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GUIDELINE

The wound/burn guidelines – 6: Guidelines for the management of burns

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ABSTRACT

Burns are a common type of skin injury encountered at all levels of medical facilities from private clinics to core hospitals. Minor burns heal by topical treatment alone, but moderate to severe burns require systemic management, and skin grafting is often necessary also for topical treatment. Inappropriate initial treatment or delay of initial treatment may exert adverse effects on the subsequent treatment and course. Therefore, accurate evaluation of the severity and initiation of appropriate treatment are necessary. The Guidelines for the Management of Burn Injuries were issued in March 2009 from the Japanese Society for Burn Injuries as guidelines concerning burns, but they were focused on the treatment for extensive and severe burns in the acute period. Therefore, we prepared guidelines intended to support the appropriate diagnosis and initial treatment for patients with burns that are commonly encountered including minor as well as moderate and severe cases. Because of this intention of the present guidelines, there is no recommendation of individual surgical procedures.

Key words: **burn index, deep burn, deep dermal burn, epidermal burn, superficial dermal burn.**

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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. Minor burns heal by topical treatment alone, but moderate to severe burns require systemic management, and skin grafting is often necessary also for topical treatment. Inappropriate initial treatment or delay of initial treatment may exert adverse effects on the subsequent treatment and course. Therefore, accurate evaluation of the severity and initiation of appropriate treatment are necessary.

To the present, the Guidelines for the Management of Burn Injuries were issued in March 2009 from the Japanese Society for Burn Injuries as guidelines concerning burns, but they were focused on the treatment of extensive and severe burns in the acute period. Therefore, we prepared guidelines intended to support the appropriate diagnosis and initial treatment of patients with burns that are commonly encountered including minor as well as moderate and severe cases. Because of this intention of the present guidelines, there is no recommendation of individual surgical procedures.

POSITION OF THE GUIDELINES FOR THE MANAGEMENT OF BURNS

The Wound/Burn Guidelines Committee consists of members commissioned by the Board of Directors of the Japanese Dermatological Association. It held several meetings and evaluations in writing since October 2008 and drafted the Guidelines for the Management of Burns by taking opinions of the Scientific Committee and Board of Directors of the Japanese Dermatological Association into consideration. The present guidelines show the current standards of the treatment for burns in Japan. However, as individual patients vary in the background including underlying diseases, severity of symptoms and complications, the physicians who conduct the diagnosis and treatment should determine the therapeutic approaches together with the patients, so the contents of their decisions are not required to be in complete agreement with the present guidelines. Also, the guidelines are not relevant for citation in lawsuits.

SPONSORS AND CONFLICTS OF INTEREST

All cost needed for drafting the present guidelines has been borne by the Japanese Dermatological Association, and no fund has been received from particular organizations, enterprises, pharmaceutical companies and so forth. If any members of the committee have been involved in the development of particular related drugs and so forth, they were excluded from the evaluation of the recommendation levels of the treatments in question. Each member of the committee has no other conflict of interest to disclose on drafting the present guidelines.

COLLECTION OF EVIDENCE

Databases used: Medline, PubMed, Japana Centra Revuo Medicina Web and Cochrane Database of Systematic Reviews of ALL EBM Reviews. References obtained by manual search of each member were also added.

Search period: The published work that could be searched between January 1980 and December 2008 was reviewed. Recent published work of importance was added when considered appropriate.

Adoption criteria: Priority was placed on systematic reviews of randomized controlled trials (RCT) and papers on individual RCT. 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.

CRITERIA FOR THE DETERMINATION OF THE 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 references.

- Evidence levels:

  I Systematic reviews/meta-analyses.
  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.

- Recommendation levels:

  A Strongly recommended (there is at least one piece of level I or good level II evidence indicating the effectiveness).
  B Recommended (there is at least one piece of inferior level II, good level III or very good level IV evidence).
  C1 Recommended as an option despite the lack of good evidence (there is inferior level III–IV evidence, several pieces of good level V evidence or level VI evidence endorsed by the committee).
  C2 (Presently) not recommendable due to the lack of sufficient evidence (there is no evidence indicating effectiveness or there is evidence indicating ineffectiveness).
  D Disrecommended (there is good evidence indicating ineffectiveness or harmfulness).

The recommendation levels mentioned in the text are not necessarily in agreement with the above, because they were determined at some points according to consensus of the

committee (by showing evidence levels) in consideration of the international lack of evidence concerning the diagnosis and treatment of the conditions in question, inappropriateness of directly applying overseas evidence to Japan and practicality of the guidelines.

REVIEWS BEFORE DISCLOSURE

Prior to the disclosure of the guidelines, progresses in drafting were presented at the Annual Meetings of the Japanese Dermatological Association from 2008 to 2011, opinions were invited from the association members and necessary revisions were made. Also, the drafts were distributed to representatives, who were considered to be typical prospective users of the guidelines, their opinions were collected and summarized, and the results were reflected in the drafts.

UPDATING POLICIES

The present guidelines will be updated in 3–5 years. However, if partial updating becomes necessary, update information is presented on the website of the Japanese Dermatological Association when appropriate.

TERMINOLOGY

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

"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 cures after epithelialization in 1–2 weeks. Generally leaves no hypertrophic scar.
- Deep dermal burn (DDB): A burn that forms a blister. The dermis at the floor of the blister is white and anemic. The injury requires 3–4 weeks until cure by epithelialization but is likely to leave hypertrophic scar or cicatricial keloid.

"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 until cure, and hypertrophic scar or cicatricial contracture occurs without skin grafting.

"Burn index (BI)": An index devised by representing the severity of burns. Calculated as 1/2 × 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 of the pharyngeal/laryngeal or tracheal/bronchial mucosa or the pulmonary alveoli caused by inhalation of smoke, high-pressure vapor and toxic gas due to fire or explosion.

"Total body surface area (TBSA)": Total body surface area.

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

"Dressing materials": Modern wound-dressing materials aimed to create a moist environment around wounds. Conventional sterilized gauze is excluded.

"Wound-dressing materials": Wound-dressing materials are divided into dressing materials (modern wound-dressing materials) and medical materials including gauze (classic wound-dressing materials). The former are medical materials that provide an optimal environment for wound healing and must be used selectively depending on the condition of the wound and amount of exudates. The latter allow drying of the wound and cannot maintain a moist environment if effusion is insufficient. Wound-dressing materials cover the wound, retain moisture and provide an optimal environment for wound healing. Medical materials other than conventional gauze may be called wound-dressing materials or dressing materials.

"Wound bed preparation": Management of the wound surface environment to promote wound healing. Specifically, necrotic tissues are removed, bacterial load is reduced, drying of the wound is prevented, excessive effusion is controlled, and pockets and wound margins are treated.

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

"Moist wound healing": Maintaining the wound surface in a moist environment. This retains multinucleated leukocytes, macrophages, enzymes and cell growth factors contained in effusion on the wound surface. Such an environment promotes autolysis and removal of necrotic tissues and does not interfere with cell migration.

DIAGNOSTIC AND THERAPEUTIC ALGORITHMS

Diagnostic and therapeutic algorithms were prepared 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 clinical questions (CQ).

"SEVERITY EVALUATION": CQ1: WHAT IS RECOMMENDED AS A METHOD FOR ESTIMATING THE DEPTH OF BURNS?

Remarks on recommendation: A classification based on clinical symptoms is recommended as a method for estimating the depth of burns (B).

For more precise estimation, the use of laser Doppler flowmetry or video microscopy with the classification based on clinical symptoms is recommended as an option (C1).

Recommendation level: B and C1.

Comments:

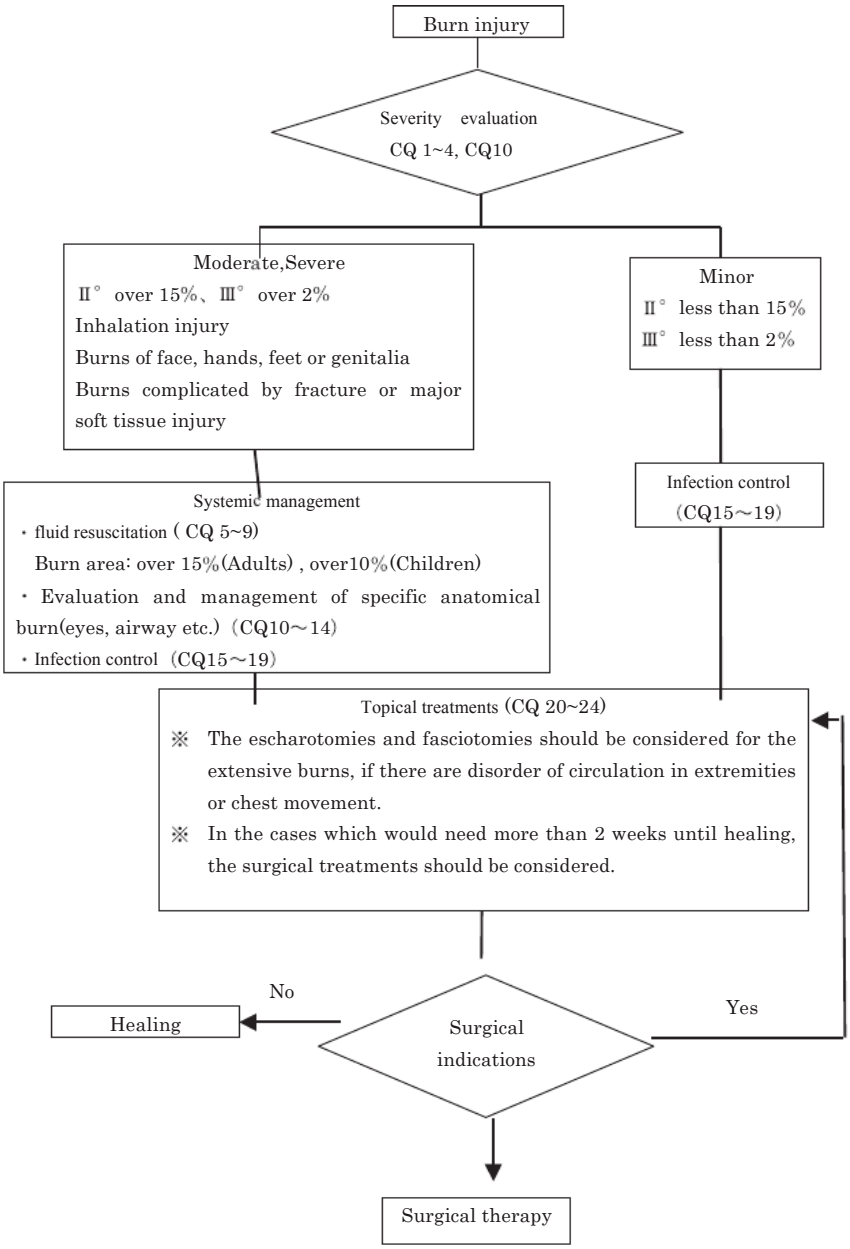


Figure 1. Diagnostic and therapeutic algorithms for burn injury.

- The method for the estimation of the depth based on clinical findings (Table 1) is regarded as a reference for depth evaluation and is in wide clinical use, but as there is only a case report,[1] the evidence level is V. However, the recommendation level was set at B, because it requires no particular instrument and is widely accepted. 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,[2] and the evidence level is III. The sensitivity for the detection of superficial partial-thickness burn, compared in 27 patients within 72 h after injury, was 100% by both methods, and the lesions

Table 1. Method for the estimation of the depth based on clinical findings

Depth	Clinical findings
Epidermal burn	Redness (+), pain (+)
Superficial dermal burn	Redness (+), blisters (+), pain (+), Blanches with pressure
Deep dermal burn	Variable color (patchy to cheesy white to red), blisters (+), pain (+/−) to (−), Does not blanche with pressure
Deep burn	Waxy white to leathery gray to charred and black, blister (−), pain (−)

diagnosed as superficial partial-thickness burn cured within 3 weeks. In addition, there are analytical epidemiological studies and case reports using laser Doppler flowmetry and video microscopy.[3–5]

REFERENCES

1 Heimbach D, Engrav L, Grube B, Marvin J. Burn depth: a review. *World J Surg* 1992; **16**: 10–15. (evidence level V).
2 McGill DJ, Sorensen K, MacKay IR, Taggart I, Watson SB. Assessment of burn depth: a prospective, blinded comparison of laser Doppler imaging and videomicroscopy. *Burns* 2007; **33**: 833–842. (evidence level III).
3 Pape SA, Skouras CA, Byrne PO. An audit of the use of laser Doppler imaging (LDI) in the assessment of burns of intermediate depth. *Burns* 2001; **27**: 233–239. (evidence level IVa).
4 Yeong EK, Mann R, Goldberg M, Engrav L, Heimbach D. Improved accuracy of burn wound assessment using laser Doppler. *J Trauma* 1996; **40**: 956–961. (evidence level IVa).
5 Isono N, Nakazawa H, Nozaki M, Sasaki K. Early assessment of second degree burn depth by means of video microscope. *J J Burn Inj* 1998; **24**: 11–18. (evidence level V).

