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Published in:
BRITISH JOURNAL OF DERMATOLOGY

DOI:
[10.1111/bjd.19893](https://doi.org/10.1111/bjd.19893)

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Document Version
Publisher's PDF, also known as Version of record

Publication date:
2021

[Link to publication in University of Groningen/UMCG research database](#)

Citation for published version (APA):

Brueggen, M. -C., Le, S. T., Walsh, S., Toussi, A., de Prost, N., Ranki, A., Didona, B., Colin, A., Horvath, B., Brezinova, E., Milpied, B., Moss, C., Bodemer, C., Meyersburg, D., Salavastru, C., Tiplica, G. -S., Howard, E., Bequignon, E., Bouwes Bavinck, J. N., ... Worswick, S. (2021). Supportive care in the acute phase of Stevens-Johnson syndrome and toxic epidermal necrolysis: an international, multidisciplinary Delphi-based consensus. *BRITISH JOURNAL OF DERMATOLOGY*, 185(3), 616-626.
<https://doi.org/10.1111/bjd.19893>

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Supportive care in the acute phase of Stevens–Johnson syndrome and toxic epidermal necrolysis: an international, multidisciplinary Delphi-based consensus

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Accepted for publication

25 February 2021

Funding sources

This work was funded by the University of Zurich.

Conflicts of interest

The authors declare they have no conflicts of interest.

The remainder of the affiliations can be found in Appendix 1.

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L.E.F. and S.I.H.O. contributed equally.

DOI 10.1111/bjd.19893

Background Supportive care is the cornerstone of management of adult and paediatric Stevens–Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN). However, consensus on the modalities of supportive care is lacking.

Objectives Our aim in this international multicentric Delphi exercise was to establish a multidisciplinary expert consensus to standardize recommendations regarding supportive care in the acute phase of SJS/TEN.

Methods Participants were sent a survey via the online tool SurveyMonkey, consisting of 103 statements organized into 11 topics: multidisciplinary team composition, suspect drug management, infection prevention, fluid resuscitation and prevention of hypothermia, nutritional support, pain and psychological distress management, management of acute respiratory failure, local skincare, ophthalmological management, management of other mucosa, and additional measures. Participants evaluated the level of appropriateness of each statement on a scale of 1 (extremely inappropriate) to 9 (extremely appropriate). The results were analysed according to the RAND/UCLA Appropriateness Method.

Results Forty-five participants from 13 countries (on three continents) participated. After the first round, a consensus was obtained for 82.5% of the 103 initially proposed statements. After the second round, a final consensus was obtained for 102 statements.

Conclusions We have reached an international Delphi-based consensus on best supportive care practice for SJS/TEN. Our expert consensus should help guide physicians in treating patients with SJS/TEN and thereby improve short-term prognosis and the risk of sequelae.

What is already known about this topic?

- Supportive care is the cornerstone of management of Stevens–Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) in the acute phase.
- There is no consensus or guideline on the best supportive care.

What does this study add?

- An international, multidisciplinary consensus on best supportive care practices for patients with SJS/TEN in the acute phase, along with practical guidance.

Stevens–Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN, or Lyell syndrome) are rare severe delayed-type hypersensitivity reactions, characterized by diffuse epidermal detachment and necrosis. Medications are recognized as the primary trigger factor of the disease, although in 15% of cases no culprit drug can be identified. The incidence varies among countries and ranges from 1–2 to 6 cases per million inhabitants per year. Mortality in the acute phase is approximately 15%. It can be predicted on an individual patient level by applying the SCORTEN (Score of Toxic Epidermal Necrolysis).^{1–11} SJS and TEN are frequently associated with long-term multiple disabling sequelae that may require prolonged follow-up.^{12,13}

