

Novifit[®]
(NoviSAmE[®])



Appropriate use of Novifit[®]



First intention **Guide**

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Geriatrics, a fast-growing new discipline:

As a result of advances in veterinary medicine and surgery over the past century, the life expectancy of our family pets has increased dramatically. Most dogs are considered geriatric after about 8 years of age depending on their breed, size, nutrition and lifestyle; cats are considered geriatric at 10 years.

It has been suggested that there are over 7 million geriatric dogs in the United States alone. As a result, veterinarians need to be prepared to recognize and thoroughly evaluate age related changes in their patients in order to satisfy a growing clientele with a strong desire to maintain the quality of life of their aging companion.



Why and how to recommend a geriatric consultation?

The goal of the geriatric consultation is to provide a complete medical evaluation of the aging animal, following the example of practices now widely applied in human medicine.

A detailed medical history and thorough physical examination are the first steps necessary for early recognition of problems. Numerous age related conditions, initially develop at a subclinical level. Waiting for the appearance of clinical signs means losing valuable time in making the diagnosis and may result in limiting the treatment options. Many disease processes can be slowed and the pet's quality of life improved with appropriate early intervention. For this reason, a complete clinical evaluation may include several simple, minimally invasive, diagnostic tests that will help the clinician to recognize the early signs of developing medical conditions.

The geriatric evaluation can be performed in conjunction with any routine consultation (including vaccination). Reception staff can mention it in the waiting area, allowing the owners time to fill out appropriate questionnaires and preparing them to discuss their concerns with the veterinarian in the exam room. Offering geriatric consultation, helps to further bond clients to the practice and can provide a daily source of satisfac-

tion for the practicing veterinarian. It is always more rewarding to detect a disease process in its early stages when intervention can slow the progress of the disease, and improve the patients quality of life as well as prolong their life expectancy.

What happens during a geriatric consultation?

❑ A geriatric consultation is above all a very complete, in-depth general medical consultation. It requires no particular specialty training and may be performed by any veterinary practitioner.

❑ Particular attention should be paid to the history: lifestyle, recent changes in the environment, past disease history, previous treatments, dietary habits, travel history, etc. In addition, the owner should be questioned thoroughly about changes in the animal's behavior as these changes may be the earliest signs of a developing disease process. The physical exam must also be very thorough as it remains an excellent way of detecting many medical conditions. Whenever possible, it is best to diagnose problems prior to the appearance of overt clinical signs, the presence of which obviously aids in the diagnosis. However, once clinical signs have

appeared, therapy is often more difficult.

The history and clinical exam allows for the most reliable assessment of the patients state of health and helps to determine the most logical selection of diagnostic tests. At this stage, an open dialog with the client is of crucial importance. This is where costs may begin to accumulate. It is necessary to explain to the client the benefit of these tests in light of the animals age and remaining life expectancy. Not all owners choose the same level of service, but age should not be considered a contraindication to a full medical work-up or to surgical intervention when appropriate.

The development of geriatric consultations leads to following patients closely and on a regular basis, which can improve client loyalty. In order to follow these patients objectively, an exhaustive clinical examination is a necessary starting point.



Dr Valérie Dramard and Dr. Laurent Kern, behaviorists graduated from French Veterinary Colleges and specialists in this field, remind us of a few key points that help for an initial approach to behavioral disorders in aging pets.

What exactly is meant by the term “Cognitive Dysfunction Syndrome”?

The main signs of cognitive dysfunction are disorientation or confusion, decreased social interactions, changes in the sleep-wake cycle and housesoiling. One study demonstrated that 68% of dogs age 15-16 had at least one of these signs of cognitive dysfunction. **Cognitive Dysfunction Syndrome is a diagnosis of exclusion.** If a pet is presented with clinical signs of cognitive impairment, medical causes for the behavioral changes should be ruled out before making a diagnosis of cognitive dysfunction.



What are the main types of behavioral disorders to be found in aging pets?

