REVIEW ARTICLE

Dermatological Conditions Inducing Acute and Chronic Pain

Mathilde HAYOUN-VIGOUROUX[1] and Laurent MISERY[1,2]
[1]Department of Dermatology, University Hospital of Brest and [2]University of Brest, LIEN, Brest, France

Pain is a common condition in dermatology. The aim of this review is to analyse the characteristics of pain in dermatology. Some skin diseases are conventionally known to cause pain; e.g. ulcers, pyoderma gangrenosum and herpes zoster. Common dermatoses, such as psoriasis or atopic dermatitis, can also cause significant pain. Some conditions are characterized by neuropathic pain and/or pruritus, without visible primary lesions: e.g. the neurocutaneous diseases, including small fibre neuropathies. Patients often fear pain in skin surgery; however, surgical procedures are rather well tolerated and any pain is mainly due to administration of local anaesthetic. Some therapies may also be uncomfortable for the patient, such as photodynamic therapy or aesthetic procedures. Thus, pain in dermatology is common, and its aetiology and characteristics are very varied. Knowledge of the different situations that cause pain will enable dermatologists to propose suitable analgesic solutions.

Key words: pain; dermatoses; dermatology; neuropathic pain.

Accepted Apr 8, 2022; Epub ahead of print Apr 8, 2022

Acta Derm Venereol 2022; 102: adv00742.

DOI: 10.2340/actadv.v102.284

Corr: Mathilde Hayoun-Vigouroux, Department of Dermatology, Centre Hospitalier Régional Universitaire Morvan, 2 avenue Foch, FR-29200 Brest, France. E-mail: vigourouxmathilde7@gmail.com

Pain is defined by the International Association for the Study of Pain (IASP) as "an unpleasant sensory and emotional experience associated with or resembling that associated with, actual or potential tissue damage (1)". In daily practice, the dermatologist encounters a wide variety of types of pain, ranging from acute surgical pain to chronic pain, inherent to many dermatoses, or acute pain from other skin pathologies, such as wounds (2). Pain can be chronic or acute. Chronic pain is defined by the IASP as ''pain without apparent biologic value that has persisted beyond the normal tissue healing time, usually taken to be 3 months". Chronic pain results from alterations at various levels of the pain pathway (3). Neuropathic pain is caused by a lesion or disease of the somatosensory nervous system, and nociceptive pain arises from actual or threatened damage to non-neural tissue and is due to the activation of nociceptors (4).

In dermatology, pruritus is the most common cutaneous symptom, and has been widely described and analysed (5). Although pain is also a common symptom in dermatology, it has been studied less than pruritus (6).

SIGNIFICANCE

In daily practice, the dermatologist encounters many situations responsible for pain, whether it be skin disorders or some therapeutic or diagnostic procedures. This article provides an updated overview of the painful conditions in dermatology. The circumstances highlighted are intentionally frequent situations, which could be met by the greatest number of dermatologists, both in hospitals or in private practice. This review is intended to be a practical guide for dermatologists to help them to identify and analyse pain or to anticipate situations that may cause pain in their daily practice, and thus to propose an appropriate analgesic approach.

The aim of this review is to analyse the circumstances of pain in dermatology.

METHODS

This narrative review was performed after a PubMed, Cochrane, Google Scholar search of papers published since 1 January 2000, using the following terms: "pain AND dermatology". Additional searches were performed with each identified painful situation: eczema, psoriasis, skin surgery, shingles, ulcers, pain repercussions, etc. Articles in a language other than English or French were excluded. Articles were initially selected based on the title, and then on the abstract. The full text of all potentially relevant articles was retrieved for detailed evaluation. Reference citations within identified articles were also searched for relevant evidence.

Chronic pain from certain skin disorders

A 2017 French study analysed the presence and frequency of pain by interviewing more than 1,565 patients with skin disorders (atopic dermatitis (AD), lower limb ulcers, pressure ulcer, psoriasis, sexually transmitted infections, and sensitive skin). The pain was chronic in 25.7% of patients and transitory in 74.3%. Only 59.3% of patients were specifically managed, and 22.6% had a 0–10 visual analogue scale (VAS) >7/10 (7).

Chronic ulcers of the lower limbs. The prevalence of wound-related background pain in a meta-analysis of chronic venous leg ulcers, varies from 46% to 100% (n = 1,446) (8). Ulcer care can be responsible for acute pain: in an observational study, 80% of patients with leg

ulcers (n=1,900) report moderate to severe pain during dressing changes (9). Patients who experience severe pain during dressing care are more likely to experience spontaneous pain (9). Classically, arterial ulcers are known to be very painful due to hypoxia (3). But venous ulcers are also painful and pain is even the main complaint reported by patients (10). A neuropathic component of pain seems to be frequent; a study has shown that 58% (n=81) of patients with leg ulcers are affected (11). An ulcer persisting for more than 90 days and the presence of pain are parameters associated with the presence of depressive symptoms (12). Depression can slow down wound healing (12). Pain diminishes the quality of life: it reduces patients' mobility and consequently reduces physical activity and leads to sleep disorders (13, 14).

Bullous diseases. There are few specific studies into pain in bullous diseases. The presence of pain is intuitively recognized, particularly during care. Concerning superficial pemphigus or pemphigus vulgaris, one study has shown that half of patients report skin pain (**Table I**). It did not find a correlation between pain intensity and pemphigus severity (15). For epidermolysis bullosa (EB), all patients (n=374) with EB in the study by Fine et al. (16) reported pain on walking or standing. Pain due to recessive dystrophic EB is more severe than other subtypes (junctional EB, dominant dystrophic EB, EB simplex) (17). A study into localized EB simplex shows that all patients (n=57) experience pain during flares of blisters or dressing changes (Table I) (18). In recessive dystrophic EB, a neuropathic component related to small fibre neuropathy has been demonstrated (19), and neuropathic component is also found in junctional EB (20) and EB simplex (18). Toxic epidermal necrolysis results in painful care, but there are no specific studies on pain characteristics (21). One study showed that one-third of patients experienced chronic pain 1 year after the reaction, no neuropathic component was found, but chronic pain in this context could be a manifestation of post-traumatic stress syndrome (Table I) (22).