SJS and TEN are considered variants on the epidermal necrolysis spectrum. Classification distinguishes them according to body surface area (BSA) involvement. SJS involves skin detachment of < 10% BSA, SJS/TEN overlap syndrome involves 10–29% BSA, and TEN describes cases with ≥ 30% BSA involvement.¹⁴ Associated dermatological manifestations are characterized by dusky macules or atypical targets that can evolve to confluent bullae and skin detachment with a positive Nikolsky sign.^{2,14,15} Mucous membranes are involved in almost all cases.^{16–18} The two most frequent complications of SJS and TEN are (i) sepsis,¹⁹ as injured skin can serve as a portal of entry, together with venous, arterial or bladder catheters, and (ii) respiratory failure, with the need for mechanical ventilation.^{20–23}

The management of patients with SJS/TEN in a referral centre has been shown to improve patient prognosis.^{24–27} To date, there are no standardized recommendations or treatment guidelines for adjuvant treatment in SJS/TEN. Apart from an unsuccessful trial with thalidomide,²⁸ and a nonblinded randomized trial with etanercept vs. corticosteroids showing a reduced time to epithelialization with etanercept,²⁹ there have been no prospective controlled and blinded clinical studies investigating the efficacy of adjuvant, immunomodulatory treatments for SJS/TEN. A variety of different approaches are used in practice, including systemic corticosteroids, intravenous immunoglobulins, ciclosporin, and tumour necrosis factor antagonists (etanercept).^{24,26,30–32}

In contrast, there is a published consensus that supportive care is the cornerstone of management of adult and paediatric SJS/TEN in the acute phase.^{24,26,33} These supportive measures include aspects such as screening and treatment of infectious complications, fluid management, and local wound and mucosal care. Although previous studies have shown that improving supportive care may reduce mortality,⁶ there is no consensus

about best practices related to specific modalities of supportive care treatment. Our aim in this multicentre Delphi exercise is to harmonize supportive care in the acute phase of SJS/TEN.

Materials and methods

Panel selection

The project was initiated by the SJS/TEN subgroup (ToxiTEN Group) of the skin European Reference Network (ERN-skin), composed only of dermatologists. An international panel of experts in the field of SJS/TEN was established. Participants were identified from academic centres that provide inpatient dermatology or intensive care services specialized in the care of patients with SJS/TEN. In total, 65 experts were identified and invited via email to participate in the Delphi consensus-building exercise. Fifty-five of the identified experts were dermatologists, and the additional nondermatologists were experts in the fields of intensive care and burns (four experts), stomatology (one), ear, nose and throat (one), ophthalmology (one) and psychiatry (one). In addition, two nurses specialized in the care of SJS/TEN were solicited. The nondermatologist experts were allowed to reply only to the statements they had enough expertise in.

Of the 65 identified experts, four did not respond to the invitation to participate, none declined, and the remaining 61 agreed to participate (Figure 1).

First round

In the first round, participants were sent an online survey consisting of 103 statements regarding SJS/TEN. Statements were organized into 11 topic categories, namely professionals involved, drug management, prevention of infection, fluid resuscitation and prevention of hypothermia, nutritional support, management of pain and psychological distress, management of acute respiratory failure, local skincare, ophthalmological management, management of other mucosa, and additional measures. SurveyMonkey, an online tool, was used to distribute surveys (<https://www.surveymonkey.co.uk>). Participants were asked to evaluate the level of appropriateness of statements on a scale of 1 (extremely inappropriate) to 9 (extremely appropriate). Participants were given the option of selecting 'not applicable' if they felt they did not have the necessary expertise to rank a particular statement. Participants also had the opportunity to submit comments to be incorporated into subsequent Delphi rounds. Statements

Figure 1 Flowchart illustrating the work steps of the Delphi exercise.

were constructed based on recommendations from existing guidelines on SJS/TEN care.^{24,26,33} Additional literature was identified through ClinicalTrials.gov and PubMed. Survey results were anonymized prior to releasing them to participants, and participants were able to suggest new statements. Members of the steering committee (M.-C.B., L.E.F., S.W., S.I.-H.-O., S.T.L. and E.M.) did not respond to the survey.