The four main categories of behavioral changes associated with cognitive dysfunction can be remembered by applying the acronym DISH; **D**isorientation, changes in social **I**nteractions with people and other pets, changes in the **S**leep-wake cycle and loss of **H**ousetraining skills. The aging pet with cognitive dysfunction may act confused. He/she may wander aimlessly around the house and act lost. He/she may fail to recognize the owner or other familiar people and appear less interested in petting and other social interaction. Sometimes pets with cognitive dysfunction stand on the wrong side of the door while waiting



to be allowed outside. The pet may act as if it no longer remembers the rules that it had complied with for years; climbing onto the bed or furniture that it had previously been restricted from and eliminating throughout the house. Finally, there may also be a reversal of the sleep-wake cycle with the pet sleeping much of the day and staying awake at night.

Some pets with cognitive dysfunction become more irritable and less tolerant of handling and interaction than when they were younger. They may also begin exhibiting increased anxiety related problems. They may follow their owners constantly through the house and panic when separated from them for even a few minutes. They may become extremely anxious as night approaches and pace, pant or vocalize while seeking attention from the owner. Some pets may

also begin to demonstrate repetitive behaviors such as licking their own feet or legs or surfaces in the home. Owners may quickly become intolerant of these behaviors in their previously well trained pet and the bond between pet and owner can be severely damaged.



What are the main causes of behavioral disorders in aging pets?

➤ Cognitive Dysfunction Syndrome in pets is similar to Alzheimer's disease in humans. Many of the processes that lead to CDS are the same as those which lead to Alzheimer's.

- **The natural aging process in the central nervous system** – As nerve cells age, their membranes become less fluid resulting in decreased sensitivity of membrane receptors (receptors for neurotransmitters and hormones); neurotransmission

decreases (in particular, neurotransmission of dopamine a neurotransmitter involved in cognitive processes); dendrites shorten; the number of synapses decrease and the rate of neuronal death increases (apoptosis).

- Another process, similar to that occurring in Alzheimer's disease, is the deposition of beta amyloid plaques. Beta amyloid is neurotoxic and further disrupts neuronal function.
- Finally, aging cells produce more neurotoxic free radicals and less of the enzymes that normally remove them from the body, resulting in increased neuronal damage.



- Physical illnesses can also contribute to the behavioral changes seen in aging pets. Some examples include: hypothyroidism, hyperadrenocorticism (Cushing's disease) and brain neoplasia. The behavioral signs of hypothyroidism include lethargy, mental dullness, and exercise intolerance. An inability to maintain body temperature may cause the hypothyroid dog to constantly, seek out warmth. Cushing's disease can lead to increased



lethargy, disturbances in the sleep-wake cycle and excess panting which may cause the pet to appear anxious. Polyuria, polydipsia and polyphagia are also common and may contribute to an increase in housesoiling problems. Mental dullness may also be a sign of a developing brain tumor. However, in these cases other neurological signs usually become apparent rather quickly (paresis, paralysis, syncope, walking in circles, running into walls, etc.).



How does one diagnose Cognitive Dysfunction Syndrome?

The practitioner must attempt to determine if the presenting clinical signs are due to a disease process, age related effects on the brain and body systems, primary behavior problems or a combination of several of these factors. Any condition that is associated with pain or discomfort may lead to increased irritability, fear and aggression. Organ failure, degenerative conditions, endocrinopathies, sensory deficits and any disease that affects the central nervous system can all contribute to profound changes in an animal's behavior. A thorough behavioral history will help the clinician to determine if the presenting clinical signs are due to an existing behavioral condition that has been exacerbated by the aging process or disruptive changes in the pet's environment.

The diagnosis of cognitive dysfunction is a diagnosis of exclusion. Once medical

problems have been ruled out or treated and primary behavioral conditions have been ruled out, a diagnosis of cognitive dysfunction can be made in the pet presenting with signs consistent with impaired cognitive function. A senior pet questionnaire can be used to pinpoint each problem and monitor response to therapy.

When and how should an aging pet be treated?

As always when confronted with behavioral problems, the earlier the treatment, the better the chances for improvement. However, the client must consider the behavior sufficiently disruptive in order to convince them to begin treatment. If the owner does not believe there is a problem, then compliance with recommended treatment is likely to be poor. Educating the client about the fact that age related changes are more likely to worsen, rather than improve if left untreated will help them to understand the importance of the recommended intervention.

