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GUIDELINE

Wound, pressure ulcer and burn guidelines – 6: Guidelines for the management of burns, second edition

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ABSTRACT

"Wound, pressure ulcer and burn guidelines – 6: Guidelines for the management of burns, second edition" is revised from the first edition which was published in the Japanese *Journal of Dermatology* in 2016. The guidelines were drafted by the Wound, Pressure Ulcer and Burn Guidelines Drafting Committee delegated by the Japanese Dermatological Association, and intend to facilitate physicians' clinical decisions in preventing, diagnosing and treating burn injury. All sections are updated by collecting documents published since the publication of the first edition. Especially, the recommendation levels of dressing materials newly covered by the Japanese national health insurance are mentioned. In addition, the clinical questions (CQ) regarding the initial treatment of electrical (CQ15) and chemical burns (CQ16), and also the use of escharotomy (CQ22), are newly created.

Key words: burn, chemical burn, escharotomy, fluid resuscitation, topical agents.

1) BACKGROUND OF THE DRAFTING OF THE GUIDELINES FOR THE MANAGEMENT OF BURNS

Burns are a common type of skin injury encountered at all levels of medical facilities, from private clinics to core hospitals. While minor burns may heal by topical treatment alone, moderate to severe burns require systemic management, and skin grafting is often necessary for local treatment as well. Inappropriate or delayed initial treatment may have an unfavorable effect on subsequent treatment and prognosis. Therefore, accurate evaluation of the severity and timely commencement of initial treatment are necessary.

To date, the "Guidelines for the management of burn injuries" was issued in March 2009 by the Japanese Society for Burn Injuries, and a revised edition was released in 2015. These guidelines focus on the acute phase and intensive care for extensive and severe burns. Therefore, our guidelines intend to facilitate the appropriate diagnosis and initial treatment of patients with minor to severe burns that are commonly encountered. Based on the concept of the current guidelines, we will not mention the recommendation for surgical procedures, aside from escharotomy.

2) POSITION OF THE "GUIDELINES FOR THE MANAGEMENT OF BURNS"

The committee that drafted these guidelines (Table 1) consists of members delegated by the Board of Directors of the Japanese Dermatological Association. It has met and created written deliberations several times since October 2008, and it has drafted guidelines for diagnosis and treatment by taking into consideration the opinions of the Scientific Committee and the Board of Directors of the Japanese Dermatological Association, with revision work commencing in June 2013. The present guidelines establish the current standards for the diagnosis and treatment of burns in Japan. However, patients have varying background characteristics, including underlying disease, severity of symptoms and complications. Therefore, physicians who conduct diagnosis and treatment should determine their approach together with the patient, and the contents of their decisions are not required to be in complete agreement with the present guidelines. Furthermore, these guidelines are not relevant for citation in lawsuits or the like.

3) MAIN CHANGES IN THE SECOND EDITION

- The content was updated by collecting and adding documents for all sections.
- We determined the level of recommendation of dressing materials that are newly covered by the Japanese national health insurance.
- We added clinical questions (CQ), namely new CQ regarding the initial treatment of electrical and chemical burns, and the use of escharotomy, were generated.

4) SPONSORS AND CONFLICTS OF INTEREST

All expenses incurred in the drafting of these guidelines have been borne by the Japanese Dermatological Association, and no aid has been rendered by specific organizations, enterprises or pharmaceutical companies. Moreover, in the case that a committee member (Table 1) participating in the drafting of these guidelines was involved in the development of a specific, relevant drug, that member abstained from determining to what degree the item in question could be recommended. Otherwise, no other committee member has any conflict of interest to disclose in the drafting of these guidelines.

5) COLLECTION OF EVIDENCE

Databases used: Medline, PubMed, Japana Centra Revuo Medicina Web and Cochrane Database of Systematic Reviews of all evidence-based medicine reviews. References obtained by manual search were also added.

Search period: The searchable work published between January 1980 and December 2013 was reviewed. Recently published important works were added when considered appropriate.

Adoption criteria: Systematic reviews of randomized controlled trials (RCT) and papers on individual RCT were prioritized. If they were not available, papers on cohort studies and case–control studies were adopted. Although some papers on case series studies were also used as references, the published work on basic experiments was excluded.

Table 1. Wound/Pressure Ulcer/Burn Guideline Drafting Committee (the head of each section is shown in bold)

Chairperson: Hironobu Ihn	
Vice-chairperson: Takao Tachibana	
Wounds in General	**Yuji Inoue**
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	Hiroyuki Kanoh
	Yoichi Shintani
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	Keisuke Sakai
	Naotaka Doi
	Akira Hashimoto
	Masahiro Hayashi
	Naoki Madokoro
	Yuichiro Yoshino
EBM	Takeshi Kono

6) CRITERIA FOR THE DETERMINATION OF EVIDENCE AND RECOMMENDATION LEVELS

The criteria adopted in the "Guidelines for the diagnosis and treatment of malignant tumors" edited by the Japanese Dermatological Association mentioned below were used as a reference for the evidence levels.

- Evidence levels:

  I. Systematic reviews/meta-analysis.
  II. One or more RCT.
  III. Non-RCT (including before/after comparative studies with statistical analysis).
  IVa. Analytical epidemiological studies (cohort studies).
  IVb. Analytical epidemiological studies (case–control studies/cross-sectional studies).
  V. Descriptive studies (case reports and case series studies).
  VI. Opinions of special committees and individual experts.

In addition, the *Minds Handbook for Clinical Practice Guideline Development 2014* was referenced for the recommendation levels.

- Recommendation levels:

  There are two levels of recommendation indicated:

1. Strong recommendation.
2. Weak recommendation (proposal).

If the level of recommendation cannot be determined, the level of recommendation is "none", which includes cases when a clear recommendation cannot be made.

The recommendations state the strength of evidence (described as A, B, C and D) together with the level of recommendation as in the following examples:

1. Treatment I is recommended for patient P (1A) (i.e. strong recommendation based on strong evidence).
2. Treatment I is proposed as an option for patient P (2C) (i.e. weak recommendation based on weak evidence).
3. We propose that treatment I not be performed for patient P (2D) (i.e. weak recommendation based on very weak evidence).
4. We recommend that treatment I not be performed for patient P (1B) (i.e. strong recommendation based on moderate evidence).

7) REVIEW BEFORE PUBLICATION

Prior to the publication of these guidelines, the Annual Meetings of the Japanese Dermatological Association from 2013 to 2015 were used to present annual progress in the drafting of the guidelines, solicit opinions from association members and make necessary revisions. In addition, the drafts were distributed to representatives who were considered typical prospective users of the guidelines, their opinions were collected and summarized, and the results are reflected in the final manuscript.

8) PLANS FOR UPDATES

There is a planned update of the present guidelines in 3–5 years. However, if a partial update becomes necessary, it will be presented on the website of the Japanese Dermatological Association.

9) DEFINITIONS OF TERMINOLOGY

The terminology used in these guidelines is defined below based on reviews and textbooks in Japan. Some terms are quoted from the burn terminology list of the Japanese Society for Burn Injuries and the terminology list of the Japanese Society of Pressure Ulcers Terminology Committee, taking into account consistency within the "Wound, pressure ulcer and burn guidelines".

"First-degree burn": Epidermal burn that shows only reddening of the injured area and cures without scarring.

"Second-degree burn": Usually classified into two types according to the depth:

- "Superficial dermal burn" (SDB): A burn that forms a blister. The dermis at the floor of the blister is red. Usually heals after epithelialization in 1–2 weeks. Generally leaves no hypertrophic scar.
- "Deep dermal burn" (DDB): A burn that forms a blister. The dermis as the floor of the blister is white and anemic. The injury requires 3–4 weeks until healing occurs by epithelialization, but it is likely to leave a hypertrophic or keloid scar.

"Third-degree burn": Deep burn causing necrosis of the full thickness of the skin. It includes burns with a white or brown leather-like appearance and burns with completely charred skin. Because epithelialization progresses only from the margins of the injury, 1–3 months or longer is needed for healing, and hypertrophic scars or scar contracture occur unless skin grafting is performed.

"Burn index" (BI): An index proposed by Schwarz *et al.*,[1] that represents the severity of burns, calculated as one-half × area of second-degree burn (%) + area of third-degree burn (%). A BI of 10–15 or higher is considered severe.

"Prognostic burn index" (PBI): An index representing the severity of burns, calculated as age (years) + BI.

"Inhalation injury" (burn): Damage to the pharyngeal/laryngeal or tracheal/bronchial mucosa or alveoli caused by inhalation of smoke, high-pressure water vapor, toxic gas or the like as a result of fire or explosion.

"Chemical burn": Various corrosive phenomena with tissue necrosis caused by chemical agents such as acids, alkalis, heavy metals, toxic gases or the like contacting or adhering to the skin or a mucous membrane.

"Electrical burn": A burn caused by an electrical hazard such as electric shock, lightning strike, electrical sparks, electrical arcs or the like. Electrical burns include those directly caused by electrical current, those caused by Joule heating and those caused by sparks.

"Total body surface area" (TBSA): The total surface area of the body.

"Topical agents": Drugs administrated through the skin or applied directly to skin lesions for local treatment. Prepared by compounding various active components with a base.

"Dressing materials": Modern wound-dressing materials for creating a moist environment for wounds. Conventional sterilized gauze is excluded.

"Wound-dressing materials": Wound-dressing materials can be broadly divided into dressing materials (modern dressing materials) and medical materials such as gauze (classic dressing materials). The former are medical materials that provide conditions optimal for wound healing by maintaining a moist environment, and must be used selectively depending on the state of the wound and the amount of exudate. Gauze allows drying of the wound and cannot maintain a moist environment if exudate volume is insufficient. Medical materials other than conventional gauze that provide an optimal environment for wound healing by covering the wound and maintaining moisture may also be called wound-dressing materials or dressing materials.

"Wound bed preparation": Management of the wound surface environment to promote wound healing. Specifically, this consists of removing necrotic tissue, reducing bacterial load, preventing wound drying, controlling excessive exudates, and treating undermining and wound margins.

"TIME": Practical principles for wound bed preparation based on the concept of evaluating factors that prevent wound healing from the viewpoints of tissue (T), infection/inflammation (I), moisture (M) and wound edge (E), and using the results for treatment and care.

"Moist wound healing": A method to maintain the wound surface in a moist environment. Such an environment retains polynuclear leukocytes, macrophages, enzymes and cell growth factors contained in exudates on the wound surface. It also promotes autolysis, contributes to debridement and does not interfere with cell migration.

"Escharotomy": Also known as "decompressive incisions". Performed to prevent obstruction to respiratory movements at the neck and torso and circulatory disturbance at the peripheral areas of the limbs due to swelling caused by deep burns to the entire periphery of the torso, limbs or neck. Depending on the depth of the burns, either escharotomy or fasciotomy is performed.

10) DIAGNOSTIC AND THERAPEUTIC ALGORITHMS

Diagnostic and therapeutic algorithms were prepared based on the assumption that the severity evaluation is performed first when a burn patient is encountered. Figure 1 shows the diagnostic and therapeutic algorithms and CQ.

11) SUMMARY OF CQ

Table 2 presents the CQ along with their respective level of recommendation and description of each recommendation.

SEVERITY EVALUATION

CQ1: What is the recommended method for estimating the depth of burns?

Description of recommendation: A classification based on clinical symptoms (1C) is the recommended method for estimating the depth of burns.