Second round

During the second round, participants rated the revised statements that failed the previous round and new suggested statements (Figure 1).

Statistics

The results were analysed according to the RAND/UCLA Appropriateness Method. The median rating for appropriateness, interpercentile range (IPR), interpercentile range adjusted for symmetry (IPRAS), and disagreement index (DI) were calculated ($DI = IPR/IPRAS$) for each statement.³⁴ Median appropriateness values were assessed as follows: 1.0–3.4 was considered 'inappropriate', 3.5–6.9 as 'uncertain' and 7.0–9.0 as 'appropriate'. A $DI \geq 1$ indicated a lack of consensus among the participants in terms of a statement's appropriateness.

Results

Participants and Delphi exercise

Forty-five of the 61 participants (coming from 14 countries, on three continents) who agreed to participate in the Delphi exercise responded in the first round (74% response rate). In the second round, 41 participants responded (response rate 67%). The statements that the panel 'agreed' on were 'appropriate' and were used to establish a consensus.

First round

A consensus was reached for 85 of 103 statements (82.5%). All statements and their respective DIs and medians are displayed in Table S1 (see Supporting Information). Eighteen of the 103 statements had a $DI \geq 1$ and therefore did not reach the necessary level of agreement (Figure 1). The section in which participants showed the most disagreement were 'Professionals involved in the care of patients with active SJS/TEN' (section I, 10 statements). Consensus was lacking for the number of specialists (pneumologist, infectious disease specialist, otolaryngologist, dentist, gynaecologist, urologist, psychiatrist, dietician, social worker) that should be involved in SJS/TEN care. Five statements were labelled as 'uncertain' and two as 'disagreed on' in the section 'Infection prevention'

(section III). These addressed the use of antiseptic baths, and the type and frequency of urine analyses and cultures, and blood and catheter cultures. Additional uncertain statements were on fluid resuscitation (use of standardized formula), nutritional support (residual gastric volume monitoring) and noninvasive ventilation.

Second round

All of the proposed modified statements passed, with the exception of two statements. The two statements that did not reach consensus were removed from the Delphi (Table S2; see Supporting Information). In total, after the two rounds, a consensus was reached for 102 statements (Tables 1–4).

Discussion

The aim of this Delphi exercise was to establish a multidisciplinary consensus for optimal and standardized acute-phase supportive care of patients with SJS/TEN.

Consensus was obtained in key fields of patient management: admission or transfer of the patient in a specialized unit with a medical multidisciplinary team available adapted to the needs of the patient, withdrawal of suspect drug(s), fluid resuscitation, prevention of hypothermia, prevention of infections, topical skin and mucosal care, nutritional

support, management of main and psychological distress, management of acute respiratory failure and mechanical ventilation in an intensive care unit (ICU), and additional measures such as prevention of thrombosis and stress ulceration. Based on this consensus, we provide a summary of the main key principles of the supportive care to help clinicians in the management of the patient in routine practice (Table 5).

Patients should be admitted or transferred without delay to a specialized unit, within or in close proximity to an intensive care or burn unit, with nurses trained in the management of skin loss. Participants agreed with strong concordance on the involvement of a core team to treat patients with SJS/TEN, which should include a dermatologist, paediatrician, intensive care specialist and ophthalmologist. As emphasized in the second Delphi round, other disciplines (such as gynaecologist, psychiatrist and social worker) should only be involved based on the need of that particular patient. No consensus was reached on the involvement of urologists, even when suggested as optional. Although they were initially included in the Delphi survey due to potential urethral involvement and strictures in SJS/TEN, we thereafter excluded recommending involvement of a urologist.

