

# Treatment of coronary infections with Intra Repiderma

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## **Swine lameness**

When a sow is lame, it leads to lower feed intake (especially during lactation), decreased reproductive performance and ultimately early exit from the herd. Intra Repiderma, developed and produced by Intracare, can help farmers with the treatment of claw lesions, this to increases swine welfare and help to improve the efficiency of pork production through the treatment and prevention of lameness.

## **Diseases of the Foot**

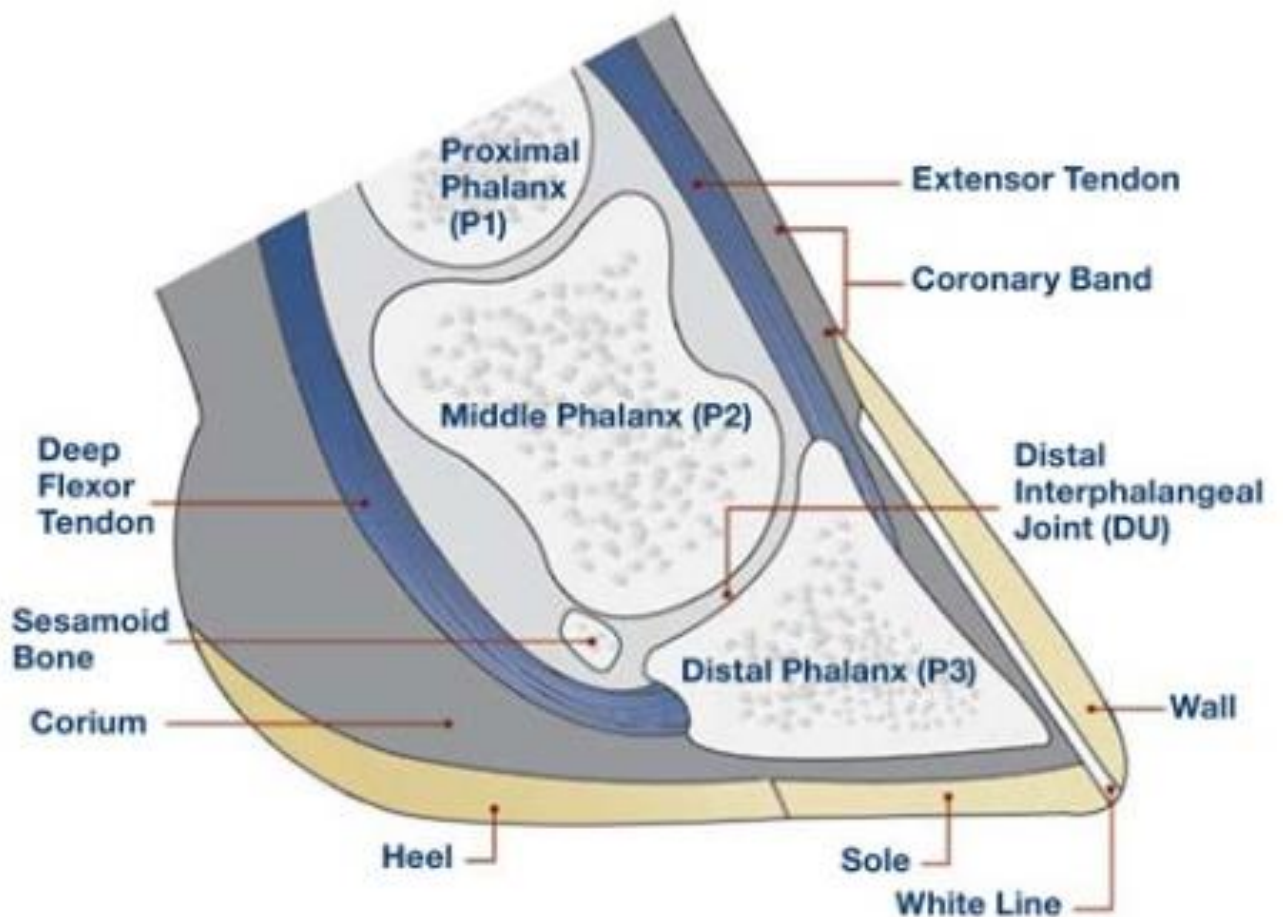
Foot lesions fall into two main categories—either the sole or heel is damaged by the floor, or the hoof wall is traumatized by the sow standing on a pig's foot or by entrapment in the flooring.

