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# Pathogenesis and pathology of shoulder ulcerations in sows with special reference to peripheral nerves and behavioural responses to palpation

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ABSTRACT

Shoulder ulcerations are common in breeding sows in production systems but the consequences for the animals in terms of pain or discomfort are not well-described. This study presents data from a histopathological examination of shoulders of sows, specially focusing on the peripheral nerves in the region and the behavioural responses towards palpation of animals with traumatic neuromas but without ulcers. The study included 155 sows from seven Danish herds initially screened and stratified according to absence/presence and size of shoulder ulcers 3–4 weeks post-partum, out of which 71 were free of ulcerations and 84 had different stages of ulceration. Before collection, sows were subjected to shoulder palpation and behavioural responses were registered. From the consecutive pattern of development of ulcerations it is evident that shoulder ulcerations develop from top-to-bottom.

A high frequency of traumatic neuromas was found in both healed and unhealed lesions. The observation of viable nerve-ends in shoulder ulcerations makes it likely that ulcerations are associated with pain. Moreover, the presence of traumatic neuromas in healed ulcerations indicates that there is discomfort even after the lesions have healed. This is further supported by the behavioural finding that rubbing behaviour in response to palpation was increased on the day of sample collection of the shoulders in sows with traumatic neuromas but without shoulder ulcers ($P = 0.053$). Further studies are needed for final confirmation but these results suggest that shoulder ulcers may be associated with pain even after healing.



## Introduction

Shoulder ulcerations in sows are common in the modern swine industry (Lund et al., 2003; Bonde, 2008; Ivarsson et al., 2009; Kilbride et al., 2009). These lesions are a significant animal welfare problem (Jensen and Svendsen, 2006; Herskin et al., 2011a; Larsen et al., 2012) and are associated with increased risk of infection leading to increased use of antibiotics and rejection of carcasses at meat inspection. To date most research concerning shoulder ulcerations has dealt with possible causes, side effects and ways to prevent or treat the ulcerations (Kaiser et al., 2007, 2010, 2013), whereas the relationship between shoulder ulcerations and the degree of pain or discomfort experienced by the sows has received only limited attention (Herskin et al., 2011a; Larsen et al., 2012).

Shoulder ulcerations can be graded post mortem on a patho-anatomical scale from 0 to 4 (Lund et al., 2003; Jensen, 2009), with the following characteristics: Stage 0, no lesions, or lesions related to biting or fighting; stage 1, lesions are restricted to the epidermis, and may be covered with some crust; stage 2, lesions involve the dermis and are often covered with extensive crust formation and some fibrosis and granulation tissue; stage 3, lesions involve the subcutis, heavy fibrosis and granulation tissue is present; stage 4, necrosis of the bone, excessive periosteal bone proliferation.

Development of shoulder ulcerations is considered to be caused by external pressure against the spine of the scapula, which is covered only by skin and subcutaneous fat tissue (Davies et al., 1997; Jensen and Svendsen, 2006; Kaiser et al., 2007; Herskin et al., 2011a) and has been shown to be related to the duration of sows' lying bouts (Rolandsdotter et al., 2009). Shoulder ulcerations are often compared to human pressure ulcers, but there are some important differences which should be considered. Firstly, human pressure ulcers always develop due to an underlying condition, e.g. in neurologic or paralytic patients, or in patients who are bedridden or wheelchair-bound (Campbell and Parish, 2010). In contrast, porcine shoulder ulcerations develop in otherwise healthy animals (Jensen and Svendsen, 2006). Secondly, human pressure ulcers can develop in two ways, from top-to-bottom where the initial changes occur in the superficial skin layers and progress

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inward, or from bottom-to-top, where deep tissue injury develops under intact skin and later erupts on the surface (Ankrom et al., 2005; Berlowitz and Brienza, 2007; Campbell and Parish, 2010). The latter, bottom-to-top pathogenesis has not been demonstrated in shoulder ulcerations in sows (Jensen, 2008, 2009).

It has been suggested that the pain associated with porcine shoulder ulcerations can be limited in cases with severe necrosis (Reese et al., 2005); human pressure ulcers have also been reported as not necessarily being painful when being debrided (Gist et al., 2009). However, patients with pressure ulcers stages II, III, and IV (stage IV being most severe) have described the pain from the ulcers as 'distressing', 'discomforting', and 'horrible', respectively (Günes, 2009). Furthermore, patients with stage II pressure ulcers often experience 'intermittent pain', whereas patients with stages III and IV pressure ulcers more often experience 'constant pain' (Günes, 2009). Furthermore, in pigs a possible positive relation between behavioural responses toward palpation and ulcer depth has been suggested (Jensen et al., 2011), indicating that even though the central part of an ulcer is necrotic, the tissues surrounding it are still capable of sensing pain. One behaviour suggested to be indicative of shoulder pain in sows is rubbing (Herskin et al., 2009) and recently Larsen et al. (2012) observed the undisturbed behaviour of sows with shoulder ulcers vs. control sows, and found that the ulcers were associated with increased rubbing behaviour.

A traumatic neuroma is a peripheral nerve's attempt to self-repair after injury. The axons of the proximal nerve-end sprout and form a disorderly bundle embedded in fibrous tissue (Summers et al., 1995; Foltán et al., 2008). In humans, traumatic neuromas are often painful and can be associated with increased pain sensitivity as well as periods of non-evoked pain (Zimmermann, 2001; Lewin-Kowalik et al., 2006; Dorsi et al., 2008). Traumatic neuromas have been described in animals and humans, e.g. in docked tails of pigs (Simonsen et al., 1991), in rats which are often used as animal models for neuroma formation in humans (Dorsi et al., 2008), and post-surgically in humans, e.g. after mastectomy (Wang et al., 2007), radical neck dissection (Huang et al., 2000), or amputations (Sehirlioglu et al., 2009). Information about the presence or absence of traumatic neuromas in the shoulder regions of sows with shoulder ulcers would be an important part of evaluating the consequences of the ulcers in terms of pain, but to date this has not been evaluated.