Atopic dermatitis. Skin pain is an important part of AD. Pain is reported by 40–60% of patients with any severity of AD (Table I) (7, 23–25). Thyssen et al. (26) showed that the intensity of skin pain is proportional to the severity of AD. Vakharia et al. (27) also found that severe skin pain is associated with increased severity of AD (23). The most painful areas in Maarouf's study were the excoriated areas as well as the hands, toes, and perioral region. These locations were also found in the

Table I. Data from studies about pain prevalence and characteristics according to skin conditions

Pathologies	Authors, year	Participants n	Skin pain prevalence (%)	Pain evaluation	Mean pain intensity score	Pain type
Chronic venous leg ulcers	Leren et al. 2019 (8)	10 studies, (n=1,446)	46–100% Weighted mean of 80%	NRS 0–10	2.3–6.6/10	Unspecified
Chronic leg ulcers	Meaume et al. 2004 (9)	1,900	Moderate to severe pain at dressing changes: 80%	Subjective 4-point scale: none, minor, moderate or severe		Unspecified
Chronic leg ulcers	Eusen et al. 2016 (11)	81	Unspecified	VAS 0–10	3.9/10	DN4≥3: 58%
Pemphigus	Tamasi et al. 2019 (15)	109	50	VAS 0–100	68/100	Unspecified
Epidermolysis bullosa	Fine et al. 2004 (17)	374	100	VAS 0–10		Unspecified
Epidermolysis bullosa simplex	Brun et al. 2017 (18)	57	100	VAS 0–10 FLACC FPS	7/10 6.8/10 6.8/10	DN4 ≥3: 75%
Epidermal necrolysis	Lefaucheur et al. 2021 (22)	81	36	NRS 0–10	4.7/10	Low neuropathic profile (mean DN4-Interview score: 3.4/7 and mean NPSI score: 25.4/100)
Atopic dermatitis	Misery et al. 2017 (7)	153	54.7	NRS 0–10	Unspecified	DN4 ≥3: 57.5%
	Paras P. Vakharia, 2017 (23)	305	42.7	NRS 0–10	Unspecified	Unspecified
	Silverberg et al. 2019 (25)	365	61	NRS 0–10	4.3/10	Unspecified
	Huet et al. 2020 (24)	185	54.6	VAS 0–10	5.91/10	DN4 ≥3: 73.6%
Psoriasis	Ljosaa et al. 2021 (32)	139	41.7	Patients indicated (yes/no) whether they experienced skin pain or skin discomfort	Unspecified	Unspecified
	Misery et al. 2020 (30)	244	33.2	VAS 0–10	5,83/10	DN4 ≥3: 63.9%
	Patruno et al. 2015 (31)	163	43.6	NRS 0–10	7,1/10	Unspecified
	Misery et al. 2017 (7)	212	51.9	NRS 0–10	Unspecified	DN4 ≥3: 58.3%
	Loft et al. 2021 (34)	4,016 patients with psoriasis of whom 847 had psoriatic arthritis (PsA)	Moderate to severe skin pain: 30% of those with PsA 21% of those without PsA Moderate to severe joint pain: 69% of those with PsA 45% of those without PsA	NRS 0–10 No (NRS of 0) Mild (NRS of 1–3), Moderate (NRS of 4–6) Severe (NRS of 7–10)		Unspecified
Hidradenitis suppurativa	Matusiak et al. 2017 (40)	103	97.1	NRS 0–10 VAS 0–10	4.9/10 4.6/10	Unspecified
	Garcovich et al. 2020 (42)	110	80% reported a 1-year-long pain history	NRS 0–10	5/10	Pain-DETECT questionnaire: "likely neuropathic pain"=30%

NRS: numerical rating scale; VAS: visual analogue scale; FLACC: Face Legs Activity Cry Consolability; FPS: Faces Pain Scale; DN4: Douleur Neuropathique en 4 Questions); PsA: psoriatic arthritis; NPSI: Neuropathic Pain Symptom Inventory.

Thyssen study, which added the thoracic region (26). The skin pain described by patients suggests a neuropathic component (7, 23–25, 28) (see Table I). The pain triggers seem to be similar to those that trigger pruritus: sweating, ambient heat, emotional stress, hot-water baths, rubbing the skin, wearing wool or synthetic clothing (27, 28). Topical calcineurin inhibitors, dermocorticoids and topical crisaborole may cause pain and burning (27, 28). Note that topical calcineurin inhibitor activates TRPV1 channels, which mediates an antipruritic effect, and can cause a burning sensation that disappears with repeated use.

Severe pain is also associated with poor sleep, depressive symptoms and poor quality of life (23). Taking pain into account is therefore important in assessing the impact of AD and to optimize its therapeutic management (28).

It has been shown that pain and pruritus coexist, while it is classically accepted that painful stimuli inhibit the itchy sensation, yet Vakharia (23) showed that 72% ($n=144$) of patients link their pain to scratching and itching, and Maarouf et al. (27) showed that 78% ($n=103$) of patients had itching and associated pain. Ikoma showed that nociceptive stimuli induced pruritus instead of pain in patients with AD, unlike in the healthy control group and the psoriasis group. This study raises the possibility of central pruritus sensitization mediated by C nociceptors, whereby a painful stimulus would induce pruritus instead of pain (29). However, it is not known if the pain is caused by pruritus, which leads to itching and therefore excoriation. The link between pruritus and pain in AD is therefore not yet understood. What is highlighted is that, in AD, the pain and pruritus pathways are not antagonistic, as is generally accepted.