CQ2: WHAT IS RECOMMENDED AS A METHOD FOR ESTIMATING THE BURNED AREA?

Remarks on recommendation: As methods to estimate the burned area, the use of the rule of nines, rule of fives, and Lund and Browder Chart is recommended (B).

The palm method is recommended as a method for local estimation of the burned area (B).

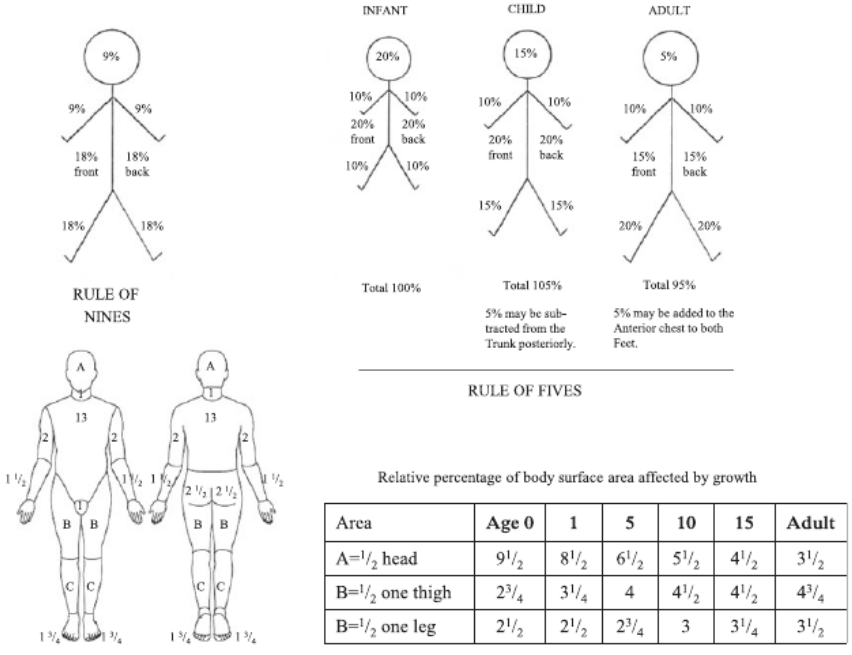
Recommendation level: B.

Comments:

- Concerning the methods to estimate the burned area using the rule of nines, rule of fives, and Lung and Browder Chart, there are only expert opinions,[6–8] and the evidence level is VI. However, the recommendation level was set at B, because they are in wide clinical use, and in consideration of the historical background. Regarding the palm method, there are some differences in the method to determine the reference TBSA, but there are analytical epidemiological studies that the palm area, corresponding to approximately 1% (range, 0.7–0.95%) of the TBSA, is useful for the estimation of the burned area,[9–11] and the evidence level is IVa. However, the recommendation level was set at B, because it is clinically applicable and practical.
- See Figure 2 for the rule of nines, rule of fives, and Lund and Browder Chart. The palm method estimates the burned area by assuming the area of the palm to be approximately 1% of the TBSA in adults.

REFERENCES

6 Wallace AB. The exposure treatment of burns. *Lancet* 1951; **1**: 501–504. (evidence level VI).
7 Blocker TG. Local and general treatment of acute extensive burns: the open-air regime. *Lancet* 1951; **1**: 498–501. (evidence level VI)
8 Lund CC, Browder NC. The estimation of areas of burns. *Surg Gynecol Obste* 1944; **79**: 352–358. (evidence level VI).
9 Sheridan RL, Petras L, Basha G *et al.* Planimetry study of the percent of body surface represented by the hand and palm: sizing irregular burns is more accurately done with the palm. *J Burn Care Rehabil* 1995; **16**: 605–606. (evidence level IVa).
10 Perry RJ, Moore CA, Morgan BD, Plummer DL. Determining the approximate area of a burn: an inconsistency investigated and re-evaluated. *BMJ* 1996; **312**: 1338. (evidence level IVa).



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. Calculation of burn area.

11 Nagel TR, Schunk JE. Using the hand to estimate the surface area of a burn in children. *Pediatr Emerg Care* 1997; **13**: 254–255. (evidence level IVa).

CQ3: ARE ARTZ'S CRITERIA USEFUL FOR THE SEVERITY EVALUATION OF BURNS?

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

Recommendation level: C1.

Comments:

- Artz's criteria and their modification (Moylan's criteria) are in the widest clinical use for the severity evaluation of burns and are practical as a severity scale. However, the evidence level is VI for both, because there are only expert opinions.[12,13]
- Artz's criteria and their modification (Moylan's criteria) grade the severity of burns according to their area, depth and complications, and show at which facilities the patients should be treated (Table 2).

Table 2. Artz's criteria

Critical burns (must be referred to a well-equipped general hospital that has a surgeon experienced in burn care)
2° Burns of over 30% TBSA
3° Burns of face, hands, feet over 10% TBSA
Burns complicated by:
Respiratory tract injury
Major soft tissue injury
Fractures
Electrical burns
Moderate burns (may be treated in a small community hospital)
2° of 15–30% TBSA
3° of less than 10% TBSA, except hands, face, feet
Minor burns (may be treated on an outpatient basis)
2° of less than 15% TBSA
3° of less than 2% TBSA

Artz and Moncrief (1969).[12] TBSA, total body surface area.

REFERENCES

12 Artz CP, Moncrief JA. *The Treatment of Burns*. Philadelphia, PA: W.B. Saunders, 1969; 94–98. (evidence level VI).
13 Moylan JA. First aid and transportation of burned patients. In: Artz CP, Moncrief JA, Pruitt BA Jr, eds. *Burns: A Team Approach*. Philadelphia, PA: W.B. Saunders, 1979; 151–158. (evidence level VI).

CQ4: WHAT ARE USEFUL AS PROGNOSTIC FACTORS AND FOR THE PROGNOSIS OF BURNS?

Remarks on recommendation: The presence or absence of airway damage, area of third-degree burn, burned area (percentage relative to the TBSA: %TBSA), PBI and burn index are recommended as prognostic factors (B).

Recommendation level: B.

Comments:

- While there are only expert opinions concerning the burned area (%TBSA), it is a fundamental index for the evaluation of the severity of burns in the published work on the prognosis of burns.[14–29] Also, as it has been suggested by many to be useful for the prognosis, the recommendation level was set at B. Many papers have mentioned age (evidence level: IVa–V)[14–16,18,20,21,24,25] and airway burn (evidence level IVa–IVb),[15,21,23,25,26,29] and some have reported the area of third-degree burn (evidence level: IVa),[24,25] as prognostic factors. All studies involved hundreds to thousands of burn patients, so their recommendation levels were set similarly to that of the burned area. The evidence levels of the burn index[26] and PBI[17] are IVa–IVb, but their recommendation level was set at B, as they are in wide clinical use in Japan. There is also the published work suggesting that burns due to suicide attempts[27] and complication by psychiatric disorders[24] contribute to the mortality rate.

REFERENCES

14 Tobiasen J, Hiebert JH, Edlich RF. Prediction of burn mortality. *Surg Gynecol Obstet* 1982; **154**: 711–714. (evidence level IVa).
15 Ryan CM, Schoenfeld DA, Thorpe WP, Sheridan RL, Cassem EH, Tompkins RG. Objective estimates of the probability of death from burn injuries. *N Engl J Med* 1998; **338**: 362–366. (evidence level IVa).
16 Iwasaki Y, Okabayashi K, Hatano Y, Mihara S, Noda H, Sera A, Yamamoto S. Treatment of 55 children with severe burns compared with 121 adult cases. *Jpn J Dermatol* 1997; **107**: 1253–1261. (evidence level IVb).
17 Iwasaki Y, Takahashi H, Mori T, Yamamoto S, Miyamoto Y. A study of the cases of fatal severe burn relationship of burn index, age, inhalation injury and surgical treatment to the prognosis. *Rinsho Derma (Tokyo)* 1991; **33**: 1387–1392. (evidence level IVb).
18 Saffle JR, Gibran N, Jordan M. Defining the ratio of outcomes to resources for triage of burn patients in mass casualties. *J Burn Care Rehabil* 2005; **26**: 478–482. (evidence level V).
19 Berry CC, Patterson TL, Wachtel TL, Frank HA. Behavioural factors in burn mortality and length of stay in hospital. *Burns* 1984; **10**: 409–414. (evidence level IVb).
20 Moreau AR, Westfall PH, Cancio LC, Mason AD Jr. Development and validation of an age-risk score for mortality predication after thermal injury. *J Trauma* 2005; **58**: 967–972. (level IVa).
21 Belgian Outcome in Burn Injury Study Group. Development and validation of a model for prediction of mortality in patients with acute burn injury. *Br J Surg* 2009; **96**: 111–117. (evidence level IVb).
22 George RL, McGwin G Jr, Schwacha MG *et al.* The association between sex and mortality among burn patients as modified by age. *J Burn Care Rehabil* 2005; **26**: 416–421. (evidence level IVa).
23 Lionelli GT, Pickus EJ, Beckum OK, Decoursey RL, Korentager RA. A three decade analysis of factors affecting burn mortality in the elderly. *Burns* 2005; **31**: 958–963. (level IVa).
24 Berry CC, Wachtel TL, Frank HA. An analysis of factors which predict mortality in hospitalized burn patients. *Burns* 1982; **9**: 38–45. (evidence level IVa).
25 Benito-Ruiz J, Navarro-Monzonis A, Baena-Montilla P, Mirabet-Ippolito V. An analysis of burn mortality: a report from a Spanish regional burn centre. *Burns* 1991; **17**: 201–204. (evidence level IVa).

26 Kobayashi K, Ikeda H, Higuchi R *et al*. Epidemiological and outcome characteristics of major burns in Tokyo. *Burns* 2005; **31** (Suppl 1): S3–S11. (evidence level IVa).
27 Thombs BD, Bresnick MG. Mortality risk and length of stay associated with self-inflicted burn injury: evidence from a national sample of 30,382 adult patients. *Crit Care Med* 2008; **36**: 118–125. (evidence level IVa).
28 Kerby JD, McGwin G Jr, George RL, Cross JA, Chaudry IH, Rue LW 3rd. Sex differences in mortality after burn injury: results of analysis of the National Burn Repository of the American Burn Association. *J Burn Care Res* 2006; **27**: 452–456. (evidence level IVa).
29 Meshulam-Derazon S, Nachumovsky S, Ad-El D, Sulkes J, Hauben DJ. Prediction of morbidity and mortality on admission to a burn unit. *Plast Reconstr Surg* 2006; **118**: 116. (evidence level IVa).

SYSTEMIC MANAGEMENT: FLUID RESUSCITATION
CQ5: WHAT KIND OF PATIENTS HAVE INDICATIONS FOR FLUID RESUSCITATION?

Remarks on recommendation: Fluid resuscitation is recommended to adults with a burned area of 15% TBSA or higher and children with a burned area of 10% TBSA or higher. However, early fluid resuscitation may be initiated in patients with a smaller burned area depending on the general condition.

Recommendation level: B.

Comments:

- There has been no detailed report on the evaluation of the appropriateness of fluid resuscitation based on the injured area in adults, and the evidence level is VI as there are only expert opinions. However, according to Artz's diagnostic criteria,[30] the area of minor burns manageable by outpatient care is a second-degree burn area of 15% or less. When patients with extensive burned area are treated by hospitalization, fluid resuscitation is considered, and is actually implemented as, a nearly essential treatment. Therefore, the recommendation level was set at B. In children, also, there are only expert opinions, and the evidence level is VI. According to the criteria of the American Burn Association, fluid resuscitation should be initiated when the burned area is 20% TBSA or greater.[31] Also, as patients with second-degree burns affecting 10% or more of the body surface area are referred to a burn treatment center according to the Advanced Burn Life Support,[32] we judged that fluid resuscitation should be performed in children with a burned area of 10% TBSA or greater. Moreover, the recommendation level was set at B on the basis of consensus of the committee.
- According to Artz's criteria, treatment by hospitalization is indicated for patients with a third-degree burn area of 2% or greater, so fluid resuscitation may as well be initiated in the acute period of burns. Also, hypovolemic shock early after injury has been reported to be avoided by appropriate fluid resuscitation.[31,33–36]
- Artz's criteria and their modification (Moylan's criteria)[37] are guidelines for the severity grading of burns according to their area, depth and complications, and for the selection of facilities appropriate for their treatment (see Table 2 concerning CQ3).