Given that early discontinuation of the culprit drug is a well-recognized prognostic factor,³⁵ experts emphasized the need for rapid drug discontinuation, and that identifying the

Table 1 Statements that the panel agreed were appropriate for professionals involved and drug management in patients with active Stevens–Johnson syndrome/toxic epidermal necrolysis (SJS/TEN)

Item	Disagreement index ^a
I. Professionals involved in the care of patients with active SJS/TEN	
Patients should be admitted or transferred to a specialty service (e.g. dermatology, intensive care unit, burn surgery unit)	0.00
Specialty units (e.g. dermatology, intensive care unit, burn unit) should be notified immediately upon admission of patients	0.01
Patients should be managed by a multidisciplinary team led by either dermatology, burn surgery or intensive care	0.03
A dermatologist should be involved in the management of SJS/TEN	0.01
An intensive care specialist should be involved in the management of SJS/TEN	0.20
A paediatrician (if child affected) should be involved in the management of SJS/TEN	0.30
An ophthalmologist should be involved in the management of SJS/TEN	0.02
A specialized nurse (e.g. burn nurse) should be involved in the management of SJS/TEN	0.10
A pulmonologist is sometimes helpful in the management of SJS/TEN	0.49
An infectious disease specialist is sometimes helpful in the management of SJS/TEN	0.29
An otolaryngologist is sometimes helpful in the management of SJS/TEN	0.49
A specialized dentist (e.g. stomatologist) is sometimes helpful in the management of SJS/TEN	0.82
A gynaecologist (if female affected) is sometimes helpful in the management of SJS/TEN	0.45
A gastroenterologist is sometimes helpful in the management of SJS/TEN	0.65
A psychiatrist (or psychologist) is sometimes helpful in the management of SJS/TEN	0.29
A dietician is sometimes helpful in the management of SJS/TEN	0.38
A social worker is sometimes helpful in the management of SJS/TEN	0.38
II. Drug management in patients with active SJS/TEN	
Suspected drugs should be immediately discontinued	0.00
Unsuspected essential drugs should not be discontinued, even if they have known associations with SJS/TEN	0.38
The ALDEN (or similar score) is helpful in assessing drug causality	0.25
The ALDEN (or similar score) should be calculated for every drug suspected	0.33
A centre for drug evaluation (i.e. pharmacovigilance centre) should be contacted if drug causality is unclear	0.84

^aA disagreement index value < 1 indicates consensus among the participants.

causal medication may be estimated by using the ALDEN score.⁸

Prevention of infection includes hand hygiene, single-use nonsterile gloves, a surgical face mask, and daily use of antiseptics. However, a recent French audit of practices showed that aseptic care in burns units is often preferred. However, the impact on the infection risk of sterile vs. non-sterile local care and antiseptics in SJS/TEN is unknown.³⁶ Experts agreed that systemic antibiotics should be prescribed

only in documented cases of sepsis, according to the international consensus definition of sepsis and septic shock,³⁷ or in patients with clinical evidence of infection, and guided by susceptibility patterns of bacteria cultured on the patient's skin, urine, blood and/or catheter. Topical antibiotics should be reserved for actively infected areas and for short durations, and guided by local microbiology. The use of silver-containing products such as silver sulfadiazine or flammacerium should be very limited (< 5% BSA).

Table 2 Statements that the panel agreed were appropriate for infection prevention, fluid resuscitation and nutritional support