Psoriasis. The prevalence of skin pain is important, affecting 30–50% of patients with psoriasis (see Table I) (7, 30–32). Epidemiologically, the most painful patients are women, with a low socioeducational level, chronic comorbidities and a long duration of psoriasis evolution. On the other hand, the studies are contradictory with regard to the influence of age (31, 33). Regarding the intensity of skin pain, Misery et al. (30) found a median score of 6/10 (numerical rating scale (NRS) 0–10), and Patruno et al. found a median score of 7/10 (NRS 0–10) (31). Moderate to severe joint pain concerned 69% of patients with psoriatic arthritis ($n=847$) and 45% of those without ($n=3,169$) (34) (see Table I). Moreover, skin pain seems to have a neuropathic component for more than half of the patients (7, 30) (see Table I). The most painful areas are the palms, plantar regions, scalp, and genital areas. The lumbosacral region is the least painful. The affected area is not necessarily correlated with the intensity of pain: palmoplantar or inverted psoriasis will be painful, even if the affected area is limited (31, 33). Patients with depression experience more severe skin pain than others, and the reverse is true: patients with skin pain present more symptoms of anxiety or depression (33, 35). Pain is a major contributor to the psychosocial impact of psoriasis, but is largely underestimated in psoriasis severity scores alone. It is not taken into account in the Psoriasis Area and Severity Index (PASI) (36, 37) and is the subject of only one question in the Dermatology Life Quality Index (DLQI) (38). Pain relief is one of the most important criteria for satisfactory treatment according to the patients, along with a reduction in pruritus, a reduction in burning sensations, and skin clearance (33, 39).

Hidradenitis suppurativa. Most patients experience lesion-linked pain in the course of hidradenitis suppurativa (HS) (40) (see Table I). Pain is one of the most debilitating symptoms of HS, it can be acute due to nodules and abscesses during outbreaks, and can become chronic in cases of advanced disease (41, 42). A neuropathic component is also possible in 30% of patients with HS (41, 42) (see Table I). The pain intensity is approximately 5/10 (40, 42) (see Table I) and is more intense than in many dermatological pathologies, such as psoriasis, eczema, acne, or skin tumours (41).

Quality of life is significantly diminished in HS, with sleep disturbances, discomfort in daily activities, discomfort in social and sexual interactions, and depression. The prevalence of depression is higher among people with HS than among those with other dermatological conditions (41).

Post-herpetic neuralgia. In patients with herpes zoster, neuropathic pain appears with a dermatomal distribution that does not cross the midline, which gives way to an erythemato-vesicular eruption (43). Post-herpetic neuralgia is defined as pain persisting for 90 days after acute onset. The risk of post-herpes zoster pain increases with age, lesion size and immunosuppression, especially among those taking anti-tumour necrosis factor (TNF)-alpha drugs (44). People over 70 years of age are at increased risk of more persistent pain (43). Post-herpetic neuralgia significantly impacts quality of life, including the ability to perform activities of daily living, and may lead to depression, chronic fatigue, and weight loss (44).

Neurocutaneous diseases. These pathologies lead to neuropathic pain and/or neuropathic pruritus of the skin due to nerve damage without primary skin lesions. There are different syndromes depending on the location and the nerve involved: e.g. scalp dysesthesia, vulvodynia, brachio-radial pruritus, paraesthetic notalgia, and paraesthetic meralgia (2, 45, 46).

In addition, this category includes small fibre neuropathies that cause autonomic symptoms and sensory symptoms (pain, pruritus, burning) that dominate the limbs in a distal-to-proximal gradient. A diminution of intraepidermal nerve fibre density, which is assessed on skin biopsies, is a major diagnostic criterion (47).

Sensitive skin syndrome. Sensitive skin is a syndrome defined by the Special Interest Group on Sensitive Skin

of the International Forum for the Study of Itch (IFSI): "The occurrence of unpleasant sensations (stinging, burning, pain, pruritus, and tingling sensations) in response to stimuli that normally should not provoke such sensations. These unpleasant sensations cannot be explained by lesions attributable to any skin disease. The skin can appear normal looking or be accompanied by erythema. Sensitive skin can affect all body locations, especially the face (48)". Cosmetics seem to be the main triggering factor of sensitive skin (49).

Acute pain induced by dermatological procedures

Surgical procedures. The consideration of acute postoperative pain is crucial. If it is neglected or underestimated there is a greater risk of complications, such as delayed healing, bleeding, insomnia, cardiovascular

Table II. Proposal of available analgesics tools in dermatology and their indications