REFERENCES

30 Artz CP, Moncrief JA. *The Treatment of Burns*, 2nd edn. Philadelphia, PA: W.B. Saunders, 1969; 94–98.
31 Pham TN, Cancio LC, Gibran NS. American Burn Association Practice Guidelines Burn Shock Resuscitation. *J Burn Care Res* 2008; **29**(1): 257–266.
32 American Burn Association. *Advanced Burn Life Support Course Providers Manual*. Chicago, IL: American Burn Association, 2001.
33 Atiyeh BS, Gunn SW, Hayek SN. State of the art in burn treatment. *World J Surg* 2005; **29**: 131–148. (evidence level VI).
34 Warden GD. Burn shock resuscitation. *World J Surg* 1992; **16**: 16–23. (evidence level VI).
35 Monafo WW. Initial management of burns. *N Engl J Med* 1996; **335**: 1581–1586. (evidence level VI).
36 Hettiaratchy S, Papini R. Initial management of a major burn: II – assessment and resuscitation. *BMJ* 2004; **329**: 101–103. (evidence level VI).
37 Moylan JA. First aid and transportation of burned patients. In: Artz CP, Moncrief JA, Pruitt BA Jr, eds. *Burns: A Team Approach*. Philadelphia, PA: W.B. Saunders, 1979; 151–158. (evidence level VI).

CQ6: WHEN SHOULD EARLY FLUID RESUSCITATION BE INITIATED?

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

Recommendation level: B.

Comments:

- Concerning the time of initiation of early fluid resuscitation, there are case–control studies,[38,39] and the evidence level is IVb, but the recommendation level was set at B on the basis of consensus of the committee.
- When the burned area is 15–20% or greater, hypovolemic shock is caused by an increase in the vascular permeability without appropriate fluid resuscitation. Edema often occurs during the first 6–8 h and persists for 18–24 h or longer.[40,41] Also, 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 those who survived and those who died (1.7 ± 1.0 vs 4.4 ± 21.1 h).[38]
- In a review of 24 patients treated in 1966–1983 and 36 patients treated in 1984–1997, the mortality rate was 100% in the former group but decreased to 56% in the latter. The time from injury to the beginning of fluid resuscitation was 8.6 ± 1.7 and 3.0 ± 0.5 h, respectively. Also, among those treated after 1984, fluid resuscitation was started earlier in those who survived than in those who died (1.7 ± 0.5 vs 4.8 ± 0.9 h).[41]

REFERENCES

38 Chrysopoulo MT, Jeschke MG, Dziewulski P, Barrow RE, Herndon DN. Acute renal dysfunction in severely burned adults. *J Trauma* 1999; **46**: 141–144. (evidence level IVb).
39 Jeschke MG, Barrow RE, Wolf SE, Herndon DN. Mortality in burned children with acute renal failure. *Arch Surg* 1998; **133**: 752–756. (evidence level IVb).
40 Monafo WW. Initial management of burns. *N Engl J Med* 1996; **335**: 1581–1586. (evidence level VI).

41 Hettiaratchy S, Papini R. Initial management of a major burn: II – assessment and resuscitation. *BMJ* 2004; **329**: 101–103. (evidence level VI).

CQ7: WHAT SHOULD BE USED FOR I.V. FLUID RESUSCITATION?

Remarks on recommendation: The use of isotonic crystalloid resuscitation preparations (lactated Ringer's solution, acetated Ringer's solution) is recommended for fluid resuscitation (B).

The concomitant use of colloid and hypertonic lactated saline (HLS) are recommended as an option for fluid resuscitation (C1).

Recommendation level: B and C1.

Comments:

- Concerning the usefulness of isotonic crystalloid resuscitation preparations for initial fluid resuscitation of burn patients, there are only expert opinions, and the evidence level is VI. There are RCT comparing an isotonic crystalloid resuscitation preparation and colloid and reporting no significant difference,[42,43] and one meta-analysis comparing the mortality rate between patients with trauma, burn and postoperative patients treated by crystalloid and those treated by HLS infusion and reporting no significant difference.[44] Also, as colloid or HLS have not been shown to be more advantageous than crystalloid, the recommendation level was set at B for crystalloid resuscitation, which are the most widely used, and C1 for concomitant colloid administration and HLS on the basis of consensus of the committee.
- Infusion of colloids immediately after burn injury, a period with enhanced vascular permeability, has been reported to have no advantage compared with crystalloid resuscitation.[45] 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 necessary in the lactated Ringer's solution group than in the colloid plus lactated Ringer's solution group (3.81 vs 2.98 mL/kg bodyweight/%TBSA). However, no significant improvement in the circulation was observed even in the colloid plus lactated Ringer's solution group, and pleural effusion increased in the period of diuresis.[42] Also, when the intravascular pressure was measured as the intra-abdominal pressure (IAP) in 15 patients administrated lactated Ringer's solution (Parkland method) and 16 administrated a colloid, the IAP increased significantly in the lactated Ringer's solution group, and more solution was needed for the initial infusion than in the colloid group. In both groups, a correlation was observed between the total volume of infusion and IAP, and, while the IAP remained less than the complication threshold (25 mmHg), and the treatment was effective for controlling the increase in the IAP, in the plasma administration group, no clear difference was noted in survival.[43]
- In a study evaluating the relationship between the colloid administration and mortality rate in severely injured patients, the mortality rate was higher in the colloid administrated group than in the control group with a relative risk of 2.40 (range, 1.11–5.19) in burn patients, indicating that colloid administration increased the mortality rate.[46] In a report of evaluation in 70 patients with burns of 20% TBSA or less, aged 19 years or below, treated by administrating colloid while maintaining the serum albumin level at 2.5–3.5 g/dL (36 patients) or administrating colloid only when the serum albumin level decreased to less than 1.5 g/dL (34 patients), no difference was observed in complications, the mortality rate, duration of hospitalization and necessity of management using a respirator.[47]
- From these observations, colloid administration is considered to reduce the total volume of infusion and suppress the increase in the IAP but not to be effective at present for improving the life prognosis. 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 the colloid osmotic pressure 8–12 h after injury is affecting the respiration or circulation,[48] and fluid resuscitation incorporating colloid administration such as the Evens method and Brooke method is performed in actual clinical practice.
- When 14 patients in the HLS group and 22 patients in the lactate Ringer's solution group were compared by maintaining the 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 per kg $\times$ %TBSA, respectively, the urine volume could be maintained with a smaller infusion volume, IAP and maximum inspiratory pressure were significantly lower, and the incidence of intra-abdominal hypertension was lower (14% vs 50%), in the HLS than lactate Ringer's solution group.[49] However, there is also a report that the incidence of renal insufficiency and mortality rate were higher in the HLS than lactated Ringer's solution group and that no difference was observed in the total infusion volume.[50] According to a meta-analysis evaluating whether or not HLS reduces the mortality rate of hypovolemic patients, when a hypotonic, isotonic or nearly isotonic solution was administrated to trauma, burn and postoperative patients, the relative risk of death in the HLS-treated group was 0.84 in trauma, 1.49 in burn and 0.51 in postoperative patients.[44]
- In conclusion, while no data indicating that HLS has a higher survival-improving effect than an isotonic solution have been obtained to the present, it is considered to be effective for reducing the total infusion volume and suppressing the increase in the IAP. HLS is prepared by adding sodium to lactated Ringer's solution. It was devised to supplement ECF and sodium, which are lost after burn, and to reduce the total infusion volume compared with an isotonic solution. Monafo HLS, Fox HLS and Osaka University HLS are known as its variations.

REFERENCES

42 Goodwin CW, Dorethy J, Lam V, Pruitt BA Jr. Randomized trial of efficacy of crystalloid and colloid resuscitation on hemodynamic

response and lung water following thermal injury. *Ann Surg* 1983; **197**: 520–531. (evidence level II).
43 O'Mara MS, Slater H, Goldfarb IW, Caushaj PF. A prospective, randomized evaluation of intra-abdominal pressures with crystalloid and colloid resuscitation in burn patients. *J Trauma* 2005; **58**: 1011–1018. (evidence level II).
44 Bunn F, Roberts I, Tasker R, Akpa E. Hypertonic versus near isotonic crystalloid for fluid resuscitation in critically ill patients. *Cochrane Database Syst Rev*, 2004; (3): CD002045. (evidence level I).
45 Monafo WW. Initial management of burns. *N Engl J Med* 1996; **335**: 1581–1586. (evidence level VI).
46 Cochrane Injuries Group Albumin Reviewers. Human albumin administration in critically ill patients: systematic review of randomised controlled trials. *BMJ* 1998; **317**: 235–240. (evidence level I).
47 Greenhalgh DG, Housinger TA, Kagan RJ *et al.* Maintenance of serum albumin levels in pediatric burn patients: a prospective, randomized trial. *J Trauma* 1995; **39**: 67–74. (evidence level II).
48 Warden GD. Burn shock resuscitation. *World J Surg* 1992; **16**: 16–23. (level VI).
49 Oda J, Ueyama M, Yamashita K *et al.* Hypertonic lactated saline resuscitation reduces the risk of abdominal compartment syndrome in severely burned patients. *J Trauma* 2006; **60**: 64–71. (level III).
50 Huang PP, Stucky FS, Dimick AR, Treat RC, Bessey PQ, Rue LW. Hypertonic sodium resuscitation is associated with renal failure and death. *Ann Surg* 1995; **221**: 543–554. (level IVb).

CQ8: HOW SHOULD THE INITIAL INFUSION VOLUME BE CALCULATED?

Remarks on recommendation: It is recommended to initiate fluid resuscitation using the Parkland method (also called the Baxter method).

Recommendation level: B.

Comments:

- There is one meta-analysis concerning the initial fluid resuscitation,[51] and the evidence level is I. While the Parkland method is widely used, the necessary infusion volume has been reported to have exceeded that calculated by this method, so its recommendation level was reduced to B.
- Baxter carried out an animal experiment for the hemodynamic evaluation using a radioisotope in the acute period of burn injury and showed that infusion at 3.7–4.3 mL/kg per %TBSA was necessary, that functional extracellular fluid (ECF) decreased rapidly after burn injury depending on the burned area, but that shock due to burn could be avoided, and the mortality rate could be reduced, by the administration of lactated Ringer's solution.[52] There is also a report that, when lactated Ringer's solution was administrated to patients with a target urine volume of 40 mL/h and according to the level of consciousness, the infusion volume during the 24 h after injury was 3.7–4.3 mL/kg per %TBSA in 70% of adults and 98% of children aged 12 years or less.[53]
- Recently, the initial infusion volume greater than that calculated by the Parkland method has been reported to have been necessary,[51,54,55] but excessive infusion has been suggested to promote edema and increase compartment syndrome of the limbs, pneumonia, acute respiratory distress syndrome, multiple organ failure, sepsis and the mortality rate.[56,57] According to a study in which 50 burn patients with a burned area of 20% TBSA or higher 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, and intravascular dehydration was observed within 48 h by the Parkland method, but there was no difference in preload or the cardiac output, or in the mortality rate or incidence of complications.[58] Therefore, crystalloid resuscitation in amounts greater than those indicated by the Parkland method is not considered to improve preload or the cardiac output. While initial infusion therapy is still performed according to the Parkland method at many facilities of the world,[59,60] further evaluation is awaited for a conclusion concerning the appropriate volume and rate of fluid resuscitation.

REFERENCES

51 Kramer G, Hoskins S, Copper N, Chen JY, Hazel M, Mitchell C. Emerging advances in burn resuscitation. *J Trauma* 2007; **62**: S71–S72. (evidence level I).
52 Baxter CR, Shires GT. Physiological response to crystalloid resuscitation of severe burns. *Ann NY Acad Sci* 1968; **150**: 874–894.
53 Baxter CR. Problems and complications of burn shock resuscitation. *Surg Clin North Am* 1978; **58**: 1313–1322.
54 Friedrich JB, Sullivan SR, Engrav LH *et al.* Is supra-Baxter resuscitation in burn patients a new phenomenon? *Burns* 2004; **30**: 464–466.
55 Mitra B, Fitzgerald M, Cameron P, Cleland H. Fluid resuscitation in major burns. *Anz J Surg* 2006; **76**: 35–38.
56 Dulhunty JM, Boots RJ, Rudd MJ, Muller MJ, Lipman J. Increased fluid resuscitation can lead to adverse outcomes in major-burn injured patients, but low mortality is achievable. *Burns* 2008; **34**: 1090–1097.
57 Klein MB, Hayden D, Elson C *et al.* The association between fluid administration and outcome following major burn: a multicenter study. *Ann Surg* 2007; **245**: 622–628.
58 Holm C, Mayr M, Tegeler J. A clinical randomized study on the effects of invasive monitoring on burn shock resuscitation. *Burns* 2004; **30**: 798–807.
59 Nguyen TT, Gilpin DA, Meyer NA, Herndon DN. Current treatment of severely burned patients. *Ann Surg* 1996; **223**: 14–25.
60 Hettiaratchy S, Papini R. Initial management of a major burn: II – assessment and resuscitation. *BMJ* 2004; **329**: 101–103.

