance of skin cultures to guide antimicrobial therapy.
218 Severe ear-nose-throat (ENT) involvement has been associated with pulmonary infection.¹¹¹
219 Evaluation using nasal fiberoptic endoscopy should be considered when dysphonia or dyspnea
220 are present. For intubated patients, there was disagreement and uncertainty (median 5, DI > 1.02)
221 regarding the need of routine fiberoptic bronchoscopy to obtain bronchoalveolar lavage
222 specimens for culture and sensitivity testing, in the absence of signs of infection.¹¹²
223 Hand hygiene and hospital infection control measures should be followed to prevent infection.
224 Prophylactic antibiotic coverage in the absence of proven or suspected infection may select for
225 resistant organisms and contribute to increased mortality.¹¹³ Antibiotic-therapy should be tailored
226 to culture data^{12,113,114} and local antibiogram.¹¹⁵ Data suggest *Staphylococcus aureus*,
227 *Pseudomonas aeruginosa*, and *Enterobacteriaceae* organisms are the most common causes of
228 blood stream infection in SJS/TEN.¹⁰⁶
229 Patients with SJS/TEN may develop neutropenia, especially in severe cases.^{116,117} The role of
230 recombinant human G-CSF in this setting is uncertain (median 5, DI 0.32).^{118,119}

231 Fluid management and electrolytes

232 Electrolytes abnormalities occur in approximately 20% of patients with SJS/TEN.⁹⁵ Due to
233 extensive skin failure, patients may have large insensible losses.¹¹ Oropharyngeal lesions
234 contribute to decreased oral intake. Electrolytes can be lost in blister fluid, which is rich in
235 sodium, potassium, and chloride.¹³ Hypophosphatemia is also common.¹³ Fluid balance and
236 electrolytes should be monitored daily to ensure adequate correction during treatment.¹²⁰
237 Fluid resuscitation in SJS/TEN is adapted from the management of burn patients, though fluid
238 losses, in general, are less.¹²¹ Current evidence supports the use of crystalloid for resuscitation,
239 though there are no prospective data to guide fluid selection.¹²¹⁻¹²³ Evidence regarding colloid
240 fluids and albumin is controversial,^{121,124-127} and their use was considered uncertain by the expert
241 panel (median 6, DI 0.65). Appropriate calculation of fluid resuscitation volume based on the
242 percent of detached skin was also uncertain (median 5, DI 0.55).^{14,123,126} The expert panel
243 recommended resuscitation be guided by physiologic parameters, with a target urine output of
244 0.5 – 1 mL/kg/hr.^{25,128,129}

245

246 Nutrition and stress ulcer prophylaxis

247 Caloric requirements in SJS/TEN are increased.¹¹ Caloric intake should be 30-35 kcal/kg.¹³ In
248 patients unable to eat, a nasogastric tube should be used to provide enteral nutrition unless there
249 is involvement of the nasopharyngeal mucosa.¹³⁰⁻¹³² Enteral nutrition is preferable to prevent
250 stress ulcer formation and infectious complications.¹³³ If adequate nutritional requirements
251 cannot be met enterally, parenteral nutrition can be used to supplement deficiencies,^{99,134}
252 however it has been associated with higher mortality rates.¹³⁵

253 Hyperglycemia is common in SJS/TEN and is associated with increased mortality, therefore,
254 careful glucose monitoring to ensure adequate glycemic control is recommended.¹³¹ Tight
255 glycemic control regimens (serum glucose 80–110 mg/dl) have been associated with increased
256 hypoglycemic events and mortality among adults in the ICU; thus, glycemic control regimens
257 maintaining glucose levels between 110 -180 mg/dl are preferable.¹³⁶⁻¹³⁹

258 In patients receiving enteral nutrition, pharmacologic stress ulcer prophylaxis (SUP) is not
259 recommended based on studies performed in ICU patients.¹⁴⁰⁻¹⁴²

260

261 **Airway management**

262 Patients with SJS/TEN may experience sloughing of the respiratory tract epithelium which
263 cannot be predicted by the extent of cutaneous involvement.¹¹ Chest x-ray and arterial blood gas
264 measurement should be obtained as part of the baseline evaluation.^{16,143-145} Appropriate
265 pulmonary toilet and positioning may help keep the upper airway clear.¹³ Attention should be
266 paid to the nose to maintain a clear respiratory passage.

