Sebaceous Adenitis in the Akita :

"The Mysterious Skin Disease"

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Current Overview

Sebaceous Adenitis (SA) in dogs is primarily an advancing inflammatory destruction of the sebaceous glands of the skin. This disease occurs in various dog-breeds with certain breeds showing a higher predisposition.

Most frequently affected are e.g. Akitas, American Akitas, Poodles, Vizslas, Samoyedes, Chow Chows and English Springer Spaniels. Furthermore cases of SA have been found in cats, rabbits, horses and humans (Bensignor & Guaguère, 2012).

Within this context, the current scientific knowledge about sebaceous adenitis, specifically in the Akita (Fig), will be discussed.

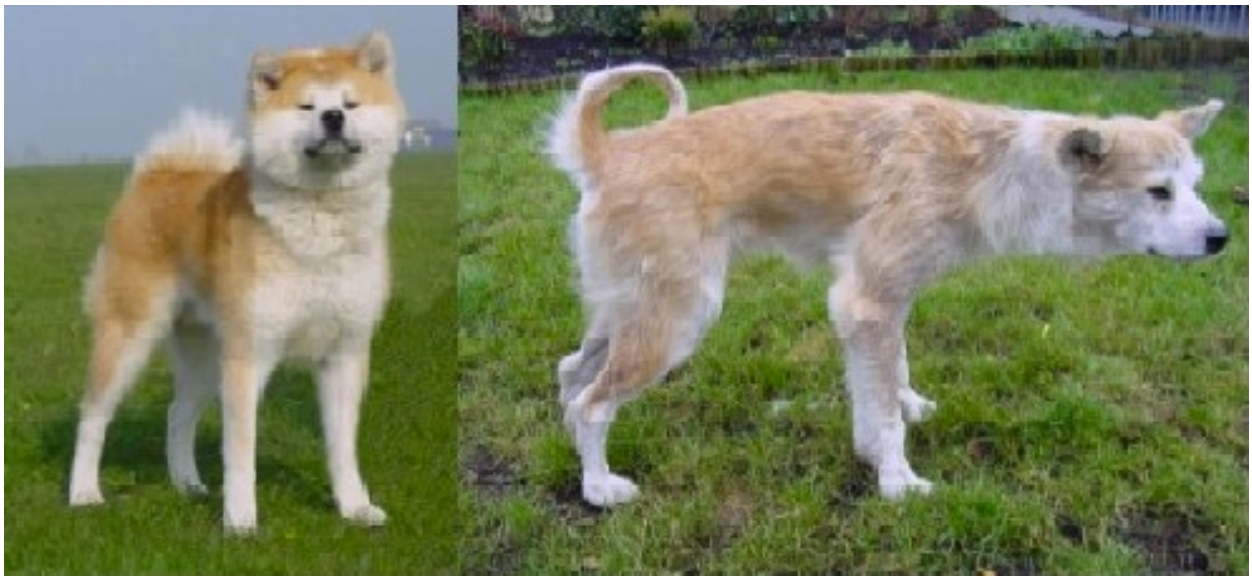

Fig. 1: On the left a healthy Akita, on the right an Akita with sebaceous adenitis

Anatomy of the skin

The Sebaceous Glands

As already mentioned, the sebaceous glands of the skin (*glandulae sebaceae*) play a major role in this condition.

Figure 2 (Fig.:2) shows in detail the anatomical structure of the skin as well as the precise localisation of the gland. The *Glandulae sebaceae* can be found in the dermis and opens via a small duct horizontally into the cavity containing the hair follicle.

The glandular product, the sebum, is secreted from the sebaceous glands via the follicular duct to the surface of the skin. The fatty substances subsequently spread, as a kind of protective film, on the surface of the skin and the hair.

I addition to the lubrication of the skin, the sebum functions as a physico-chemical barrier protecting the skin from potential pathogens.

Salts and several proteins are also found in the produced sebum, e.g. glycoproteins, interferons and immuno-globulines, in order to ensure a specific protection (Sousa, 2006). Furthermore other fatty acids support the barrier effect.