For a more precise estimation, the use of laser Doppler flowmetry (2B) or video microscopy (2B) together with the

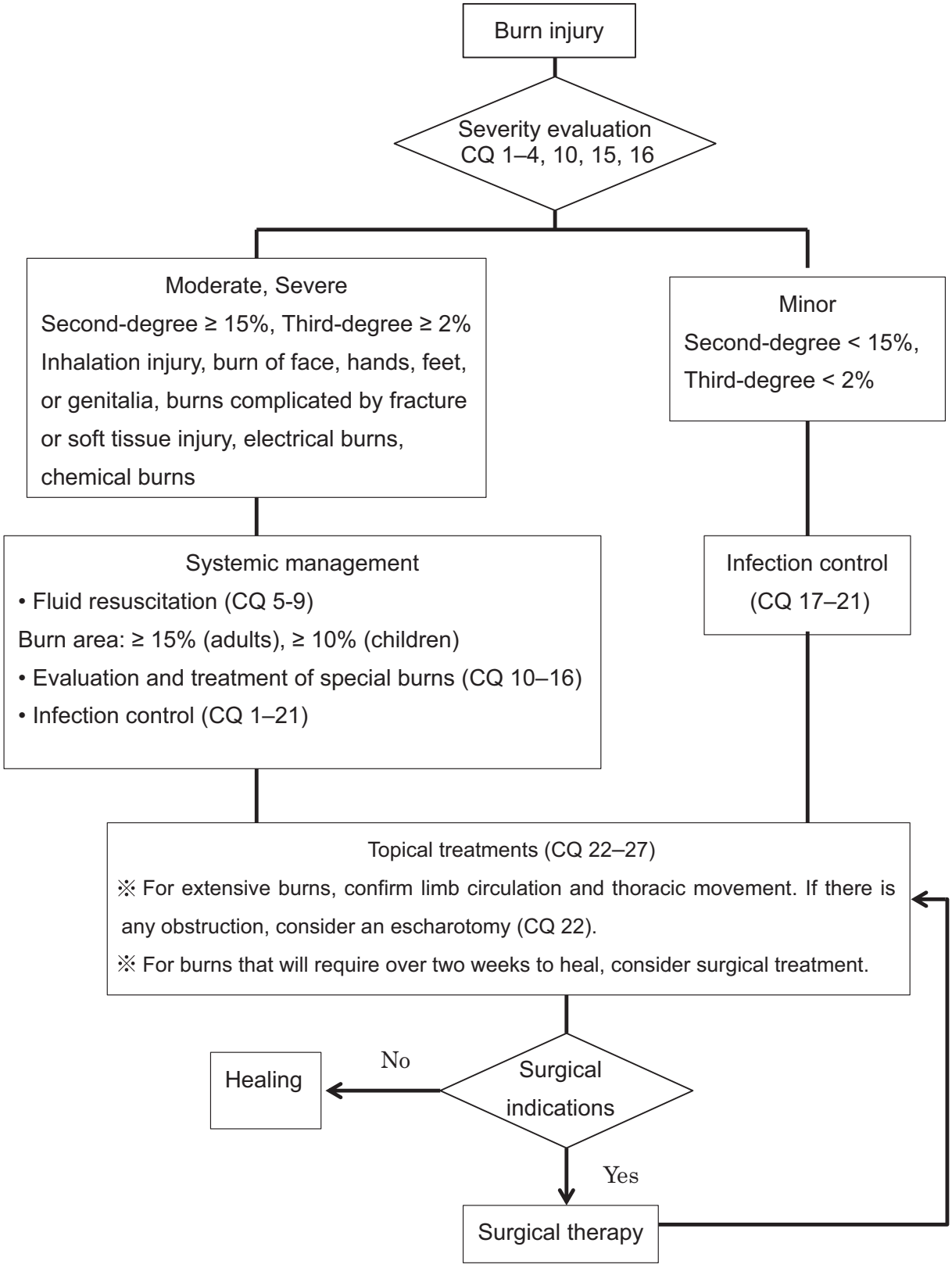

Figure 1. Diagnostic and therapeutic algorithms for burn injury. CQ, clinical question.

Table 2. Summary of clinical questions

Clinical question (CQ)	Description of recommendation
Severity evaluation	A classification based on clinical symptoms (1C) is recommended as a method for estimating the depth of burns. For a more precise estimation, the use of laser Doppler flowmetry (2B) or video microscopy (2B) together with the classification based on clinical symptoms is proposed as an option. Recommendation level: 1C for classification based on clinical symptoms; 2B for laser Doppler flowmetry and video microscopy.
CQ1: What is the recommended method for estimating the depth of burns?	
CQ2: What is the recommended method for estimating the burn area?	For estimating the burn area, the use of the rule of nines (1D), the rule of fives (1D), and the Lund and Browder Chart (1D) is recommended. Recommendation level: 1D for the rule of nines, the rule of fives, and the Lund and Browder Chart; 1C for the palm method.
CQ3: Are Artz's criteria useful for the severity evaluation of burns?	The use of Artz's criteria or their modification (Moylan's criteria) is recommended as a tool to evaluate the severity of burns. Recommendation level: 1D.
CQ4: What are useful prognostic factors for burns?	For estimating prognosis, factors such as burn area (percentage relative to the total body surface area [TBSA]: %TBSA) (1D), presence of airway damage (1C), area of third-degree burns (1C), prognostic burn index (PBI) (1C), age (1C) and burn index (BI) (1C) are recommended. Recommendation level: 1D for burn area; 1C for presence of airway damage, area of third-degree burns, PBI, age and BI.
Systemic management	Fluid resuscitation is recommended for adults with a burn area of approximately 15% TBSA or higher (1D) and for children with a burn area of approximately 10% TBSA or higher. However, early fluid resuscitation may be initiated in patients with a smaller burn area depending on their general condition. Recommendation level: 1D for adults with a burn area of approximately 15% TBSA or higher and children with a burn area of approximately 10% TBSA or higher.
CQ5: Which patients have indications for fluid resuscitation?	
CQ6: When should early fluid resuscitation be initiated?	In patients who require fluid resuscitation, it is recommended to initiate it as early as possible after injury. Recommendation level: 1C.
CQ7: What should be used for the initial infusion?	The use of isotonic electrolyte fluids (e.g. lactated Ringer's solution, acetated Ringer's solution) (1B) is recommended for the initial infusion. The concomitant use of colloids (2A) and hypertonic lactated saline (HLS) (2A) is proposed as a strategy for reducing the total administrated fluid dose. Recommendation level: 1B for isotonic electrolyte fluids; 2A for concomitant colloids and HLS.
CQ8: How should the initial infusion volume be calculated?	The Parkland method (also called the Baxter method) is recommended for initiating fluid resuscitation. Recommendation level: 1A.
CQ9: What are the appropriate indicators for determining the infusion rate?	Urine volume is recommended as an index for the infusion rate. The infusion rate should be adjusted to maintain a urine volume of 0.5 mL/kg per h or 30–50 mL/h or more in adults and 1–2 mL/kg per h or more in children. Recommendation level: 1D.
CQ10: What factors are suggestive of airway burns?	Circumstances of injury (injury in a narrow space due to inhalation of hot vapor or liquid) (1C) and physical findings (e.g. soot in the mouth or sputum, burned ends of nasal hair, burns of the face) (1C) are recommended as the findings that suggest airway burns. Recommendation level: 1C for circumstances of injury and physical findings.
CQ11: Is bronchoscopy useful for the diagnosis of airway burns?	Diagnosis by bronchoscopy is recommended when bronchoscopy findings support a diagnosis. Recommendation level: 1C.
CQ12: Is plain chest radiography useful for the diagnosis of respiratory disorders due to airway burns?	Serial plain chest radiography is recommended for the early diagnosis of respiratory disorders. Recommendation level: 1C.

Table 2. (continued)

Clinical question (CQ)	Description of recommendation
CQ13: Should endotracheal intubation be performed when airway burns are suspected?	When airway burns are suspected, preventive intubation is recommended if possible. Recommendation level: 1C.
CQ14: Is steroid administration useful for the management of airway burns?	Steroid administration (systemic or local) for the treatment of airway burns does not have sufficient evidence (at present), and therefore it is recommended not to be performed. Recommendation level: 1B (recommended not to be performed).
CQ15: How should burns caused by electric shock be treated?	Inpatient care is recommended for burns due to high-voltage electric shock to enable systemic monitoring. Recommendation level: 1C.
CQ16: What is the recommended initial response for chemical burns?	With some exceptions, lavage with a sufficient volume of water is recommended for the initial response to chemical burns. However, phenols, hydrogen fluoride, cement, quicklime and the like require specialized initial treatment. Recommendation level: 1C.
Infection control CQ17: Is the early, preventive systemic administration of antibiotics after burns useful?	In patients with contaminated wounds (2B), immunocompromised patients such as those with diabetes (2B), children (2B) and perioperative patients (2B), it is recommended to determine the target bacteria taking into consideration the facility and local characteristics as well as the results of bacterial cultures from the wound and to administrate preventive systemic antibiotics. Uniform preventive systemic administration of antibiotics (B) cannot be clearly recommended at present because of the absence of sufficient evidence supporting its effectiveness. Recommendation level: 2B for patients with contaminated wounds, immunocompromised patients, children and perioperative patients.
CQ18: Is an anti-tetanus treatment of burns necessary for the prevention of tetanus?	For contaminated burns, the administration of tetanus toxoid (Tt) or human tetanus immunoglobulin (TIG) is recommended. Recommendation level: 1D.
CQ19: Is hydrotherapy (shower, bathing, lavage) useful for the treatment of burns?	Hydrotherapy is recommended for patients with relatively minor burns not requiring hospitalization (1D). For patients with extensive severe burns judged to benefit from hydrotherapy, it is proposed as an option assuming that anti-infection measures are being taken (2C). Recommendation level: 1D for hydrotherapy in patients with relatively minor burns not requiring hospitalization; 2C for hydrotherapy in patients with extensive severe burns with anti-infection measures.
CQ20: Is disinfection useful for the prevention of infection in burns?	Disinfection is proposed as an option by evaluating the condition of the wound along with the causative bacteria and antibacterial spectra of various drugs. Recommendation level: 2B.
CQ21: Is a fecal management tube useful for the prevention of infection in perianal burns?	The use of a fecal management tube is recommended for perianal burns according to the patient's general condition and state of the wound as it may reduce the incidence of wound and urinary tract infections and the frequency of gauze changes due to fecal contamination to the wound area. Recommendation level: 1B.
Local treatment CQ22: When should escharotomy be performed?	Escharotomy is recommended for reducing pressure, because full-circumference or nearly full-circumference deep burns to the limbs or precordium have no elasticity and subsequent fluid resuscitation can cause breathing impairment or circulatory impairment at the peripheral areas of the limbs. Recommendation level: 1A.
CQ23: Are dressing materials useful for the treatment of second-degree burns?	Silver-containing Hydrofiber® (1A) (Convatec, Deeside, UK) is recommended. Silver alginate (2A), silver-containing polyurethane foam/soft silicone (2A), alginate (2B), hydrocolloid (2B), hydrogel, polyurethane film (2B), chitin (2C) and polyurethane foam (2C) are proposed as options. Recommendation level: 1A for silver-containing Hydrofiber; 2A for silver alginate and silver-containing polyurethane foam/soft silicone; 2B for alginate, hydrocolloid, hydrogel and polyurethane film; 2C for chitin and polyurethane foam.

Table 2. (continued)

Clinical question (CQ)	Description of recommendation
CQ24: What topical agents should be used for the treatment of second-degree burns?	For the initial treatment of second-degree burns, ointments with oleaginous bases such as zinc oxide, dimethyl isopropylazulene, petrolatum and the like are recommended (1D). For second-degree burns, trafermin (1A), tretinoin tocopherol (1B), bucladesine sodium (1B) and prostaglandin E1 (1B) are recommended. Aluminum chlorohydroxy allantoinate (Alcloxa) (2B) and lysozyme hydrochloride (2B) are proposed as options. For chronic ulcers accompanied by necrotic tissue resulting from deep second-degree burns, bromelain ointment (1A), cadexomer iodine (1B), dextranomer (1B) and silver sulfadiazine (1D) are recommended for removing necrotic tissue. Recommendation level: (Initial treatment) 1D for ointments with oleaginous bases. (Second-degree burns) 1A for trafermin; 1B for tretinoin tocopherol, bucladesine sodium, and prostaglandin E1; 2B for aluminum chlorohydroxy allantoinate (Alcloxa) and lysozyme hydrochloride. (Chronic ulcers with necrotic tissue) 1A for bromelain ointment, 1B for cadexomer iodine and dextranomer; 1D for silver sulfadiazine.
CQ25: Is silver sulfadiazine useful for the treatment of extensive third-degree burns?	Silver sulfadiazine is recommended for treating extensive third-degree burns. Recommendation level: 1B.
CQ26: What topical agents should be used to remove necrotic tissue from small third-degree burns?	As topical agents aimed to remove necrotic tissue from small third-degree burns, bromelain (1A), cadexomer iodine (1B), dextranomer (1B) and silver sulfadiazine (1D) are recommended. Recommendation level: 1A for bromelain; 1B for cadexomer iodine and dextranomer; 1D for silver sulfadiazine.
CQ27: Are topical steroid preparations useful for the treatment of first-degree burns and shallow second-degree burns?	The use of topical steroid preparations is proposed as an option for the initial period after injury owing to their anti-inflammatory effects. Recommendation level: 2D.

classification based on clinical symptoms is proposed as an option.

Recommendation level:
(1C) for classification based on clinical symptoms.
(2B) for laser Doppler flowmetry and video microscopy.
Commentary:

- The method for estimating depth based on clinical findings (Table 3) is regarded as a reference for depth evaluation and is in wide clinical use. However, as it is only supported by a case report,[2] the evidence level is V. No particular instruments are needed and it is widely accepted, so the recommendation level is 1C.
- Regarding the method for the estimation of the depth of burns, there is a prospective non-randomized comparative trial comparing laser Doppler flowmetry and video microscopy;[3] therefore, the evidence level is III. The sensitivity for the detection of SDB was compared in 27 patients within 72 h after injury and was 100% by both methods, and the patients who were diagnosed with SDB healed within 3 weeks. In addition, although there are analytical epidemiological studies and case reports using laser Doppler flowmetry and video microscopy,[4–6] the equipment is not widespread; therefore, the recommendation level is 2B.