267 Patients with hypoxemia, dyspnea, or tachypnea should undergo fiberoptic bronchoscopy to
268 evaluate the extent of bronchial involvement while minimizing iatrogenic trauma.^{145,146}

269 Pulmonary function testing and computed tomography scanning are indicated in those with
270 ongoing respiratory symptoms.^{14,147}

271 Patients with SJS/TEN may experience airway compromise requiring intubation and early
272 tracheostomy (before ventilator day 10) prior to the onset of respiratory failure, predicted by oral
273 mucosal involvement and initial BSA of 70% or more, progression of BSA from hospital day 1
274 to hospital day 3 by 15% or more, neurologic diagnosis preventing airway protection, or
275 documented airway involvement on direct laryngoscopy.¹⁴⁸ Improved survival is attributed to

276 aggressive wound care after airway protection. Ventilation strategies should mimic those used in
277 acute respiratory distress syndrome, such as low tidal volume¹⁴⁹ and early prone
278 positioning.^{144,150}

279

280 **Anticoagulation**

281 Patients with SJS/TEN are at increased risk of venous thromboembolism. Prophylaxis with low
282 weight molecular heparin is recommended.¹⁵¹⁻¹⁵⁴ Patients who are bleeding or at high risk of
283 major bleeding should receive graduated compression stockings or intermittent pneumatic
284 compression instead.^{152,154} Early mobilization of patients should be encouraged.¹⁵⁵

285

286 **LIMITATIONS AND CONCLUSION**

287 These guidelines address supportive care treatment options for adult patients with SJS/TEN.
288 Systemic treatment options, management of sequelae, and considerations in special populations
289 (e.g., pediatric, pregnant) will be addressed in future guidelines. Judgment regarding the
290 appropriateness of any specific therapy lies with the treating clinician. Future studies will
291 necessitate revisions and updates to these recommendations.

292

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Table 1. Clinical Question**What supportive care treatment strategies are safe and effective for adult patients with SJS, SJS-TEN overlap, or TEN?**

1.	Hospital setting and care team
2.	Wound care
3.	Ocular care
4.	Oral care
5.	Urogenital care
6.	Pain management
7.	Infection surveillance
8.	Fluid and electrolyte management
9.	Nutrition and stress ulcer prophylaxis
10.	Airway management
11.	Anticoagulation

SJS, Steven-Johnson syndrome; TEN, toxic epidermal necrolysis

Table 2. Recommendations

	Level of evidence*	Strength of Recommendation*	DI**	Median
<i>Hospital setting and care team</i>				
Management of patients with SJS/TEN requires a multidisciplinary team that may include dermatology, intensive care, pulmonology, ophthalmology, otorhinolaryngology, gynecology, urology, nephrology, plastic surgery, nutrition, nursing, psychology/psychiatry, and other fields.	4	D (GPP)	0.00	9.0
Dermatologists are experts in the disease state of SJS/TEN and should directly participate in the management of such patients.	4	D (GPP)	0.00	9.0
Staff should have specific training in the care of patients with SJS/TEN.	4	D (GPP)	0.13	9.0
Chronic conditions and comorbidities play a significant role in the mortality of SJS/TEN patients and the need for specialized care, and hospital transfers should take into account these comorbidities.	3	C	0.00	9.0
Medical or burn ICU settings of care for SJS/TEN patients are recommended.	2-/3	D	0.00	9.0
SJS/TEN patients must be cared for in a private room.	3	D	0.13	9.0
Patient rooms should be controlled for humidity.	4	D	0.26	7.5
Sterile sheets should be obtained and used for patient bedding, where available	4	D	0.65	8.0
At least one nurse should take care of one SJS/TEN patient (at least 1:1 ratio).	4	D	0.32	8.0
<i>Wound care</i>				
Determine % BSA of epidermal detachment (only skin that is already necrotic, detached, or skin with positive Nikolsky sign).	3	D	0.06	9.0
Avoid unnecessary wound manipulation by limiting the number of dressing changes.	3	D	0.13	8.0
Use an air-fluidized bed to minimize friction.	3	D	0.15	8.0
Gently cleanse all areas with sterile water, normal saline, or dilute chlorhexidine (0.05%) solution with dressing changes.	4	D	0.26	8.0
The detached and detachable epidermis should be left in place as a biological dressing.	4	D (GPP)	0.13	8.0
Lyse large or painful bullae for comfort only.	4	D (GPP)	0.20	8.0
Wound debridement of necrotic skin is not recommended.	4	D (GPP)	0.82	7.0
Apply topical emollients such as petroleum jelly on the entire epidermis.	3	D	0.13	8.5
Apply non-adherent sterile dressings to denuded skin.	3	D	0.13	9.0
Select non-adherent silver-impregnated primary dressings for optimal moisture retention and antibacterial properties.	2+/3	D	0.59	6.5
Apply secondary dressing to absorb exudate.	3	D	0.37	7.0
<i>Ocular care</i>				
Patients thought to have SJS/TEN should be examined by an ophthalmologist as part of the initial assessment.	4	D (GPP)	0.00	9.0
Patients should be examined at least every 24 hours until it is clear there is no worsening, and thereafter the frequency of follow-up should be determined on a case-by case basis.	4	D (GPP)	0.13	9.0
Educate the appropriate staff regarding the need for immediate ophthalmologic evaluation of all SJS/TEN	4	D (GPP)	0.00	9.0