Bruises or lacerations can develop on either the sole or heel. The lesions are associated with worn and rough floor surfaces and with floors that have solid as well as perforated surfaces. Rough flooring can also cause bruising in soft tissue below the hoof wall. If spaces between slats are large, digits can be entrapped, and lameness results from bruising or infection at the

coronary band. Pigs on expanded metal floors can incur heel and wall injuries leading to loss of accessory digits. Second and third digits may be damaged as the pigs thrust with their feet during suckling and catch their toes against sharp metal edges.

### Coronary band infection

The most common claw lesions within a sow herd can vary based on several factors including management, nutrition and genetics. The lesions of greatest concern are those which penetrate the horn wall into the corium of the foot and cause an inflammatory response. These types of lesions cause pain and locomotion problems. One big problem of claw related lesions are coronary band infections that are located just above the claw, more and more farmers experience problems with this type of lesion.



**Figure 1.** - Cross section of a pig claw with the location of the coronary band

The main attributers to coronary band infection are:

- Bad floors
- Fighting between sows
- Floor surface is too wet
- Not enough ventilation

Coronary band infection is an infection of the claw, which becomes swollen and extremely painful around the coronary band (the area where the hoof meets the skin of the leg). It usually starts through an opening on the sole of the foot (caused by a puncture wound or cut), cracks at the coronary band, or from hoof splitting. The infection enters through the crack, or puncture wound, and progresses inside the hoof. The claw becomes swollen and infection and inflammation of the joint often develops. Because the bone of the foot is so close to this area, osteomyelitis (an infection in the bone) can occur and destroy those bones in the foot if left untreated. Signs to look for include lameness/limping, swollen claw, or swelling and heat around the coronary band, which may form an abscess on the surface.



**Figure 2.** - Typical example of a coronary band infection.

The infection does not heal spontaneously and requires intensive treatment. Untreated sows cannot walk anymore, resulting in less feed consumption. In many cases, these sows are euthanized.

Treatment of this condition requires a high dose of antibiotics for longer time periods, since a poor blood supply travels to the infected tissue. Also, topical treatment and foot wraps to keep the abscess clean and prevent further infection may be required.

Because of the weight of an adult domestic pig, prevention of this condition is difficult. Walking on frozen, rutted ground, or stepping on sharp stones, can cause cuts in the foot pads. Cracks are also a problem in older pigs due to the large amount of weight they carry.



**Figure 3.** – Pigs lying on a metal surface.

### **Intra Repiderma**

Intra Repiderma is a skin care product with an immediate effect. The active ingredients are chelated minerals which - unlike traditional minerals - can be absorbed easily by the skin. Therefore, Repiderma is not only active 'on' the skin, but also 'under and within' the skin. This process is intensified because the chelated minerals are micronized, using the latest nanotechnology techniques. Minerals are ground into tiny particles of app. 3 µm, using specialized equipment. This is 25,000 times smaller than a sand grain. As a result, the particles quickly penetrate deeply into the skin.

### **Adhesion and protection**

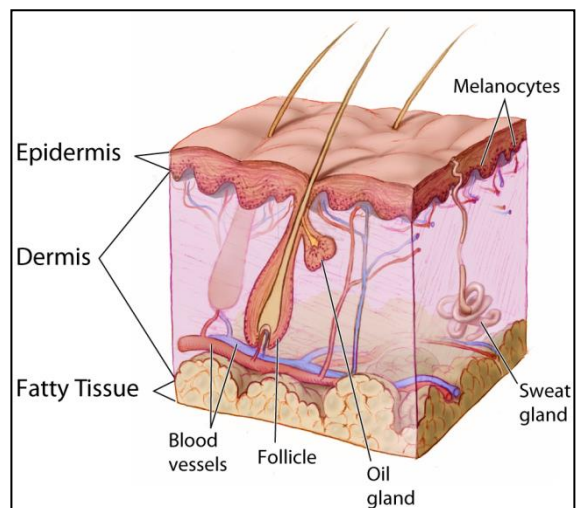
Intra Repiderma contains adhesive substances, ensuring a long contact time with the skin. In addition to these adhesive substances, Intra Repiderma contains numerous active ingredients that protect the skin against external influences. After applying the spray, Intra Repiderma forms a covering layer on the skin.