CQ9: WHAT SHOULD BE USED AS THE INDEX FOR THE DETERMINATION OF THE INFUSION RATE?

Remarks on recommendation: The urine volume is recommended as an index for the infusion rate. The infusion rate should be adjusted to maintain the urine volume at 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: B.

Comments:

- There are only expert opinions about indices of the appropriate volume and rate of initial infusion, and the evidence level is VI. However, the recommendation level was set at B, because the urine volume per hour reflects the 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 the urine volume, which reflects the renal blood flow, is widely used as an index for the evaluation of the organ blood fow.[61–63] However, caution is needed as the urine volume cannot be used as the sole index in patients with compromised renal function. The hemodynamics should also be evaluated using other general vital signs (e.g. blood pressure, heart rate, peripheral circulation and tachypnea), central venous pressure and lactate level.

REFERENCES

61 Warden GD. Burn shock resuscitation. *World J Surg* 1992; **16**: 16–23. (evidence level VI).
62 Monafo WW. Initial management of burns. *N Engl J Med* 1996; **335**: 1581–1586. (evidence level VI).
63 Hettiaratchy S, Papini R. Initial management of a major burn: II – assessment and resuscitation. *BMJ* 2004; **329**: 101–103. (evidence level VI).

SYSTEMIC MANAGEMENT: AIRWAY BURNS CQ10: WHAT ARE FACTORS THAT SUGGEST AIRWAY INJURY?

Remarks on recommendation: Circumstances of injury (injury in a narrow space due to inhalation of hot vapor or liquid) and physical findings (soot in the mouth or sputum, burned ends of nasal hair, burns of the face) are recommended as findings that suggest airway burns.

Recommendation level: B.

Comments:

- There is a case–control study investigating the presence or absence of airway burns according to physical findings,[64] and the evidence level is IVb. However, the recommendation level was set at B, because they are common diagnostic indices and can be examined easily.
- Most experts use the circumstances of injury and physical findings as non-invasive indices of inhalation injury.[65] 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 the correlations to be higher than that with edema of the vocal cord detected by laryngoscopy.[64]

REFERENCES

64 Madnani DD, Steele NP, de Vries E. Factors that predict the need for intubation in patients with smoke inhalation injury. *Ear Nose Throat J* 2006; **85**: 278–280. (evidence level IVb).
65 American Burn Association. Inhalation injury: diagnosis. *J Am Coll Surg* 2003; **196**: 307. (evidence level VI).

CQ11: IS BRONCHOSCOPY USEFUL FOR THE DIAGNOSIS OF AIRWAY INJURY?

Remarks on recommendation: The diagnosis by bronchoscopy is recommended.

Recommendation level: B.

Comments:

- Concerning the diagnosis of inhalation injury using the bronchoscope, there is a cohort study,[66] and the evidence level is IVa. However, the recommendation level was set at B, because it is a widely practiced examination with a high diagnostic value.
- Presence of soot inside the bronchi and pallor and ulceration of the bronchial mucosa observed by bronchoscopy have been reported to be in agreement with diagnoses of inhalation injury.[67,68]

REFERENCES

66 Masanès MJ, Legendre C, Lioret N, Saizy R, Lebeau B. Using bronchoscopy and biopsy to diagnose early inhalation injury: macroscopic and histologic findings. *Chest* 1995; **107**: 1365–1369. (evidence level IVa).
67 American Burn Association. Inhalation injury: diagnosis. *J Am Coll Surg* 2003; **196**: 307.
68 Masanes MJ, Legendre C, Lioret N, Maillard D, Saizy R, Lebeau B. Fiberoptic bronchoscopy for the early diagnosis of subglottal inhalation injury: comparative value in the assessment of prognosis. *J Trauma* 1994; **36**: 59–67.

CQ12: IS PLAIN CHEST RADIOGRAPHY USEFUL FOR THE DIAGNOSIS OF RESPIRATORY DISORDERS DUE TO INHALATION INJURY?

Remarks on recommendation: It is recommended to serially perform plain chest radiography in the acute period for the early diagnosis of respiratory disorders.

Recommendation level: B.

Comments:

- Concerning the diagnosis of respiratory disorders by plain chest radiography, there are cohort studies,[69,70] and the evidence level is IVa. However, the recommendation level was set at B, because it is a useful examination that can be performed relatively easily.
- The grading by plain chest radiography correlated well with the extravascular lung water content, intrapulmonary shunt ratio (Qs/Qt) and static lung compliance.[69] Abnormalities detected by early plain chest radiography are important prognostic factors that make the selection of patients that are likely to need respirator management possible.[70] It is an easy-to-perform examination compared with computed tomography, and serial radiographic evaluation is recommended in the acute period.

REFERENCES

69 Peitzman AB, Shires GT 3rd, Teixidor HS *et al.* Smoke inhalation injury: evaluation of radiographic manifestations and pulmonary dysfunction. *J Trauma* 1989; **29**: 1232–1239. (evidence level IVa).
70 Lee MJ, O'Connell DJ. The plain chest radiograph after acute smoke inhalation. *Clin Radiol* 1988; **39**: 33–37. (evidence level IVa).

CQ13: SHOULD ENDOTRACHEAL INTUBATION BE PERFORMED WHEN INHALATION INJURY IS SUSPECTED?

Remarks on recommendation: When inhalation injury is suspected, preventive intubation is recommended if possible.

Recommendation level: B.

Comments:

- There is a cohort study about preventive endotracheal intubation,[71] and the evidence level is IVa. However, the recommendation level was set at B because of the seriousness of the disadvantage when intubation becomes impossible later.
- Respiratory disorders associated with burns may be caused by restriction of respiratory motions and compression of the trachea due to burns of the neck/chest as well as airway injury.[72] Therefore, whether the patient should be intubated or not cannot be determined according to the presence or absence of airway injury alone. However, if airway edema is caused by burns of the face/neck or airway, preventive intubation is recommended, because intubation may become difficult with the progression of the course. Also, there is a report that early preventive intubation and respiratory management by continuous positive airway pressure may have contributed to the prevention of respiratory organ-related deaths early after burns.[71]

REFERENCES

71 Venus B, Matsuda T, Copiozo JB, Mathru M. Prophylactic intubation and continuous positive airway pressure in the management of inhalation injury in burn victims. *Crit Care Med* 1981; **9**: 519–523. (evidence level IVa).

72 Gartner R, Griffe O, Captier G, Selloumi D, Otman S, Brabet M, Baro B. Acute respiratory insufficiency in burn patients from smoke inhalation. *Pathol Biol* 2002; **50**: 118–126.

CQ14: IS STEROID ADMINISTRATION USEFUL FOR THE MANAGEMENT OF INHALATION INJURY?

Remarks on recommendation: Steroid administration (systemic or topical) for the treatment of inhalation injury cannot be recommended (at present) because of the lack of sufficient evidence.

Recommendation level: C2.

Comments:

- Concerning the systemic steroid administration for inhalation injury, there is an RCT,[73] and the evidence level is II. However, systemic steroid administration has not been shown to be useful for reducing the mortality rate or preventing complications. The recommendation level was set at C2 also in consideration of increased susceptibility to infection in a state of disruption of the mucosal barrier function due to burns. The recommendation level of topical steroid administration was set similarly.
- There are reports that systemic steroid administration caused no difference in lung-related conditions or the mortality rate in burn patients with airway injury.[74,75] There is also a report that laryngeal edema was alleviated, and the reintubation rate was reduced, in non-burn adult patients who underwent intubation for 36 h or longer with systemic steroid administration before extubation,[76] suggesting that the treatment is useful for alleviating edema. However, these patients cannot be compared with those with damages in the airway mucosa due to differences in the condition.

REFERENCES

73 Levine BA, Petroff PA, Slade CL, Pruitt BA Jr. Prospective trials of dexamethasone and aerosolized gentamicin in the treatment of inhalation injury in the burned patient. *J Trauma* 1978; **18**: 188–193. (evidence level II).

74 Robinson NB, Hudson LD, Riem M *et al.* Steroid therapy following isolated smoke inhalation injury. *J Trauma* 1982; **22**: 876–879.

75 Cha SI, Kim CH, Lee JH *et al.* Isolated smoke inhalation injuries: acute respiratory dysfunction, clinical outcomes, and short-term evolution of pulmonary functions with the effects of steroids. *Burns* 2007; **33**: 200–208.

76 François B, Bellissant E, Gissot V *et al.* 12-h pretreatment with methylprednisolone versus placebo for prevention of postextubation laryngeal oedema: a randomised double-blind trial. *Lancet* 2007; **369**: 1083–1089.

INFECTION CONTROL
CQ15: IS PREVENTIVE SYSTEMIC ADMINISTRATION OF ANTIBIOTICS EARLY AFTER BURNS USEFUL?

Remarks on recommendation: In patients with contaminated wounds, immunocompromised patients such as those with diabetes, children and perioperative patients, it is recommended to determine target microorganisms in consideration of facility and local characteristics as well as the results of bacterial cultures from the wound and to perform preventive systemic administration of antibiotics as an option (C1).

Uniform preventive systemic administration of antibiotics cannot be recommended (at present) because of the absence of sufficient evidence supporting its effectiveness (C2).

Recommendation level: C1 for administration according to the patient's condition and situation. C2 for uniform preventive systemic administration.

Comments:

- Concerning preventive systemic administration in the perioperative period, there are two RCT, and the evidence level is II.[77,78] While it may improve the survival rate of skin grafts or reduce the incidence of bacteremia, the recommendation level was set at C1 due to the lack of data that it improved the survival rate.
- There is an RCT concerning uniform systemic administration of antibiotics for the prevention of infection of burns, and the evidence level is II.[79] In this trial, no improvement in the outcome or decrease in the incidence of infection was observed despite uniform systemic administration of antibiotics. Moreover, as the treatment may induce microbial substitution, the recommendation level was set at C2.

- There are many negative reports concerning uniform preventive systemic administration of antibiotics. Ergün *et al.* treated 77 children with extensive burns with and without preventive systemic administration of antibiotics in 47 and 30, respectively, and reported that the frequency of wound infection was significantly higher in the treatment (21.3%) than non-treatment (16.7%) group, that seven of the eight patients who developed sepsis belonged to the treatment group, that the duration of hospitalization was longer in the treatment group and that the treatment was related to secondary infections of other sites (respiratory organs, urinary tract).[79] In a multicenter collaborative study carried out in Italy, 634 patients with extensive burns (mean age, ~40 years; mean burned area, 35% TBSA) were treated by topical application of silver sulfadiazine and 4-day administration of pefloxacin (a quinolone). As a result, 104 (16%) showed no infection, but the burns of all these patients were relatively minor, and bacteria resistant to quinolones and aminoglycosides increased after the administration, so the usefulness of preventive systemic administration of antibiotics by this protocol could not be confirmed.[80]
- Concerning studies on minor burns, Boss *et al.* retrospectively compared the wound infection rate between 133 who underwent systemic administration of antibiotics and 161 who did not of the 294 outpatients with burns and reported that there was no difference in the infection rate (3.8% vs 3.1%) and that, while antibiotics were administrated to a significantly higher percentage of patients in those with a burned area of 5% TBSA or more than in those with a burned area of less than 5% TBSA, the infection rate was not reduced in the first group.[81]
- Various reports and opinions have been presented concerning what kind of patients should receive preventive administration of antibiotics. In children, the incidence of toxic shock syndrome (TSS) is reported to be higher than in adults and to be often lethal.[82] Sheridan *et al.* compared children with burns administrated antibiotics for the prevention of group A β-hemolytic streptococcal infection and those administrated antibiotics only when group A β-hemolytic streptococci were detected by cultures of samples from the wound and considered the treatment unnecessary, because the incidence of group A β-hemolytic streptococcal infection was originally low, and because no difference was observed in its incidence with or without preventive administration.[83] Patients with extensive burns have been reported to temporarily develop bacteremia in wound lavage and surgery.[84] However, according to Steer *et al.*, who evaluated the incidence of bacteremia and outcome after perioperative preventive administration of teicoplanin, the incidence of bacteremia was reduced, but the outcome was comparable between the teicoplanin-treated and non-treated groups.[78]
- On the other hand, there are considerable numbers of reports suggesting the effectiveness of preventive administration and opinions recommending it in patients considered to be at high risk of infection and perioperative patients. Takuma recommended to specify bacteria that may infect patients with contaminated wounds, those who have complications such as diabetes and are immunocompromised, and to prophylactically administrate antibiotics to which the bacteria are susceptible.[85] Rashid *et al.* administrated antibiotics for the prevention of TSS in children with burns and reported a decrease in its incidence.[86] In the perioperative period, also, as *Staphylococcus aureus* and *Pseudomonas aeruginosa* are predominantly and widely detected, Wolf *et al.* stated that they administrate vancomycin and amikacin in combination between 1 h before and 24 h after surgery.[87]
- Regarding the effects on the survival of skin grafts, Ramos *et al.* compared the survival rate of 90 skin grafts in 77 patients (mean age, 41.7 years; mean burned area, 21.8% TBSA) between 44 and 46 surgeries performed with and without topical application of polymyxin and preventive systemic administration of antibiotics and reported that any part of the skin graft was lost in 23% and 50%, and 10% or greater area of the skin graft was lost in 9% and 35%, respectively, with significant differences.[79]
- Because of the marked variation in underlying disease, and condition of the wound, among the patients, opinions as to what kind of patients are candidates for preventive administration of antibiotics and which antibiotics should be used vary widely. In patients with contaminated wounds, immunocompromised patients such as those with diabetes, children and perioperative patients, preventive administration of antibiotics effective for the control of bacteria 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 international guidelines for management of severe sepsis and septic shock: 2008.[88]

Supplementary comments: According to the systematic review concerning the preventive systemic administration of antibiotics and outcome in severely burned patients issued in February 2010,[89] the mortality rate was significantly lower with than without the treatment. The review states, "The current guidelines do not recommend preventive systemic administration of antibiotics except in the perioperative period, but the results of this review are contradictory to this view. Also, as the data collected include those based on weak methodologies, a large-scale randomized controlled trial is necessary for the future."