Chronic pain management from skin disorders		Acute pain management in dermatological procedures	
Nociceptive pain (e.g. eczema, psoriasis, burn injury, hidradenitis suppurativa, chronic ulcers, bullous diseases)	*Neuropathic pain* (e.g. post-herpetic neuralgia, small-fibre neuropathies, scalp dysesthesia, vulvodynia and to screen for eczema, psoriasis, chronic ulcers)	*Pharmacological interventions*	*Non-pharmacological interventions*
Acetaminophen (WHO level 1) (3, 4, 63) As first-line treatment for mild to moderate pain.	*Pregabalin, gabapentin:* Can be used as a first-line treatment (64–66).	*Acetaminophen:* Can be used 1 h before the procedure as a preventive measure and after the procedure in case of post-operative pain (50).	*Hypnosis* (67–70): Photodynamic therapy (PDT) Neurotoxin or filler injections Laser procedures Skin surgery (in combination with locoregional anaesthesia) Ulcer detersion
Codeine, tramadol (WHO level 2) (3, 4, 63) As first-line treatment for mild to moderate pain and in case of failure of level 1.	*Oxcarbamazepine:* Can be used as a second-line treatment (71).	*AINS (except aspirin):* Can be used in the postoperative setting as a second-line treatment (for up to 7 days) (72) or 1 h before the procedure (50)	*Virtual reality and augmented reality (73, 74):* For anxiolytic purposes. Few studies.
Morphine, oxycodone (WHO level 3) (3, 4, 63, 75) Immediately in case of severe pain, or failure of levels 1 and 2. Combine paracetamol for its synergistic effect.	*Duloxetine, venlafaxine* Can be used as a first-line treatment (65, 76).	*Opioids:* Rarely needed, so it is not advisable to prescribe them routinely (52).	*Cold anaesthesia:* – Applying ice packs or cold air before injection (77, 78) – Pulsed cold air systems for laser procedures (51, 79, 80) – Cryoflurane (81–83): refrigerant spray, can be used for injections (neurotoxins, fillers, locoregional anaesthesia)
	Nortriptyline, amitriptyline Can be used as a second-line treatment (65, 84).	*Topical anaesthetics (54, 57, 85, 86):* Before using an injectable anaesthetic on the face or perineum Neurotoxins or filler injections Laser Ulcer detersion	*Music interventions (77, 87–89):* During surgical procedures
	Lidocaine 5% patch (4, 90): For localized neuropathic pain.	*Locoregional anaesthetics:* Skin surgery, skin biopsy Neurotoxins and filler injections Buffering lidocaine 1%/epinephrine 1:100,000 solution with sodium hydrogen carbonate ($NaHCO_3$) (3/1 ratio) significantly reduces burning pain during infiltration (91).	*Transcutaneous electrical nerve stimulation (TENS) (92):* Applied during PDT the device appears to reduce pain (few studies).
	Topical capsaicin 8% (high-concentration) (4, 93): For localized neuropathic pain. High-concentration topical capsaicin is better than very low- concentration capsaicin.	*Meopa (94):* Paediatric procedures Skin surgery (in combination with locoregional anaesthesia) Photodynamic therapy Laser procedures Ulcer detersion	
	Botulinum toxin injection (95–97): Is still being studied with encouraging results in case of recalcitrant post-herpetic neuralgia and chronic localized pruritus.	*Benzodiazepines (midazolam, alprazolam):* Before the procedure, for the most anxious patients because it has been proven that preoperative anxiety can lead to greater postoperative pain (50, 57).	
	Transcutaneous electrical nerve stimulation (TENS) (92): Promising for treatment of post-herpetic neuralgia, but also for prevention of post-herpetic neuralgia.		

It should be noted that some drugs have not been specifically studied in dermatology: e.g. acetaminophen, codeine, tramadol, morphine, oxycodone, benzodiazepines.
Notes on level of evidence and effectiveness:
pregabalin, gabapentin: Cochrane reviews show moderate-quality evidence of important efficacy on pain in some people with moderate or severe neuropathic pain after shingles, or due to diabetes (64, 66).
Oxcarbazepine: Cochrane review found "little evidence to support the effectiveness of oxcarbazepine in painful diabetic neuropathy, neuropathic pain from radiculopathy and mixed neuropathies of various causes" (71).
Duloxetine, venlafaxine: "There is moderate quality evidence of duloxetine are efficacious for treating pain in diabetic peripheral neuropathy" according to a Cochrane review.
Nortriptyline, amitriptyline: Cochrane review found "little evidence to support the use of nortriptyline to treat the neuropathic pain conditions (cancer-related neuropathy, painful diabetic neuropathy, post-herpetic neuralgia …)" (65). There is no convincing evidence about the effectiveness of amitriptyline according to Cochrane review. Amitriptyline probably does provide good pain relief to some people with neuropathic pain, but only a minority of them (84).
Lidocaine patch: Cochrane review found no evidence from good-quality randomized controlled studies to support the use of topical lidocaine to treat neuropathic pain (mainly in post-herpetic neuralgia), but clinical experience supports efficacy in some patients (90).
Topical capsaicin 8%: high-concentration topical capsaicin generated moderate or substantial levels of pain relief (post-herpetic neuralgia, HIV neuropathy, painful diabetic neuropathy). The quality of the evidence was moderate or very low according to a Cochrane review (93).

sequelae, and a risk of chronic pain, substance abuse and negative psychological repercussions (50).

The mean pain score during surgical procedures and biopsies, found by Talour et al. (51), is 2.2/10 (NRS 0–10), which corresponds to the pain associated with injection of the anaesthetic. The pain is rather mild to moderate in Mohs' surgery (50); between 2.5/10 and 3.5/10 (51–53) (NRS 0–10). Although surgical procedures and biopsies are well tolerated by patients, with a local anaesthetic usually deemed appropriate, administration of the anaesthesia is painful for most patients (88.5%, $n=120$). On average, this pain is evaluated at a level of 2.8/10 (VAS 0–10) (54). The pain is maximal on the day of surgery (52, 53, 55, 56), reaches its peak at 4 h, and decreases sharply 12 h after the intervention (57). Forty to 50% ($n=212$ and $n=433$, respectively) of patients used an analgesic postoperatively, especially on the first day, and the majority used acetaminophen (52, 55). A single dose of acetaminophen is sufficient in the majority of cases (53). The consumption of opiates varies from 7% to 20% ($n=433$ and $n=212$, respectively) (52, 55, 56). The most painful locations are the extremities, the axillary hollow, and the head (51, 55), and, especially on the face: the lips, the nose, ears, and forehead (58). The perineum is also a painful localization, especially for injection of an anaesthetic. In the absence of premedication by topical application, 42% ($n=18$) of patients with perineal lesions prefer general anaesthesia, and this proportion is increased if the size of the lesion is large (>2 cm) (54). The sites least prone to significant postoperative pain are the trunk and limbs (51, 55).

The characteristics of the surgery, the number of anatomical sites operated on the same day or the type of closure may influence the intensity of postoperative pain, but the results are contradictory among studies (52, 55, 56).