The present study was performed in connection with a study that developed a clinical scale suitable for grading of shoulder ulcerations in living sows (Jensen et al., 2011) and presents data from a thorough histopathological examination of shoulders of sows, focusing especially on the pathogenesis and pathology of shoulder ulcers and the peripheral nerves in the region, as well as on the behavioural responses of the animals towards palpation.

## Materials and methods

### Tissue samples

A total of 155 shoulders originating from sows in seven Danish production herds were examined. All the sows were in their third or fourth week of lactation and ranged in age from single to multiple parities. Data were collected from September 2009 to January 2010. The sampling of shoulders was stratified according to: (1) the absence or presence of clinically visible scar tissue when the sows were transferred to the farrowing unit, and (2) the absence or presence as well as size (smaller or larger than 5 cm in diameter) of a shoulder ulcer at weeks 3–4 of lactation. The sampling pattern ensured that shoulders with ulcerations in different stages, shoulders without ulcerations and shoulders with and without visible scar formation were all included in the study. A scar was defined as a round, well-defined area of the skin covering the shoulder with loss of hair.

The shoulders were cross-sectioned and grossly evaluated as previously described (Jensen, 2009), followed by tissue sampling for histology. When an ulcer was present, representative tissue samples were taken from the central part of the ulcer. When no ulcer was present, tissue samples were taken from the tissues overlaying the spine of the scapula, i.e. epidermis, dermis, and subcutis. The osseous tissue of the spine of the scapula was in all cases sampled for histology.

### Histology and immunohistochemistry

Tissue samples were fixed in 10% neutral buffered formalin for 3 days, then processed through graded concentrations of ethanol and xylene and finally embedded in paraffin wax. Tissue sections were cut at 4–5 μm and stained with haematoxylin and eosin (HE). Samples including the spine of the scapula were decalcified for 3 weeks in 85% formic acid and processed as above (Bancroft and Gamble, 2008).

Two immunohistochemical stains were applied in selected cases for optimized visualization of the outline of nerves. For immunohistochemistry, tissue slides were deparaffinised, blocked for endogenous peroxidase and treated with primary antibodies towards S-100 (polyclonal rabbit anti-s-100, 1:3000, Dako) and glial fibrillary acidic protein (GFAP) (polyclonal rabbit anti-glial fibrillary acidic protein, 1:100, Dako), as recently described (Nielsen et al., 2011). Masson's trichrome stain was used for optimized characterization of granulation tissue and fibrosis. Toluidine blue stain was used for visualization of glycosaminoglycans (GAGs) (Bancroft and Gamble, 2008).

### Evaluation

Apart from characterization of the ulcerations at gross examination, the degree of fibrosis (⩽2.0 mm; >2.0 mm but ⩽5.0 mm; >5.0 mm) and the presence of haemorrhages and oedema in the subcutis overlaying the spine of the scapula were recorded. Based on macroscopic and histological observations on the cross-sectioned shoulders, lesions were grouped as follows: Group A = no lesions, Group B = patho-anatomical stages 1 + 2, and Group C = patho-anatomical stages 3 + 4.

### Behavioural registrations and data processing

On the day of sample collection, the shoulder regions of the sows were subject to standardized palpation while the sows were standing in their farrowing crate. A 15 cm diameter area surrounding the spine of the scapula was examined in all sows and the occurrence of rubbing behaviour (the sow performed rubbing movements with the shoulder region against the fixtures of the stall (Herskin et al., 2009)) in response to palpation was registered using 1/0-sampling (Martin and Bateson, 2007).

After pathological evaluation of the shoulders, behavioural data were selected in order to characterize the behavioural responses of sows without lesions, and split according to the presence of traumatic neuromas. Behavioural data from Group B and C sows have been reported elsewhere (Herskin et al., 2011b) and showed that the occurrence of rubbing increased with increasing pathological stage (up to 24% in Group B and 33% in Group C, respectively; $P < 0.05$).

## Results

### Group A: No lesions in the shoulder region

Seventy-one shoulder regions had no ulcers and belonged to Group A. These had the following features at gross inspection: intact skin, loss of hair, varying degrees of redness of the skin and thickening of the epidermis. In cross-section, haemorrhages and oedema (Fig. 1) were present in the subcutis of more than half of the cases (Table 1). A low grade fibrosis (Fig. 2) was only observed in a few cases at gross examination (Table 1). Histologically, the tissues of Group A included areas of haemorrhage and oedema in the subcutis, corresponding to the gross observations, but this was never accompanied by necrosis. In 38% of the cases, traumatic neuromas surrounded by fibrosis (Fig. 3) were present in the subcutis (Table 1). The presence of traumatic neuromas was associated with further fibrosis in subcutis of almost all cases (Table 2) but not whether there was a visible scar at the time of movement to the farrowing unit (Table 3).

The behavioural analyses showed that within Group A sows, rubbing behaviour was observed in a larger proportion of sows with traumatic neuromas than in sows without neuromas (11% vs. 0%, respectively; Fisher's exact test: $P = 0.053$). In all cases of rubbing behaviour the sows also had fibrosis in the subcutis.