Item	Disagreement index ^a
III. Infection prevention for patients with SJS/TEN with active disease	
Hand hygiene, single-use nonsterile gloves, and a surgical face mask should always be used	0.07
Strict standard operating procedures should be followed for invasive procedures such as central catheter placement	0.00
Prophylactic systemic antibiotics are not recommended without indication	0.05
Systemic antibiotics should only be administered in cases of sepsis or invasive infection, or in patients with vital signs, laboratory findings (e.g. positive blood cultures) or clinical presentation consistent with infection	0.01
Routine skin cultures should be used to investigate and follow bacterial skin colonization every 2–3 days, especially on sloughy or crusted areas	0.65
Topical antimicrobial agents should not be routinely used due to risk of allergy and microbial resistance	0.88
If used, topical antimicrobial agents (e.g. fusidic acid or silver sulfadiazine) should only be applied for short durations and in the treatment of actively infected areas	0.24
Choice of topical antimicrobial agents should be guided by knowledge of local microbiology	0.23
Choice of antimicrobial agents should be guided by susceptibility patterns of bacteria cultured on the patient's skin, urine, blood and/or catheter	0.02
Silver-containing products (e.g. silver sulfadiazine or flammacerium) should not be used in patients with sulfonamide-triggered SJS/TEN	0.89
If used, silver-containing products should be limited to 5% or less of body surface area due to risk of absorption	0.89
Peripheral (or central if no peripheral access) catheters should be used, inserted into unbroken skin when possible	0.02
Central catheters containing antimicrobial agents (e.g. silver sulfadiazine or chlorhexidine) may be considered except if contraindicated	0.35
Eroded or vesicular skin, particularly in a genital or oral distribution, should be investigated for herpes simplex virus	0.19
Routine blood cultures should be obtained at baseline	0.89
Routine blood cultures should occur regularly, especially in cases of any clinical suspicion of sepsis	0.49
Routine urine analysis (e.g. dipstick) should be obtained at baseline	0.38
Routine urine analysis (e.g. dipstick) should occur regularly, especially in cases of any clinical suspicion of sepsis	0.66
Routine intravenous catheter culture should be performed when changing the device	0.49
Application of antiseptic agents (e.g. diluted aqueous chlorhexidine) should be used daily	0.63
IV. Fluid resuscitation and prevention of hypothermia in patients with active SJS/TEN	
Fluid resuscitation should be adapted on a case-by-case basis	0.03
Fluid resuscitation should be less aggressive than for patients with burns to avoid pulmonary, cutaneous or intestinal oedema	0.36
Haemodynamic status should be monitored every 2–4 h	0.24
Fluid volume should be tailored to urine output (e.g. 0.5–1 mL kg ⁻¹ h ⁻¹)	0.18
Development of hypothermia should be actively monitored and prevented	0.01
Room temperature should be kept at 25–32 °C	0.16
Warmed inspired gases, warmed or room-temperature fluids, and warming blankets should be used if necessary	0.08
A standardized formula (e.g. modified Brooke formula or Parkland formula) may be used to guide initial fluid resuscitation	0.16
V. Nutritional support for patients with active SJS/TEN	
Early nutritional support by continuous enteral nutrition should be used	0.26
The nutritional target is 20 kcal kg ⁻¹ per day, to be slowly increased to 30 kcal kg ⁻¹ per day	0.30
Enteral nutrition should be avoided in patients with extensive oesophageal involvement	0.83
Parenteral nutrition should be used in patients with oesophageal involvement	0.29
Blood glucose levels should be monitored at least once a day	0.19
Insulin treatment should be initiated if two consecutive blood glucose readings exceed 180 mg dL ⁻¹ , with a target glucose ≤ 180 mg dL ⁻¹	0.37

SJS/TEN, Stevens–Johnson syndrome/toxic epidermal necrolysis. ^aA disagreement index value < 1 indicates consensus among the participants.

Table 3 Statements that the panel agreed were appropriate for psychological distress, acute respiratory failure, local skincare and ophthalmological management