Preoperative anxiety and "pain catastrophization" lead to higher postoperative pain scores, and anxiety plays a role in the risk of chronic postoperative pain (57, 59).

Photodynamic therapy. Pain during photodynamic therapy (PDT) is the main limiting adverse effect the use of this technique in dermatology (60). Traditional topical and oral anaesthetics are ineffective in PDT (61). No significant correlation has been found between pain during PDT and age or sex (61, 62). Lesions on the face and scalp are more painful than other body sites, and larger lesions are more painful during PDT (60, 61). Actinic keratosis is more painful than basal cell carcinoma (62). PDT using a MAL or 5-aminolevulinic acid methyl ester (METVIXIA*) photosensitizer is less painful than using ALA or 5-aminolevulinic acid (AMELUZ*) (60). Daylight PDT is less painful than conventional red light PDT, or may even be painless, but the efficiency is similar (61, 62).

In conlusion, pain in dermatology occurs in a variety of circumstances and is inherent in a large number of skin disorders. It is widely known and studied for some conditions, such as ulcers or zoster. However, pain is less recognized in certain common pathologies, such as AD or psoriasis, even though its relief is among the most important criteria according to patients. In addition, pain and itch are generally regarded as antagonistic, but they coexist in many of dermatoses, highlighting that although separate specific pathways have been identified, the mechanisms underlying pain and itch overlap.

Moderate to severe pain has a strong negative impact on quality of life. In particular, it alters the quality and quantity of sleep, interferes with activities of daily living, social interactions, school or professional performance, sexual relations, and causes depressive symptoms, etc. Therefore, pain management is important, and dermatologists must be able to propose appropriate therapies and master the main analgesic tools (**Table II**; (63–97)).

Conflicts of interest: H-V have no conflicts of interest to declare. LM: Galderma, Lilly, Pfizer: speaker, investigator, consultant, and Pierre Fabre: speaker, consultant.

REFERENCES

1. Terminology | International Association for the Study of Pain. International Association for the Study of Pain (IASP). [accessed 2021 Sept 1]. Available from: https: //www.iasp-pain.org/resources/terminology/.
2. Al-Ghazawi FM, Ramien ML, Brassard A, Shear NH, Beecker J. Management of pain associated with selected conditions in dermatology. Am J Clin Dermatol 2016; 17: 463–474.
3. Beiteke U, Bigge S, Reichenberger C, Gralow I. Pain and pain management in dermatology. J Dtsch Dermatol Ges 2015; 13: 967–987.
4. Enamandram M, Rathmell JP, Kimball AB. Chronic pain management in dermatology: a guide to assessment and nonopioid pharmacotherapy. J Am Acad Dermatol 2015; 73: 563–573; quiz 573–574.
5. Misery L, Ständer S. Pruritus, 2nd edn. USA, Springer International Publishing.
6. Rafaa M, de la Tour A, Sigal M-L. Prise en charge de la douleur en dermatologie: aspects fondamentaux. Ann Dermatol Venereol 2011; 138: 436–441.
7. Misery L, Saint Aroman M, Zkik A, Briant A, Martin L, Sigal M-L, et al. Chronic pain in patients with skin disorders. Acta Derm Venereol 2017; 97: 986–988.
8. Leren L, Johansen E, Eide H, Falk RS, Juvet LK, Ljoså TM. Pain in persons with chronic venous leg ulcers: a systematic review and meta-analysis. Int Wound J 2020; 17: 466–484.
9. Meaume S, Téot L, Lazareth I, Martini J, Bohbot S. The importance of pain reduction through dressing selection in routine wound management: the MAPP study. J Wound Care 2004; 13: 409–413.
10. Green J, Jester R, McKinley R, Pooler A. The impact of chronic venous leg ulcers: a systematic review. J Wound Care 2014; 23: 601–612.
11. Eusen M, Brenaut E, Schoenlaub P, Saliou P, Misery L. Neuropathic pain in patients with chronic leg ulcers. J Eur Acad Dermatol Venereol 2016; 30: 1603–1605.
12. Zhou K, Jia P. Depressive symptoms in patients with wounds: a cross-sectional study. Wound Repair Regen 2016; 24: 1059–1065.
13. González-Consuegra RV, Verdú J. Quality of life in people with venous leg ulcers: an integrative review. J Adv Nurs 2011; 67: 926–944.
14. Persoon A, Heinen MM, van der Vleuten CJM, de Rooij MJ, van de Kerkhof PCM, van Achterberg T. Leg ulcers: a review of their impact on daily life. J Clin Nurs 2004; 13: 341–354.
15. Tamási B, Brodszky V, Péntek M, Gulácsi L, Hajdu K, Sárdy