patients and the proper application of topical ocular medications (drops and ointments).				
The entire ocular surface should be examined daily- eyelid skin, eyelid margin, conjunctiva, and cornea. The eyelids should be everted, and the eyes rotated to look for forniceal and tarsal conjunctival epithelial defects and early symblephara.	4	D (GPP)	0.13	8.0
Fluorescein staining should be done in all patients.	4	D	0.65	6.5
Resting eyelid position should be assessed for lagophthalmos.	4	D	0.37	8.0
Grade the ocular exam findings to facilitate medical decision making (eAppendix5).	3	D	0.65	7.0
Consider amniotic membrane transplantation (AMT) during the initial evaluation of any patient thought to have SJS/TEN and at each follow-up exam during the acute phase.	1+/2+	B	0.13	8.0
Offer AMT to patients with moderate to severe conjunctival injection, significant conjunctival epithelial defects (especially the eyelid margin, tarsal conjunctiva, fornices), significant corneal epithelial defects or membranes / pseudo-membranes.	1+/2+	B	0.13	8.0
AMT is ideally performed within 5 days of onset but may be offered later.	1+/2+	B	0.13	8.0
Amniotic membrane should cover the entire ocular surface.	1+/2+	B	0.00	8.0
Apply artificial tears every 1-2 hours for any patient with any ocular surface inflammation.	4	D	0.13	8.0
Apply ophthalmic ointment to the eyelid margin every 2-24 hours.	4	D	0.13	8.0
Eye drops containing preservatives should be avoided.	4	D	0.48	8.0
Apply a moisture chamber over the eyes for lagophthalmos. A facemask or moist occlusive dressing may be used for this purpose.	4	D	0.56	8.0
Rinse the eyes every 2-24 hours with sterile saline.	4	D	0.16	7.5
Remove/lyse adherent debris and membranes daily.	4	D	0.16	8.0
Apply a topical anesthetic (e.g. proparacaine or tetracaine) if needed.	4	D	0.12	8.0
Apply a corticosteroid containing ointment to the eyelid margin and eyelashes at least once daily and a corticosteroid drop to the ocular surface at least twice daily for any patient with any ocular surface inflammation.	2-	D	0.59	8.0
If there is clinical suspicion of infectious conjunctivitis, obtain a bacterial (and consider a fungal) culture of the ocular surface and begin application of a topical broad-spectrum antibiotic (4th generation quinolone commonly used).	4	D	0.00	8.0
Avoid chloramphenicol drops and tetracycline containing ointment, as these have been associated with late complications, particularly dry eyes.	3	D	0.65	8.0
Oral Care				
The mouth should be examined as part of the initial assessment of a patient with SJS/TEN.	4	D (GPP)	0.00	9.0
Daily oral exam is required during acute illness.	4	D (GPP)	0.00	9.0
Have a low threshold for HSV PCR, bacterial, and fungal cultures if infection is suspected.	4	D (GPP)	0.00	9.0
Petrolatum ointment should be applied on the lips immediately, and then every 2 hours throughout the acute illness.	3	D	0.29	8.0
Viscous lidocaine 2%, 15 ml per application, can be used every three hours (and prior to cleanses) as an oral rinse to control pain.	3	D	0.13	8.0
Clean the mouth daily with warm saline mouthwashes or an oral sponge, sweeping the sponge gently in the labial and buccal sulci to reduce the risk of fibrotic scars and prevent buildup of hemorrhagic crust.	3	D	0.13	8.0