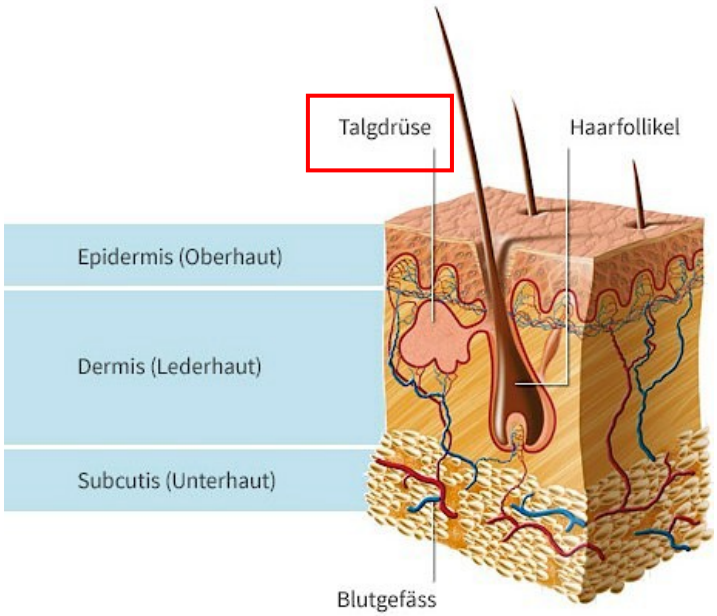

Fig. 2: Schematic illustration of the anatomic structure of the skin (Fabre, 2014)

The sebaceous glands can be found all over the dogs skin with exception of the teats, nose leather and the soles of the paws. Depending on the region of the body, there are variations of sebaceous glands e.g. in size, number and occurrence. Extremely large glands are located in the regions of the chin, neck and the tail.

Clinical Signs

Idiopathic (= without detectable cause) sebaceous adenitis can be characterized by an inflammation of the sebaceous glands leading to a total destruction of the gland. (Bensignor & Guaguère, 2012).

As a result, the production of the sebum decreases in the affected skin areas causing numerous negative effects on the skin and coat.
How the lack of the secretion influences hair growth, is still unknown (Sousa, 2006).

Fig. 3: Agglomerated brownish coloured follicular casts

Box 1: Clinical signs of sebadenitis in Akita (Bensignor & Guaguère, 2012; Simpson & McKay, 2012)
symptoms
• Keratin cast (Fig 4 A/B) on hair line
• Itching (pruritus) of the skin, generally caused by fungi and bacteria
• In case of acute pyoderma (bacterial skin infection with pus formation): o blisters (papules) (Fig 4 C) o pustules (Fig 4 D) o inflammatory collarette (FigE)
• Symmetric hair loss (alopecia) up to complete hair loss
• Hair: o brittle o dull o as if eaten by moths
• White-haired dogs develop a brown-red colouring caused by brownish crust formation

Microscopic examinations shows a dry and scaly skin-surface and some SA-dogs even demonstrate blisters (Fig 4 C) and pustules (Fig 4 D) (Simpson & McKay, 2012).

Moreover keratin casts, an agglomeration of brown crusts and scales stucked together at the hair shaft, are typical characteristics for sebaceous adenitis in the Akita-dogs (Fig 3). In addition to the loss of undercoat, the fur is described as dry, dull, and fragile (Sousa, 2006).

The loss of sebum generally triggers a broad range of secondary skin infections: Bacteria, viruses, or fungi (Bensignor & Guaguère, 2012). Typically a bad odor, like socks worn for several days, accompanies the individual appearance of SA.