Item	Disagreement index ^a
VI. Pain and psychological distress management for patients with active SJS/TEN	
Pain and the efficacy of pain medications should be regularly assessed and documented	0-00
Evaluation and treatment of pain should be a priority in the acute-phase management of SJS/TEN, particularly during wound care	0-01
The efficacy of pain medications should be assessed with a visual analogue scale according to the age of the patient	0-05
Opioids should be used in most cases of SJS/TEN	0-28
High-potency opioids (e.g. morphine) should be used if the visual analogue scale score is elevated	0-27
Non-oral formulations of opioids (e.g. intranasal diamorphine or sublingual fentanyl) may be used for limited procedures, unless active disease in these distributions precludes use	0-38
Non-opioid agents (e.g. ketamine infusions) may be used over opioids during wound care in the intensive care unit	0-29
Sedation and mechanical ventilation may be used to achieve pain control	0-17
Psychiatric and/or psychological evaluation should be effected to reduce post-traumatic stress disorder	0-10
VII. Management of acute respiratory failure in patients with active SJS/TEN	
Patients should be monitored closely in cases of respiratory decompensation	0-00
Patients should be transferred to the intensive care unit in cases of respiratory decompensation	0-00
Chest X-ray and arterial blood gases should be obtained upon admission to assess respiratory status	0-06
Active disease in the tracheobronchus should be suspected in the presence of respiratory signs or symptoms (e.g. productive cough, dyspnoea, hypoxaemia) or consistent radiological findings	0-03
Bronchoscopy may be considered for diagnostic and therapeutic purposes	0-27
Endotracheal intubation and mechanical ventilation should be used in the presence of impaired consciousness, haemodynamic instability, or acute respiratory distress	0-00
If needed, invasive ventilation should be preferred to noninvasive ventilation given the risk of upper-airway obstruction	0-16
VIII. Local skincare for patients with active SJS/TEN	
Pressure should be limited on affected skin by use of appropriate beds	0-00
Detached epidermis should not be removed in patients with SJS/TEN	0-22
Surgical debridement should only be used if conservative management fails (e.g. clinical deterioration, extension of epidermal detachment, local sepsis of subepidermal pus, or delayed healing)	0-17
Tense bullae should be pierced and aspirated, allowing the blister roof to settle onto the underlying dermis	0-10
The entire skin surface may be covered with nonadherent dressings or white petroleum	0-13
The denuded skin surface should be covered with nonadherent dressings	0-07
Synthetic skin substitutes or other biological products (human placenta-derived extracellular matrix containing bioactive molecules of cryopreserved placental membrane) may be considered, but there is insufficient evidence of their efficacy in early wound coverage	0-26
Catheters should be secured with nonadhesive dressings	0-13
IX. Ophthalmological surveillance in patients with active SJS/TEN	
Ophthalmological evaluation should occur within 24 h of presentation	0-00
Follow-up ophthalmological evaluation should occur at least twice a week until discharge	0-01
Power score (e.g. mild, moderate, severe) or simplified grading (e.g. no involvement, mild, severe, very severe) should be used to evaluate the severity of eye involvement	0-07
Local eye care (e.g. lubricant eyedrops without preservatives and/or vitamin A ophthalmic ointment) should be administered every 2 h	0-06
Antimicrobial eyedrops without preservatives may be used if necessary	0-10
Broad-spectrum topical antibiotic prophylaxis may be recommended in the presence of deficits on corneal fluorescein staining or frank ulceration (when microbial keratitis has been excluded)	0-33
Symblepharon lysis should be performed as often as necessary by an ophthalmologist	0-02
Topical corticosteroids may be considered	0-18
The use of topical corticosteroid therapy is debated	0-64
Amniotic membrane transplantation and plastic symblepharon rings MAY be considered if conservative measures fail	0-12

SJS/TEN, Stevens–Johnson syndrome/toxic epidermal necrolysis. ^aA disagreement index value < 1 indicates consensus among the participants.

Fluid resuscitation guided by urine output (e.g. 0.5–1 mL kg⁻¹ h⁻¹), maintenance of room temperature at 25–32 °C, and nutritional support are aimed at compensating for the effects resulting from acute skin detachment, which include hypothermia, and loss of fluid, nutrient and electrolytes.³⁸

In patients with SJS/TEN, evaluation and treatment of pain are considered a priority, particularly during wound care, and patients may require high-potency opioids. In recalcitrant cases, pain may warrant transfer to an ICU for ketamine infusions or sedation if the intensity of pain prevents

Table 4 Statements that the panel agreed were appropriate for mucosal surveillance and additional measures of Stevens–Johnson syndrome/toxic epidermal necrolysis (SJS/TEN) care