## Mode of action

### The skin and cutaneous wound healing

The skin is the largest organ of the body and it fulfills an important role in the defense against pathogens, regulation of the body temperature, and the prevention from dehydration. The skin consist of two major layers: The dermis with on top the epidermis (**Fig. 4**). The dermis is the thickest layer and consists of a loose layer of connective tissue (mainly type I collagen and elastic fibers), containing collagen-producing fibroblasts as the major cell type. The dermis is covered with the epidermis: a relatively thin layer of densely packed cells called keratinocytes. At the basal layer, these keratinocytes are quite undifferentiated, and while moving upwards they slowly differentiate to form the protecting cornified horny layer.

When the skin is wounded, the wound healing process is activated to restore its structure and protective function as quickly as possible. The classic model of wound healing comprises three sequential, yet overlapping, phases: (1) inflammation, (2) proliferation and (3) remodeling. Within the first few minutes after the injury, platelets join together at the injury site to form a fibrin clot, which reduces active bleeding (hemostasis). During the inflammation phase, bacteria and cell debris are phagocytosed and removed from the wound by white blood cells. The proliferation phase is characterized by angiogenesis, collagen deposition, granulation tissue formation, epithelialization, and wound contraction. Vascular endothelial cells form new blood vessels (angiogenesis), fibroblasts grow and form a new, provisional extracellular matrix (ECM) by excreting collagen and fibronectin. Concurrently, re-epithelialization of the epidermis occurs, whereby epithelial cells proliferate and 'crawl' over the wound bed, covering the new tissue. During maturation and remodeling, collagen is remodeled and realigned along tension lines, and apoptosis removes unnecessary cells.



**Figure 4.** – Schematic representation of the layers and components of the skin

### **Antimicrobial properties of copper**

Copper at low concentrations is required for living organisms, including bacteria. At higher concentrations however, copper can be bactericidal or bacteriostatic. The bactericidal properties of copper have been known for many years and this has been used as a disinfectant for veterinary purposes and in the food industry. Several metal ions, especially heavy metals like copper and zinc, show this so-called oligodynamic effect to various degrees. Bacteria are in general affected by the oligodynamic effect, but the exact mechanism of action is still unknown. Data from silver suggest that these ions denature enzymes of the target cell or organism by binding to reactive groups, resulting in their precipitation and inactivation.

For copper, it has been suggested that the antibacterial effects are caused by different mechanisms including substitution of essential ions and blocking of functional groups of proteins, inactivation of enzymes, production of hydroperoxide free radicals by membrane bound copper and alterations of membrane integrity (Fáundez, 2004). Copper toxicity is caused mainly by the intrinsic properties of copper, as free copper ions undergo redox cycling reactions alternating between Cu(I) and Cu(II) (Santo, 2010).

### **The role of copper in cutaneous wound healing**

Besides the bactericidal and bacteriostatic effects, copper also has an effect in wound repair (Sen, 2002). An important aspect of wound healing is the formation of new blood vessels (angiogenesis). The most prevalent, efficacious, and long-term signal to stimulate angiogenesis in wound healing is the vascular endothelial growth factor (VEGF) (Stefanini, 2008). It induces migration and proliferation of endothelial cells and enhances vascular permeability consistent with the purported ability to promote angiogenesis. The expression of VEGF is copper sensitive, which means that when Cu<sup>2+</sup> is topically applied, the wound healing process is accelerated. Another effect of topical Cu<sup>2+</sup> is the accelerated closure of dermal wounds (Sen, 2002). In addition, copper is required for a proper functioning of the extracellular matrix protein lysyl oxidase (LOX), that is responsible for the crosslinking and thus stabilization and maturation of collagen and elastin, which is an important aspect of the wound healing process. The authors conclude that copper-based therapeutics are a feasible approach to improve wound healing, also given the fact that topical application of copper is simple and copper is effectively absorbed by the skin.