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Table 3. Depth classification based on clinical findings

Classification	Clinical findings
First-degree burn (epidermal burn)	Redness, pain
Superficial second-degree burn (superficial dermal burn)	Redness, blisters, pain, blisters blanche with pressure
Deep second-degree burn (deep dermal burn)	Redness, purple-white, blisters, desensitization, blisters do not blanche with pressure
Third-degree burn (deep burn)	Black, brown or white blister (–), pain (–)

Adapted from the *Comprehensive Handbook of Clinical Dermatology*, 2. Tokyo, Nakayama Shoten: 2003, p. 241.

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CQ2: What is the recommended method for estimating the burn area?

Description of recommendation: As methods for estimating the burn area, the use of the rule of nines (1D), the rule of fives (1D), and the Lund and Browder Chart (1D) are recommended.

The palm method (1C) is recommended as a method for the local estimation of the burn area.

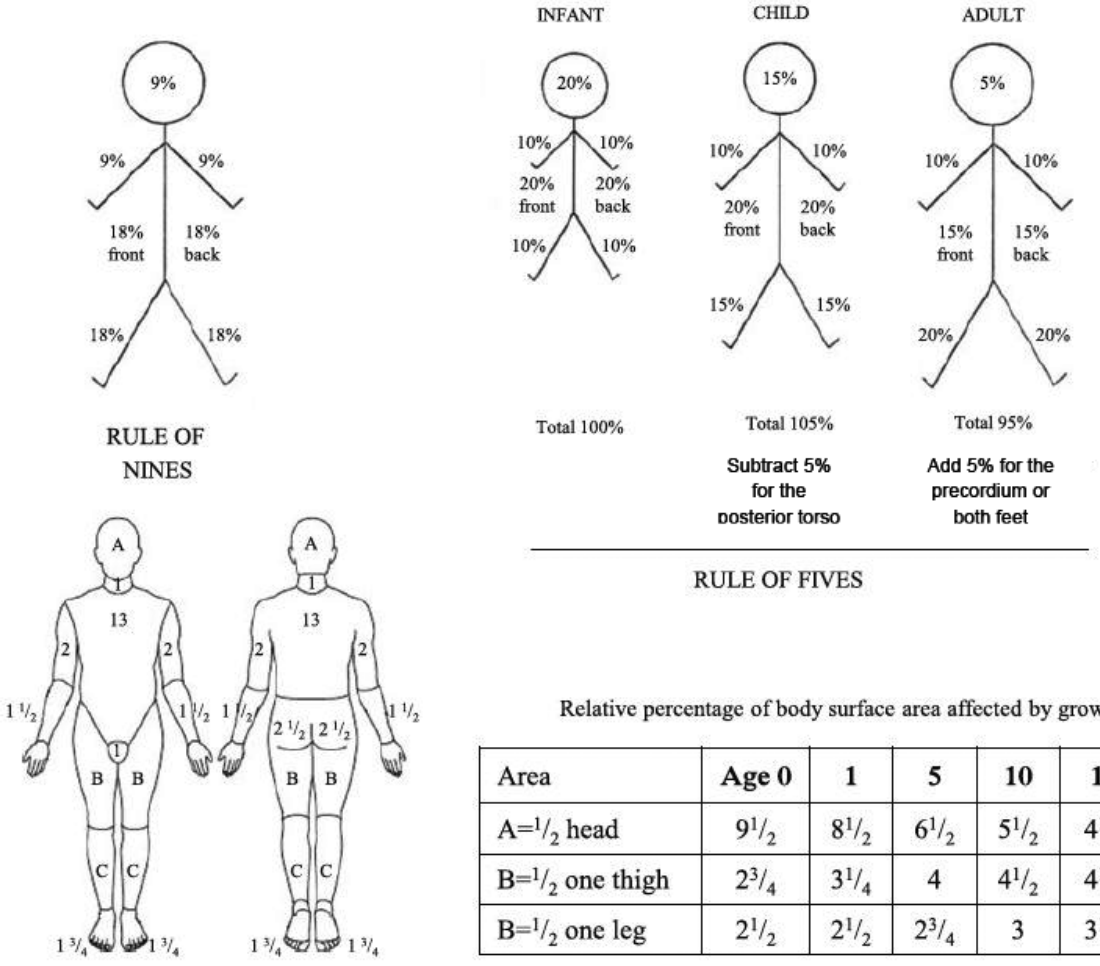
Recommendation level:

(1D) for the rule of nines, the rule of fives, and the Lund and Browder Chart.

(1C) for the palm method.

Commentary:

- The methods for estimating the burn area using the rule of nines, the rule of fives, and the Lund and Browder Chart are all supported only by expert opinion;[7–9] therefore, the evidence level is VI. However, because they are in wide clinical use, the recommendation level is 1D in light of the historical background. Regarding the palm method, there are some variations in determining the reference TBSA. However, the palm area can estimate a burn area that is approximately 1% (range, 0.7–0.95%) of the TBSA according to analytical epidemiological studies;[10–12] therefore, the evidence level is IVa. Because it is useful in the clinical setting, the recommendation level is 1C. See Figure 2 for the rule of nines, rule of fives, and the Lund and Browder Chart. In addition,



Relative percentage of body surface area affected by growth

Area	Age 0	1	5	10	15	Adult
A=1/2 head	9 1/2	8 1/2	6 1/2	5 1/2	4 1/2	3 1/2
B=1/2 one thigh	2 3/4	3 1/4	4	4 1/2	4 1/2	4 3/4
B=1/2 one leg	2 1/2	2 1/2	2 3/4	3	3 1/4	3 1/2

The Lund and Browder chart

Figure 2. Methods for estimating the burn area. Quoted from *Burn Treatment Manual*, Chugai-Igakusha: 2007, 72–76.

the palm method is a method that calculates the area of the palm to be approximately 1% of the TBSA in adults.

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CQ3: Are Artz's criteria useful for the severity evaluation of burns?

Description of recommendation: The use of Artz's criteria or their modification (Moylan's criteria) is recommended as a tool for the severity evaluation of burns.

Recommendation level: 1D.

Commentary:

- Since Artz's criteria and their modification (Moyland's criteria) for evaluating the severity of burns are both supported only by expert opinion,[13,14] the evidence level is VI. However, owing to their widespread clinical use and practicality as definitions for evaluating severity, the recommendation level is 1D.
- Artz's criteria and their modification (Moylan's criteria) grade the severity of burns according to their area, depth and complications, and indicate at which type of facility the patient should be treated (Table 4).

Table 4. Artz's criteria

Severe burns
• Second-degree burns over at least 30% TBSA
• Third-degree burns over at least 10% TBSA
• Third-degree burns of the face, hands, or feet
• Burns complicated by respiratory tract burns
• Burns complicated by soft tissue damage or fractures
• Electric shock
Moderate burns (requiring inpatient care at a general hospital)
• Second-degree burns over 15–30% TBSA
• Third-degree burns over <10% TBSA (excluding the face, hands and feet)
Minor burns (may be treated on an outpatient basis)
• Second-degree burns of <15% TBSA
• Third-degree burns of <2% TBSA

Adapted from Artz and Moncrief.[13] TBSA, total body surface area.

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CQ4: What are the useful prognostic factors for burns?

Description of recommendation: For estimating prognosis, factors such as burn area (percentage relative to the TBSA: % TBSA) (1D), presence of airway damage (1C), area of third-degree burns (1C), PBI (1C), age (1C) and BI (1C) are recommended.

Recommendation level:

(1D) for burn area.

(1C) for presence of airway damage, area of third-degree burns, PBI, age and BI.

Commentary:

- Although the burn area (%TBSA) is supported only by expert opinion with an evidence level of VI, it is a fundamental index for the evaluation of the severity of burns according to the published work on estimating the prognosis of burns.[15–30] Furthermore, as it is commonly considered useful for determining a prognosis, the recommendation level is 1D.
- Many studies have mentioned age (evidence level Iva–V)[15–17,19,21,22,25,26] and airway burns (evidence level Iva–IVb),[16,22,24,26,27,30] and some have reported the third-degree burn area (evidence level IVa)[25,26] as prognostic factors. Because those studies involved hundreds to thousands of burn patients, the recommendation level has been set to 1C. While the evidence level for the burn index[27] and PBI[18] is Iva–IVb, they are not in wide clinical use in Japan; therefore, their recommendation level is 1C. There is additional published work suggesting that burns due to suicide attempts[28] and complication by psychiatric disorders[25] also contribute to the mortality rate.

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SYSTEMIC MANAGEMENT

CQ5: Which patients have indications for fluid resuscitation?

Description of recommendation: Fluid resuscitation is recommended for adults with a burn area of around 15% TBSA or higher (1D), and children with a burn area of around 10% TBSA or higher. However, early fluid resuscitation may be initiated in patients with a smaller burn area depending on their general condition.

Recommendation level:

(1D) for adults with a burn area of approximately 15% TBSA or higher and children with a burn area of approximately 10% TBSA or higher.

Commentary:

- Because no detailed report has evaluated the appropriateness of fluid resuscitation based on the size (area) of the injury and it is based only on expert opinion, the evidence level is VI.[31–38] According to Artz's diagnostic criteria,[31] the area of minor burns manageable by outpatient care is a second-degree burn area of 15% or less. When patients with a burn area greater than that are treated on an inpatient basis, fluid resuscitation is considered virtually mandatory. Therefore, the recommendation level has been set at 1D. For children, according to the criteria of the American Burn Association, fluid resuscitation should be initiated when the burn area is at least 20% TBSA.[32] However, according to Advanced Burn Life Support,[32] cases with second-degree burns covering at least 10% TBSA are referred to a burn treatment center (Table 5); therefore, fluid resuscitation for pediatric patients with a burn area of at least 10% TBSA, which is considered a severe case, has been set to 1D.
- According to Artz's criteria, inpatient treatment is necessary for patients with a third-degree burn area of at least 2% so that fluid resuscitation may be initiated during the acute period.
- Appropriate fluid replacement has been reported to prevent hypovolemic shock early after injury.[32,34–37]
- Artz's criteria and their modification (Moylan's criteria) are standards for grading the severity of burns according to their area, depth and complications, and for the selection of the appropriate facilities for treatment (see Table 4 concerning CQ3).

Table 5. Burn center referral criteria according to Advanced Burn Life Support

1. Second-degree burns >10% TBSA
2. Burns that involve the face, hands, feet, genitalia, perineum or major joints
3. Third-degree burns in any age group
4. Electrical burns including lightning injury
5. Chemical burns
6. Inhalation injury
7. Burn injury in patients with a medical history that could affect treatment or mortality
8. A patient with burns and concomitant trauma affecting morbidity or mortality
9. Burned children in hospitals at which the quality of pediatric care is not assured
10. Patients requiring special social or emotional care or long-term rehabilitation

Adapted from American Burn Association.[32] Other issues regarding specific cases can be resolved through diagnosis and treatment at a burn center. TBSA, total body surface area.

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CQ6: When should early fluid resuscitation be initiated?

Description of recommendation: In patients who require fluid resuscitation, it is recommended to initiate it as early as possible after injury.

Recommendation level: 1C.

Commentary:

- For the case–control studies on the timing of initiation for early fluid resuscitation,[39,40] the evidence level is IVb, and the recommendation level is 1C.
- When the burn area is 15–20% or greater, hypovolemic shock can occur due to increased vascular permeability in the absence of appropriate fluid resuscitation. Edema often occurs during the first 6–8 h and persists for 18–24 h or longer.[41,42] In addition, in 76 adult burn patients who developed renal insufficiency, the time until the beginning of early fluid resuscitation was reported to have differed significantly between the surviving cases and the fatal cases (1.7 ± 1.0 vs 4.4 ± 2.1 h).[39]
- In a review of 24 patients treated from 1966 to 1983 and 36 patients treated from 1984 to 1997, the mortality rate was 100% in the former group but decreased to 56% in the latter. While the time from injury to the beginning of fluid resuscitation was 8.6 ± 1.7 h in the former, it had been reduced to 3.0 ± 0.5 h in the latter. Among those treated since 1984, fluid resuscitation was started earlier in the surviving patients than in those who died (1.7 ± 0.5 vs 4.8 ± 0.9 h).[42]

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CQ7: What should be used for the initial infusion?

Description of recommendation: The use of isotonic electrolyte fluids (e.g. lactated Ringer's solution, acetated Ringer's solution) (1B) is recommended for the initial infusion.