M, et al. Validity of the EQ-5D in patients with pemphigus vulgaris and pemphigus foliaceus. Br J Dermatol 2019; 180: 802–809.
16. Fine J-D, Johnson LB, Weiner M, Suchindran C. Assessment of mobility, activities and pain in different subtypes of epidermolysis bullosa. Clin Exp Dermatol 2004; 29: 122–127.
17. Brun J, Chiaverini C, Devos C, Leclerc-Mercier S, Mazereeuw J, Bourrat E, et al. Pain and quality of life evaluation in patients with localized epidermolysis bullosa simplex. Orphanet J Rare Dis 2017; 12: 119.
18. von Bischhoffshausen S, Ivulic D, Alvarez P, Schuffeneger VC, Idiaquez J, Fuentes C, et al. Recessive dystrophic epidermolysis bullosa results in painful small fibre neuropathy. Brain 2017; 140: 1238–1251.
19. Schräder NHB, Yuen WY, Jonkman MF. Pain quality assessment scale for epidermolysis bullosa. Acta Derm Venereol 2018; 98: 346–349.
20. Valeyrie-Allanore L, Ingen-Housz-Oro S, Colin A, Thuillot D, Sigal M-L, Binhas M. Prise en charge de la douleur dans le syndrome de Stevens-Johnson/Lyell et les autres dermatoses bulleuses étendues. Ann Dermatol Venereol 2011; 138: 694–697; quiz 692–693, 698.
21. Lefaucheur J-P, Valeyrie-Allanore L, Ng Wing Tin S, Abgrall G, Colin A, Hajj C, et al. Chronic pain: a long-term sequela of epidermal necrolysis (Stevens-Johnson syndrome/toxic epidermal necrolysis) – prevalence, clinical characteristics and risk factors. J Eur Acad Dermatol Venereol 2021; 35: 188–194.
22. Vakharia PP, Chopra R, Sacotte R, Patel KR, Singam V, Patel N, et al. Burden of skin pain in atopic dermatitis. Ann Allergy Asthma Immunol 2017; 119: 548–552.e3.
23. Huet F, Shourick J, Séité S, Taïeb C, Misery L. Pain in atopic dermatitis: an online population-based survey. Acta Derm Venereol 2020; 100: adv00198.
24. Silverberg JI, Gelfand JM, Margolis DJ, Boguniewicz M, Fonacier L, Grayson MH, et al. Pain is a common and burdensome symptom of atopic dermatitis in united states adults. J Allergy Clin Immunol Pract 2019; 7: 2699–2706.e7.
25. Thyssen JP, Halling-Sønderby A-S, Wu JJ, Egeberg A. Pain severity and use of analgesic medication in adults with atopic dermatitis: a cross-sectional study. Br J Dermatol 2020; 182: 1430–1436.
26. Maarouf M, Kromenacker B, Capozza KL, Kempton D, Hendricks A, Tran K, et al. Pain and itch are dual burdens in atopic dermatitis. Dermatitis 2018; 29: 278–281.
27. Misery L, Belloni Fortina A, El Hachem M, Chernyshov P, von Kobyletzki L, Heratizadeh A, et al. A position paper on the management of itch and pain in atopic dermatitis from the International Society of Atopic Dermatitis (ISAD)/Oriented Patient-Education Network in Dermatology (OPENED) task force. J Eur Acad Dermatol Venereol 2021; 35: 787–796.
28. Ikoma A, Fartasch M, Heyer G, Miyachi Y, Handwerker H, Schmelz M. Painful stimuli evoke itch in patients with chronic pruritus: central sensitization for itch. Neurology 2004; 62: 212–217.
29. Misery L, Shourick J, Taieb C. Skin pain and psoriasis. J Am Acad Dermatol 2020; 83: 245–246.
30. Patruno C, Napolitano M, Balato N, Ayala F, Megna M, Patrì A, et al. Psoriasis and skin pain: instrumental and biological evaluations. Acta Derm Venereol 2015; 95: 432–438.
31. Ljosaa TM, Bondevik H, Halvorsen JA, Carr E, Wahl AK. The complex experience of psoriasis related skin pain: a qualitative study. Scand J Pain 2020; 20: 491–498.
32. Pithadia DJ, Reynolds KA, Lee EB, Wu JJ. Psoriasis-associated cutaneous pain: etiology, assessment, impact, and management. J Dermatolog Treat 2019; 30: 435–440.
33. Loft N, Nguyen TT, Kristensen LE, Thyssen JP, Egeberg A. Disease burden, symptoms, and use of analgesics in patients with psoriasis with or without psoriatic arthritis: a cross-sectional study. J Am Acad Dermatol 2021; 86: 590–597.
34. Gallo L, Megna M, Cirillo T, Caterino P, Lodi G, Mozzillo R, et al. Psoriasis and skin pain: real-life effectiveness of calcipotriol plus betamethasone dipropionate in aerosol foam formulation. J Eur Acad Dermatol Venereol 2019; 33: 1312–1315.