An antiseptic oral rinse should be used twice daily to reduce bacterial colonization of the mucosa.	3	D	0.65	6.5
A topical steroid (ultrapotent) ointment can be applied up to 4 times a day during the acute phase.	3	D	0.58	8.0
Consider diluted chlorhexidine digluconate mouthwash (2-3 times daily).	3	D	0.37	7.0
Consider the use of oral coating agents for pain reduction in patients with oral mucosal involvement.	4	D	0.13	8.0
<i>Urogenital care</i>				
Examine the urogenital tract as part of the initial assessment of a patient with SJS/TEN.	4	D (GPP)	0.00	9.0
Urogenital exam should ideally be performed by a gynecologist, urologist, or urogynecology specialist.	4	D (GPP)	0.13	8.0
Daily exam is required during the acute illness.	4	D (GPP)	0.13	8.0
If there is clinical suspicion for vaginal candidiasis in the setting of vaginal steroid use, consider obtaining a KOH and fungal culture and beginning treatment with antifungal medications.	4	D (GPP)	0.13	8.0
During the acute phase of the disease, the vulvar/urogenital skin/mucosa should be coated with an ointment and/or ointment gauze to help reduce pain, reduce adhesion formation, and facilitate healing.	3	D	0.13	8.0
An intravaginal device such as a dilator/tampon/vaginal mold/roll of gauze covered in a lubricated condom can be utilized to treat vaginal disease.	3	D	0.13	9.0
Intravaginal devices may be left in place for no longer than 24hrs, at which time they should be replaced.	3	D	0.03	8.0
Even for virginal patients, use of a small mold or a condom-covered tampon should be encouraged if the patient is emotionally and physically comfortable with the regimen.	4	D	0.65	7.0
Patients uncomfortable with using an intravaginal device, can apply medication twice daily with a vaginal applicator.	4	D	0.06	8.0
Topical anesthetics (i.e., lidocaine 5% ointment) can be used at the vaginal introitus, once open sores have healed, to reduce discomfort with use of the vaginal dilators.	3	D	0.01	8.0
It is at the provider's discretion to use either a non-steroidal ointment (i.e., petrolatum jelly) with reapplication as frequently as necessary (2-4x daily) to maintain barrier protection and/or consider 1-2x daily application of a high potency steroid ointment if active inflammation is observed, with the caveat that consideration for tapering of steroid use should be based on clinical improvement.	3	D	0.00	8.0
Consider the medication on the dilator can be changed to, or alternated with, estrogen cream to help promote healing of the vaginal mucosa.	4	D	0.55	7.0
Consider menstrual suppression to reduce discomfort and possibly to decrease the risk of vaginal adenosis.	3	D	0.69	8.0
Consider division of any fine [vaginal] adhesions to prevent the development of thick fibrous bands that could lead to problems inserting tampons and during sexual intercourse later in life.	3	D	0.22	8.0
Consider urinary catheters to decrease pain with urination, prevent urinary obstruction, and monitor fluid balance.	3	D	0.13	8.0
<i>Pain management</i>				
Evaluation and treatment of pain is a priority in the acute phase, especially during wound management.	4	D (GPP)	0.00	9.0
Pain should be evaluated on a 4-hourly basis.	4	D (GPP)	0.13	9.0
A validated pain tool should be used to assess pain in all conscious patients at least once a day.	4	D (GPP)	0.13	9.0
If the score is mild, pain control with acetaminophen should be introduced.	3	D	0.00	8.0
If acetaminophen is not enough, oral synthetic opiates such as tramadol should be considered.	3	D	0.23	8.0
If the pain score is moderate to severe, then morphine or fentanyl should be delivered enterally, by PCA, or by infusion.	3	D	0.13	8.0