❖ First, all medication being given to the pet should be reviewed, mainly to eliminate any medications that could be causing or aggravating behavioral problems. Neuroleptics and benzodiazepines, for example, decrease overall activity levels and can make a lethargic animal appear even less responsive. Other, less sedating, anti-anxiety drugs may be preferable. The review also provides an opportunity to eliminate the least relevant drugs and supplements. An aging pet with the behavior problems mentioned above will be treated with newer veterinary pharmaceuticals. To improve compliance with new treatment, the overall number of tablets and capsules given to

the pet each day should be limited if possible. One way to do this is to eliminate the least useful products.

❖ Simple measures can improve quality of life for an aging pet. Decreasing the quantity of food fed to the pet may be helpful, especially if the pet is overweight. Obesity contributes to decreased activity in aging pets and makes them appear more apathetic and unresponsive. Increased weight also contributes to the pain and discomfort associated with arthritis. Special diets fortified with anti-oxidants are also available and may help with managing the aging pet.

❖ If the pet has arthritis, it will need pain relief. It has been proven in humans that chronic pain significantly affects behavior, possibly leading to depression and decreasing the effectiveness of the immune system. Moreover, if the pet is more comfortable, it may regain its ability to move and its desire to play, thus increasing its interaction with its owner and possibly improve a weakening bond between the owner and the pet.

❖ The treatment of concurrent illness is essential. Working to improve diseases that cause pain and discomfort (skin diseases, arthritis, etc) and treating endocrinopathies can lead to significant improvement in some behaviors.

❖ Novifit is the product of choice for aging pets that are showing signs of cognitive dysfunction. Novifit has been shown to be safe and there are no known contraindications in aging animals suffering other disease processes or taking other medications. Its systemic action (methyl group donor in all body tissues) is particularly beneficial in aging animals. SAME has been



shown to improve cognitive function, mood and speed of mental processing in humans with Alzheimer's disease. Clinical trials have been completed in dogs (Accepted for U.S. publication in the peer-reviewed journal, *Veterinary Therapeutics*) and demonstrated significant improvement in the behavior of dogs with cognitive dysfunction within two months. The majority of owners were satisfied with the results and, given the challenges of living with a dog with cognitive dysfunction, this criteria is of critical importance.

How does one manage Cognitive Dysfunction Syndrome?

As is usually the case with behavioral disorders, medical treatment is combined with behavioral therapy.

➤ **The first and most important step is to identify and treat any concurrent disease.** It is therefore crucial when evaluating an aging animal to perform a complete examination

and collect blood for diagnostic testing. At the very least, glucose, cholesterol, T_4 , kidney and liver function tests should be performed.

➤ **Behavioral treatment is usually straightforward.** Animals with cognitive dysfunction may be



confused and anxious so any punishment, including verbal reprimands should be discontinued because it is likely to make the situation worse. It is more appropriate to "set the pet up to succeed" by limiting its opportunities for performing inappropriate behaviors. For example, a dog with a housesoiling problem should be confined to a crate or a limited part of the house when it cannot be closely supervised. Interactions with the dog should be encouraging

and positive. The dog should be rewarded with appropriate treats, toys or play for responding to commands.

➤ **Owners should also be reminded that continuing mental stimulation may help slow the deterioration of mental function.** They should try to encourage interaction with their pets that involve games, play, training and appropriate exercise. Increasing stimulation during the day will help to tire the pet so that it sleeps at night.

➤ **Medical measures may also be necessary** when behavioral disorders are affecting the good relationship between the pet and its owners. Such disorders are in particular, disruptions of the sleep-wake cycle, loss of housetraining, excess vocalization or destruction. Instead of waiting, action should be taken immediately after a request for help from the owners in order to decrease the risk of a decision to euthanize the animal. Novifit is the product of choice in this situation. Clinical trials show that the pet becomes more active and this significantly reassures its owners. If

improvements to behavior are still insufficient or not quick enough, then a psychotropic drug can be prescribed. Novifit may be continued in combination with these other treatments, as there are no known contraindications.

❖ **Behavioral problems resulting from cognitive dysfunction can be improved but the disease causing the problems cannot be cured.** In pets, as in humans with Alzheimer's, it is possible to slow the progress of the disease and improve the corresponding behavioral problems but the illness itself is incurable.