35. Feldman SR, Krueger GG. Psoriasis assessment tools in clinical trials. Ann Rheum Dis 2005; 64: ii65–68; discussion ii69–73.
36. Ljosaa TM, Stubhaug A, Mork C, Moum T, Wahl AK. Improvement in Psoriasis Area and Severity Index score predicts improvement in skin pain over time in patients with psoriasis. Acta Derm Venereol 2013; 93: 330–334.
37. Finlay AY. Quality of life assessments in dermatology. Semin Cutan Med Surg 1998; 17: 291–296.
38. Blome C, Gosau R, Radtke MA, Reich K, Rustenbach SJ, Spehr C, et al. Patient-relevant treatment goals in psoriasis. Arch Dermatol Res 2016; 308: 69–78.
39. Matusiak Ł, Szczęch J, Kaaz K, Lelonek E, Szepietowski JC. Clinical characteristics of pruritus and pain in patients with hidradenitis suppurativa. Acta Derm Venereol 2018; 98: 191–194.
40. Patel ZS, Hoffman LK, Buse DC, Grinberg AS, Afifi L, Cohen SR, et al. Pain, psychological comorbidities, disability and impaired qualify of life in hidradenitis suppurativa. Curr Pain Headache Rep 2017; 21: 49.
41. Garcovich S, Muratori S, Moltrasio C, Buscemi AA, Giovanardi G, Malvaso D, et al. Prevalence of neuropathic pain and related characteristics in hidradenitis suppurativa: a cross-sectional study. J Clin Med 2020; 9: E4046.
42. Le P, Rothberg M. Herpes zoster infection. BMJ 2019; 364: k5095.
43. Guenther LC, Lynde CW. A refresher on herpes zoster, current status on vaccination, and the role of the dermatologist. J Cutan Med Surg 2011; 15: 185–191.
44. Shumway NK, Cole E, Fernandez KH. Neurocutaneous disease: neurocutaneous dysesthesias. J Am Acad Dermatol 2016; 74: 215–228; quiz 229–230.
45. Zagarella S. Nerve entrapment syndromes in dermatology: review and practical approach to treatment. Australas J Dermatol 2018; 59: 286–290.
46. Misery L, Bodere C, Genestet S, Zagnoli F, Marcorelles P. Small-fibre neuropathies and skin: news and perspectives for dermatologists. Eur J Dermatol 2014; 24: 147–153.
47. Misery L, Ständer S, Szepietowski JC, Reich A, Wallengren J, Evers AWM, et al. Definition of sensitive skin: an expert position paper from the special interest group on sensitive skin of the International Forum for the Study of Itch. Acta Derm Venereol 2017; 97: 4–6.
48. Misery L, Weisshaar E, Brenaut E, Evers AWM, Huet F, Ständer S, et al. Pathophysiology and management of sensitive skin: position paper from the special interest group on sensitive skin of the International Forum for the Study of Itch (IFSI). J Eur Acad Dermatol Venereol 2020; 34: 222–229.
49. Glass JS, Hardy CL, Meeks NM, Carroll BT. Acute pain management in dermatology: risk assessment and treatment. J Am Acad Dermatol 2015; 73: 543–560; quiz 561–562.
50. Talour K, Schollhammer M, Garlantezec R, Quinio B, Misery L. Facteurs prédictifs de la douleur dans les gestes techniques dermatologiques. Ann Dermatol Venereol 2013; 140: 5–14.
51. Harris K, Curtis J, Larsen B, Calder S, Duffy K, Bowen G, et al. Opioid pain medication use after dermatologic surgery: a prospective observational study of 212 dermatologic surgery patients. JAMA Dermatol 2013; 149: 317–321.
52. Lopez JJ, Warner NS, Arpey CJ, Baum CL, Brewer JD, Otley CC, et al. Opioid prescribing for acute postoperative pain after cutaneous surgery. J Am Acad Dermatol 2019; 80: 743–748.
53. Beqqal K, Debie J, Constantin S, Chau E, Burnouf M, Stephanazzi J, et al. Evaluation of local anesthesia and pain control in dermatological surgery: a prospective study of 120 patients. Eur J Dermatol 2010; 20: 349–353.
54. Firoz BF, Goldberg LH, Arnon O, Mamelak AJ. An analysis of pain and analgesia after Mohs micrographic surgery. J Am Acad Dermatol 2010; 63: 79–86.
55. Limthongkul B, Samie F, Humphreys TR. Assessment of postoperative pain after Mohs micrographic surgery. Dermatol Surg 2013; 39: 857–863.
56. Theunissen M, Peters ML, Bruce J, Gramke H-F, Marcus MA. Preoperative anxiety and catastrophizing: a systematic review and meta-analysis of the association with chronic postsurgical pain. Clin J Pain 2012; 28: 819–841.