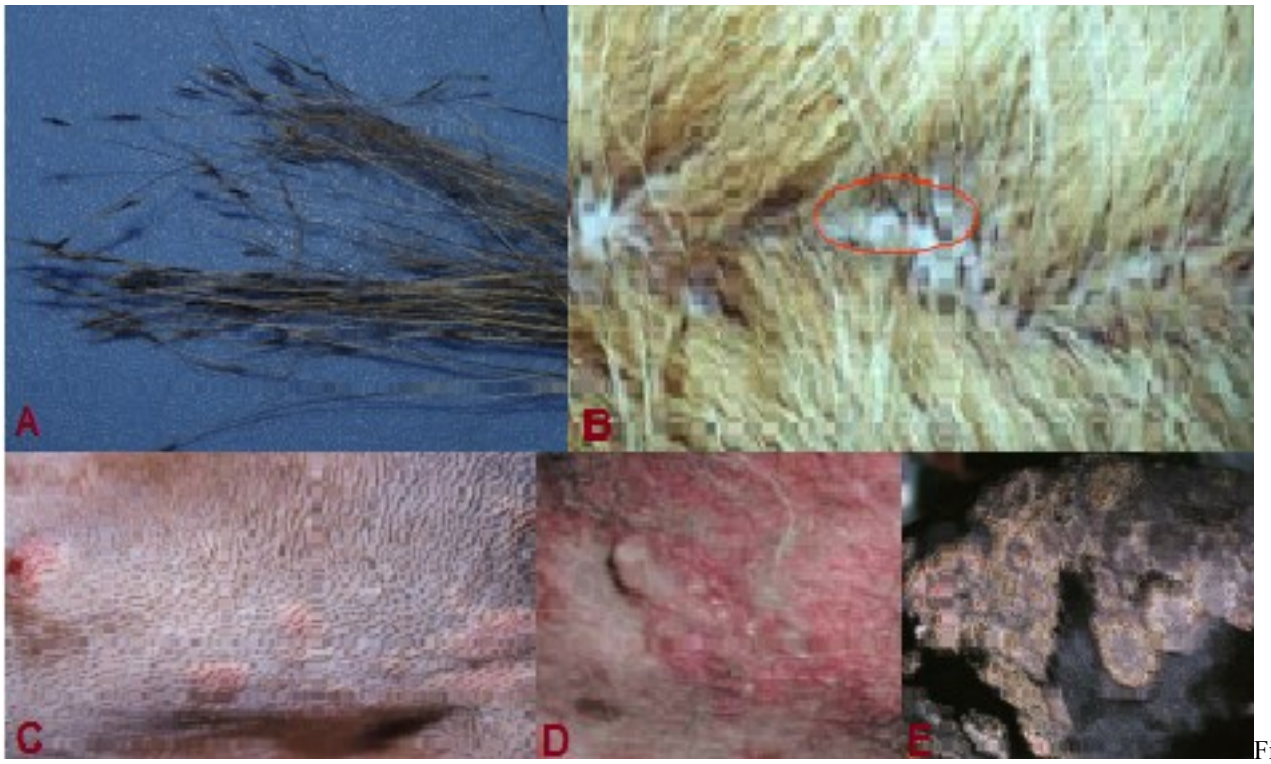

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Fig. 4: **A-E**: Depiction of the symptoms of sebadenitis in Akita dogs:
A: "featherlike“ keratin cast (Bensignor & Guaguère, 2012), **B**: keratin casts at the hairline (red circle), **C**: blisters (papules) (Noli, 2008), **D**: pustules (Noli, 2008), **D** : collarettes (Noli, 2008)

In general, the first clinical symptom will most often appear on the dogs head. More precise on the outer ear as a brown crumbling residue which can be mistaken for mites. Later on, the SA-signs spread all over the body to the tail (Simpson & McKay, 2012). During the chronic phase of disease, the coat appears thinner - as if eaten by moths (Simpson & McKay, 2012) - while the remaining hair shows a grayish cast and resembles a “puppy coat“.

Especially in Akitas, a diffuse hyperkeratosis (Greek*:* *hyper* “over“, *keratos* “keratin“, an over-production of keratin in the skin) can be seen sometimes, appearing similar to symmetric alopecia (loss of hair) (Bensignor & Guaguère, 2012).

In Akitas, both, male and female dogs are affected. There appears to be no correlation between SA and the coat colour of the dog. In general, the first symptoms usually appear with the beginning of sexual maturity. A significant correlation between the duration of the disease and the severity of the disorder could not be demonstrated.

Additionally there was no correlation observed between the degree of illness and the age of the dog. The progression of SA does moreover not follow a rigid pattern: Some individuals demonstrate a rapid progression (2 months), while others progress over a period of many years (Reichler, et al., 2001).

In the Akita, it is assumed that SA probably follows an autosomal recessive mode of inheritance (Fig 5) (Reichler, et al., 2001). That is why the term genodermatosis (geno = for genetic reasons, dermatosis = skin disease) is frequently used in relation to SA. Presumably, hormonal changes play a key-role in triggering the disease. But also pregnancy or any stressful situations cannot be totally excluded as a possible contributor for this health issue.