The concomitant use of colloids (2A) and hypertonic lactated saline (HLS) (2A) is proposed as a strategy for reducing the total administrated fluid dose.

Recommendation level:

(1B) for isotonic electrolyte fluids.

(2A) for concomitant colloids and HLS.

Commentary:

- For the RCT comparing isotonic electrolyte fluids and colloid administration for the initial fluid resuscitation of burn patients,[43,44] the evidence level is II, though no significant difference was demonstrated. In addition, because one meta-analysis has compared the mortality rate between patients with trauma, burns and postoperative patients treated with isotonic electrolyte fluids and those treated with HLS,[45] the evidence level is I despite its failure to show a significant difference. Because colloids and HLS have not been shown to be more advantageous than isotonic electrolyte fluids, the recommendation level has been set to 1B for isotonic electrolyte fluids, which are the most widely used. The recommendation level is 2A for concomitant colloids and HLS as they are a promising approach to reducing the total administrated fluid dose despite their failure to improve mortality.
- Administration of colloids immediately after a burn injury, which is a period of enhanced vascular permeability, has been reported to have no advantage compared with isotonic electrolyte fluids.[46] In an RCT in which 79 patients with burns were divided into those treated with a lactated Ringer's solution and those treated with a colloid (2.5% albumin) plus lactated Ringer's solution, a larger volume of infusion was needed in the lactated Ringer's solution group than in the group with concomitant colloid use (3.81 vs 2.98 mL/kg bodyweight/%TBSA). However, no significant improvement in circulation was observed even in the concomitant colloid use group, and pleural effusion increased in the period of diuresis.[43] Furthermore, when the intravesical pressure was measured as the intra-abdominal pressure (IAP) in 15 patients who were administrated lactated Ringer's solution (Parkland method) and in 16 who were administrated a colloid, IAP was significantly higher in the lactated Ringer's solution group, and more solution was needed for the initial infusion compared with the colloid group. In both groups, a correlation was observed between the total volume of infusion and IAP, and while IAP remained no greater than the complication threshold (25 mmHg) in the plasma administration group, an effect of suppressing an increase in IAP was shown. Nevertheless, no clear difference was found in terms of mortality.[44]
- To date, in studies investigating the association between colloid administration and mortality rate in severely injured patients due to trauma and burns as well as in postoperative patients, colloids have not been shown to improve mortality.[47,52] In addition, in a study of 70 patients aged 19 years and under with burns of 20% TBSA or greater that compared a group (36 patients) who were administrated a colloid maintaining serum albumin levels at 2.5–3.5 g/dL to a group (34 patients) who were supplemented with the colloid only when serum albumin levels had dropped under 1.5 g/dL, there was no difference between the groups in terms of complications, mortality, hospitalization period or artificial respiration management.[48]
- According to these observations, colloid administration can be considered to reduce the total volume of infusion and to suppress increases in IAP, but at present cannot be considered effective at improving mortality. However, as a decrease in the colloid osmotic pressure exacerbates edema in non-burned areas, colloid administration has been

recommended by some when hypoalbuminemia or a decrease in colloid osmotic pressure 8–12 h after injury is affecting respiration or circulation.[49] It has also been reported that the concomitant administration of albumin within 24 h of injury stabilized circulation and decreased mortality.[53] Fluid resuscitation incorporating colloid administration, such as the Evan's method and Brooke method, is performed in actual clinical practice.

- When 14 patients in the HLS group and 22 patients in the lactated Ringer's solution group were compared, with a maintenance of urine volume at 0.5–1.0 mL/kg per h, the necessary infusion volume was 3.1 ± 0.9 versus 5.2 ± 1.2 mL/24 h/kg $\times$ %TBSA, respectively. Thus, the HLS group was able to maintain urine volume with a smaller infusion volume and had a significantly lower maximum inspiratory pressure, with a lower incidence of intra-abdominal hypertension (14% vs 50%).[50] However, in another report, the incidence of renal insufficiency and mortality rate were higher in an HLS group than in a lactated Ringer's solution group, and no decrease in the total infusion volume was observed.[51] In addition, according to a meta-analysis evaluating whether or not HLS reduces the mortality rate of hypovolemic patients, when hypotonic, isotonic and nearly isotonic solutions were administrated to trauma, burn and postoperative patients, the relative risk of death in the HLS-treated group was 0.84 for trauma, 1.49 for burns and 0.51 in postoperative patients.[45] The conclusion is that while no data indicating that HLS has a higher survival-improving effect than an isotonic solution have been obtained at present, it can be considered effective for reducing the total infusion volume and suppressing IAP increase.
- HLS is prepared by adding sodium to lactated Ringer's solution. It was devised to supplement ECF and sodium, which are lost after burns, and to reduce the total infusion volume compared with that using an isotonic solution. Monafo HLS, Fox HLS and Osaka University HLS represent some variations (Tables 6,7).

Table 6. Hypertonic lactated saline (HLS) types

Monafo formula	Transfusion of HLS250 to maintain urine volume at 30 mL/h
Fox formula	Transfusion of HLS225 to maintain urine volume at 30 mL/h
Osaka University HLS	Start transfusion with HLS300 to maintain urine volume at 30–50 mL/h

Adapted from *Burn Treatment Manual*, Chugai-Igakusha: 2007; p. 85.

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CQ8: How should the initial infusion volume be calculated?

Description of recommendation: The Parkland method (also called the Baxter method; Table 8) is recommended for initiating fluid resuscitation.

Recommendation level: 1A.

Commentary:

- For one meta-analysis concerning initial fluid resuscitation volume,[54] the evidence level is I and the recommendation level is 1A. While the Parkland method is widely used, it was shown that the necessary initial infusion volume exceeded that which was calculated by that method.
- Baxter carried out an animal experiment for hemodynamic evaluation using a radioisotope during the acute period of burn injury and showed that an infusion at 3.7–4.3 mL/kg per %TBSA was necessary and that functional extracellular

Table 7. Hypertonic lactated saline (HLS) compositions and administration methods

Preparation	Na (mEq/L)	Cl (mEq/L)	Lactate (mEq/L)	
HLS 300	300	88	212	Switch to HLS 250 after administrating 2000 mL
HLS 250	250	94	156	Switch to HLS 200 after administrating 1000 mL
HLS 200	200	100	100	Switch to HLS 150 after administrating 1000 mL
HLS 150	150	102	48	Up to 48 h after injury

Table 8. The Parkland method

Total infusion volume for the first 24 h after injury = 4 mL × TBSA(%) × bodyweight (kg)
Administrate 50% of the total infusion volume in the first 8 h after injury.
Administrate the remaining 50% during the following 16 h.
In children, maintenance infusions are concomitantly used.
Administrate the maintenance infusion at 4 mL/kg per h for each of the first 10 kg of bodyweight.
Add a maintenance infusion of 2 mL/kg per h for each kg of bodyweight exceeding 10 kg up to 20 kg.
Add a maintenance infusion of 1 mL/kg per h for each kg of bodyweight exceeding 20 kg.
Example: For a 25-kg child, the concomitant maintenance infusion is 10 × 4 + 10 × 2 + 5 × 1 = 65 mL/h.

Adapted from Hettiaratchy and Papini.[63]

fluid (ECF) decreased rapidly after a burn injury depending on the burn area, but that shock due to burn could be avoided and the mortality rate reduced by administrating lactated Ringer's solution.[55] There is also a report that, when lactated Ringer's solution was administrated to patients with a target urine volume of 40 mL/h with the level of consciousness as an indicator, the infusion volume during the 24 h after injury was in the range of 3.7–4.3 mL/kg per %TBSA in 70% of adults and 98% of children aged 12 years or less.[56]

- In recent years, there have been reports that an initial infusion volume greater than that calculated by the Parkland method is necessary,[54,57,58] but excessive infusion is believed to promote edema and increase compartment syndrome of the limbs, pneumonia, acute respiratory distress syndrome, multiple organ failure, sepsis and mortality.[59,60] According to a study in which 50 burn patients with a burn area of 20% TBSA or more were treated by the Parkland method or invasive intrathoracic blood volume monitoring, the infusion volume during the first 24 h was significantly greater in the intrathoracic blood volume monitoring group. Furthermore, intravascular dehydration was observed within 48 h by the Parkland method, but there was no difference in the preload or cardiac output between the two groups, or in the mortality rate or the incidence of complications.[61] Therefore, electrolyte fluid administration in quantities greater than those indicated by the Parkland method is not considered to improve preload or cardiac output.
- There has also been a report that on comparing a group administrated an initial infusion volume of 2 mL/kg per % TBSA and a group administrated 4 mL/kg per %TBSA, the former had a lower total infusion volume, and there were no differences in results such as mortality.[64] In addition, ABSL 2011 has established the method of starting the initial infusion at 2 mL/kg per %TBSA and then adjusting it based on responses such as urine volume.[65] Although many facilities worldwide still perform the initial infusion treatment according to the Parkland method,[62,63] further evaluation is warranted for the conclusive determination of the appropriate volume and rate of initial fluid resuscitation.

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CQ9: What are the appropriate indicators for determining the infusion rate?

Description of recommendation: Urine volume is recommended as an index for the infusion rate. The infusion rate should be adjusted to maintain a urine volume of 0.5 mL/kg per h or 30–50 mL/h or more in adults and 1–2 mL/kg per h or more in children.

Recommendation level: 1D.

Commentary:

- Because the reports on the indices for the appropriate volume and rate of initial infusion are based on expert opinion, the evidence level is VI. However, the recommendation level has been set at 1D given that hourly urine volume reflects organ blood flow and is widely accepted as an index for hemodynamic evaluation.
- The objective of initial fluid resuscitation is to resolve hypovolemic shock, and urine volume, which is reflective of renal blood flow, is generally used as an index for the evaluation of organ blood flow.[66–68] However, caution is needed as the urine volume cannot be used as the sole index in patients with compromised renal function. Hemodynamics should be evaluated using other general vital signs (e.g. blood pressure, heart rate, peripheral circulation, tachypnea), central venous pressure and lactate levels.

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SYSTEMIC MANAGEMENT: AIRWAY BURNS

CQ10: What factors are suggestive of airway burns?

Description of recommendation: The circumstances of injury (injury in a narrow space due to the inhalation of hot vapor or liquid) (1C) and physical findings (e.g. soot in the mouth or sputum, burned ends of nasal hair, burns of the face) (1C) are recommended as the findings that suggest airway burns.

Recommendation level: (1C) for the circumstances of injury and physical findings.

Commentary:

- For a case–control study investigating the presence of airway burns according to physical findings,[69] the evidence level is IVb. Because these are commonly used diagnostic methods that can be easily implemented, the recommendation level is 1C.
- Most experts use the circumstances of injury and physical findings as non-invasive indicators of airway burns.[70] In patients requiring intubation, airway burns are reported to be positively correlated with soot in the oral cavity ($P < 0.001$), burns of the face ($P = 0.025$) and burns of the trunk ($P = 0.025$), and these correlations are higher than those with edema of the vocal cords detected by laryngoscopy.[69]

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CQ11: Is bronchoscopy useful for the diagnosis of airway burns?

Description of recommendation: Diagnosis by bronchoscopy is recommended when bronchoscopy findings support a diagnosis.

Recommendation level: 1C.

Commentary:

- For a cohort study on the diagnosis of airway burns using bronchoscopy,[71] the evidence level is IVa. As it is a widely implemented examination with a high diagnostic value, the recommendation level is 1C.
- The presence of soot inside the bronchi along with pallor and ulceration of the bronchial mucosa observed by bronchoscopy have been reported to be consistent with diagnoses of airway burns.[72,73]

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CQ12: Is plain chest radiography useful for the diagnosis of respiratory disorders due to airway burns?

Description of recommendation: Chronological plain chest radiography is recommended for the early diagnosis of respiratory disorders.

Recommendation level: 1C.

Commentary:

- For cohort studies investigating the diagnosis of respiratory disorders by plain chest radiography,[74,75] the evidence level is IVa. As this is a relatively simple examination, the recommendation level is 1C.
- The categorization into groups based on plain chest radiography was found to correlate well with the extravascular lung water volume, intrapulmonary shunt ratio (Qs/Qt) and static lung compliance.[74] Abnormalities detected by early plain chest radiography are important prognostic factors that enable the selection of patients who are likely to need respiratory management.[75] It is an easy-to-perform examination compared with computed tomography and the like; therefore, serial radiographic evaluation is recommended in the acute period.

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CQ13: Should endotracheal intubation be performed when airway burns are suspected?

Description of recommendation: When inhalation injury is suspected, preventive intubation is recommended if possible.

Recommendation level: 1C.