Item	Disagreement index ^a
X. Surveillance of other mucosae in patients with active SJS/TEN	
Mucosal lesions should be evaluated thoroughly	0.00
Accessible sites (including the outer ear) should be evaluated daily	0.02
The oropharyngeal and gynaecological distribution of mucosa should be examined at admission and at least once weekly until discharge	0.03
Antimicrobial and analgesic mouthwashes should be used several times daily	0.11
Paraffin-based ointments should be frequently applied to the lips (e.g. every 2 h)	0.13
Paraffin-based ointments should be applied on the glans in men and the vagina in women	0.13
Daily foreskin mobilization should be performed in men	0.13
XI. Additional measures in patients with active SJS/TEN	
Upper gastrointestinal stress ulcer prophylaxis should be used in patients without enteral nutrition	0.13
Proton pump inhibitors should be used for ulcer prophylaxis except when suspected as a trigger	0.13
Prophylactic anticoagulation (e.g. low-molecular-weight heparin) should be used unless contraindicated	0.68
Blood pressure, heart rate, temperature, respiratory rate and oxygen saturation should be monitored every 2–4 h	0.15
Routine weight monitoring should be performed every 2–3 days until discharge	0.26

^aA disagreement index value < 1 indicates consensus among the participants.

local care. Post-traumatic stress is a major long-term complication of SJS/TEN, especially in patients with previous psychological fragility.³⁹ Regular psychological evaluation is indicated for anticipatory management of this important sequela.

The pathophysiology of SJS/TEN differs from that of burns, as healing begins after 7–10 days. As such, consensus was that the detached epidermis should not be removed. Thus, surgical debridement should only be used if conservative management fails (e.g. clinical deterioration, extension of epidermal detachment, local sepsis or subepidermal pus, or delayed healing). Several previous studies have also pointed to the need to avoid debridement.^{40,41} Due to the lack of convincing efficacy data to date, synthetic skin substitutes or other biological products are not recommended as first-line therapy. White petrolatum and/or nonadherent dressings are recommended for covering the entire body.

Ophthalmological assessment several times a week is of major importance. Indeed, the severity of ocular involvement during the acute phase is the main risk factor for severe sequelae.⁴² The cornerstone of ocular care is the use of lubricant eyedrops (without preservatives) and/or vitamin A ophthalmic ointment every 2 h, with lysis of symblepharons as often as necessary. Topical steroids or antibiotics may be considered on a case-by-case basis, such as amniotic membrane transplantation in the most severe involvements and failure of conservative measures. A recent publication suggested a simple classification of four stages to assess local severity.⁴³ That publication also included the result of a literature review showing the lack of evidence for topical steroids and antibiotics, encouraging results of amniotic membrane transplantation in the most severe cases, and lack of data concerning symblepharon rings.⁴³

Recently, a Delphi exercise was conducted by the Society of Dermatology Hospitalists on the acute-phase care of patients with SJS/TEN.⁴⁴ Recommendations about general measures, treatment of acute skin failure, wound care and airway management were overall similar to ours. However, our consensus statements regarding pain management and ocular care were different. For the latter, the US group's recommendation for use of topical corticosteroids in the eyes, which has been controversial and lacks consensus in the literature, was not in our group's recommendations.⁴³ Of note, the American dermatologists' Delphi exercise was not assessed by an international expert panel, and combined several messages in contrast to our larger number of more specific recommendations. Methodologically, the median set as the threshold for agreement was 6.5 in that study, as opposed to 7 in ours.

Several limitations need to be considered with regard to our study. The respondents of this Delphi were multidisciplinary – from intensive care and burn units, ophthalmology, stomatology, ear, nose and throat, paediatrics, psychiatry and dermatology – with the latter representing the majority of the solicited experts. The numerical predominance of dermatologists is due to the fact that this Delphi was initiated by the ToxiTEN ERN-skin dermatologist expert group and because in European and many other countries, dermatologists are the cornerstone of SJS/TEN management. The under-representation or lack of certain other specialists, especially burns surgeons, is reflected in our consensus and may have skewed our results. Future studies should aim at soliciting these groups of experts. Also, although many of our statements are applicable to the paediatric setting, it will be worth further specifying child-specific aspects of SJS/TEN care. An additional limitation could be that the response rate was slightly lower in the second round than in the first round of the Delphi (74% and 67%, respectively).