REFERENCES

77 Ergün O, Celik A, Ergün G, Ozok G. Prophylactic antibiotic use in pediatric burn units. *Eur J Pediatr Surg* 2004; **14**: 422–426. (evidence level II).
78 Steer JA, Papini RP, Wilson AP, McGrouther DA, Nakhla LS, Parkhouse N. Randomized placebo-controlled trial of teicoplanin in the antibiotic prophylaxis of infection following manipulation of burn wounds. *Br J Surg* 1997; **84**: 848–853. (evidence level II).
79 Ramos G, Resta M, Machare Delgado E, Durlach R, Fernandez Canigia L, Benaim F. Systemic perioperative antibiotic prophylaxis may improve skin autograft survival in patients with acute burns. *J Burn Care Res*, 2008; **29**: 917–923. (evidence level II).

80 Donati L, Periti P, Andreassi A *et al.* Increased burn patient survival with once-a-day high dose teicoplanin and netilmicin. An Italian multicenter study. *J Chemother* 1998; **10**: 47–57. (evidence level IVa).
81 Boss WK, Brand DA, Acampora D, Barese S, Frazier WH. Effectiveness of prophylactic antibiotics in the outpatient treatment of burns. *J Trauma* 1985; **25**: 224–227. (evidence level IVa).
82 Church D, Elsayed S, Reid O, Winston B, Lindsay R. Burn wound infections. *Clin Microbiol Rev* 2006; **19**: 403–434.
83 Sheridan RL, Weber JM, Pasternack MS, Tompkins RG, Antibiotic Prophylaxis for Group. A streptococcal burn wound infection is not necessary. *J Trauma* 2001; **51**: 352–355. (evidence level IVa).
84 Mozingo DW, McManus AT, Kim SH, Pruitt BA Jr. Incidence of bacteremia after burn wound manipulation in the early postburn period. *J Trauma* 1997; **42**: 1006–1011.
85 Takuma K. The characteristics of burn wound infection and its control. *MB Derma* 2008; **146**: 54–65. (In Japanese) (evidence level VI).
86 Rashid A, Brown AP, Khan K. On the use of prophylactic antibiotics in prevention of toxic shock syndrome. *Burns* 2005; **31**: 981–985. (evidence level IVa).
87 Wolf SE, Pruitt BA. Infection in burns. In: Burke AC, ed. *Infectious Diseases in Critical Care Medicine*. New York, NY: Informa Healthcare, 2007; 507–526. (evidence level VI).
88 Dellinger RP, Levy MM, Carlet JM *et al.* Surviving Sepsis Campaign: international guidelines for management of severe sepsis and septic shock. *Crit Care Med* 2008; **36**: 296–327. (evidence level I).
89 Avni T, Levcovich A, Ad-El DD, Leibovici L, Paul M. Prophylactic antibiotics for burns patients: systematic review and meta-analysis. *BMJ* 2010; **340**: c241. (evidence level I).

TETANUS
CQ16: IS ANTI-TETANUS TREATMENT OF BURNS NECESSARY FOR THE PREVENTION OF TETANUS?

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

Recommendation level: B.

Comments:

- There have been three descriptive studies reviewing the previous published work on anti-tetanus treatment for wounds in general including burns,[90–92] and the evidence level is V. It is recommended to treat contaminated burns similarly to other wounds in general.[90] While there is no clear standard for anti-tetanus treatment for burn patients in Japan, the recommendation level was set at B on the basis of consensus of the committee, because tetanus can be lethal once it occurs, and because there is an opinion recommending anti-tetanus treatment for contaminated burns.[93]
- *Clostridium tetani* is an anaerobic bacterium widely distributed in nature including rice paddies, vegetable fields and house gardens,[94] and tetanus may occur following burns.[95,96] There is a report that 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.[97] For the prevention of tetanus at the time of injury including burns, topical treatment of wounds including the removal of foreign bodies and debridement is considered essential. In addition to it, Church *et al.* 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".[90] 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 of Tt and condition of the wound (whether or not it is a tetanus-prone wound).[91,98,99]
- Clinically, it is difficult to strictly distinguish between "tetanus-prone" and "non-tetanus-prone" wounds, and tetanus occurs not infrequently from a minor wound such as a scratch sustained during gardening and a burn of 1% TBSA or less or even without a clear wound. Therefore, Rhee *et al.* recommended to "administer Tt and TIG to those more than 10 years after the last vaccination and those with an unclear state of immunity regardless of the severity of the wound",[92] but, in the present medical circumstances in Japan, it is considered difficult to administrate Tt or TIG to all patients with traumas including minor ones. Also, according to the survey of five emergency medical facilities in the USA, none of the 504 patients with "tetanus-prone wounds" in a state of incomplete primary immunity was administrated both Tt and TIG, suggesting a gap between the guidelines and actual use of TIG.[92] However, as 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 more than 5 or 10 years after the last vaccination depending on the degree of contamination of the wound similar to anti-tetanus treatment for wounds in general. In Japan, Takeuchi *et al.*[100] 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, but, according to our review, there is no evaluation or report concerning burns.

REFERENCES

90 Church D, Elsayed S, Reid O, Winston B, Lindsay R. Burn wound infections. *Clin Microbiol Rev* 2006; **19**: 403–434. (evidence level V).
91 Brook I. Current concepts in the management of *Clostridium tetani* infection. *Expert Rev Anti Infect Ther* 2008; **6**: 327–336. (evidence level V).
92 Rhee P, Nunley MK, Demetriades D, Velmahos G, Doucet JJ. Tetanus and trauma: a review and recommendations. *J Trauma* 2005; **58**: 1082–1088. (level V).
93 Aikawa N, Aoki K, Yamazaki M. Burn would infection. *Antibiot Chemother* 1999; **15**: 671–673. (In Japanese) (evidence level VI).
94 Ebisawa I, Takayanagi M, Kurata M, Kigawa M. Density and distribution of *C. tetani* in the ground. *J Jpn Assoc Infect Dis* 1984; **60**: 277–282. (In Japanese).
95 Miyazawa N, Matsuura Y, Seino H. Severe tetanus with diabetic foot ulcers. *J Jpn Soc Intern Med* 2005; **94**: 1155–1157. (In Japanese) (evidence level V).

96 Sakaguchi E, Sakai K. Treatment of tetanus in a patient of advanced age. *Nishinihon J Dermatol* 1990; **52**: 696–700. (In Japanese) (evidence level V).
97 Karyoute SM, Badran IZ. Tetanus following a burn injury. *Burns Incl Therm Inj* 1988; **14**: 241–243. (evidence level V).
98 Kruszon-Moran DM, McQuillan GM, Chu SY. Tetanus and diphtheria immunity among females in the United States: are recommendations being followed?. *Am J Obstet Gynecol* 2004; **190**: 1070–1076. (evidence level IVb).
99 Larkin JM, Moylan JA. Tetanus following a minor burn. *J Trauma* 1975; **15**: 546–548. (evidence level V).
100 Takeuchi Y, Sono M, Iguchi M, Kusafuka H. Management and prevention of tetanus in trauma patients. *J Jpn Assoc Surg Trauma* 2007; **21**: 367–374. (In Japanese) (evidence level V).

CQ17: IS HYDROTHERAPY (SHOWER, BATHING, LAVAGE) USEFUL FOR THE TREATMENT OF BURNS?

Remarks on recommendation: Hydrotherapy is recommended for patients with minor burns not requiring hospitalization (B).

Because hydrotherapy using shared equipment may induce nosocomial infection including *P. aeruginosa* and methicillin-resistant *S. aureus* (MRSA) infections and exacerbate the survival rate in patients with extensive severe burns, it is recommended as an option to perform hydrotherapy with anti-infection measures in patients with a stable general condition and those who are expected to benefit from hydrotherapy (C1).

Recommendation level: B for hydrotherapy of relatively minor burns not requiring hospitalization. C1 for hydrotherapy of extensive severe burns with anti-infection measures.

Comments:

- The published work on hydrotherapy for patients with relatively minor burns not requiring hospitalization is mostly expert opinions, and the evidence level is VI.[101–104] However, as there are many opportunities for giving guidance concerning taking a shower or bath at home in daily clinical practice, the recommendation level was set at B on the basis of consensus of the committee in consideration of the huge number of cases accumulated to the present. Concerning hydrotherapy for extensive severe burns and their infection, there is one case–control study, and the evidence level is IVb.[105]
- Hydrotherapy for burns is performed at many facilities. According to an investigation by a burn unit of the USA and Canada reported in 1994, of the surveyed facilities, hydrotherapy was carried out at 94.8%, with immersion performed at 81.4%, and hydrotherapy was performed regardless of the burned area at 82.8% and throughout the period of hospitalization at 86.9%.[106] However, hydrotherapy using shared equipment has been suggested to cause nosocomial infections including *P. aeruginosa* and MRSA infections.[105,107,108] In the study by Tredget *et al.*, 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 immersed using shared equipment.[108] They observed that immersed hydrotherapy may increase the number of bacteria on the normal skin and other non-infected wounds or cause infection of wounds and loss of skin grafts.
- The above bacteria settle at parts of the hydrotherapy equipment difficult to sterilize such as stainless plates and pipes,[105,108] and complete prevention of their settlement is difficult. However, Akin *et al.* 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 contamination of wound from the stretcher being observed.[109] Patients with extensive burns are obliged to be hospitalized for a long time 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 refresh them, there is no published work to our knowledge concerning the effects of hydrotherapy on the patient's psychology.
- On the other hand, hydrotherapy is recommended by a number of reports for minor burns not requiring hospitalization,[101,102] and guidance about how to take a shower or bath at home is considered to be given on various opportunities in daily clinical practice. While we have encountered no report of comparison of the infection rate between hydrotherapy and no hydrotherapy groups, hydrotherapy is considered recommendable for minor burns in consideration of the rich 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.[110,111] Also, according to many expert opinions, minor burns "should be washed with sterile saline or sterilized water",[101,103,104] but, when minor burns are regarded as simple wounds, the infection rate is not considered to differ whether they are washed with tap water or sterile saline. Presently, however, there is no report comparing the procedures.