Commentary:

- For a cohort study on preventive endotracheal intubation,[76] the evidence level is IVa and the recommendation level is 1C.
- Respiratory disorders associated with burns may be caused by the restriction of respiratory motion and compression of the trachea due to burns of the neck/chest as well as airway burns.[77] Therefore, whether the patient should be intubated cannot be determined according to the presence of airway burns alone. However, if airway edema develops due to burns of the face/neck or airway, preventive intubation is recommended because intubation may become

subsequently difficult, leading to a potentially dangerous situation. In addition, there is a report that early preventive intubation and respiratory management by continuous positive airway pressure (CPAP) may prevent respiratory organ-related mortality after burns.[76]

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CQ14: Is steroid administration useful for the management of airway burns?

Description of recommendation: Because steroid administration (systemic or local) for the treatment of airway burns does not have sufficient evidence (at present), it is recommended not to be performed.

Recommendation level: 1B (recommended not to be performed).

Commentary:

- For an RCT on systemic steroid administration for airway burns,[78] the evidence level is II. However, systemic steroid administration has not been shown to be useful for reducing the mortality rate or preventing complications. In addition, taking into consideration the increased susceptibility to infection when the mucosal barrier function is disrupted due to burns, the recommendation level is 1B. The recommendation level for localized steroid administration is also set at 1B.
- There are reports that systemic steroid administration in burn patients with airway burns caused no difference in lung-related conditions or the mortality rate.[79,80] Although it does not pertain to burn patients, there is a report that systemic steroid administration prior to extubation in adult patients who had undergone intubation for at least 36 h alleviated laryngeal edema and reduced the reintubation rate,[81] suggesting that the treatment is effective in reducing edema. However, due to the differences in circumstances, these patients cannot be compared with those who have damage to the airway mucosa.

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CQ15: How should burns caused by electric shock be treated?

Description of recommendation: Inpatient care is recommended for burns due to high-voltage electric shock to enable systemic monitoring.

Recommendation level: 1C.

Commentary:

- Electric shocks can cause damage not only to the skin but also to a variety of organs and tissues as a result of electrical current flowing through the body. It is difficult to make comparisons between patients as the cause of injury, site of injury, pathway of electrical current, duration of contact and so forth vary on a case-to-case basis. Given that the available reports are primarily retrospective cohort studies and case collection studies,[82–85] the evidence level is IVb. The recommendation level for inpatient treatment is 1C as the encroachment on the body is evident in cases of high-voltage electric shock.
- When examining electric shock patients, monitoring and blood tests must be serially performed in accordance with the individual patient.[84,85] A decision must also be made as to the early debridement of significantly damaged muscle tissue,[82] and constant supervision is necessary. A comparison of causes of injury is shown in Table 9.
- Care is particularly necessary for electric shocks caused by high-voltage, and early debridement was indicated in one report because muscle tissue damage can cause myoglobinemia and kidney damage.[82] Fluid resuscitation is performed as expected owing to the extent of the skin burns.[84] A target urine volume of approximately 3 mL/kg per h is in accordance with the treatment for crush syndrome.[86]
- The most common causes of fatal electrocution are contact with the power transmission grid and lightning strikes.[83,85]

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CQ16: What is the recommended initial response for chemical burns?

Description of recommendation: With some exceptions, lavage with a sufficient volume of water is recommended for the initial

Table 9. Comparison by cause of injury

	Lightning strike	High-voltage	Low-voltage
Voltage (V)	$>30 \times 10^6$	>1000	<600
Current (A)	>200 000	<100	<240
Contact time	Instantaneous	Brief	Prolonged
Current type	DC	DC or AC	Mainly AC
Cardiac arrest (cause)	Systolic failure	Ventricular fibrillation	Ventricular fibrillation
Respiratory arrest (cause)	Direct central nervous system damage	Indirect trauma or tetanic contraction of the respiratory muscles	Tetanic contraction of the respiratory muscles
Muscle contraction	Muscle twitching	DC: muscle twitching; AC: tetanic	Tetanic
Burns	Unusual, surface	Deep burns arise	Arise on the body surface
Rhabdomyolysis	Does not ordinarily occur	Occurs very frequently	May occur
Blunt trauma	Caused by air blast or shock wave	Caused by falling due to muscle contraction	Caused by falling
Mortality rate (acute phase)	High	Moderate	Low

Adapted from Hussmann *et al*.[82]

response to chemical burns. However, phenols, hydrogen fluoride, cement, quicklime and the like require specialized initial treatment.

Recommendation level: 1C.

Commentary:

- For three cohort and case–control studies regarding the initial treatment of chemical burns, the evidence level is IVa–IVb and the recommendation level is 1C.
- Chemical burns exhibit a different clinical progression than burns caused by flame or hot water, and the progression even differs according to the causative substance. In addition, while lavage with water is habitually performed as the initial response, all the reports on the initial treatment of chemical burns are retrospective cohort studies in which a group that received appropriate treatment was compared with a group that did not. The appropriate treatment group had a lower mortality rate and fewer hospitalization days as well as a shallower burn depth.[87–89] Although the reports define the optimal treatment differently, timely treatment (ideally within 10 min of injury) and sufficient lavage (at least 15 min) are the critical components.[89]
- In addition, some injurious substances require specialized initial treatment, including the following:[90]

Phenols: These do not dissolve in water, so polyethylene glycol must be used.

Hydrogen fluoride: Recognized to have a pain-reducing effect. Use calcium gluconate topically and as an intra-arterial injection (2–5% calcium gluconate).[91]

Cement: It is a strong alkali that is powerfully water absorbent, so remove clothing and wipe it off thoroughly before lavage with water.

Quicklime: Reacts exothermically with water, so wipe it off thoroughly before lavage with water.

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INFECTION CONTROL

CQ17: Is the early, prophylactic administration of systemic antibiotics useful for burns?

Description of recommendation: In patients with contaminated wounds (2B), immunocompromised patients such as those with diabetes (2B), children (2B) and perioperative patients (2B), it is recommended to consider the prophylactic administration of systemic antibiotics by determining the target bacteria and taking into consideration the facility and local characteristics of antibiogram as well as the results of bacterial cultures from the wound.

Uniform prophylactic administration of systemic antibiotics (B) cannot be recommended at present owing to the absence of sufficient evidence supporting its effectiveness.

Recommendation level: (2B) for patients with contaminated wounds, immunocompromised patients, children and perioperative patients.

Commentary:

- For two RCT on prophylactic administration of systemic antibiotics in the perioperative period,[92,93] the evidence level is II. While it may improve the intake rate of skin grafts or reduce the incidence of bacteremia, the recommendation level has been set at 2B due to the lack of data that it would improve the patient's survival rate.
- For one RCT concerning the prophylactic administration of systemic antibiotics for the prevention of infection in burns,[94] the evidence level is II. In this trial, no improvement in outcomes or decrease in the incidence of infection was

observed despite the uniform administration of systemic antibiotics. Moreover, because the treatment may induce microbial substitution, a clear recommendation could not be made, resulting in a recommendation level of B.

- There are many negative reports concerning the uniform prophylactic administration of systemic antibiotics. Ergün *et al.*[92] investigated 77 children with extensive burns, applying the prophylactic administration of systemic antibiotics in 47 subjects (treatment group) and no administration in 30 subjects (non-treatment group), and reported that the frequency of wound infection was significantly higher in the treatment group than in the non-treatment group (21.3% vs 16.7%), that seven out of the eight patients who developed sepsis were in the treatment group, that the duration of hospitalization was longer in the treatment group, and that the treatment was associated with secondary infections of other sites (respiratory organs, urinary tract). In a multicenter collaborative study carried out in Italy, 634 patients with extensive burns (mean age, ~40 years; mean burn area, 35% TBSA) were treated with topical application of silver sulfadiazine and a 4-day administration of pefloxacin (a quinolone). As a result, 104 patients (16%) showed no infection, though the burns of these patients were relatively minor. However, the frequency of detected bacteria which is resistant to quinolones and aminoglycosides increased following treatment administration, and the usefulness of prophylactic administration of systemic antibiotics with this protocol could not be confirmed.[95]
- Concerning studies on minor burns, Boss *et al.*[96] retrospectively compared the wound infection rate among 294 outpatients with burns, with 133 subjects who underwent systemic administration of antibiotics and 161 who did not, and reported that there was no difference in the infection rate (3.8% vs 3.1%). Moreover, while antibiotics were administrated to a significantly higher percentage of patients with a burn area of 5% TBSA or more than to those with a burn area of less than 5% TBSA, the infection rate was not decreased in the first group.
- Various reports and suggestions have been described as to what kind of patients should be administrated prophylactic antibiotics. The incidence of toxic shock syndrome (TSS) is reported to be higher in children than in adults and to be often lethal.[97] Sheridan *et al.*[98] compared children with burns who received prophylactic antibiotics for group A β-hemolytic streptococcal infection and those who received antibiotics only when group A β-hemolytic streptococci were detected by cultures of samples from the wound. Ultimately, the treatment was considered unnecessary because the incidence of group A β-hemolytic streptococcal infection was originally low and because no difference in its incidence was observed with or without prophylactic administration. Patients with extensive burns have been reported to temporarily develop bacteremia during wound manipulation and surgery.[99] However, according to Steer *et al.*[93] who evaluated the incidence of bacteremia and outcome after the perioperative prophylactic administration of teicoplanin (a glycopeptide antibiotic), the incidence of bacteremia was reduced, but outcomes were comparable overall between the teicoplanin-treated and non-treated groups.
- Meanwhile, reports suggesting the effectiveness of prophylactic administration and opinions recommending it in patients considered at higher risk of infection and perioperative patients are not uncommon. Rashid *et al.*[100] administrated antibiotics for the prevention of TSS in children with burns and reported a decrease in its incidence. According to Wolf and Pruitt,[101] as *Staphylococcus aureus* and *Pseudomonas aeruginosa* are predominantly and widely detected in wound sites in the perioperative period, vancomycin and amikacin can be administrated in combination between 1 h before and 24 h after surgery.
- In terms of the effects on the survival of skin grafts, Ramos *et al.*[94] compared the survival rate of 90 skin grafts in 77 patients (mean age, 41.7 years; mean burn area, 21.8% TBSA) between 44 and 46 surgeries performed with and without topical application of polymyxin and preventive systemic administration of antibiotics, respectively. They reported that some of the skin graft was lost in 23% and 50% of the groups, respectively, and that 10% or greater area of the skin graft was lost in 9% and 35% of the groups, respectively; these findings demonstrated significant differences.
- Owing to the marked variation in underlying diseases and wound condition among patients, opinions vary widely as to which patients are candidates for the prophylactic administration of systemic antibiotics and which antibiotics should be used. In patients with contaminated wounds and in immunocompromised patients, such as those with diabetes, children and perioperative patients, prophylactic administration of systemic antibiotics for the control of either bacteria that has been isolated by bacterial cultures or those suspected to be infecting the patient should be considered.
- If severe infection or sepsis has occurred in burn patients, it should be treated according to "The Japanese Clinical Practice Guidelines for Management of Sepsis and Septic Shock" (2013).[102] According to a systematic review published in February 2010 on prognosis and prophylactic administration of systemic antibiotics in severe burn patients,[103] the treated group had a significantly lower mortality rate compared with the untreated group. The review states, "The current guidelines do not recommend prophylactic administration of systemic antibiotics except in the perioperative period, but the results of this review are contradictory to this view. In addition, as the data collected include those based on weak methodologies, a large-scale randomized controlled trial is necessary for the future."

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TETANUS

CQ18: Is an anti-tetanus treatment of burns necessary for the prevention of tetanus?

Description of recommendation: For contaminated burns, the administration of tetanus toxoid (Tt) or human tetanus immunoglobulin (TIG) is recommended.

Recommendation level: 1D.