Keratinocytes express transmembrane receptors called integrins that mediate the attachment between a cell and its surroundings, such as other cells or the extracellular matrix (ECM). Some integrins expressed by basal layer keratinocytes play an essential part in wound healing, whose expression and distribution in epidermis are modified during the re-epithelialization phase. The inductive effect of zinc was particularly notable on integrins affecting cellular mobility in the proliferation phase of wound healing (alpha3, alpha6, alphaV) and that of copper on integrins expressed by suprabasally differentiated keratinocytes during the final healing phase (alpha2, beta1 and alpha6) (Tenaud, 1999).

### **The role of zinc in cutaneous wound healing**

Zinc is an essential element for both animals and humans. In the skin, zinc is located intracellularly and in extracellular matrix in epidermal and dermal tissues in the form of protein complexes where zinc acts as a stabilizer of cell membranes and an essential cofactor, and satisfies a central role in mitosis, migration, and maturation (Lansdown, 2007). It serves as a cofactor for numerous transcription factors and enzyme systems including the zinc-dependent matrix metalloproteinases. These metalloproteinases are enzymes capable of degrading essentially all components of the extracellular matrix and are upregulated after injury and involved in matrix remodeling and keratinocyte migration during wound repair. Zinc deficiency of hereditary or dietary cause can lead to pathological changes and delayed wound healing.

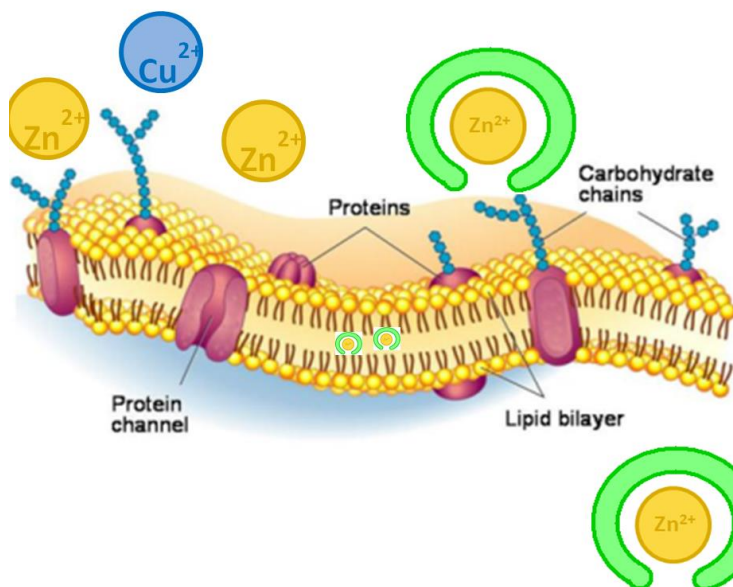
Recent studies have shown unequivocally that topical zinc therapy reduces wound debris and advances epithelialization in surgical wounds in the rat (Lansdown, 2007). Zinc oxide advanced the enzymatic breakdown of collagen fragments in vitro through MMPs, which exhibit substrate specificity for most ECM molecules. Locally applied zinc oxide also enhanced the repair of ulcerated skin. Conversely, inhibition of MMPs dramatically delays wound healing. Topical administration of zinc appears to be superior to oral therapy due to (1) its action in reducing super infections and necrotic material via enhanced local defense systems, (2) its collagenolytic activity and (3) the sustained release of zinc ions that stimulates epithelialisation of wound.

Also the expression of the metallothionein gene is up-regulated in the skin following topical application of zinc and copper, and in wound margins particularly in regions of high mitotic activity. Metallothioneins are a family of low molecular weight proteins that complex up to 20% of intracellular zinc. This induction of metallothionein in the wound margin may reflect its role in promoting cell proliferation and re-epithelialiation. The action of metallothioneins in these

processes may result from the large number of Zinc-dependent and copper-dependent enzymes required for cell proliferation and matrix remodeling.

### Chelated forms of copper and zinc

Often copper and zinc are used as inorganic form (e.g. copper sulphate, zinc chloride, etc). In Intra Repiderma the copper and zinc are in the form of organic chelated complexes. This allows a deeper penetration into cells / skin layer which gives rise to a better efficacy of the product as the infectious diseases are often also present in deeper skin layers. This improved efficacy has been demonstrated in several practical field trials.