REFERENCES

101 Takayanagi K, Kumagai N. Minor burn treatment in an out-patient clinic. *Jpn J Acute Med* 2003; **27**: 83–84. (In Japanese) (evidence level VI).
102 Deguchi E. Management of burns, chemical burns, and electric injuries in children. *Jpn J Pediatr Surg* 2003; **35**: 966–970. (In Japanese) (evidence level VI).
103 Kawakami M. Emergency management of burn injuries. *Jpn J Acute Med* 2001; **25**: 346–348. (In Japanese) (evidence level VI).
104 Suzuki T. Acute burn. *J Clin Surg* 2004; **59**: 343–345. (In Japanese) (evidence level VI).
105 Simor AE, Lee M, Vearncombe M *et al.* An outbreak due to multiresistant *Acinetobacter baumannii* in a burn unit: risk factors for acquisition and management. *Infect Control Hosp Epidemiol* 2002; **23**: 261–267. (evidence level IVb).
106 Shankowsky HA, Callioux LS, Tredget EE. North American survey of hydrotherapy in modern burn care. *J Burn Care Rehabil* 1994; **15**: 143–146.
107 Embil JM, McLeod JA, Al-Barrak AM *et al.* An outbreak of methicillin resistant *Staphylococcus aureus* on a burn unit: potential role

of contaminated hydrotherapy equipment. *Burns* 2001; **27**: 681–688. (evidence level V).
108 Tredget EE, Shankowsky HA, Joffe AM *et al.* Epidemiology of infections with *Pseudomonas aeruginosa* in burn patients: the role of hydrotherapy. *Clin Infect Dis* 1992; **15**: 941–949. (evidence level V).
109 Akin S, Ozcan M. Using a plastic sheet to prevent the risk of contamination of the burn wound during the shower. *Burns* 2003; **29**: 280–283. (evidence level V).
110 Valente JH, Forti RJ, Freundlich LF, Zandieh SO, Crain EF. Wound irrigation in children: saline solution or tap water? *Ann Emerg Med* 2003; **41**: 609–616.
111 Moscati RM, Mayrose J, Reardon RF, Janicke DM, Jehle DV. A multicenter comparison of tap water versus sterile saline for wound irrigation. *Acad Emerg Med* 2007; **14**: 404–409.

DISINFECTION
CQ18: IS DISINFECTION USEFUL FOR THE PREVENTION OF INFECTION OF BURNS?

Remarks on recommendation: It is recommended as an option to disinfect burns by evaluating the condition of the wound along with the causative bacteria and antibacterial spectra of various drugs.

Recommendation level: C1.

Comments:

- Regarding the effectiveness of disinfectants for burns, there is one RCT comparing silver sulfadiazine alone and silver sulfadiazine plus chlorhexidine,[112] and the evidence level is II. The frequency of colonization of *S. aureus* at the wound has been shown to be reduced, but the recommendation level was set at C1, because whether or not the treatment improves the outcome is unclear.
- There are various opinions and reports concerning disinfection of burns, and the matter still remains controversial. In Japan, some investigators consider that chlorhexidine or povidone iodine should be used for disinfection of burns,[113–116] but others consider that disinfection itself should be avoided.[117,118] The guidelines concerning burn of New South Wales, Australia,[119] recommend that burns "should be washed with 0.05% chlorhexidine gluconate, sponge saturated with chlorhexidine gluconate, or sterile saline". Snelling *et al.* studied 253 burn patients with a mean burned 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 silver sulfadiazine and 0.2% chlorhexidine gluconate or soap containing 4% chlorhexidine gluconate at gauze changes compared with topical application of 1% silver sulfadiazine alone.[112]
- As for povidone iodine, there is a report that it is toxic to fibroblasts and epidermal keratinized cells *in vitro* at clinically used concentrations,[120] but there is another report that no significant difference was observed in the time until cure when split-thickness mesh skin grafts were treated by topical application of povidone iodine or petrolatum.[121] However, caution is necessary in applying povidone iodine over an extensive area in patients with kidney or thyroid dysfunction or elderly patients because of its absorption from the wound surface (iodine poisoning).[122]

REFERENCES

112 Snelling CF, Inman RJ, Germann E *et al.* Comparison of silver sulfadiazine 1% with chlorhexidine digluconate 0.2% to silver sulfadiazine 1% alone in the prophylactic topical antibacterial treatment of burns. *J Burn Care Rehabil* 1991; **12**: 13–18. (evidence level II).
113 Takayanagi K, Kumagai N. Minor burn treatment in an out-patient clinic. *Jpn J Acute Med* 2003; **27**: 83–84. (In Japanese) (evidence level VI).
114 Kawakami M. Emergency management of burn injuries. *Jpn J Acute Med* 2001; **25**: 346–348. (In Japanese) (evidence level VI).
115 Suzuki T. Acute burn. *J Clin Surg* 2004; **59**: 343–345. (In Japanese) (evidence level VI).
116 Aikawa N, Aoki K, Yamazaki M. Burn would infection. *Antibiot Chemother* 1999; **15**: 671–673. (In Japanese) (evidence level VI).
117 Natsui M. The principles of wound healing. *J Clin Surg* 2008; **63**: 915–919. (In Japanese) (evidence level VI).
118 Mizuhara A. Basic management of would. *Surgery* 2008; **70**: 293–300. (In Japanese) (evidence level VI).
119 Available from URL: http://www.health.nsw.gov.au/resources/gmct/burninjury/pdf/clinical_practice_guidelines.pdf (evidence level VI).
120 Ward RS, Saffle JR. Topical agents in burn and wound care. *Phys Ther* 1995; **5**: 526–538.
121 Vehmeyer-Heeman M, Van den Kerckhove E, Gorissen K, Boeckx W. Povidone-iodine ointment: no effect of split skin graft healing time. *Burns* 2005; **31**: 489–494. (evidence level IVa).
122 Aiba M, Ninomiya J, Furuya K *et al.* Induction of a critical elevation of povidone-iodine absorption in the treatment of a burn patient: report of a case. *Surg Today* 1999; **29**: 157–159. (evidence level V).

DEFECATION CONTROL INSTRUMENTS/SYSTEMS
CQ19: IS THE FECAL DIVERSION TUBE USEFUL FOR THE PREVENTION OF INFECTION OF BURNS AROUND THE ANUS?

Remarks on recommendation: In patients with perianal burns, the use of the fecal diversion tube is recommended as an option in consideration of the patient's general condition, and state of the wound because it may reduce the frequency of gauze changes due to contamination by stools and the incidence of wound or urinary tract infection.

Recommendation level: C1.

Comments:

- There is one non-randomized comparative trial concerning the use of the fecal diversion tube for burn patients,[123] and the evidence level is III.
- 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. Also, sedated patients have fecal incontinence and require gauze change at each bowel movement, and patients with fecal incontinence are reported to increase the risk of nosocomial infection including *Clostridium difficile* infection.[124]
- Recently, the fecal diversion tube has been reported to be useful for the management of skin detachment and wounds around the anus. When it was used in 42 patients with fecal incontinence discharging liquid or semi-liquid stools, the treatment was effective for maintaining or improving the condition of the gluteal and perianal skin in 92% or more of

patients even with risk factors of skin vulnerability.[125] When 106 patients with perianal burns managed with the fecal diversion tube were compared with a previous 106 patients managed without it, no significant difference was observed in the mortality rate, but 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 cost wise.[123]

- In a prospective study in seven perianal burns and 13 with severe perianal excoriations, the severity score of perianal skin damage was significantly reduced after intubation, the mean frequency of gauze change was reduced from 3.3 to 1.5 times/day, and the frequency of changes of bed linen for patients with fecal incontinence was reduced from 9.3 to 1.2 times/day.[126] In Japan, Nishibori *et al.* 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.[127] While the fecal diversion tube is recommended as a non-invasive treatment that should be considered before ostomy,[126] caution is needed as there have been reports of anal ulceration and laxity,[128] and lower gastrointestinal bleeding in patients receiving anticoagulant therapy the relationship of which with anal intubation cannot be excluded.[125]

REFERENCES

123 Echols J, Friedman BC, Mullins RF, *et al.* Clinical utility and economic impact of introducing a bowel management system. *J Wound Ostomy Continence Nurs* 2007; **34**: 664–670. (evidence level III).

124 Donskey CJ. The role of the intestinal tract as a reservoir and source for transmission of nosocomial pathogens. *Clin Infect Dis* 2004; **39**: 219–226.

125 Padmanabhan A, Stern M, Wishin J, Mangino M, Richey K, DeSane M, Flexi-Seal Clinical Trial Investigators Group. Clinical evaluation of a flexible fecal incontinence management system. *Am J Crit Care* 2007; **16**: 384–393. (evidence level V).

126 Keshava A, Renwick A, Stewart P, Pilley A. A nonsurgical means of fecal diversion: the Zassi Bowel Management System. *Dis Colon Rectum* 2007; **50**: 1017–1022. (evidence level IVa).

127 Nishibori A, Hiramatsu Y, Kato T, Kato Y, Asai S. Clinical evaluation of a flexible fecal incontinence management system (FLEXI-SEAL®). *J J Burn Inj* 2008; **34**: 284–289. (In Japanese) (evidence level V).

128 Bordes J, Goutorbe P, Asencio Y, Meaudre E, Dantzer E. A non-surgical device for faecal diversion in the management of perineal burns. *Burns* 2008; **34**: 840–844. (evidence level V).

TOPICAL TREATMENTS: DRESSING MATERIALS

CQ20: ARE DRESSING MATERIALS USEFUL FOR THE TREATMENT OF SECOND-DEGREE BURNS?

Remarks on recommendation: Dressing materials such as hydrocolloid, hydrogel, polyurethane film, chitin, polyurethane foam, alginate and Hydrofiber® are recommended as an option for topical treatment for second-degree burns.

Recommendation level: C1.

Comments:

- There are five RCT concerning hydrocolloid and two RCT each concerning polyurethane film and hydrogel,[129] and the evidence level is II for each. However, because no significant difference was observed in the time until cure compared with oil-based ointments, the recommendation level was set at C1.
- There is one case series study each concerning chitin and polyurethane foam,[130,131] and the evidence level is V for each.
- While the use of alginate and Hydrofiber for second-degree burns is not covered by insurance, there is one RCT concerning each,[129] and the evidence level is II for both. However, as no significant difference was noted in the time until cure compared with silver sulfadiazine, the recommendation level was set at C1.
- SDB are usually not an indication for surgery and cure by appropriate topical treatment. In DDB, a thin layer of necrotic tissue is observed on the wound surface, but, if their area is limited, they are manageable by conservative treatment after lysing the necrotic tissue by appropriate topical agents or surgical debridement. Dressing materials are used for the treatment of SDB and DDB after removal of necrotic tissue. Third-degree burns, which have thick necrotic tissue, are usually indications for surgery and not treated with dressing materials.
- In the Cochrane review in 2008 concerning the effects of dressing materials on second-degree burns,[129] 26 RCT comparing various dressing materials with paraffin gauze or silver sulfadiazine are mentioned. Among them, dressing materials available in Japan are evaluated in 11. Because the dressing materials used in the remaining 15 trials are unapproved in Japan, they are excluded. The material referred to as paraffin in the Western published work is comparable with a grease base such as white petrolatum used in Japan. While it is expressed as “oil-based ointment” in the Remarks on recommendation, it is referred to as “paraffin” in the Comments by respecting the original articles.
- There are three RCT comparing hydrocolloid and paraffin gauze in 236 patients.[129] No significant difference was observed in the time until cure compared with paraffin gauze in any of the reports. There are two RCT comparing hydrocolloid and silver sulfadiazine in 72 patients,[129] and the time until cure did not significantly differ in one but was significantly shorter with hydrocolloid in the other.
- Two RCT have been reported by the same authors concerning hydrogel.[129] In these reports, data including those concerning paraffin gauze and silver sulfadiazine are used as controls, and the time until cure was shorter with hydrogel in both reports, but the difference was significant in one but not in the other.
- There is one RCT comparing polyurethane film and paraffin gauze in 55 patients,[129] but the time until cure showed no

significant difference. Also, there is an RCT comparing polyurethane film and paraffin gauze saturated with chlorhexidine, and the time until cure was significantly shorter with polyurethane film.[129] Whether or not this difference was due to chlorhexidine is unclear, but the cure rate was higher with polyurethane film until day 10, and the difference disappeared thereafter.

- There is one each RCT concerning alginate and Hydrofiber using silver sulfadiazine as a control, and neither showed a difference in the time until cure.[129] 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 subcutaneous tissue.
- 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 in 120 patients including those with donor site wounds and traumas.[130] Of the 120 patients, 21 had burns, and the treatment was effective or very effective in 80% of them. However, the hemostatic and analgesic effects were included in the evaluation, and the effect on wound healing is unclear. Also, there is no report evaluating the effectiveness of polyurethane foam exclusively for the treatment of burns, and there is only one case series study in 150 patients including those with donor site wounds and pressure ulcers.[131] Of these 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 for the treatment of burns include those concerning hydrocolloid,[132,133] Hydrofiber[134,135] and hydrogel,[136,137] the effectiveness of the dressing material itself is evaluated in each report without comparing it with other treatments.
- Of the studies on the effects of dressing materials in the management of second-degree burns mentioned in the Cochrane review,[129] six evaluated the incidence of wound infection. They consist of three RCT comparing hydrocolloid and paraffin gauze, one RCT comparing polyurethane film and paraffin gauze, one RCT comparing polyurethane film and paraffin gauze saturated with chlorhexidine, and one RCT comparing silver-containing Hydrofiber and silver sulfadiazine, and they are 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,[129] eight RCT evaluated the frequency of dressing changes. The frequency of changes was reported to be higher with the dressing material in one but to be lower compared with paraffin gauze or silver sulfadiazine in six and not to be different in one.
- 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. Actually, however, as it is difficult to apply a dressing material over a wide area, and as there is a cost restriction, dressing materials are used for the treatment of relatively small burns that can be covered with them. Because there is no RCT comparing dressing materials, no evidence for recommending particular products among a large number of dressing materials is available. Therefore, dressing materials must be used by understating their characteristics and considering the area and site of the wound, presence or absence or risk of infection, amount of effusion and age. Caution against wound infection is also necessary, and, if the risk of wound infection is considered high, topical treatments other than a dressing material are recommended.