Commentary:

- For three descriptive studies reviewing the published work on anti-tetanus treatment for wounds in general including burns,[104–106] the evidence level is VI. It is recommended to treat contaminated burns similarly to other wounds.[104] While there is no clear standard for the anti-tetanus treatment of burn patients in Japan, the recommendation level has been set at 1D because tetanus can be lethal once it occurs and anti-tetanus treatment for contaminated burns has been recommended.[107]
- *Clostridium tetani* is an anaerobic bacterium widely distributed in nature including rice paddies, vegetable fields and home gardens,[108] and tetanus may occur following burns.[109,110] In one report, an 18-month-old girl who had undergone anti-tetanus vaccination three times and was considered to have complete immunity against tetanus developed the disease 11 days after sustaining a burn of 25% TBSA.[111] For the prevention of tetanus at the time of injury, including burns, local treatment of wounds including the removal of foreign bodies and debridement is considered essential. In addition, Church *et al.*[104] recommended, "at burn centers, to usually administer human tetanus immunoglobulin (TIG) at 250–500 U and to administer tetanus toxoid (Tt) to patients who have not acquired complete primary immunity or those more than 10 years after the last vaccination". Concerning wounds in general, including burns, the American Academy of Pediatrics Advisory Committee on Immunization Practices and Advisory Committee on Immunization Practices recommend the administration of Tt or TIG depending on the patient's history of inoculation with Tt and the condition of the wound (whether or not it is a tetanus-prone wound).[105,112]
- Clinically, it is difficult to strictly distinguish between "tetanus-prone" and "non-tetanus-prone" wounds, and tetanus can arise from minor wounds such as scratches sustained during gardening, burns of 1% TBSA or less,[113] and even in the absence of a obvious wound at all. Therefore, Rhee *et al.*[106] recommended "administering Tt and TIG to those more than 10 years since the last vaccination and those with an unclear state of immunity regardless of the severity of the wound". Nevertheless, based on the present medical circumstances in Japan, the administration of Tt or TIG to all patients with traumas including minor ones is considered challenging in practicality. Furthermore, according to the survey of five emergency medical facilities in the USA, none of the 504 patients with "tetanus-prone wounds" and a state of incomplete primary immunity were administrated both Tt and TIG, which suggests a gap between the guidelines and actual use of TIG.[106] In addition, although administrating TIG increases the antibody titer against tetanus within 24 h, administration of Tt requires at least 4 days to achieve an increase in the antibody titer; therefore, minimal effect can be expected from it for prevention during the acute phase. Nevertheless, if basic immunity based on vaccinations is complete, it is said that the prevention of tetanus can be achieved by increasing the antibody titer through Tt administration.[114] The annual number of patients with tetanus reported in Japan is approximately 100, and the mortality rate is relatively high at approximately 10%. Consequently, given that tetanus can be lethal once it occurs, the administration of Tt or TIG is recommended for patients with incomplete or unclear primary immunity against tetanus and those with contaminated burns and more than 5 or 10 years since the last vaccination, depending on the degree of contamination of the wound, similarly to the anti-tetanus treatment of wounds in general (see Table 10).
- In Japan, Takeuchi *et al.*[115] performed anti-tetanus preventive treatment in 89 trauma patients (TIG in 60, Tt in nine, both in 20) and reported no occurrence of tetanus or adverse reactions. However, to the extent of our search of the published work, there is no evaluation or report addressing such treatment in burns.
- Because the number of supplementary Tt vaccinations differs by patient age and level of immunity, the information accompanying each pharmaceutical must be consulted.

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Table 10. Anti-tetanus therapy for wounds

	Wound type	
Immune state	Clean, minor	Other wound
History of at least three Tt injections	No TIG Vaccinate with 0.5 mL Tt if at least 10 years have elapsed since the most recent Tt injection	No TIG Vaccinate with 0.5 mL Tt if at least 5 years have elapsed since the most recent Tt injection
Fewer than three Tt injections or injection history is unknown	No TIG Inject 0.5 mL Tt	Inject 500 U TIG, 0.5 mL Tt

TIG, human tetanus immunoglobin; Tt, Tetanus toxoid.Adapted from Brook.[104]

105 Brook I. Current concepts in the management of *Clostridium tetani* infection. *Expert Rev Anti Infect Ther* 2008; **6**: 327–336. (evidence level VI).
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CQ19: Is hydrotherapy (shower, bathing, lavage) useful for the treatment of burns?

Description of recommendation: Hydrotherapy is recommended for patients with relatively minor burns not requiring hospitalization (1D). For patients with extensive severe burns judged to benefit from hydrotherapy, it is a viable option assuming anti-infection measures are being taken (2C).

RECOMMENDATION LEVEL:

(1D) for hydrotherapy in patients with relatively minor burns not requiring hospitalization.

(2C) for hydrotherapy in patients with extensive severe burns along with anti-infection measures.

Commentary:

- Because the published work on hydrotherapy for patients with relatively minor burns not requiring hospitalization comprises mostly expert opinion, the evidence level is VI.[116–119] However, as there are many opportunities to offer guidance concerning showering or bathing at home in daily clinical practice, the recommendation level has been set at 1D due to the significant number of accumulated cases at present. For one case–control study investigating hydrotherapy for extensive severe burns and their infection,[120] the evidence level is IVb, though the recommendation level is only 2C as anti-infection measures are required to prevent nosocomial infection.
- Hydrotherapy for burns is performed at many facilities. According to an investigation by burn units in the USA and Canada reported in 1994, hydrotherapy was carried out at 94.8% of the surveyed facilities, with immersion performed at 81.4%, and hydrotherapy was performed irrespective of the burn area at 82.8% and throughout the period of hospitalization at 86.9%.[121] However, hydrotherapy using shared equipment has been suggested to cause nosocomial infections including *P. aeruginosa*, *S. aureus* and methicillin-resistant *S. aureus* infections.[120–123] Furthermore, one study showed that the mortality rate, sepsis-related mortality rate and *P. aeruginosa*-related mortality rate were all significantly lower and the resistance of *P. aeruginosa* to aminoglycosides was reduced in a group that received bedside lavage using sterilized water and chlorhexidine without immersion compared with a group that was immersed using shared equipment.[123] They observed that immersed hydrotherapy may increase the number of bacteria on the normal skin and other non-infected wounds or cause infection in wounds and skin graft loss.
- The above bacteria settle in parts of the hydrotherapy equipment that are difficult to sterilize such as stainless plates and pipes,[120,123] and complete prevention of their settlement is difficult. However, Akin and Ozcan[124] applied a shower to patients on a stretcher covered with a sterilized disposable plastic sheet and reported that the measure was effective for the prevention of infection, with no observed contamination of wounds from the stretcher.
- Patients with extensive burns must be hospitalized for an extended period and are exposed to physical and psychological stress associated with treatments, surgery and so forth. Although hydrotherapy is expected to relieve the patient's psychological stress and to have a refreshing effect, there is no published work concerning the effects of hydrotherapy on the patient's psychology, to our knowledge.

- On the other hand, hydrotherapy is recommended by a number of reports for minor burns not requiring hospitalization,[116,117] and there are frequent opportunities to offer guidance as to how to take a shower or bath at home in daily clinical practice. Although we have not encountered a report comparing the infection rate between hydrotherapy and no hydrotherapy groups, hydrotherapy is considered recommendable for minor burns given the extensive clinical experience in the past. There are reports that no difference was observed in the infection rate of simple wounds that can be closed by primary suturing whether they were washed with tap water or sterile saline.[125,126] In addition, according to many experts, minor burns "should be washed with sterile saline or sterilized water",[116,118,119] but when minor burns are regarded as simple wounds, the infection rate is not expected to differ whether they are washed with tap water or sterile saline. Nevertheless, there are currently no reports comparing the procedures.

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DISINFECTION

CQ20: Is disinfection useful for the prevention of infection of burns?

Description of recommendation: Disinfection is proposed as an option by evaluating the condition of the wound along with the causative bacteria and antibacterial spectra of various drugs.

Recommendation level: 2B.

Commentary:

- For one RCT that assessed the effectiveness of disinfectants for burns by comparing silver sulfadiazine alone and silver sulfadiazine plus chlorhexidine,[127] the evidence level is II. While disinfection has been shown to reduce the frequency of *S. aureus* colonization in wounds, the recommendation level has been set at 2B because it is unclear whether the treatment improves outcomes.
- There are various opinions and reports concerning the disinfection of burns, and the matter remains controversial. In Japan, some investigators contend that chlorhexidine or povidone iodine should be used to disinfect burns,[128–131] while others believe that disinfection should be avoided.[132,133] The burn guidelines of New South Wales, Australia,[134] recommend that burns "should be washed with 0.05% chlorhexidine gluconate, sponge saturated with chlorhexidine gluconate, or sterile saline". Snelling *et al.*[127] studied 253 burn patients with a mean burn area of approximately 20% TBSA and reported that the frequency of colonization of *S. aureus* was reduced by washing the wounds with a mixture of 1% silver sulfadiazine and 0.2% chlorhexidine gluconate or soap containing 4% chlorhexidine gluconate when the gauze was changed compared with the topical application of 1% silver sulfadiazine alone.
- As for povidone iodine, there is a report that it is toxic to fibroblasts and epidermal keratinized cells *in vitro* at clinically used concentrations.[135] However, in another report, no significant difference was observed in the healing time when split-thickness mesh skin grafts were treated by the topical application of povidone iodine or petrolatum.[136] However, caution is necessary in applying povidone iodine over an extensive area in patients with kidney or thyroid dysfunction or elderly patients owing to its absorption from the wound surface (iodine poisoning).[137]

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FECAL MANAGEMENT DEVICES/SYSTEMS

CQ21: Is a fecal management tube useful for the prevention of infection in perianal burns?

Description of recommendation: The use of a fecal management tube is recommended for perianal burns according to the patient's general condition and the state of the wound as it may reduce the incidence of wound and urinary tract infection as well as the frequency of gauze changes due to fecal contamination to the wound area.

Recommendation level: 1B.

Commentary:

- For one non-randomized comparative trial concerning the use of fecal management tubes in burn patients,[138] the evidence level is III and the recommendation level is 1B.
- In patients with burns of the gluteal, femoral and perineal regions, contamination of the wound associated with defecation often poses problems, and the patients are exposed to the risk of infection and loss of skin grafts. In addition, sedated patients have fecal incontinence and require gauze changes at each bowel movement, and fecal incontinence is associated with an increased risk of nosocomial infection including *Clostridium difficile* infection.[139]
- To avoid wound infection, fecal control has been performed through a variety of methods including ostomy, fasting, narcotic drugs and the like. Recently, fecal management tubes have been reported to be useful for the management of perianal skin excoriations and wounds. When they were used in 42 patients with fecal incontinence involving the discharge of liquid or semi-liquid stools, the treatment was effective for maintaining or improving the condition of the gluteal and perianal skin in at least 92% of patients, including those with risk factors of skin vulnerability.[140] When 106 patients with perianal burns managed with a fecal management tube were compared with 106 previous patients who were managed without it, no significant difference was observed in the mortality rate. However, the incidences of subcutaneous and urinary tract infections were reduced significantly from 46.2% to 19.8% and from 27.4% to 14.2%, respectively, and the treatment was also advantageous in terms of cost-effectiveness.[138]
- In a prospective study of 20 patients, seven with perianal burns and 13 with severe perianal excoriations, the severity score of the perianal skin damage decreased significantly after intubation, the mean frequency of gauze change decreased from 3.3 to 1.5 times/day for burn patients, and the frequency of bed linen changes for patients with fecal incontinence was reduced from 9.3 to 1.2 times/day.[141] In Japan, Nishibori *et al.*[142] anally intubated five burn patients (three after surgery for gluteal burns and two with extensive burns) and reported that the treatment was effective for defecation control with no wound contamination. Fecal management tubes have been recommended as a potential non-invasive treatment before ostomy procedures.[141]
- Patient condition must be taken into consideration as there have been reports of anal ulceration and laxity,[143] rectal ulcers[144] and lower gastrointestinal bleeding[140,144] in patients receiving anticoagulant therapy, and a relationship to anal intubation cannot be excluded.

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LOCAL TREATMENT

CQ22: When should escharotomy be performed?

Description of recommendation: Escharotomy is recommended for decompressive procedures because full-circumference or nearly full-circumference deep burns to the limbs or chest have loss of elasticity; therefore, fluid resuscitation can cause circulatory compromise at the extremities and digits or respiratory compromise.

Recommendation level: 1A.

Commentary:

- For one systematic review on escharotomy, the evidence level is I.[145] Although it is unclear whether it is associated with improved outcomes, the recommendation level is 1A.
- Escharotomy should be considered in the case of full-thickness (third-degree) circumferential (and sometimes partial thickness) burns at a limb or the chest taking into consideration circulatory or respiratory compromise of the patient. Fasciotomies may also be required and should be considered especially in patients with electrical burns or very deep thermal injuries.
- For full-thickness third-degree circumferential burns to the limbs, escharotomies are performed as a releasing skin

incision allowing the subcutaneous tissues in a longitudinal fashion to be decompressed.[146] Salisbury *et al.*[147] prospectively evaluated the use of digital escharotomies in addition to standard limb escharotomies. Although the sample size was small, there was a reduced incidence of digital necrosis (7.5% vs 20.8%) in those patients with digital escharotomies. Ischemia was assessed by means of pulse oximetry in circumferentially burned extremities (26 limbs in 15 patients). For O_2 saturations of less than 95%, two patients (four limbs) had escharotomies with subsequent restoration of O_2 saturations.[148] Intramuscular pressure (IMP) was measured compared with clinical and Doppler findings. A threshold for escharotomies was IMP of 30 mmHg or more, or absent pulses.[149]

- In a review of clinical experiences and physiological changes of circumferential chest burns (compared with body burns) in 10 patients with escharotomy, hemodynamic and pulmonary abnormalities were not reversed but improved with escharotomy.[150]

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CQ23: Are dressing materials useful for the treatment of second-degree burns?