Procedures such as dressing changes and bathing may require additional pain control.	3	D	0.00	9.0
Consider adding low dose ketamine infusions.	3	D	0.65	6.5
Consider adding gabapentin or pregabalin.	3	D	0.65	7.0
NSAIDs should be avoided due to renal or gastric injury.	3	D	0.35	7.0
<i>Infection surveillance</i>				
Hand hygiene and other infection control measures should be strictly applied.	3	D (GPP)	0.00	9
Patients should be monitored carefully for signs of systemic infection, such as confusion, hypotension, reduced urine output and reduced oxygen saturation.	3	D	0.00	9
Cutaneous infection may be accompanied by increase in skin pain.	3	D	0.13	8.5
Consider activation of HSV in eroded or vesicular areas which are slow to heal, particularly in genital and oral sites. Take viral swabs if herpes virus infection is suspected.	3	D	0.00	9
In patients with diarrhea who are immobile, consider a fecal management system to prevent fecal soiling of wounds.	3	D	0.13	8.5
Prophylactic antibiotic treatment is not recommended.	4	D	0.13	8.5
Administer systemic antibiotics only if there are clinical signs of infection. The choice of systemic antibiotic should be guided by local microbiological resistance patterns.	3	D	0.13	9
Severe ENT involvement is significantly associated with pulmonary infection. ENT evaluation using nasal fiberoptic endoscopy should be suggested when dysphonia or dyspnea are present.	3	D	0.16	8.0
<i>Fluid and electrolyte management</i>				
Peripheral catheters preferred for vascular access with implantation in uninjured skin and fixed with non-adhesive dressings.	3	D	0.13	9
Change peripheral venous cannulas every 48 hours if possible.	3	D	0.65	7
Monitor electrolytes and fluid balance daily.	4	D (GPP)	0.00	9
Consider invasive fluid balance monitoring with Foley catheter.	3	D	0.33	8
Fluid administration should be titrated to urine output (0.5-1 ml/kg/hr).	3	D	0.16	8
<i>Nutrition and stress ulcer prophylaxis</i>				
Maintain adequate nutrition orally; utilize nasogastric tube if necessary. Enteral feeding reduces stress ulcers and reduces bacterial translocation and enterogenic infection.	3	D	0.13	9
Supplement enteral nutrition with parenteral if intake via the enteral route is insufficient to meet caloric needs.	3	D	0.39	8
Avoid nasogastric tube placement if there is involvement of the nasopharyngeal mucosa.	3	D	0.37	7
Deliver daily caloric requirement of 30-35 kcal/kg.	3	D	0.33	8
Maintain close glycemic control.	3	D (GPP)	0.03	8
In patients receiving enteral nutrition, pharmacologic stress ulcer prophylaxis is not recommended.	4	D (GPP)	0.65	8
Pharmacologic stress ulcer prophylaxis with PPIs should be limited to patients at high risk for clinically important bleeding (respiratory failure, coagulopathy, liver disease, use of renal replacement therapy, three or more co-existing diseases).	4	D (GPP)	0.16	8
PPIs should be used over H2 receptor antagonists (due to decrease in GI bleeding events).	4	D (GPP)	0.5	7.5
<i>Airway management</i>				
The nose should be examined as part of the initial assessment of a patient with SJS/TEN.	4	D (GPP)	0.13	9

Daily nasal exams are required during acute illness.	4	D (GPP)	0.07	8
Pulmonary care includes normal saline aerosols, bronchial aspiration and postural drainage by turning the patient to different sides.	4	D	0.11	8
Severe ENT involvement is significantly associated with pulmonary infection. ENT evaluation using nasal fiberoptic endoscopy should be suggested when dysphonia or dyspnea are present.	3/4	D	0.16	8
Chest X-ray and arterial blood gases should be obtained upon admission for baseline respiratory function assessment.	3/4	D	0.65	7
Patients with ongoing respiratory symptoms should be closely monitored with pulmonary function testing and high-resolution computed tomography (CT) scanning.	3	D	0.37	8
Fiberoptic bronchoscopy should be undertaken in patients with respiratory symptoms and hypoxia.	3	D	0.00	8
Bronchoscopy should be done by an experienced technician due to risk of post-instrumental endobronchial bleeding.	3	D	0.13	8
Consider intubation and early tracheostomy in patients with oral involvement AND one of the following: <ul style="list-style-type: none"> • Initial BSA 70% or more • Progression of BSA involved from DOH1 to DOH3 > 15% • Underlying neurologic diagnosis prevents airway protection • Documented airway involvement on direct laryngoscopy 	3	D	0.40	7
Ventilation strategies should mimic ARDS management guidelines (low tidal volume and early prone positioning).	4	D	0.65	7
<i>Anticoagulation</i>				
Immobile patients should receive low molecular weight heparin.	4	D (GPP)	0.07	8
For acutely ill patients at increased risk of thrombosis who are bleeding or at high risk for major bleeding, mechanical thromboprophylaxis with graduated compression stockings or intermittent pneumatic compression is recommended.	4	D (GPP)	0.16	8

*For level of evidence and grade of recommendation calculation see eAppendix2. GPP, good practice point. A GPP is a recommendation for best practice based on the experience of the guideline development group.

**Statements were appraised on a Likert scale of 1 (strongly disagree) to 9 (strongly agree), medians and disagreement indexes (DI) were calculated for each statement. Items with a $DI \leq 1$ and a median ≥ 6.5 were deemed appropriate and included in the guidelines, and all other items were not included as recommendations. (eAppendix4)

SJS, Steven-Johnson syndrome; TEN, toxic epidermal necrolysis; BSA, Body Surface Area; DI, disagreement index; DOH, Day of hospitalization; ENT, Ear-Nose-Throat; ICU, Intensive Care Unit; NSAIDs, Non-steroidal anti-inflammatory drugs; PCA, patient-controlled analgesia; PPI, proton pump inhibitor.