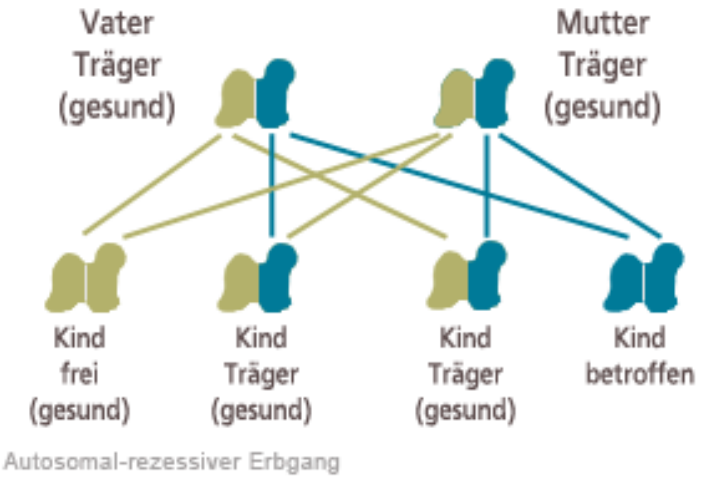

Fig. 5: Diagram of an autosomal recessive inheritance (Brüggemann, 2014)

Clinical Diagnostics

Diagnosing SA is very difficult without a skin biopsy (Histological examination). SA exhibits numerous similarities with other diseases, such as canine demodicosis (skin disorder caused by parasitic mites), dermatophytosis (fungal infection of the skin) folliculitis (inflammation of the follicles) or leishmaniosis (infectious disease) to name a few (Bensignor & Guaguère, 2012).

Hence the veterinarians should first investigate and eliminate the above mentioned diseases in order to avoid misdiagnosis.

Biopsy

A definitive diagnosis can only be found by means of a skin biopsy. In cases of suspected sebaceous adenitis, multiple skin biopsies and samples from different body regions should be taken, in order to identify the varying inflammatory phases of the sebaceous glands.

Three phases of sebaceous glands with inflammatory symptoms can be observed: In the first phase the excretory duct of the sebaceous gland is inflamed (Bensignor & Guaguère, 2012). During the second phase various “defensive cells” of the immune system are found in the tissue samples (Fig 7).

The so called “defencive cells” were represented by makrophages, lymphocytes, and neutrophilic granulocytes. In more scientific term, representing a perifollicular (= around the follicle) granulosum, i.e. accumulation of many cells without connective tissue (Linek, et al., 2005).

In phase 3, the destruction of the gland tissue has taken place, which is probably caused by the infiltrating immune cells. The tissue develops a perifollicular fibrosis (Bensignor und Guaguère, 2012). In other words, in the end only scar tissue remains and can be seen in the inflamed regions (Klöppel, et al., 2008). Because of the complete destruction of the sebaceous glands, the degree of inflammation decreases.

It is vital to stress, that SA is **not** caused by microbial infection – neither an attack of viruses, nor bacteria or fungi can be observed in the affected gland tissue.

SA can be seen as a disorder of the auto-immune system which means that the body's own defence attacks its own structures. In conclusion, an auto-immune mediated disease is possibly the main reason for sebaceous adenitis in the Akita.

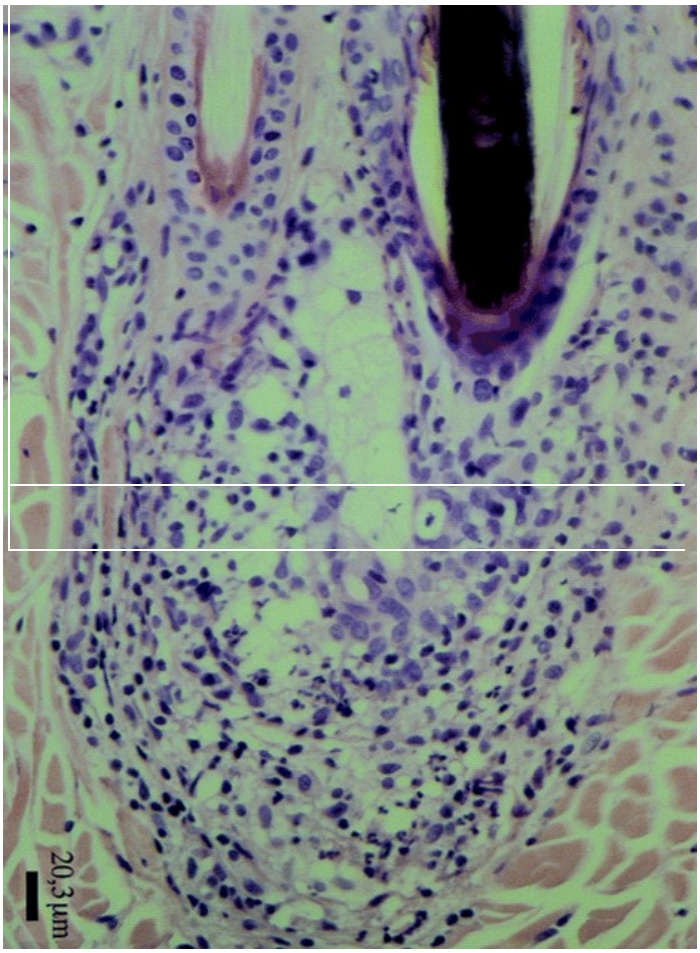

Fig. 6: Histological image of a sebaceous gland with an inflammatory reaction (Reichler, et al., 2001)

