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ALERT: administration of gabapentin in the treatment of arthritis leads to serious side-effects in rabbits !!!

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Arthritis is difficult to diagnose in rabbits as clinical signs may also be indicative of other health problems. Signs are furthermore individual to each rabbit. Even so, one common sign is the loss of litter habits and refusal to jump in the litter-box.

Arthritis is becoming more and more frequent as pet rabbits suffer from obesity or grow older. Rarely, there is a genetic predisposition. Arthritis can also develop

secondary to splay leg or amputation, as the remaining limbs will have to support the weight of the body. Active rabbits that jump on hard floors are also more prone to

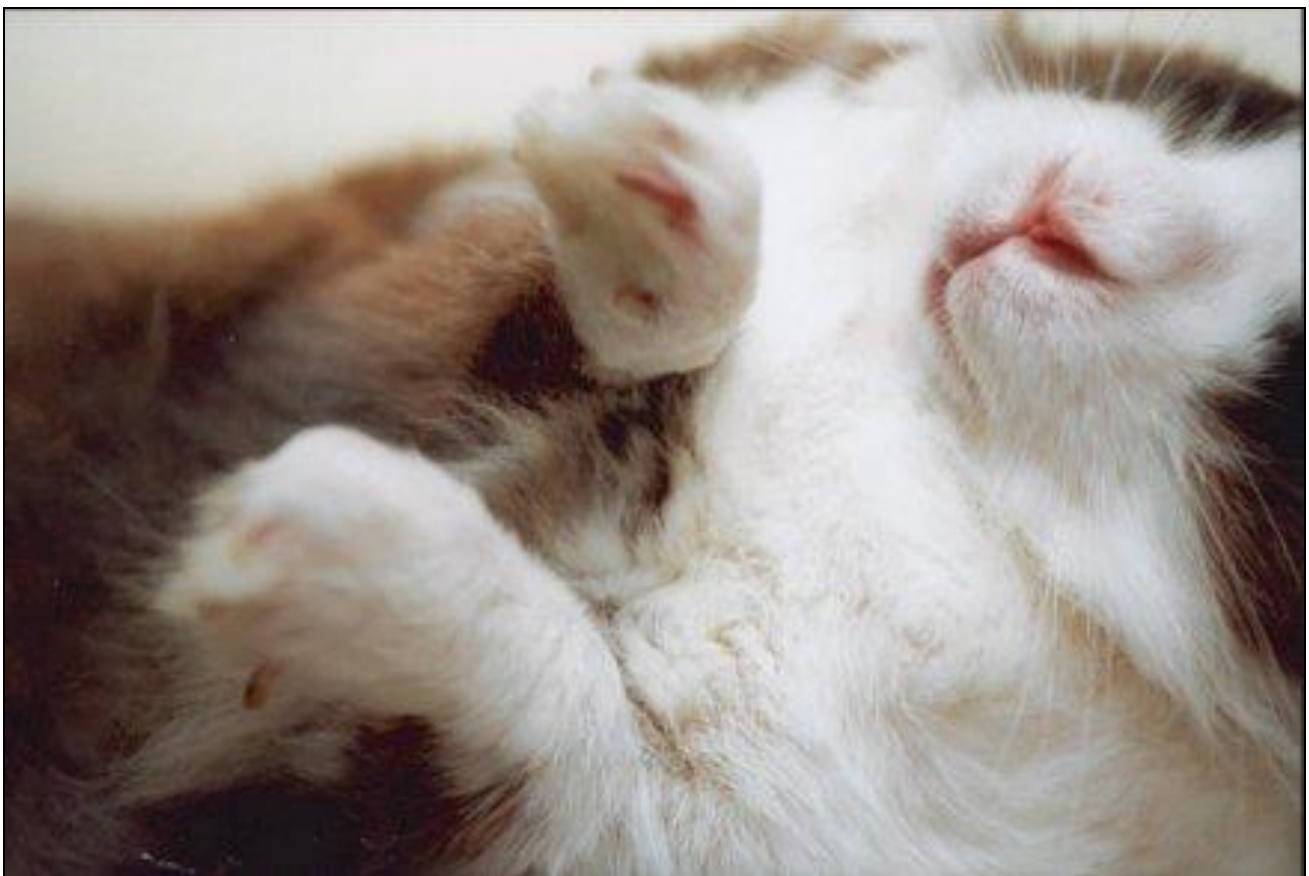


Figure 1: Stampi, a small female rabbit aged 6 years with severe deformation of the front limbs due to arthritis.