Description of recommendation: Silver-containing Hydrofiber® (1A) is recommended.

Silver alginate (2A), silver-containing polyurethane foam/soft silicone (2A), alginate (2B), hydrocolloid (2B), hydrogel, polyurethane film (2B), chitin (2C) and polyurethane foam (2C) are proposed as other options.

Recommendation level:

(1A) for silver-containing Hydrofiber®.

(2A) for silver alginate and silver-containing polyurethane foam/soft silicone.

(2B) for alginate, hydrocolloid, hydrogel and polyurethane film.

(2C) for chitin and polyurethane foam.

Commentary:

- For two RCT on silver-containing Hydrofiber,[151,152] the evidence level is II. It is significantly superior compared with silver sulfadiazine in terms of pain alleviation, treatment repetition, scar formation and cost, and was also approved for Japanese national health insurance coverage for burns reaching the dermis in 2014; therefore, the recommendation level is 1A.
- In terms of silver-containing dressing materials approved in Japan, one randomized trial has investigated silver alginate,[153] and the evidence level is II. Compared with silver sulfadiazine, it was found to reduce the healing time. For two RCT regarding silver-containing polyurethane foam/soft silicone,[154,155] the evidence level is II. The subject of comparison was silver-containing polyester rayon, and its associated healing time was inferior in one study and significantly improved in another. However, because both dressing materials are only covered by the national health insurance for wounds extending to subcutaneous tissue, the recommendation level is 2A. Insurance coverage must be taken into account.
- For five RCT on hydrocolloids, three on hydrogels and two on polyurethane film,[151] the evidence level is II. However, because no significant difference in healing time was found compared to ointments with oleaginous bases, the recommendation level is 2B. In addition, for one RCT that investigated alginate,[151] the evidence level is II. However, because no significant difference was found compared with silver sulfadiazine in the period until wound healing, the recommendation level is 2B.
- For one case study on chitin and one on polyurethane foam,[157,158] the evidence level is V. Owing to the small sample size involving their use in burns, the recommendation level is 2C.
- Surgery is not ordinarily indicated for shallow second-degree burns that heal with appropriate local treatment. In deep second-degree burns, although a shallow layer of necrotic tissue is visible at the wound surface, it only covers a small area and can be lysed through an appropriate topical agent or surgically debrided, followed by conservative treatment to achieve a cure. Dressing materials for burns are appropriate for both shallow second-degree burns and deep second-degree burns after elimination of the necrotic tissue. Because third-degree burns have a thick layer of necrotic tissue and must be surgically treated, ordinary dressing materials are not applicable.
- The 2013 Cochrane review[151] on the effect of dressing materials on second-degree burns included 30 RCT comparing various dressing materials with paraffin gauze and silver sulfadiazine, among which there were 13 RCT investigating the use of dressing materials in Japan. The other 17 were excluded as they evaluated dressing materials that are not approved for use in Japan. The paraffin described in Western documents is comparable with an oleaginous base such as white petrolatum in Japan. Therefore, although the description of recommendation states “ointments with oleaginous bases”, the commentary states “paraffin” in deference to the authors.
- There are two RCT comparing silver-containing Hydrofiber and silver sulfadiazine,[151,152] that used 152 subjects. Both found that silver-containing Hydrofiber was superior in terms

of pain alleviation, treatment repetition, scar formation and cost. One study demonstrated a significant difference in healing time. The other did not find a significant difference in the healing rate, although silver-containing Hydrofiber exhibited a greater rate than silver sulfadiazine, at 74% versus 60%. A non-randomized comparative trial[156] also found a significant difference in the healing time compared with paraffin gauze.

- There are three RCT comparing hydrocolloids and paraffin gauze in 236 patients.[151] No significant difference was observed in the healing time compared with paraffin gauze in any of the reports. In two RCT comparing hydrocolloids and silver sulfadiazine in 72 patients,[151] the healing time did not differ significantly in one but was significantly shorter with the use of hydrocolloids in the other.
- Three RCT have been reported by the same authors concerning hydrogels,[151] in which data on paraffin gauze and silver sulfadiazine were used as controls. The healing time was shorter with the hydrogels than with the controls, but the difference was only significant with regard to silver sulfadiazine and not to paraffin gauze.
- In one RCT comparing polyurethane film and paraffin gauze in 55 patients,[151] the healing time showed no significant difference. In addition, in an RCT comparing polyurethane film and paraffin gauze saturated with chlorhexidine, the healing time was significantly shorter with polyurethane film.[151] Whether or not this difference was due to chlorhexidine is unclear, but the cure rate was higher with polyurethane film until day 10, after which the difference disappeared.
- There is one RCT each concerning alginate and Hydrofiber using silver sulfadiazine as a control, and neither showed a difference in the healing time.[151] It must be noted that, in Japan, the use of alginate and Hydrofiber is covered by insurance only when they are applied to wounds reaching the subcutaneous tissue level.
- Chitin has been used in Japan as a dressing material for wounds including burns, but reports evaluating its effectiveness for the treatment of burns are few, and there is only one case series study of 120 patients including those with donor site wounds and traumas.[157] Of the 120 patients, 21 had burns, and the treatment was effective or very effective in 80%. However, its hemostatic and analgesic effects were included in the evaluation, and the actual effect on wound healing remains unclear. Moreover, no report has assessed the effectiveness of polyurethane foam exclusively for the treatment of burns, and there is only one case series study of 150 patients including those with donor site wounds and pressure ulcers.[158] Of those patients, 35 had burns, and the treatment was effective or very effective in 94% for improving the condition of the wound surface.
- While the reports in Japan on the use of dressing materials in the treatment of burns include those on hydrocolloid,[159-162] hydrofiber[163,164] and hydrogel,[165,166] the effectiveness of the dressing material itself is evaluated in each of these reports without comparing it with other treatments.
- Among the studies on the effects of dressing materials in the management of second-degree burns mentioned in the Cochrane review,[151] seven evaluate the incidence of wound infection. They consist of three RCT comparing hydrocolloids and paraffin gauze, one RCT comparing polyurethane film and paraffin gauze, one RCT comparing polyurethane film and paraffin gauze saturated with chlorhexidine, one RCT comparing hydrogels and silver sulfadiazine against *P. aeruginosa* infection, and one RCT comparing silver-containing Hydrofiber and silver sulfadiazine. They are all in agreement in that there was no significant difference in the incidence of wound infection between the trial and reference materials.
- In the Cochrane review,[151] eight RCT evaluate the frequency of dressing changes. The frequency of changes was reported to be higher with the use of dressing materials in one study, but to be lower compared with paraffin gauze or silver sulfadiazine in six. One study showed no difference.
- For dressing materials to sufficiently function as a preserver of an appropriate moist environment or a barrier against bacterial infection, they must be in close contact with the normal skin around the wound. However, as the application of a dressing material over a wide area is challenging, and there are cost restrictions, dressing materials tend to be used for the treatment of relatively small burns that can be covered by them. Dressing materials must be used with consideration of their specific characteristics and the area and site of the wound, presence or risk of infection, amount of effusion and age. Caution is advised regarding wound infection; if the risk of infection is considered high, the use of a silver-containing dressing material or a topical treatment is required.

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LOCAL TREATMENT: TOPICAL AGENTS

CQ24: What topical agents should be used for the treatment of second-degree burns?

Description of recommendation: For the initial treatment of second-degree burns, ointments with oleaginous bases such as zinc oxide, dimethyl isopropylazulene, petrolatum and the like are recommended (1D).

For second-degree burns, trafermin (1A), tretinoin tocopherol (1B), bucladesine sodium (1B) and prostaglandin E1 (1B) are recommended.

Aluminum chlorohydroxy allantoinate (Alcloxa) (2B) and lysozyme hydrochloride (2B) are proposed as options.

For chronic ulcers accompanied by necrotic tissue resulting from deep second-degree burns, bromelain ointment (1A), cadexomer iodine (1B), dextranomer (1B) and silver sulfadiazine (1D) are recommended for removing necrotic tissue.

RECOMMENDATION LEVEL:

(Initial treatment) (1D) for ointments with oleaginous bases.

(Second-degree burns) (1A) for trafermin, (1B) for tretinoin tocopherol, bucladesine sodium and prostaglandin E1, and (2B) for aluminum chlorohydroxy allantoinate (Alcloxa) and lysozyme hydrochloride.

(Chronic ulcers with necrotic tissue) (1A) for bromelain ointment, (1B) for cadexomer iodine and dextranomer, and (1D) for silver sulfadiazine.

Commentary:

- Because the use of ointments with oleaginous bases for second-degree burns is supported only by expert opinion,[167] the evidence level is VI. Because maintaining a moist environment at the wound surface during initial treatment is considered important, the recommendation level is 1D.
- For one systematic review indicating the efficacy of trafermin for second-degree burns,[168] as well as two RCT,[169,170] the evidence level is I and II, respectively, and the recommendation level is 1A.
- For one double-blind RCT on tretinoin tocopherol compared with bendazac for various skin ulcers including burns,[171] and one non-blinded RCT comparing it with lysozyme hydrochloride,[172] the evidence level is II. For one double-blind RCT on bucladesine sodium compared with a base for various skin ulcers including burns and another double-blind RCT comparing it with lysozyme hydrochloride,[173,174] the evidence level is II. For a non-blinded RCT on prostaglandin E1 compared with lysozyme hydrochloride for various skin ulcers including burns,[175] the evidence level is II. However, because these reports do not include details as to the condition of burns such as burn depth, the recommendation level is 1B.
- For one RCT on lysozyme hydrochloride for various skin ulcers including burns compared with a base (placebo) and bendazac,[176] and one case series study on burns,[177] the evidence levels are II and V, respectively. For one double-blind RCT on aluminum chlorohydroxy allantoinate compared with a base for skin ulcers including burns, erosion, eczema and dermatitis in 62 patients,[178] the evidence level is II. However, because it was not specifically focused on burns, the number of subjects was low and there was no detailed description or evaluation of burns, the recommendation level is 2B.
- In second-degree burns, damage to the dermis is partial, and the selection of appropriate topical agents must also take into account not only the antibacterial action but also the wound healing effect. In general, the principles of topical treatment for wounds converge on protecting the wound surface and maintaining a moist environment.[179] However, as it is difficult to accurately determine the depth of burns shortly after injury, and burns ranging from first-degree burns to DDB are often mixed, it is challenging to specify the optimal topical agents to use. Therefore, oleaginous ointments may be used in the stage of initial treatment to protect the wound surface, but topical agents appropriate for the condition of the wound surface must be selected as the status becomes clear.
- Ointments containing antibiotics (antibacterial agents) are oleaginous ointments. While they may be used for the protection of the wound surface and maintenance of the moist environment, their use should be restricted to a short period, because lengthy use may invite the development of resistant bacteria.
- For chronic ulcers caused by burns, topical agents should be selected for wound bed preparation based on the TIME concept or for moist wound healing. In addition, it is critical to appropriately select not only the principal agent but also the base according to the condition of the wound surface.

The following local treatments are recommended as topical agents appropriate for wound bed preparation by the "Guidelines for the management of pressure ulcers", except that the topical agents used for T (removal of necrotic tissue) and M (maintenance of the moist environment) are the same in burns:

T (removal of necrotic tissue): Cadexomer iodine, silver sulfadiazine, dextranomer, bromelain ointment and the like.
I (control/elimination of infection): Cadexomer iodine, silver sulfadiazine.
M (maintenance of the moist environment):

When effusion is excessive: cadexomer iodine, dextranomer and bucladesine sodium.
When effusion is deficient: aluminum chlorohydroxy allantoinate, ointments containing antibiotics (antibacterial agents), tretinoin tocopherol, prostaglandin E1, lysozyme hydrochloride and ointments with an oleaginous base such as petrolatum.

E (management of wound edges): No recommendable topical agents.