57. Sniezek PJ, Brodland DG, Zitelli JA. A randomized controlled trial comparing acetaminophen, acetaminophen and ibuprofen, and acetaminophen and codeine for postoperative pain relief after Mohs surgery and cutaneous reconstruction. Dermatol Surg 2011; 37: 1007–1013.
58. Chen AF, Landy DC, Kumetz E, Smith G, Weiss E, Saleeby ER. Prediction of postoperative pain after Mohs micrographic surgery with 2 validated pain anxiety scales. Dermatol Surg 2015; 41: 40–47.
59. Fink C, Enk A, Gholam P. Photodynamic therapy – aspects of pain management. J Dtsch Dermatol Ges 2015; 13: 15–22.
60. Wang B, Shi L, Zhang YF, Zhou Q, Zheng J, Szeimies RM, et al. Gain with no pain? Pain management in dermatological photodynamic therapy. Br J Dermatol 2017; 177: 656–665.
61. Ang JM, Riaz IB, Kamal MU, Paragh G, Zeitouni NC. Photodynamic therapy and pain: a systematic review. Photodiagnosis Photodyn Ther 2017; 19: 308–344.
62. Organization WH. Traitement de la douleur cancéreuse. Genève: Organisation mondiale de la Santé. 1987. [Accessed 2021 Jan 26]. Available from: https: //apps.who.int/iris/handle/10665/41712.
63. Wiffen PJ, Derry S, Bell RF, Rice AS, Tölle TR, Phillips T, et al. Gabapentin for chronic neuropathic pain in adults. Cochrane Database Syst Rev 2017; 6: CD007938.
64. Derry S, Wiffen PJ, Aldington D, Moore RA. Nortriptyline for neuropathic pain in adults. Cochrane Database Syst Rev 2015; 1: CD011209.
65. Derry S, Bell RF, Straube S, Wiffen PJ, Aldington D, Moore RA. Pregabalin for neuropathic pain in adults. Cochrane Database Syst Rev 2019; 1: CD007076.
66. Thompson T, Terhune DB, Oram C, Sharangparni J, Rouf R, Solmi M, et al. The effectiveness of hypnosis for pain relief: a systematic review and meta-analysis of 85 controlled experimental trials. Neurosci Biobehav Rev 2019; 99: 298–310.
67. Maillard H, Bara C, Célérier P. Intérêt de l'hypnose dans les injections palmaires de toxine botulique A. Ann Dermatol Venereol 2007; 134: 653–654.
68. Paquier-Valette C, Wierzbicka-Hainaut E, Cante V, Charles S, Guillet G. Évaluation de l'hypnose à visée antalgique dans la photothérapie dynamique: étude pilote. Ann Dermatol Venereol 2014; 141: 181–185.
69. Shenefelt PD. Anxiety reduction using hypnotic induction and self-guided imagery for relaxation during dermatologic procedures. Int J Clin Exp Hypn 2013; 61: 305–318.
70. Zhou M, Chen N, He L, Yang M, Zhu C, Wu F. Oxcarbazepine for neuropathic pain. Cochrane Database Syst Rev 2017; 12: CD007963.
71. Watson Brown T, Nelson S, Nelson T. Should nonselective nonsteroidal anti-inflammatory drugs be avoided following dermatological surgery? A critically appraised topic with a proposed approach to postoperative analgesia. Clin Exp Dermatol 2020; 45: 134–136.
72. Obagi ZA, Rundle CW, Dellavalle RP. Widening the scope of virtual reality and augmented reality in dermatology. Dermatol Online J 2020; 26: 13030/qt6mz1s20x.
73. Higgins S, Feinstein S, Hawkins M, Cockburn M, Wysong A. Virtual reality to improve the experience of the Mohs patient-a prospective interventional study. Dermatol Surg 2019; 45: 1009–1018.
74. Sigal M-L, Rafaa M, Caravias J-L. Prise en charge de la douleur en dermatologie: les opioïdes forts. Ann Dermatol Venereol 2011; 138: 524–529.
75. Lunn MPT, Hughes RAC, Wiffen PJ. Duloxetine for treating painful neuropathy, chronic pain or fibromyalgia. Cochrane Database Syst Rev 2014; CD007115.
76. Gamboa J, Cameron MC, Fathi R, Alkousakis T. A review of non-pharmacologic approaches to enhance the patient experience in dermatologic surgery. Dermatol Online J 2020; 26: qt7mp372nd.
77. Al-Qarqaz F, Al-Aboosi M, Al-shiyab D, Al Dabbagh Z. Using cold air for reducing needle-injection pain. Int J Dermatol 2012; 51: 848–852.
78. Greveling K, Prens EP, Liu L, van Doorn MBA. Non-invasive anaesthetic methods for dermatological laser procedures: a systematic review. J Eur Acad Dermatol Venereol 2017; 31: 1096–1110.
79. Tierney EP, Hanke CW. The effect of cold-air anesthesia during fractionated carbon-dioxide laser treatment: Prospective study and review of the literature. J Am Acad Dermatol 2012; 67: 436–445.
80. Baelen E, Dalmas S, Ducloux B, Scherpereel P. Cryoanesthésie par pulvérisation de fréon pour ponction veineuse chez l'enfant. Ann Fr Anesth Reanim 1994; 13: 6–9.
81. Kontochristopoulos G, Gregoriou S, Zakopoulou N, Rigopoulos D. Cryoanalgesia with dichlorotetrafluoroethane spray versus ice packs in patients treated with botulinum toxin-A for palmar hyperhidrosis: self-controlled study. Dermatol Surg 2006; 32: 873–874.
82. Zhu Y, Peng X, Wang S, Chen W, Liu C, Guo B, et al. Vapocoolant spray versus placebo spray/no treatment for reducing pain from intravenous cannulation: a meta-analysis of randomized controlled trials. Am J Emerg Med 2018; 36: 2085–2092.
83. Moore RA, Derry S, Aldington D, Cole P, Wiffen PJ. Amitriptyline for neuropathic pain in adults. Cochrane Database Syst Rev 2015; 2015: CD008242.
84. Sobanko JF, Miller CJ, Alster TS. Topical anesthetics for dermatologic procedures: a review. Dermatol Surg 2012; 38: 709–721.
85. Cuomo R, D'Aniello C, Grimaldi L, Nisi G, Botteri G, Zerini I, et al. EMLA and lidocaine spray: a comparison for surgical debridement in venous leg ulcers. Adv Wound Care 2015; 4: 358–361.
86. Nilsson U. The anxiety- and pain-reducing effects of music interventions: a systematic review. AORN J 2008; 87: 780–807.
87. Alam M, Roongpisuthipong W, Kim NA, Goyal A, Swary JH, Brindise RT, et al. Utility of recorded guided imagery and relaxing music in reducing patient pain and anxiety, and surgeon anxiety, during cutaneous surgical procedures: a single-blinded randomized controlled trial. J Am Acad Dermatol 2016; 75: 585–589.
88. Kühlmann AYR, de Rooij A, Kroese LF, van Dijk M, Hunink MGM, Jeekel J. Meta-analysis evaluating music interventions for anxiety and pain in surgery. Br J Surg 2018; 105: 773–783.
89. Derry S, Wiffen PJ, Moore RA, Quinlan J. Topical lidocaine for neuropathic pain in adults. Cochrane Database Syst Rev 2014; CD010958.
90. Vent A, Surber C, Graf Johansen NT, Figueiredo V, Schönbächler G, Imhof L, et al. Buffered lidocaine 1%/epinephrine 1: 100,000 with sodium bicarbonate (sodium hydrogen carbonate) in a 3: 1 ratio is less painful than a 9: 1 ratio: a double-blind, randomized, placebo-controlled, crossover trial. J Am Acad Dermatol 2020; 83: 159–165.
91. Visconti MJ, Haidari W, Feldman SR. Transcutaneous electrical nerve stimulation (TENS): a review of applications in dermatology. J Dermatolog Treat 2020; 31: 846–849.
92. Derry S, Rice AS, Cole P, Tan T, Moore RA. Topical capsaicin (high concentration) for chronic neuropathic pain in adults. Cochrane Database Syst Rev 2017; 1: CD007393.
93. Brotzman EA, Sandoval LF, Crane J. Use of nitrous oxide in dermatology: a systematic review. Dermatol Surg 2018; 44: 661–669.
94. Gharib K, Mostafa A, Elsayed A. Evaluation of botulinum toxin type A injection in the treatment of localized chronic pruritus. J Clin Aesthet Dermatol 2020; 13: 12–17.
95. Hu Y, Zou L, Qi X, Lu Y, Zhou X, Mao Z, et al. Subcutaneous botulinum toxin-A injection for treating postherpetic neuralgia. Dermatol Ther 2020; 33: e13181.
96. Kim YS, Hong ES, Kim HS. Botulinum toxin in the field of dermatology: novel indications. Toxins (Basel) 2017; 9: 403.