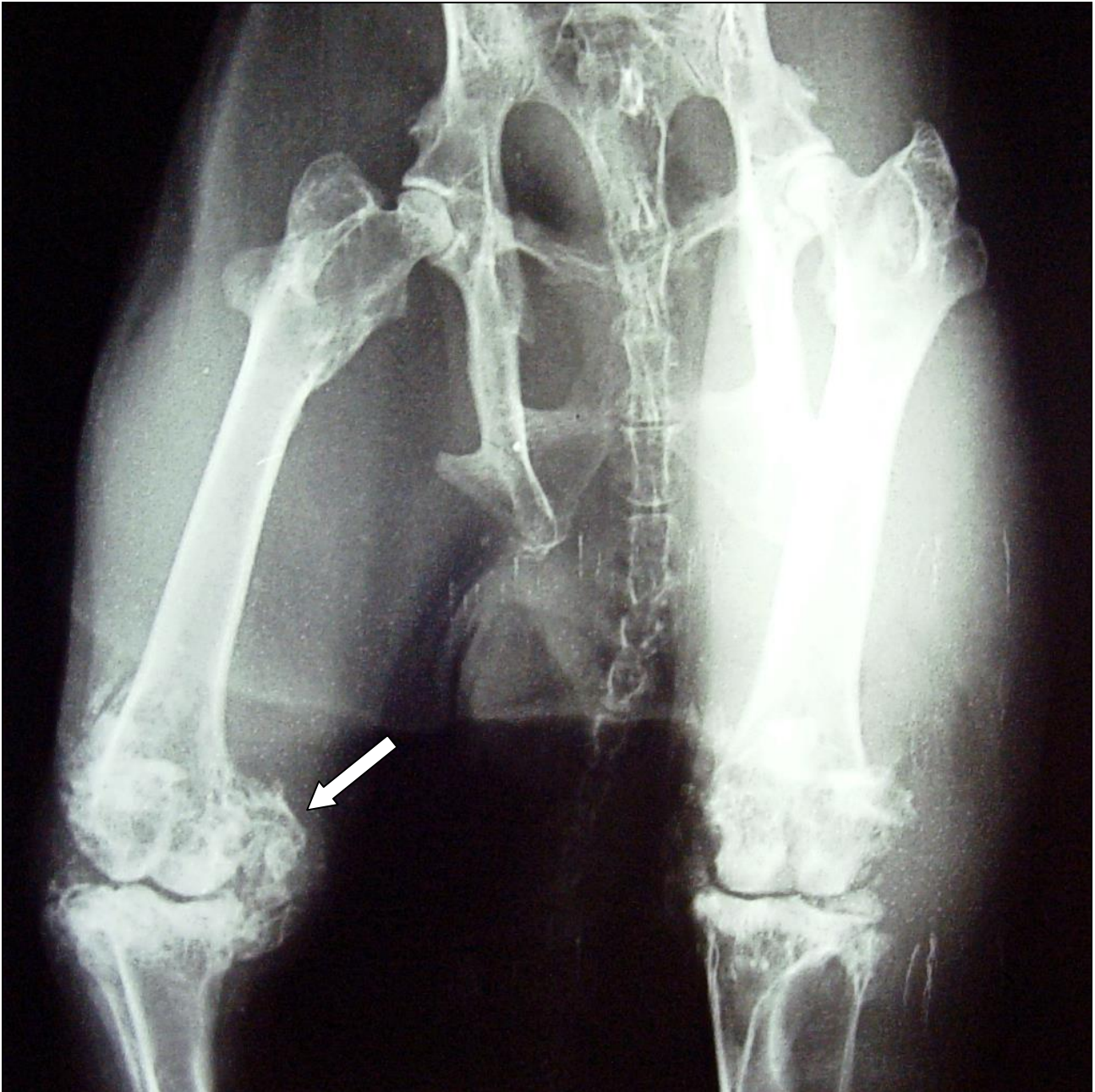


Figure 2: radiograph of arthritis in a rabbit, showing the typical haze around the affected knee joint (arrow). Photo courtesy: anonymous.