**Figure 5.-** Simulation of the penetration of chelated zinc and copper in comparison with ionized zinc and copper



## Materials and Method

A sow with a coronary band infection was treated twice a day during one week. The Intra Repiderma spray was applied for 2 seconds during treatment for a layer completely covering the lesion. The lesion was scored after 14 days of the first treatment (note: no treatment second week).

Location: Varkenshouderij Bouwens  
Hoolbeemdweg 52  
5345 DZ Oss the Netherlands

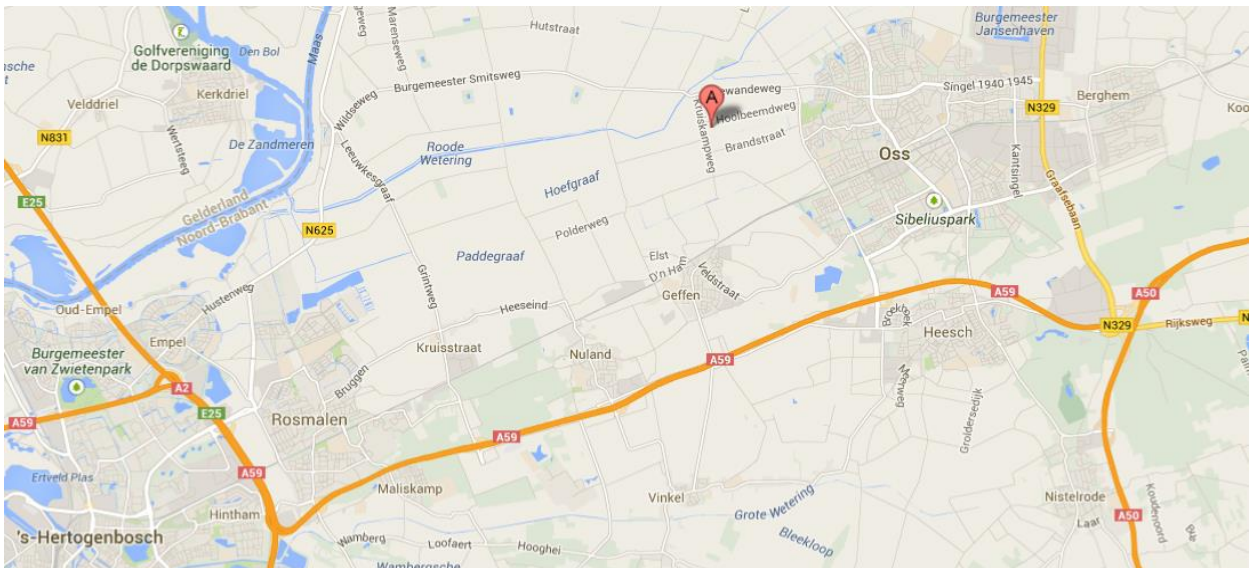


Figure 6. - Location of the farm in the Netherlands



## Results



**Figure 7.** - Coronary band infection sow A. Clearly you can see the swollen skin which indicates that the infection is spreading.



**Figure 8.** - Applying Intra Repiderma on the coronary band infection of sow A. The spray is easily applied and the spray nozzle can be used at all angles.



**Figure 9.** – After two weeks there was a significant reduction of the swollen claw.

The sow was treated twice daily during one week, after that the wound was not treated and the lesion was scored 14 days after the first treatment. There was a significant reduction of the swollen claw. Also the infection was reduced and was starting to heal now.

During our first visit (day 0) it was clear that the sow could not stand on the infected claw due to pain. On day 14 there was contact with the claw and the floor and the pain was not so severe anymore.

### **Pharmacovigilance**

During the study and also during two weeks after the last treatment, the sows were checked daily on any adverse effects. No adverse effects were observed.



**Figure 10.** – Farmer Gerard Bouwens in conversation with Robbert van Berkel and Carly Vulders of Intracare.

## **Conclusion**

Intra Repiderma can be used for the treatment of coronary band infections. It can be a good alternative for the sprays based on antibiotics and has therefore the potential to substantially contribute to a reduction in the use of antibiotics.

**Author**



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