- If ulcers accompanied by necrotic tissue have developed as a result of DDB, topical agents should be selected from the above after surgical debridement. If the general condition is poor, or if the necrotic tissue is thin and surgical debridement cannot be performed, the topical application of bromelain, silver sulfadiazine, cadexomer iodine or dextranomer should be considered for the removal of necrotic tissue (see CQ26).
- In a systematic review of growth factor therapy including trafermin for second-degree burns,[168] it is noted that there is insufficient consideration of the optimal dose, but it is determined to be a safe and effective therapy that can be used as a standard treatment.
- Akita *et al.*[169] performed an RCT by randomizing 102 adults with second-degree burns into trafermin and non-trafermin groups. As a result, it was reported that the healing time was significantly shorter in the trafermin group, with significantly higher elasticity and hardness scores for the scar and moisture-retaining ability in the trafermin group. Hayashida and Akita[170] reported in an RCT of 20 children with second-degree burns that the trafermin treatment group had significantly improved results in terms of healing time and scarring.
- Komuro *et al.*[180] evaluated 32 patients (including children) with second-degree burns conservatively treated using trafermin, comparing those who were administrated the drug within 3 days and 4 days or more after injury. They reported that the mean number of days until epithelialization and the cumulative cure rate were both statistically superior in the group treated within 3 days. Fujiwara *et al.*[181] evaluated 20 patients with fresh second-degree burns in whom treatment was initiated within 48 h after injury by comparing those treated with trafermin and those treated with white petrolatum alone as a control group, and they reported that the number of days until epithelialization was significantly fewer in the trafermin group. Furthermore, Shiozawa *et al.*[182] performed a case–control study comparing 171 patients with DDB (including infants and children) treated with trafermin and 53 historical controls conservatively treated without trafermin and reported that significantly fewer patients showed hypertrophic scarring in the trafermin group.
- Trafermin is a spray-type liquid preparation that must be used with some topical agents or dressing material to maintain a moist environment for burns. In recent years, despite reports of the concomitant use of artificial dermis and injections into blisters,[183,184] no established method has been proposed concerning the selection of the appropriate topical agents or dressing materials to be used with this treatment.
- A double-blind RCT comparing tretinoin tocopherol and bendazac was performed by the L-300 Clinical Trial Group in 152 patients with various skin ulcers including 44 with ulcers due to burns.[171] While there is no mention of the depth of burns or time after injury, at 1 week after the application of the test drugs, granulation was reportedly significantly better in the tretinoin tocopherol group. In addition, there is a non-blinded RCT comparing tretinoin tocopherol and lysozyme hydrochloride in 217 patients with various skin ulcers including 36 with ulcers due to burns, but no detailed description is provided concerning the depth of burns or time after injury, and no significant difference was observed in the ulcers due to burns between the two groups.[172]
- Niimura *et al.*[173,174] performed double-blind RCT that compared bucladesine sodium and a base in 150 patients with pressure ulcers/skin ulcers, including 20 with ulcers due to burns, and bucladesine sodium ointment and lysozyme hydrochloride in 275 patients with pressure ulcers/skin ulcers, including 40 with ulcers due to burns.[173,174] According to these reports, bucladesine sodium was significantly superior in terms of the ulcer area reduction rate, granulation and epithelialization, but no detailed information is provided concerning the depth of burns or time after injury. There is, however, a report that the blood concentration of bucladesine sodium increased and remained elevated for a period after its topical application;[185] therefore, attention to the patient's general condition, including blood pressure, urine volume and blood glucose level, is necessary when it is topically applied to a wide area.
- Imamura *et al.*[175] performed a non-blinded RCT comparing prostaglandin E1 and lysozyme hydrochloride in 171 patients with pressure ulcers/skin ulcers including 26 with ulcers due to burns. According to their report, there is no detailed mention of the depth of burns or time after injury, but the efficacy rate in ulcers due to burns was significantly higher in the prostaglandin E1 topical application group. On the other hand, no significant difference was observed in the ulcer area reduction rate between the two groups.
- In an RCT comparing lysozyme hydrochloride, a base (placebo) and bendazac, lysozyme hydrochloride was shown to be superior to the base (placebo).[176] Kawakami *et al.*[177] performed a case series study using lysozyme hydrochloride in 28 patients with SDB and 40 with DDB. In their study, the

improvement of all second-degree burns was greater in the lysozyme hydrochloride group, though it was noted that granulation became excessive and epithelialization was delayed in patients with old DDB (topical application initiated ≥5 days after injury).

- Konjiki[178] carried out a double-blind RCT comparing aluminum chlorohydroxy allantoinate and a base in 62 patients with skin ulcers including those due to burns, erosion, eczema or dermatitis, and reported that the efficacy rate in all patients was significantly higher in the true drug group, but the number of patients with each disorder was small, and no statistical evaluation of individual disorders including burns was performed.

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CQ25: Is silver sulfadiazine useful for the treatment of extensive third-degree burns?

Description of recommendation: Silver sulfadiazine is recommended for treating extensive third-degree burns.

Recommendation level: 1B.

Commentary:

- For two non-randomized comparative trials concerning the topical use of silver sulfadiazine for the treatment of third-degree burns,[186,187] the evidence level is III and the recommendation level is 1B. The primary objective of topical agents for extensive third-degree burns is to prevent infection from the wound surface until surgical debridement. Silver sulfadiazine is widely used in Japan and abroad for the treatment of burns, and there are multiple reports indicating an excellent antibacterial effect. In addition, it is convenient for application to a wide area because of the emulsion base.
- Pegg *et al.*[186] performed a non-randomized comparative trial in patients with burns of various degrees by treating 314 with silver sulfadiazine, 156 with maphenide (not sold in Japan), and 175 historical controls with gentamycin sulfate and so forth, and reported that the mortality rate, positive rate of bacterial cultures and detection rates of *P. aeruginosa*, staphylococci, *Proteus* and *Candida* through bacterial cultures were significantly reduced in the silver sulfadiazine group compared with the control and maphenide groups. In Japan, Ohyama *et al.*[186] carried out a non-randomized comparative trial evaluating the effects of silver sulfadiazine and gentamycin sulfate in 31 patients with moderate to severe burns according to Artz's criteria, and they reported that silver sulfadiazine was markedly effective against *Klebsiella*, *Serratias*, other Gram-negative bacteria and *Candida*.
- Ono *et al.*[188] evaluated the minimum inhibitory concentrations (MIC) of various antibacterial agents against *P. aeruginosa*, because its detection rate increases with time among bacteria isolated from burns. As no strain resistant to silver sulfadiazine or maphenide was observed, they were recommended as viable topical antibacterial agents for burns. In addition, Yura *et al.*[189] performed resistance-acquisition and bactericidal studies using silver sulfadiazine against *P. aeruginosa* and reported the infrequent development of resistance and a satisfactory bactericidal action of the drug. On the other hand, there have been reports of infections resistant to silver preparations including silver sulfadiazine.[190] According

to the report by Li *et al.*,[191] bacteria are shown to acquire resistance to silver in their presence at low concentrations, and Atiyeh *et al.*[192] suggested the necessity to maintain an appropriate silver concentration at the wound, because resistance to silver only develops at concentrations near the MIC and not when sufficient concentrations are present. Furthermore, in extensive burns with a large amount of exudates, silver sulfadiazine is reported to be inactivated with a marked decrease in its effect.[193] Therefore, repeated applications should be considered under such circumstances.

- Because an emulsion base is used in silver sulfadiazine preparations, they have high tissue permeability and can be expected to produce a debriding effect by promoting the autolysis of necrotic tissue (see CQ26).
- Reported adverse effects of silver sulfadiazine include leukocytopenia, methemoglobinemia, silver deposition, allergic reaction to sulfonamides and so forth. Thorough attention to these adverse effects is necessary, particularly when silver sulfadiazine is applied topically to extensive burns. However, leukocytopenia is also occasionally associated with the use of other drugs, and some contend that it should not be regarded as a side-effect that is specific to silver sulfadiazine.[194] Others suggest that the use of silver sulfadiazine should be avoided when possible for wounds showing active proliferation of epidermal keratinized cells such as donor site wounds and SDB, because the cytotoxicity of silver delays wound healing.[192]

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CQ26: What topical agents should be used to remove necrotic tissue from small third-degree burns?

Description of recommendation: As topical agents aimed to remove necrotic tissue from small third-degree burns, bromelain (1A), cadexomer iodine (1B), dextranomer (1B) and silver sulfadiazine (1D) are recommended.

Recommendation level:

(1A) for bromelain, (1B) for cadexomer iodine and dextranomer, and (1D) for silver sulfadiazine.

Commentary:

- For one RCT concerning the debriding effect of bromelain on third-degree burns,[195] the evidence level is II and the recommendation level is 1A.
- Regarding dextranomer and cadexomer iodine, there are non-randomized comparative trials in patients with various skin ulcers including ulcers due to burns,[196,197] and a case series study;[198] therefore, the evidence level is III and V, respectively, and the recommendation level is 1B. In these reports, there was a high improvement rate including the necrotic tissue debridement effect, but they did not focus on burns and the number of patients was small.
- For silver sulfadiazine, because there are no reports evaluating the debriding effect aside from expert opinion on pressure ulcers,[199,200] the evidence level is VI. However, owing to the extensive experience in the clinical use of silver sulfadiazine for burns and its expected preventive effect against infection (see CQ25), the recommendation level has been set at 1D.
- As for ointments containing calf blood extract, there is one RCT indicating its usefulness for the treatment of third-degree burns,[201] and the evidence level is II. However, as this preparation was manufactured and approved in 1963 and has been used only rarely in recent years, it was excluded from the recommendation level evaluation.
- Regarding the debriding effect of fradiomycin sulfate/crystalline trypsin, it is supported only by expert opinion, and so the evidence level is VI. As this preparation was also manufactured and approved in 1962 and has been used only rarely in recent years, it was excluded from the recommendation level evaluation.
- Anzai *et al.*[195] performed an RCT using bromelain and a placebo prepared by mixing inactivated bromelain with the same base in 33 patients with deep second- or third-degree burns (7–10 days after injury). Each patient's wound was separated into halves, the true drug or placebo was applied topically to each half, and a comparison was made in terms of the degree of lysis of the necrotic tissue, hemorrhage and pain. It was reported that the true drug showed a significantly greater debriding effect in third-degree burns. There are many other case reports indicating the usefulness of bromelain. Ogawa *et al.*[202] evaluated the debriding effect of bromelain in ulcer patients including 28 with ulcers due to burns, and reported that a response rate of 86% was obtained in ulcers due to burns. When using bromelain, attention must be paid to frequent pain. In addition, as highly water-absorbing macrogol is used as the base, its debriding effect is attenuated when the effusion or moisture of the wound surface is reduced.[199]
- Silver sulfadiazine is considered to have a wound surface cleaning effect as its emulsion base has a high water content that causes softening and lysis of necrotic tissue owing

to its osmotic characteristics.[200] However, there are a few points regarding its use that must be addressed: it may cause edema on the wound surface in wounds rich in effusion, its effect is attenuated when it is used with povidone iodine, and its concomitant use with other drugs, particularly topical cutaneous enzyme preparations, should be avoided.[199]

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CQ27: Are topical steroid preparations useful for the treatment of first-degree burns and shallow second-degree burns?

Description of recommendation: The use of topical steroid preparations is proposed as an option for the initial period after injury in expectation of their anti-inflammatory effects.

Recommendation level: 2D.

Commentary:

- Because the usefulness of topical steroid preparations for the treatment of burns is supported only by expert opinion,[203–205] the evidence level is VI and the recommendation level is 2D. On the other hand, in three RCT (including double-blind trials), topical steroid preparations showed no anti-inflammatory effect on skin that had sustained physical damage including burns.[206–208] However, we noted that the majority of the expert opinions suggest the usefulness of topical steroid preparations for the treatment of first- or second-degree burns and the wide use of topical steroid preparations for the treatment of burns in Japan.
- Yamanaka and Mizutani[203] recommend the use of a very strong class or strongest class topical steroid preparation for first-degree burns for a short period immediately after injury to rapidly remove damaged tissue and control inflammation. Takuma *et al.*[204] recommend the use of topical steroid preparations for areas of first-degree burns with marked reddening/pain. Hitoshi *et al.*[205] reported that the use of topical steroid preparation should be restricted to the first 2 days after injury in first- or second-degree burns, because they delay wound healing and suppress epithelialization even though they are very effective for suppressing reddening and edema and mitigating pain in the acute period.
- However, Pedersen *et al.*[206] performed a double-blind RCT by artificially creating first-degree burns or SDB in 12 healthy volunteers and comparing the anti-inflammatory effect between clobetasol propionate and placebo using the degree of pain and reddening as indicators and reported no significant difference between the two groups. Faurschou and Wulf[207] examined the effects of a topical steroid preparation on sun burn (ultraviolet B irradiation) in 20 healthy volunteers but observed no clinical utility when it was applied after irradiation.
- In addition, Muramatu *et al.*[208] carried out a double-blind trial concerning the effects of betamethasone valerate/gentamycin sulfate on fresh second-degree burns using gentamycin sulfate as a control drug. According to their study, no difference was observed in the alleviation of swelling or pain between the two groups, and betamethasone valerate/gentamycin sulfate promoted epithelialization during the first 2 days after the start of their use but suppressed it after 4 days or more. One group was also treated by using topical betamethasone valerate/gentamycin sulfate for 3 days followed by gentamycin sulfate, and another group by using gentamycin sulfate alone from the beginning. No significant difference in the comprehensive evaluation of objective findings, number of days until completion of epithelialization or overall pharmacological effect was observed.

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