develop arthritis at an older age. Septic arthritis has furthermore been diagnosed in rabbits suffering from respiratory bacterial infection. Rheumatoid arthritis has not been observed and it does not seem to occur spontaneously in rabbits. A recent study has shown that roughly one rabbit on 2 will be affected by this disease at the age of 6 years. The disease affects joints and is accompanied by pain, swelling and

stiffness. In a healthy rabbit, joint bones are covered by a smooth layer of cartilage and are surrounded by a capsule that produces and contains a thick fluid. This fluid protects the bone and helps smooth movement of the joint. It also absorbs shock in order to prevent bones from touching each other. These protective layers have no nerve endings and are poorly irrigated with blood.

When the protective layers are damaged due to infection, trauma or age, arthritis will develop. Indeed, the damaged cartilage will not be replaced or repaired due to poor blood supply. As a result, bones become exposed and may come into contact with each other. As arthritis worsens, the bone endings roughen and contact between bones is possible. Nerve endings in the bone are exposed, leading to pain. The damage is irreversible and the condition will progress with time.

Behavioral and clinical signs

Symptoms can be mild, moderate or severe. In general, affected rabbits will present a decreased range of motion and become reluctant to move. Some will develop an abnormal gait and stumble or present balance problems. When one limb is favored over the other, pododermatitis may appear.

Many arthritic rabbits are unable to engage into daily activities such as grooming. As the animal becomes stiffer, getting up is difficult and moving becomes slow, going and jumping into a litter-box is difficult and painful. The rabbit may urinate on the way to its litter-box, unable to reach it in time or just outside, unwilling to hop in the box. This is often wrongly diagnosed as incontinence caused by the parasite of the nervous system *Encephalitozoon cuniculi*. Consequently, an inappropriate treatment is started.

Diagnosis

Clinical examination includes examination of the skin, joints, testing of response to reflexes, and determining muscle strength. A pain reaction is often observed when rotating the joint. The presence of fluid will be determined around the joints. The arthritic joint may feel swollen upon

examination. Over time, arthritis will cause modifications of the bone structure. Some may be visible, such as knobby and deformed extremities of limbs (Figure 1). In other rabbits, the damage can only be seen on X-rays (Figure 2).

Radiography will help to visualize the degree of bone and joint destruction, or the presence of a bone spur (osteophyte). The affected joint will typically show a 'haze' or 'fuzziness' around the bone structures (Figure 2). Other imaging techniques can also be used to assess the degree of damage, like ultrasound, computed tomography (CT), magnetic resonance imaging (MRI) or arthroscopy.

Additional blood and urine tests may be necessary to rule out other underlying health problems or diseases.

Treatment

The initial treatment includes rest and pain management. These help reduce the pain and inflammation caused by arthritis.

Pain management

Pain management is very important and is possible thanks to the administration of NSAID or opioid analgesics. Those commonly used are meloxicam (Metacam), tramadol or buprenorphine.

Depending on the severity of arthritis and the behavior of the rabbit, analgesics do not need to be given on a daily basis. Once or twice a week may be enough. There is no rule, just observation of the rabbit and detecting signs of discomfort or pain: behavior, eating, moving, etc. The frequency of pain medication can be increased or decreased. In one case, the rabbit showed regular relapses with meloxicam. When it happened, ketoprofen was given instead, as long as needed. One or two injections were usually sufficient.

Use of gabapentin

Gabapentin (Neurontin) passes the blood-brain barriers and enters the nervous system and the brain to prevent seizures. As a consequence, it is used as an anticonvulsant/antiepileptic drug, but also in the management of neurological pain caused by postherpetic neuralgia or diabetic peripheral neuropathy. It has addictive properties and should be used with care, especially in animals.

Gabapentin is not used for minor pain or arthritis even if its use in persons suffering from osteoarthritis and fibromyalgia has been studied.