REFERENCES

129 Wasiak J, Cleland H, Campbell F. Dressings for superficial and partial thickness burns. *Cochrane Database Syst Rev*, 2008; **8**: CD002106. (evidence level II).

130 Beschitin® Study Group in Kyusyu. Examination of usability of chitin dressing (Beschitin® W) for wounds – multicenter clinical study in Kyusyu. *Nishi J Dermatol*, 1993; **55**: 941–946. (evidence level V).

131 Nozaki M, Soejima K, Nakazawa H. Clinical application of lyofoam for the treatment of skin defects (pressure ulcers, burns and donor sites of split-thickness skin grafts), and the site of insertion of tubes. *Prog Med* 1996; **16**: 1101–1114. (evidence level V).

132 Ishibashi Y, Nakagawa H, Nakanishi H *et al.* Clinical study of DuoDERM on skin ulcers. *J Clin Therap Med* 1986; **2**: 1575–1584. (evidence level V).

133 Ono I, Gunji H, Tateshita T, Kaneko F, Takiguchi Y. Examination of usability of hydrocolloid covering material (HCD-02) for suture wound, burn and skin ulcer wound. *Nishi J Dermatol* 1996; **58**: 319–329. (evidence level V).

134 Ueno T, Tsukada S, Heshiki T, Akaba N, Ihara E. Clinical trial results of Hydrocel for donor sites and thermal burns. *Nishi J Dermatol* 1998; **60**: 206–211. (evidence level V).

135 Kishibe M, Kawakami S, Nozaki M *et al.* Clinical effects of carboxymethylcellulose (AQUACEL®) for the treatment of dermal burns. *J J Burn Inj* 2006; **32**: 249–257. (evidence level V).

136 Aikawa N, Nozaki M, Takuma K *et al.* Clinical trial of hydrogel dressing (NMD-101) on dermal burns, split-thickness skin donor sites, and skin defect injuries. *Jpn Pharmacol Ther* 2002; **30**: 863–874. (evidence level V).

137 Kato T, Asai S, Hiramatsu Y, Nishihori A. Application of VIEWGEL (a new hydrocolloidal dressing) on burn wounds. *J J Burn Inj* 2006; **32**: 44–51. (evidence level V).

TOPICAL TREATMENTS: TOPICAL AGENTS

CQ21: WHAT TOPICAL AGENTS SHOULD BE USED FOR THE TREATMENT OF SECOND-DEGREE BURNS?

Remarks on recommendation: For the initial treatment of second-degree burns, ointments with oleaginous bases such as petrolatum, zinc oxide and dimethyl isopropylazulene are recommended as an option (C1).

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

Lysozyme hydrochloride, aluminum chlorohydroxy allantoinate (Alcloxa) and so forth are recommended as an option (C1).

For chronic ulcers accompanied by necrotic tissue resulting from DDB, the use of bromelain ointment, cadexomer iodine,

dextranomer and silver sulfadiazine is recommended as an option for the removal of necrotic tissue (C1).

Recommendation level: B and C1.

Comments:

- For chronic ulcers caused by burns, topical agents should be selected for wound bed preparation based on the TIME concept or moist wound healing. It is also important to appropriately select not only the principal agent but also the base according to the condition of the wound surface. The following topical treatments are recommended by the Guidelines for the Management of Pressure Ulcers as topical agents appropriate for wound bed preparation, but the topical agents used for T (removal of necrotic tissue) and M (maintenance of the moist environment) in burns are the same:

  T (removal of necrotic tissue): Cadexomer iodine, silver sulfadiazine, dextranomer, bromelain ointment.
  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 a oil base such as petrolatum.
  E (management of wound edges): No recommendable topical agents.

- Concerning the use of oil-based ointments for second-degree burns, there is only an expert opinion,[138] and the evidence level is VI. There is one RCT showing the effectiveness of trafermin for the treatment of second-degree burns,[139] and the evidence level is II. Regarding tretinoin tocopherol, there is one double-blind RCT comparing it with bendazac in patients with various skin ulcers including those caused by burns[140] and one non-blinded RCT comparing it with lysozyme hydrochloride,[141] and the evidence level is II. However, no details such as the depth of the burns are provided. Concerning bucladesine sodium, there is one double-blind RCT each comparing it with the base and lysozyme hydrochloride in patients with various skin ulcers including those caused by burns,[142,143] and the evidence level is II. However, no detailed description concerning the burns is provided. As for prostaglandin E1, there is a non-blinded RCT comparing it with lysozyme hydrochloride in patients with various skin ulcers including those due to burns,[144] and the evidence level is II, but no detailed information including the depth is provided about the burns, and the number of patients is small. However, as tretinoin tocopherol, bucladesine sodium and prostaglandin E1 are rated similarly to trafermin in the Guidelines for the Management of Pressure Ulcers, which are similar chronic skin lesions, the recommendation levels of these topical agents were determined similarly to trafermin on the basis of consensus of the committee. Concerning lysozyme hydrochloride, there is one RCT comparing it with bendazac in patients with various skin ulcers including those due to burns[145] and one case series study in patients with ulcers due to burns,[146] and the evidence level is II and V, respectively. However, the recommendation level of the former was set at C1 because of the lack of detailed description about the burns. Regarding aluminum chlorohydroxy allantoinate, there is a double-blind RCT comparing it with the base in 62 patients with skin ulcers including those due to burns, erosion, eczema and dermatitis,[147] but the recommendation level was set at C1, because there was no detailed description or evaluation about the burns.
- In second-degree burns, damage of the dermis is partial, and the selection of topical agents in consideration of not only the antibacterial action but also wound healing is necessary. The principle of topical treatment for wounds in general converges on protecting the wound surface and maintaining a moist environment.[148] However, as it is difficult to accurately determine the depth of burns early after injury, and as burns ranging from first-degree burns to DDB are often mixed, topical agents to be used are difficult to specify. Therefore, oil-based ointments may be used in the stage of initial treatment, but topical agents appropriate for the condition of the wound surface must be selected as it becomes clear.
- Ointments containing antibiotics (antibacterial agents) are oil-based 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 their long-time use may invite the development of resistant bacteria.
- Akita *et al.* performed an RCT by randomizing 102 adults with second-degree burns into trafermin and non-trafermin groups.[139] As a result, they reported that the time until cure was significantly shorter in the trafermin group and that the elasticity and hardness scores of the scar and moisture-retaining ability were all significantly higher in the trafermin group compared with a control group consisting of 51 healthy volunteers. Komuro *et al.* evaluated 32 patients (including children) with second-degree burns conservatively treated using trafermin, comparing those administrated the drug within 3 days and after 4 days or more after injury, and reported that the mean number of days until epithelialization and cumulative cure rate were both statistically superior in the group treated within 3 days.[149] Fujiwara *et al.* 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 and reported that the number of days until epithelialization was significantly shorter in the trafermin group.[150] Also, Shiozawa *et al.* 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[151] and reported that patients who showed hypertrophic scarring were significantly fewer in the trafermin group.

- Trafermin is a spray type liquid preparation, and it must be used with some topical agents or dressing material to maintain a moist environment for burns. Recently, there have been reports of the concomitant use of artificial dermis and intra-bulla injection,[152,153] but no established method has been proposed concerning the selection of the topical agents or dressing materials to be used with these treatments.
- A double-blind RCT comparing tretinoin tocopherol and bendazac has been performed in 152 patients with various skin ulcers including 44 with ulcers due to burns by the L-300 Clinical Trial Group.[140] While there is no mention of the depth of burns or time after injury, granulation 1 week after the application of the test drugs was reported to be significantly better in the tretinoin tocopherol group. There is also a unblended 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 reported to be observed in the ulcers due to burns between the two groups.[141]
- Shinmura *et al.* performed double-blind RCT comparing bucladesine sodium and the base in 150 patients with pressure ulcers/skin ulcers including 20 with ulcers due to burns and comparing bucladesine sodium and lysozyme hydrochloride in 275 patients with pressure ulcers/skin ulcers including 40 with ulcers due to burns.[142,143] According to these reports, bucladesine sodium was significantly superior in 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,[154] so attention to the general condition including the blood pressure, urine volume and blood glucose level is necessary when it is topically applied to a wide area.
- Imamura *et al.* performed a non-blinded RCT comparing prostaglandin E1 and lysozyme hydrochloride in 171 patients with pressure ulcer/skin ulcer including 26 with ulcers due to burns.[144] 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.
- Kawakami *et al.* performed a case series study using lysozyme hydrochloride in 28 patients with SDB and 40 with DDB.[146] In this study, the improvement of all second-degree burns was greater in the lysozyme hydrochloride group, but granulation was suggested to become excessive, and epithelialization to be delayed, in patients with old (topical application initiated ≥5 days after injury) DDB.
- Konjiki carried out a double-blind RCT comparing aluminum chlorohydroxy allantoinate and the base in 62 patients with skin ulcers including those due to burns, erosion, eczema or dermatitis,[147] 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 burn was performed.
- 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, topical application of bromelain, silver sulfadiazine, cadexomer iodine or dextranomer for the removal of necrotic tissue should be considered (see CQ23).

REFERENCES

138 Kamiya T, Ono I. A practical concept of topical therapy in burn wound (moist wound care). *MB Derma* 2008; **146**: 21–28. (evidence level VI).

139 Akita S, Akino K, Imaizumi T, Hirano A. Basic fibroblast growth factor accelerates and improves second-degree burn wound healing. *Wound Rep Reg* 2008; **16**: 635–641. (evidence level II).

140 Clinical Research Group for L-300. Clinical evaluation of L-300 ointment in the treatment of skin ulcers – controlled comparative study by using Bendazac ointment as a control. *J Clin Therap Med*, 1991; **7**: 437–456. (evidence level II).

141 Clinical Research Group for L-300. Clinical evaluation of L-300 ointment in the treatment of skin ulcers – controlled comparative study by using Lysozyme chloride ointment. *J Clin Therap Med*, 1991; **7**: 645–665. (evidence level II).

142 Niimura M, Yamamoto K, Kishimoto S *et al.* Clinical evaluation of DT-5621 in patients with chronic skin ulcer – multicenter, placebo-controlled double blind study. *Jpn Pharmacol Ther* 1990; **18**: 245–258. (evidence level II).

143 Niimura M, Ishibashi Y, Imamura S *et al.* Clinical study of Dibutyryl cyclic AMP ointment (DT-5621) in chronic skin ulcers – well-controlled comparative study with Lysozyme ointment. *J Clin Therap Med* 1991; **7**: 677–692. (evidence level II).

144 Imamura S, Sagami S, Ishibashi Y *et al.* Clinical study of prostaglandin E1 ointment (G-511 ointment) in chronic skin ulcers – well-controlled comparative study with Lysozyme chloride ointment. *J Clin Therap Med* 1994; **10**: 127–147. (evidence level II).

145 Study Group for KH-101. Clinical evaluation of KH-101 ointment (Reflap ointment) in skin ulcers – new analysis of well controlled comparative study. *Nishinihon Derma*, 1986; **48**: 553–562. (evidence level II).

146 Kawakami S, Tsukada S, Nanba K *et al.* The effect of Lysozyme ointment for the treatment of dermal burn wounds. *J J Burn Inj* 1989; **15**: 109–117. (evidence level V).

147 Konjiki S. Clinical evaluation of Alkisa ointment in the treatment of skin disease – double blind controlled study. *Jpn Pharmacol Ther* 1977; **5**: 172–176. (evidence level VI).

148 Hinman CD, Maibach H. Effect of air exposure and occlusion on experimental human skin wounds. *Nature* 1963; **200**: 377–378.

149 Komuro A, Kishibe M, Yamamoto Y *et al.* Treatment for second-degree burn wounds using Trafermin (Fiblast® spray). *J J Burn Inj* 2009; **35**: 27–39. (evidence level III).

150 Fujiwara O, Soejima K, Nozaki M *et al.* Treatment of acute second degree burn wound with bFGF. *J J Burn Inj* 2008; **34**: 29–37. (evidence level III).

151 Shiozawa K, Mukae N, Nishimura G. Inhibition of hypertrophic scars by administration of basic fibroblast growth factor. *Jpn J Plast Surg* 2009; **52**: 543–549. (evidence level IVb).

