Dermatological Conditions Inducing Acute and Chronic Pain

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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.

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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 | Meaume et al. 2004 (9) | 1,900 | 46–100% | Subjective 4-point scale: none, minor, moderate or severe | Unspecified |
| Chronic leg ulcers | Meaume et al. 2004 (9) | 1,900 | Moderate to severe pain at dressing changes: 80% | Unspecified |
| Chronic leg ulcers | Eusen et al. 2016 (11) | 81 | Unspecified |
| Pemphigus | Tamasi et al. 2019 (15) | 109 | 50 |
| Epidermolysis bullosa | Fine et al. 2004 (17) | 374 | 100 |
| Epidermolysis bullosa simplex | Brun et al. 2017 (18) | 57 | 100 |
| Epidermal necrolysis | Lefaucheur et al. 2021 (22) | 81 | 36 |
| Atopic dermatitis | Misery et al. 2017 (7) | 153 | 54.7 |
| | Paraz P. Vakharia, 2017 (23) | 305 | 42.7 |
| | Silverberg et al. 2019 (25) | 365 | 61 |
| | Huet et al. 2020 (24) | 185 | 54.6 |
| Psoriasis | Ljosaa et al. 2021 (32) | 139 | 41.7 |
| | Misery et al. 2020 (30) | 244 | 33.2 |
| | Patruno et al. 2015 (31) | 163 | 43.6 |
| | Misery et al. 2017 (7) | 212 | 51.9 |
| | 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 |
| | Hidradenitis suppurativa | Matusiak et al. 2017 (40) | 103 | 97.1 |
| | Garchovich et al. 2020 (42) | 110 | 80% reported a 1-year-long pain history |

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, demeclocycloids 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) | Pharmacological interventions |
| Acetaminophen (WHO level 1) (3, 4, 63) | Acetaminophen: Can be used 1 h before the procedure as a preventive measure and after the procedure in case of post-operative pain (50). |
| As first-line treatment for mild to moderate pain. | |
| Topical capsaicin 8%: (high-concentration) (4, 93): | |
| High-concentration topical capsaicin generated moderate or substantial levels of pain relief (post-herpetic neuralgia, HIV neuropathy, painful diabetic neuropathy) |
| Oxcarbazepine: Can be used as a second-line treatment (71). | |
| Lidocaine 5% patch (4, 90): | |
| For localized neuropathic pain. | |
| Topical capsaicin 8% (high-concentration) (4, 93): | |
| For localized neuropathic pain. | |
| Topical capsaicin 8%: (high-concentration) (4, 93): | |
| For localized neuropathic pain. | |
| Botulinum toxin injection (95–97): | |
| Is still being studied with encouraging results in case of recalcitrant post-herpetic neuralgia and chronic localized pruritus. | |
| Transcutaneous electrical nerve stimulation (TENS) (92): | |
| Promising for treatment of post-herpetic neuralgia, but also for prevention of post-herpetic neuralgia. |

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 (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 areas 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 of 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 conclusion, 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 1; (63–97)).

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