Some US veterinarians do, nowadays, suggest the off-label administration of gabapentin to control pain in rabbits suffering from arthritis, without studies of effects and side-effects.

Several cases of arthritic rabbits that were administered gabapentin and developed serious side-effects have been reported to the owner of MediRabbit.com and author of this article. The side-effects appeared several weeks after intake of this medication (source: private communications):

- Lack of appetite.
- Dizziness, drowsiness, fatigue.
- Weakness of the healthy limb.
- General muscular weakness with the rabbit staying in one place.
- Ataxia, reluctance or inability to move.
- Decreased urine output or urinary retention.

In one case, there was discoloration of the hard excrements and in another the rabbit developed nystagmus-like, uncontrolled, back-and-forth eye movements.

Since the above clinical signs show similarities with *Encephalitozoon cuniculi*, a parasite of the nervous system, it was

often concluded that the rabbit developed an active phase of the parasitosis, rather than reviewing the current arthritis treatment with gabapentin and its numerous known side-effects. Instead these rabbits were given the benzimidazole anthelmintic fenbendazole in addition.

In spite of warnings, the gabapentin treatment was continued in most rabbits and their health condition continued to decline.

Gabapentin treatment must not be stopped abruptly. The rabbit must be weaned of gabapentin slowly to avoid withdrawal symptoms.

Alternative remedies

Glucosamine/chondroitin has been used to relieve arthritis. According to Carpenter's formulary, Cosequin dosage for rabbits is the following: "use empirically at feline dose". For instance, Cosequin can be started with 1/4 teaspoon BID. After one month, it can be dropped to SID for maintenance. For Adequan, the used dosage is 2.2 mg/kg SC, IM, q once a week during 4 weeks, then q 14d.

Cosequin or Adequan do not relieve pain, so the administration of analgesics is recommended.

Other products include pellets with broad spectrum joint health supplements such as cetyl myristoleate fatty acid complex, methylsulfonylmethane (MSM), glucosamine-HCl and hydrolyzed collagen. Although some of these pellets are manufactured for horses, cats and dogs, they have shown positive effects in rabbits too. Another brand of supplemented pellets for rabbits contains glucosamine, turmeric, ginger root and *Yucca schidigera* extract.

These natural products do not bring an immediate relief. It may take up to 4 weeks before positive effects are noticeable.

Massage

Massage of the body and limbs as well as acupuncture have brought an increase in quality of life in arthritic rabbits. Although acupuncture uses needles, most rabbits remain calm and relaxed (Figure 3).



Figure 3: Timmy getting acupuncture. Photo courtesy: Susan Lehman

Diet and home arrangements

Diet is very important as an arthritic rabbit should not become obese due to lack of exercise.

Arrangements in the living environment of an arthritic rabbit home can improve his comfort and quality of life. Exercise should

be stimulated to build-up muscles. This can be done by adding toys and tunnels in the living environment or in a pen.

Litterboxes usually have a high entrance and the rabbit must jump in. This leads to pain. Boxes can be replaced by low entrance boxes or potting trays for larger rabbits (Figure 4).

Soft bedding in the living area helps to keep the limbs warm when resting (Figure 5). It is also possible to use a heating pad. Both bedding and heating pad help improve blood circulation. This is especially important when a rabbit becomes reluctant to move.

If the arthritic rabbit is reluctant to move and urinates while resting, waterproof sheets and soft absorbent bedding will improve comfort of both owner and rabbit. Clipping of fur in the perineal region and application of a cream will help avoid irritation of the skin from urine. Some rabbits become unable to reach their caecotrophes. If this is the case, the caecotrophes can be collected and placed in front of the rabbit. Most will eat them.

Finally, some rabbits will groom and clean the inside of their ears less. If wax has accumulated in the ear canal, it can be gently wiped off and presented to the rabbit. Most will eagerly eat it.



Figure 4: A low entrance litter-box or a potting tray is ideal for arthritic rabbits



Figure 5: Soft and warm bedding help improve blood circulation in arthritic rabbits. Here Grijsje, a female rabbit at the age of almost 8 years.

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