❖ **Novifit should be prescribed as soon as possible.** Its action stimulates cell metabolism in all tissues, thereby decreasing the processes of cell aging

and cell death. Generally speaking, it increases neurotransmission and therefore compensates for the consequences of neuronal aging.

How does one assess a senior pet?

Senior pet checklists or questionnaires should be used during geriatric consultations to assess the health and behavior of aging animals. They can be particularly useful to the veterinarian not only in making a diagnosis but in monitoring patient progress.

With behavioral problems, in order to assess improvement, approximately three objectives should be identified from the checklist or questionnaire and monitored.

For example, they might include sleep quality at night, an improvement in housetraining or other learned skills or a return to normal daytime activity. To monitor changes most accurately, owners can be asked to give a score of 1 to 10 with 10 representing perfect behavior. Or you can ask them to score the behaviors as a percentage with 0% representing total solution of the problem.

Ideally the situation should be reviewed in the clinic with the owners and the pet after no more than one month. The owners should be asked to let you know how their pet is progressing during the first two weeks of treatment, even if the behavior has not changed. Even if owners have come to terms with behavioral problems in their pet because it is part of the natural aging process, they may become much less tolerant if their pet prevents them from sleeping at night and they may quickly decide to have the pet euthanized. The fact that their veterinarian will listen to them and is available by telephone at least allows them to "hang in there" until the first treatment effects become noticeable.





❖ The pet should also be re-examined after two months of treatment so that the veterinarian can actually see any behavioral improvements, such as decreased anxiety or more energy. This is also a good opportunity to take a blood sample and monitor any changes in liver and kidney function, cholesterol, T_4 and blood glucose. It is also important to listen to the owners; any form of observation can be useful to the veterinarian in deciding on the course of treatment (continue the treatment, change doses, prescribe additional medications, etc).

❖ If there is no improvement after two months, the diagnosis should be reviewed. It is especially important at this time to look closely for physical

disorders if this has not yet been done. In addition, another psychotropic drug might be prescribed at this time to assist with the treatment of the more annoying behavior patterns such as night time waking or housesoiling due to separation anxiety.

❖ The pet should be referred to a veterinary behaviorist if minimal or no improvement is noted, especially if the owners

are seriously considering euthanasia for their pet.

Summary and key points

❖ **Cognitive dysfunction in aging pets is fairly common.** The resultant behavior problems can damage the owner-pet bond and cause the owner to consider euthanasia as the only option, especially when the animal is house-soiling or keeping them awake at night.

❖ **The sooner an aging animal with cognitive decline is recognized and appropriate treatment initiated, the greater the chances of improvement.** Treatment consists of a combination of behavioral therapy and medication required to at least restore



sleep quality and house training.

❑ As a nutraceutical, Novifit is a **safe** and **effective** first line treatment of behavioral problems associated with cognitive decline. Clients generally appreciate the fact that it is a nutraceutical.

❑ **Novifit** has been shown to be **safe** and **effective** in clinical trials of aging dogs showing signs of cognitive decline.



Dr. Valérie Dramard and Dr. Laurent Kern, behaviorists and graduates from French veterinary colleges, discuss the clinical usefulness of Novifit.

What is your clinical experience with Novifit?

We have used Novifit in two clinical trials, with general practitioners. The first was an open trial; the second was a **double blind versus placebo controlled trial** (accepted for presentation at the WSAVA Congress in Prague in October of 2006 as well as the AFVAC

Congress in Bordeaux, December 2006, and for publication in the U.S. peer-reviewed journal, *Veterinary Therapeutics*).

We have also used it in referrals, on its own or combined with other psychotropic drugs and behavior therapies.

Novifit was given to improve the **behavior of pets presenting with behavioral symptoms associated with aging** (CDS).

It was used for the following symptoms, which are found singly or jointly depending on the severity and prior duration of the clinical signs:

❖ **Confusion** resulting in aimless wandering, periods of immobility or staring, vocalizations with no identifiable reason.

❖ **Decreased activity** during the day and decreased attention: the pet reacts less to verbal commands, is lethargic and appears to have lost interest in the world around it. Owners often attribute these symptoms to deafness but in many cases they merely reflect a loss of attention.