152 Mitsukawa N, Suse T, Karube D *et al.* Clinical study of treatment skin defects using a combination of artificial dermis and bFGF preparation. *Jpn J Plast Surg* 2009; **52**: 517–527.

153 Kurokawa M, Morooka H, Jinno C. Treatment for partial thickness burns with Intra-bleb bFGF infusion therapy and hydrogel covering therapy following bFGF spray. *J J Burn Inj* 2009; **35**: 21–26.
154 Ito Y, Aoyama H, Yokoo K *et al.* Absorption of Bucladesine sodium ointment from burn wounds. *J J Burn Inj* 1998; **24**: 13–21.

CQ22: IS SILVER SULFADIAZINE USEFUL FOR THE TREATMENT OF EXTENSIVE THIRD-DEGREE BURNS?

Remarks on recommendation: Silver sulfadiazine is recommended for the treatment of extensive third-degree burns.

Recommendation level: B.

Comments:

- Concerning the topical use of silver sulfadiazine for the treatment of third-degree burns, there are two non-randomized comparative trials,[155,156] and the evidence level is III. 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 action. Also, as it is convenient for application to a wide area because of the emulsion base, its recommendation level was set at B.
- Pegg *et al.* performed a non-randomized comparative trial in patients with burns of various degrees by treating 314 with silver sulfadiazine, 156 with maphenide (unmarketed in Japan), and 175 historical controls with gentamycin sulfate and so forth,[155] and reported that the mortality rate, positive rate of bacterial cultures, and detection rates of *P. aeruginosa*, staphylococci, *Proteus* and *Candida* were significantly reduced in the silver sulfadiazine group compared with the control and maphenide groups. In Japan, Oyama *et al.* 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,[156] and reported that silver sulfadiazine was markedly effective against *Klebsiella*, *Serratias*, other Gram-negative bacteria and *Candida*.
- Ono *et al.* 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 recommended them as topical antibacterial agents for burns.[157] Also, Yura *et al.* performed resistance-acquisition and bactericidal studies using silver sulfadiazine against *P. aeruginosa* and reported infrequent development of resistance and a satisfactory bactericidal action of the drug.[158] On the other hand, there have been reports of infections resistant to silver preparations including silver sulfadiazine.[159] According to the report by Li *et al.*,[160] bacteria are shown to acquire resistance to silver in the presence of silver at a low concentration, and Atiyeh *et al.* suggested the necessity to maintain an appropriate silver concentration at the wound, because resistance to silver develops at concentrations near the MIC but not at a sufficient concentration.[161] Also, in extensive burns with a large amount of exudates, silver sulfadiazine is reported to be inactivated with a marked decrease in its effect.[162] 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 are expected to produce a debriding effect by promoting autolysis of necrotic tissue (see CQ23).
- As adverse effects of silver sulfadiazine, leukocytopenia, methemoglobinemia, silver deposition, allergic reaction to sulfonamides and so forth have been reported. Sufficient attention to these adverse effects is considered necessary, particularly when silver sulfadiazine is topically applied to extensive burns. However, leukocytopenia is also occasionally observed in the use of other drugs, and there is the opinion that it should not be regarded as a side-effect specific to silver sulfadiazine.[163] There is also the opinion that the use of silver sulfadiazine should be avoided as much as 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.[161]

REFERENCES

155 Pegg SP, Ramsay K, Meldrum L, Laundy M. Clinical comparison of maphenide and silver sulfadiazine. *Scand J Plast Reconstr Surg* 1979; **13**: 95–101. (evidence level III).
156 Ohyama K. Clinical comparison of silver sulfadiazine cream (T-107) and Gentamycin ointment in burn wound. *J J Burn Inj* 1980; **6**: 87–96. (evidence level III).
157 Ono I, Ohura T, Manabe M *et al.* Topical therapy on burned patients – comparison with silver sulfadiazine cream and other ointment. *J J Burn Inj* 1982; **8**: 3–12. (evidence level VI).
158 Yura J, Andoh M, Ishikawa S. Clinical evaluation of silver sulfadiazine (T107) in decubitus, chronic skin ulcers – comparison with placebo by a double blind method. *Chemotherapy* 1984; **32**: 208–222.
159 Heggers JP, Robson MC. The emergence of silver sulphadiazine-resistant *Pseudomonas aeruginosa*. *Burns* 1979; **5**: 184–187.
160 Li XZ, Nikaido H, Williams KE. Silver-resistant mutants of *Escherichia coli* display active efflux of Ag+ and are deficient in Silver Sulfadiazine. *J Bacteriol* 1997; **179**: 6127–6132. (evidence level VI).
161 Atiyeh BS, Costagliola M, Hayek SN, Dibo SA. Effect of silver on burn wound infection control and healing review of the literature. *Burns* 2007; **33**: 139–148. (evidence level V).
162 Hoffmann S. Silver sulfadiadine: an antibacterial agent for topical use in burns. *Scand J Plast Reconstr Surg* 1984; **18**: 119–126. (evidence level V).
163 Frederick W. The side effect of silver sulphadiazine. *J Burn Care Res* 2009; **30**: 464–470. (evidence level V).

CQ23: WHAT TOPICAL AGENTS SHOULD BE USED TO REMOVE NECROTIC TISSUE FROM SMALL THIRD-DEGREE BURNS?

Remarks on recommendation: As topical agents aimed to remove necrotic tissue from small third-degree burns, bromelain, cadexomer iodine, dextranomer and silver sulfadiazine are recommended as an option.

Recommendation level: C1.

Comments:

- Concerning bromelain, there is one RCT evaluating its debriding effect on third-degree burns,[164] and the evidence level is II. However, as its effect was similar to those of other drugs and attenuated in dried wounds, the recommendation level was set at C1.
- Regarding dextranomer and cadexomer iodine, there are non-randomized comparative trials in patients with various skin ulcers including ulcers due to burns,[165,166] and a case series study,[167] and the evidence level is III and V, respectively. In these reports, the response rate with the debriding effect included was high, but burns were not focused, and the number of patients was small. Both of these drugs are indicated for wounds rich in effusion, and caution is needed in their use for wounds deficient in effusion, because they may cause drying of the wound surface and delay wound healing.[168]
- For silver sulfadiazine, there is no report evaluating the debriding effect except for expert opinions about pressure ulcers,[166,167] and the evidence level is VI. However, there has been rich experience in the clinical use of silver sulfadiazine, and it is also expected to have a preventive effect against infection (see CQ22).
- As for the ointment containing calf blood extract, there is one RCT indicating its usefulness for the treatment of third-degree burns,[169] and the evidence level is II. However, as this preparation was manufactured and approved in 1963 and has recently been used rarely, it was excluded from the evaluation for recommendation.
- Regarding the debriding effect of fradiomycin sulfate/crystalline trypsin, there are only expert opinions, and the evidence level is VI. As this preparation was also manufactured and approved in 1962 and has recently been used rarely, it was excluded from the evaluation for recommendation.
- Anzai *et al.* performed an RCT using bromelain and placebo prepared by mixing inactivated bromelain with the same base in 33 patients with deep second-degree or third-degree burns (7–10 days after injury).[164] They separated the wound of each patient into halves, applied the true drug or placebo topically to each half, and compared the degree of lysis of necrotic tissue, hemorrhage and pain, reporting 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.* 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.[170] In using bromelain, attention to pain, which occurs frequently, is necessary. Also, as highly water-absorbing macrogol is used as the base, its debriding effect is attenuated when effusion or the moisture of the wound surface is reduced.[168]
- Silver sulfadiazine is considered to produce a wound surface cleaning effect as its emulsion base with high water content causes softening and lysis of necrotic tissue due to its permeation characteristics.[171] However, there are a few points that need attention in its use: 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.[165]

REFERENCES

164 Anzai T, Tomizawa T, Muramatsu T *et al.* Effect of Bromelain ointment in necrotic tissue. *Jpn J Plast Surg* 1972; **15**: 456–462. (evidence level II).

165 Asada Y, Higashida T, Odaka T *et al.* Clinical efficacy of NI-009 in various cutaneous ulcers (phase III study). *J Clin Therap Med* 1990; **6**: 101–117. (evidence level V).

166 Japanese Society of Pressure Ulcers "Pressure Ulcer Prevention and Control Guideline" Development Committee. *Removal of Necrotic Tissue for N to n*. 2009; 107–113. (evidence level VI).

167 Tachibana T, Miyachi Y. Conservative treatment by drug. *Jpn J Plast Surg* 2003; **46**: 459–470. (evidence level II).

168 Study Group for SK-P-9701. Clinical study results of SK-P-9701 (Dextranomer paste) in various cutaneous ulcers. *J Clin Therap Med*, 2000; **16**: 1419–1437. (evidence level III).

169 Suetsugu T, Yashiro A, Yamasaki R *et al.* Clinical efficacy of Solcoseryl ointment in burn. *The Clinical Report* 1975; **9**: 2433–2452. (evidence level II).

170 Ogawa Y, Kurooka S, Katakami S *et al.* The evaluation of the effect of Bromelain ointment on the debridement of eschar of burn, decubitus and various wound. *J New Rem Clin* 1999; **48**: 69–77. (evidence level V).

171 Kukita A, Ohura T, Aoki T *et al.* Clinical evaluation of NI-009 on various cutaneous ulcers – comparative study with Elase®-C ointment. *J Clin Therap Med* 1990; **6**: 817–848.

CQ24: ARE TOPICAL STEROID PREPARATIONS USEFUL FOR THE TREATMENT OF FIRST-DEGREE BURNS AND SDB?

Remarks on recommendation: The use of topical steroid preparations is recommended as an option in expectation of their anti-inflammatory effects.

Recommendation level: C1.

Comments:

- There are only expert opinions concerning the usefulness of topical steroid preparations for the treatment of burns,[172–174] and the evidence level is VI. On the other hand, there are three RCT (including double-blind trials) suggesting that topical steroid preparations showed no anti-inflammatory effect on the skin that has sustained physical damage including burn.[175–177] However, we noted that expert opinions suggesting the usefulness of topical steroid preparations for the treatment of first- or second-degree burns are predominant and that topical steroid preparations have been used widely for the treatment of burns in Japan.
- Yamanaka *et al.* recommend the use of a very strong or even stronger topical steroid preparation for first-degree burns for a short period from immediately after injury to rapidly repair damaged tissue and control inflammation.[172]

Takuma *et al.* recommend the use of topical steroid preparations for areas of first-degree burns with marked reddening/pain.[173] Hitoshi *et al.* 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 while they are very effective for suppressing reddening and edema and mitigating pain in the acute period.[174]

- Pederson *et al.* however, performed a double-blind RCT by artificially creating first-degree burns or SDB in healthy volunteers and compared the anti-inflammatory effect between clobetasol propionate and placebo according to the severity of pain and erythema and reported no significant difference between the two groups.[175] Faurschou *et al.*[176] examined the effects of an topical steroid preparation on sun burn (ultraviolet B irradiation) in 20 healthy volunteers but observed no clinical usefulness when it was applied after irradiation.
- Also, Matsumura *et al.* 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.[177] According to this study, no difference was observed in the alleviation of swelling or pain between the two groups, and betamethasone valerate/gentamycin sulfate promoted epithelialization until 2 days from the beginning of their use but suppressed it after 4 days or more. They also treated one group by using gentamycin sulfate after topical application of betamethasone valerate/gentamycin sulfate for 3 days but another group by using gentamycin sulfate alone from the beginning and observed no significant difference in the comprehensive evaluation of objective findings, number of days until completion of epithelialization or overall pharmacological effect.

REFERENCES

172 Yamanaka K, Mizutani H. Princple of initial treatment in burn wound. *MB Derma* 2008; **146**: 16–20. (evidence level VI).

173 Taguma K, Sasaki J. 9 Treatment and topical therapy, BURN – index of initial treatment and topical therapy antibacterial chemotherapy in burn. *Med J*, 2008; 129–156. (evidence level VI).

174 Todoroki T, Okano Y, Moriuchi H. From daily inquiry – adrenal corticosteroid. *J Pract Pharm* 1988; **39**: 1085–1093. (evidence level VI).

175 Pedersen JL, Moiniche S, Kehlet H. Topical glucocorticoid has no antinociceptive or anti-inflammatory effect in thermal injury. *Br J Anaesth* 1994; **72**: 379–382.

176 Faurschou A, Wulf HC. Topical corticosteroids in the treatment of acute sunburn a randomized, double-blind clinical trial. *Arch Dermatol* 2008; **144**: 620–624.

177 Muramatsu T, Sekiguchi T. The clinical use of corticosteroid ointment for acute second degree burn. *Jpn J Plast Surg* 1972; **15**: 318.