Trichoscopy

Using trichoscopy (Greek *trichos* “hair“, ancient Greek *skopein* ”scopy“ = method or instrument of observation and examination), a method of evaluating hair microscopically, one can get an overview of the hair density, scaling or formation of pustules, and the characteristic keratin casts (Bensignor & Guaguère, 2012).

Treatment

There is **no** treatment available at this time for curing sebaceous adenitis with a certainty of 100 percent remission. (Bensignor und Guaguère, 2012). In other words, there is no treatment available that will totally restore the coat and skin of affected Akita dogs.

It appears that the disease typically progresses in periodical cyles. In the beginning the dogs show a massive hair loss. Oil-treatment encourages hair growth almost back to normal. Followed in episodes, by an other loss of hair and the cycle starts again.

The aim of therapy is to slow down the inflammatory process as well as to reduce stress, in order to stabilize the immune system (Simpson & McKay, 2012).

Local Treatment

Local treatment means the external application of medication.

Following the individual step of treatment are outlined. The **4 step procedure** is relatively time consuming but - as practice shows - exceptionally promising (Simpson & McKay, 2012).

Step one: R*emoving scales, crusts and keratin casts*
Using a keratolytic or keratoplastic shampoo, bathe the dog to remove dry scales and crusts as well as keratin casts. Shampoos with ingredients like sulfur or salicylic acid (Scott, et al., 2001) are especially recommendable.

In cases with a secondary bacterial folliculitis, shampoos combining the ingredients mentioned above and benzoylperoxide, proved to be very effective. All shampoos should be allowed to infiltrate for 10 minutes (Simpson & McKay, 2012).

Step two: *Replacing the oily barrier on the outer skin (stratum corneum)*
Bathe the dog using generic baby oil, olive oil, or calendula oil. A treatment of 50 percent water and 50 percent oil proved beneficial. Apply the emulsion by rubbing from head to tail.
Soaking for about two hours.

Step three: Removing the excess oil.

Step four: *Skin care protective*
Moisturising products, such as conditioners (Vétoquinol Hydra-Pearls™ Shampoo, Virbac EPI-SOOTHE® Shampoo) and sprays (Virbac HUMILAC® Spray) protect the skin from drying out and support the protective function of the skin (Rosser, 1999).

Simpson and McKay (2012) suggest that this four-stage treatment plan be performed once a week for a time period of four to six weeks. The skin and haircoat should show improvement after one to two months.

Attention: There is no guarantee for the success of the treatment. The majority of the affected dogs respond very well, showing new hair growth and a certain degree of stabilization.

The outer oil treatment is a simple and “low-priced” method to restore the lipid film of the skin. According to the Bensignor and Guaguère's study (2012), olive oil supports the regression of affected skin wounds.

As shown by special analyses, the components of olive oil (up to 83 % oleic acid) are very similar to the natural composition of the sebum: 48 % cholesterol ester, 48 %wax, diesters and 4 % free fatty acids as well as a slightly acid pH-value (Bensignor & Guaguère, 2012). This is possibly a reason, why olive oil can simulate the external skin-biofilm and protect against harmful pathogens (Bensignor & Guaguère, 2012).

Using antiseborrheic shampoos or giving fatty acids orally (in the form of capsules) is **not** advisable (Bensignor & Guaguère, 2012).

Cyclosporines are often percaved by owners as expensive SA-medications. But they are frequently associated with negative side-effects. These drugs belong to a group of immunosuppressives, used to inhibit the function of the patients own immune system.
In the past, only oral treatments with cyclosporin were commonly known. But a recent study showed their use in treatments in the form of sprays resulting in an improvement of the skin, coat and also of the general state of health of the dogs.

However, it is not totally clear whether cyclosporines actually have a positive health effect or if other ingredients, such as 1,2-propanediol, vegetable oils, or mineral oils in the spray lead to the regression of SA (Bensignor & Guaguère, 2012).

In addition a remedy for the treatment of the dog's ears, namely Ortena® (with the main ingredient 1,2-Propandiol), is being discussed. One of its most important ingredients is the colourless oil "Squalane" (Bensignor & Guaguère, 2012). Nowadays it can be isolated from olive oil whereas in the past, this substance was extracted from shark liver.