Table 5 Supportive care of patients with Stevens–Johnson syndrome and toxic epidermal necrolysis

Measures	Comments
General measures	
Transfer to a specialized multidisciplinary setting	Dermatology department, intensive care unit (ICU), burn unit Always notify specialty service upon admission Additional specialities may be consulted depending on severity and involvement
Drug management	Immediate discontinuation of culprit drug(s) ALDEN score may help for causality determination
Temperature of the room	Ambient temperature between 25 °C and 32 °C
Management of pain	Regular assessment of pain using visual analogue scale Opioids (morphine, fentanyl), non-opioids (ketamine, only in ICU)
Prevention of psychological distress	Appropriate psychiatric and/or psychological evaluation
Hydration	Fluid resuscitation adapted on a case-by-case basis Standardized formula may guide initial fluid resuscitation Fluid intake adapted according to haemodynamic status and urine output (e.g. 0.5–1 mL kg ⁻¹ h ⁻¹) monitored every 2–4 h
Nutritional support	Continuous enteral nutrition except if oesophageal involvement Parenteral nutrition if oesophageal involvement Target 20–30 kcal kg ⁻¹ per day of exact bodyweight Daily monitoring of blood glucose and treat with insulin if > 180 mg dL ⁻¹
Prophylaxis of thromboembolism	Thromboprophylaxis unless contraindicated
Prevention of infections	Hand hygiene, single-use nonsterile gloves, surgical face mask Regular skin swabs or skin cultures until healing Regular bedside dipstick urinalysis (nitrites, leucocytes and glucose) Regular blood culture, especially if signs of sepsis Systemic antibiotics only if documented sepsis or strong clinical or biological signs of invasive infection
Local care	
Antiseptic measures	Antiseptics daily (e.g. diluted aqueous chlorhexidine) No topical antibiotics except if needed and according to results of local microbiology on actively infected areas No silver sulfadiazine except if needed, i.e. in actively infected areas
Skincare	Pierce blisters but do not remove the detached epidermis Surgical debridement only if failure of conservative treatment
Ocular care	Cover the entire skin, including denuded skin, with nonadherent dressings or white petroleum Lubricant eyedrops without preservatives, and/or vitamin A ophthalmic ointment every 2 h Removal of symblepharons If needed, according to ophthalmologist's opinion: <ul style="list-style-type: none"> • Topical steroids and antibiotics • Amniotic membrane transplantation and plastic symblepharon rings
Genital care	Paraffin-based ointments In men, daily foreskin mobilization
Oral care	Antimicrobial and analgesic mouthwashes several times daily Paraffin-based ointments on the lips

In conclusion, SJS and TEN are delayed-type hypersensitivity mucocutaneous reactions associated with high morbidity and mortality. To date, the recommended mainstay therapy of SJS/TEN in the acute phase is optimized supportive care, but the specifics of the elements of supportive care that are most important have not been defined in detail with a consensus of experts. Here, through multidisciplinary agreement, we expect our consensus statements to help harmonize SJS/TEN supportive care and guide physicians in treating patients with SJS/TEN, thereby improving short-term prognosis and lowering the risk of sequelae.

Acknowledgments

We thank the French patients' association Amalyste.

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Supporting Information

Additional Supporting Information may be found in the online version of this article at the publisher's website:

Table S1 Items the panel agreed were 'appropriate' for the treatment of patients with active Stevens-Johnson syndrome/toxic epidermal necrolysis (first round).

Table S2 Items the panel agreed were 'appropriate' for the treatment of patients with active Stevens-Johnson syndrome/toxic epidermal necrolysis (second round).

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