❖ **Loss of learned skills:** the pet has lost certain learned skills and may no longer comply with “house-rules” (occupying places not previously authorized such as the sofa etc.).

❖ **Spatial disorientation:** The pet gets lost in familiar environments, tries to go through the wrong door, gets stuck behind furniture, etc.

❖ **Decreased social interaction:** The pet seeks less interaction with its owners, plays less and doesn't want to be petted. It no longer welcomes its owners or people familiar to it in the same way. It may also decrease its interaction with other pets. Interaction may even annoy it and make it aggressive.

❖ **Housoiling:** a pet that was house-trained before may eliminate inappropriately in the house.

❖ **Emotional disorders:** the pet may show signs of phobia or anxiety that were not present before. These disorders are often the reason for separation anxiety (or secondary attachment) and the pet may also become destructive if left on its own.



❖ **Sleep disorders:** the pet sleeps a lot during the day and finds it difficult to sleep at night. It may wander or even vocalize at night. Secondary separation anxiety often leads the pet to seek its owner's company at night whereas, previously, it could sleep on its own.

What symptoms respond best to the use of Novifit?

In the clinical trials, the use of Novifit was particularly effective in dogs suffering from **a general decrease in activity and attention, housoiling and the loss of learned skills. Sleep disorders also responded well to Novifit.** I remember the case of a dog which, as soon as the treatment with Novifit ceased, again began to suffer from severe nocturnal insomnia and vocalizations.

How much improvement can be expected?

The clinical trials have shown a statistically significant reduction in age-related behavioral symptoms after one month's treatment.

After two months, the severity of the age-related symptoms decreased by one-half compared to the placebo group.

What about compliance?

The taking of Novifit tablets by the animal was deemed very satisfactory to satisfactory by 78% of owners. Given the absence of side effects, owners are inclined to continue the treatment, even if improvement is not obvious in the first days of treatment.

What dosage regimen should be used?

Cats should be given 1 tablet of Novifit S per day.

Dogs weighing less than 22 lbs. (<10 kg) are given 1 tablet of Novifit S per day

Dogs weighing between 22-44 lbs. (10-20 kg) are given 1 tablet of Novifit M per day.

Dogs weighing between 44-88 (20-40 kg) lbs. are given 1 tablet of Novifit L per day.

Dogs weighing over 88 lbs. (>40 kg) are given 1 tablet of Novifit L twice per day.

The tablets can be given in food but should not be crushed or divided up into smaller pieces.



What are the side effects of Novifit?

Novifit causes very few side effects: only one dog in the controlled clinical trial had a brief bout of self-limiting diarrhea, which was cured by diet alone. Blood samples were taken from the dogs in the first trial after 4 months of continuous treatment. Biochemical and hematologic parameters remained within normal limits.

It should be remembered that aging pets are often receiving a range of different drugs and it is therefore useful to be able to suggest efficient treatment with no cardiac, hepatic or renal toxicity and no side effects such as sedation or agitation.

Novifit's lack of toxicity makes it a product that is safe to use in most aging dogs and cats suffering from age-related behavior problems, including those with concomitant organic disease.

What is the recommended therapeutic protocol?

In the controlled clinical trial, two-thirds of the dogs responded well or very well to Novifit within the first two months of treatment. The case should therefore be reassessed after two months of treatment. A decision will then be made to either continue the treatment without a break or to give the treatment for specified periods of time, or, if there has been insufficient improvement, to add a psychotropic drug or replace Novifit.

Where does Novifit stand compared to the other available therapeutic options?

Compared to other possible therapeutic options, Novifit should be considered as a first intention treatment when caring for dogs and cats presenting with age-related behavior problems. It has no known contraindications.

However, if there is insufficient improvement in the disorders, it is better to prescribe a more specific psychotropic drug and keep Novifit as part of a multi-modal treatment strategy.

In general, if the dog or cat's behavior has not shown improvement in eight weeks, the treatment plan should be modified.

Finally, as always in behavioral veterinary medicine, behavioral therapy should also be used. The goal should be to minimize isolation of the elderly patient and to encourage it to re-engage in social activities, in physical activity where appropriate, and in play activity via age-appropriate, stimulating games (especially those using food rewards).