Also the thought of lipid as intermediate product of the body's own metabolism is of interest (Käser, 2014). For example Squalane has the ability to remove keratin from the *stratum corneum* and replace it with a lipid film (Bensignor & Guaguère, 2012).

Systemic Therapy

Systemic therapy can be described as use of medication in form of tablets or injections. This means the agent is transported by blood circulation.

Cyclosporine has been used several times as medication for SA. An oral dosage of 5-10 mg cyclosporine per kg body weight has been proved successful. The drug induces an inhibition of the immune systems which blocks all inflammations. Regeneration of the sebaceous glands has been observed to a certain degree, depending on the severity of the SA.

In an open study, performed by Bensignor and Guaguère (2012), 12 dogs have been treated with cyclosporine for one year. 60 % of the test-dogs showed a clinical improvement. After a treatment of 8-12 months, a stabilisation of the inflammations was detected. Discentinuing medication lead to a spontaneous recurrence of the SA (Bensignor & Guaguère, 2012).

Critical Treatment

Several systemic treatment options have resulted in unsatisfactory results in the treatment of SA. Oral fatty acids (capsules) do not lead to any positive effect on the skin conditions (Simpson & McKay, 2012). Likewise a therapy with corticoids showed mainly disappointing results (Bensignor & Guaguère, 2012; Simpson & McKay, 2012
Corticoids belong to a group of steroid hormones which are generated in the adrenal cortex. In addition to influencing many physiological effects, corticoids play a role in the metabolism – especially in the water and electrolyte balance of the body, the cardiovascular system, and the nervous system. They also suppress the immune system, thus having anti-inflammatory effects (Simpson & McKay, 2012).

As a last resort, a treatment of SA with vitamin A (retinoids) is a possibility. Like previously mentioned medications, vitamin A has a similar anti-inflammatory effect. Retinoids are also involved in the proliferation and differentiation of cells.

Under strict medical supervision, several dog breeds showed an 80-90 % improvement after three months. Synthetic retinoids (such as isotretinoin and acitretin) can possibly provide a slight reduction of manifested SA (Simpson & McKay, 2012).

A study done by Simpson and McKay (2012) showed that 60 % of dogs treated with synthetic retinoids demonstrate a 50 % percent reduction of hair loss. Although the treatment of above mentioned substances promise a certain recovery, their use is highly controversial because side effects are not yet fully evaluated.

Possible side effects are: Digestive disorders, dry eyes due to a lack of lacrimal fluid, diarrhoea, deformities during pregnancy, elevated blood fat levels (triglycerides), a risk factor for cardiovascular diseases or liver poisoning (Bensignor & Guaguère, 2012; Simpson & McKay, 2012).

Because of these secondary effects, veterinarians should attentively monitor the chosen therapy (Bensignor & Guaguère, 2012; Simpson & McKay, 2012) very careful.

Treatment of secondarily microbial infections

Skin lesions in SA-affected Akita dogs can be very often traced back on a secondary skin infiltration of bacteria, viruses or fungi.

If a veterinarian confirms this infection, a sufficient treatment with antibiotics (of about 4 to 6 weeks) should be considered (Bensignor und Guaguère, 2012).

Research perspective

SA in Akitas demonstrates a broad spectrum of unknowns. Therefore the disease opens up multiple fields of research. It is vitally important to cooperate with breeders and dog owners – especially in order to not fall behind:

EDTA blood samples (ca. 2ml) only from pure bred SA diagnosed (only by skin biopsy) Akita dogs can be an advance in research. Without this cooperation, a perspective to solve this health concerns seem to be possible.

The following question still remains: What is the reasons the defensive cells of the dog attack and destroy the body's own structures in Akitas? A continuous treatment of SA with immunosuppressants (such as cyclosporine) is normally associated with high costs and cannot be considered as a long-term solution because of the undesirable side effects.

Open questions for further studies are for example, what kind of substances trigger or cause the auto-immune reactions in the sebaceous glands? Genetic reasons for the defective regulation of the processes should likewise be further investigated.

The immune system is a rather complex and not fully understood system Therefore various motives and possibilities have to be considered in SA. The SA-disease can be seen as an eminently multifaceted problem. From the current status of knowledge, a simple and short-termed solution on

the genetic level can *not* be assumed: Several influencing factors such as different genes, the natural dogs environment and maybe several epigenetic side aspects we actually do not know about, play a major role.

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