

THE EXPERIENCE OF CHRONIC PAIN



ZOETIS
PETCARE

2019 PROCEEDINGS

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THE EXPERIENCE OF OSTEOARTHRITIS



“OA really can be what I’ve termed ‘a silent killer’ because when it robs patients of their life quality... that loss of well-being is often the motivating concern that will cause a dog owner to begin to consider end of life decisions or perhaps pursue euthanasia” – Dr. Palmer

THE EXPERIENCE OF OSTEOARTHRITIS IS PAIN

When we think about osteoarthritis (OA), our focus is primarily on the lameness and inflammation. This is not surprising based on what tools we currently have available for treatment. But we know that from the pet owner’s and pet’s perspectives, the experience of osteoarthritis is an experience of pain. From that inciting action, we see many associated clinical signs.

During OA treatment, the pet owner and veterinarian are trying to restore the pet’s quality of life which can be severely impacted by the experience of pain.

CLINICAL SIGNS OF OA PAIN CAN INCLUDE:

- Abnormalities of movement/lameness
- Musculoskeletal deterioration
- Anxiety
- Loss of vitality, energy, and enthusiasm
- Sleep impairment
- Cognitive dysfunction

Pain is the primary experience and treatable sign of OA; it is also a large part of how we measure and monitor the disease process. Pain-induced behavior changes are a common metric to understand a pet’s OA progression and to determine treatment options. In fact, research has shown that when untreated, pain becomes its own disease state, impacting the pet’s physical and emotional well-being.

Dr. Lascelles: “Pain is an experience, so we’re measuring the impact of this negative experience. And then the next stage I think we have to appreciate is that the impact of pain is multifactorial. And that differs from individual to individual - it may affect your ability to perform certain activities, it may affect sleep, it may affect anxiety, or different combinations of these depending on the individual. It has so many different impacts. All of those are measurable, but there is no one measure of pain.”

A MIXED STATE

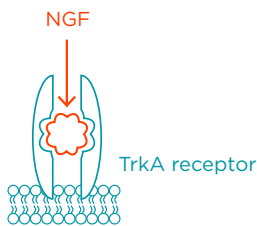
OA pain progression has been traditionally depicted as a linear process: undertreated or untreated acute, inflammatory pain evolves into chronic, refractory pain over weeks, months, and even years.

Deeper study into the distinct behaviors of the multiple proinflammatory mediators in the joint, such as PGE-2 and Nerve Growth Factor (NGF), has demonstrated it is, in fact, non-linear. The groundwork for chronic pain is laid immediately following trauma, allowing pain to take on a life of its own at the onset of OA.

The effects of the proinflammatory mediators in OA pain create a mixed state of acute, or adaptive, pain and chronic, or maladaptive, pain from the start.¹

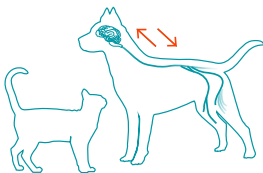
THE PATHOLOGY OF MIXED PAIN

Research has shown that not all proinflammatory mediators have the same impact on pain signaling. For example, in the periphery, PGE-2 sensitizes nerves to noxious stimuli. Nerve Growth Factor (NGF), on the other hand, has additional effects.



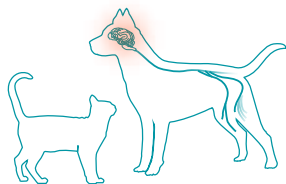
NERVE GROWTH FACTOR (NGF)

NGF is a mediator involved in the synthesis of nerves during early development. In the adult, NGF is a mediator released in the inflamed joint at the same time that PGE-2 is released. However, in addition to sensitizing nerves, it stimulates development of additional receptors on the cell's surface to increase the cell's sensitivity to stimuli, and contributes to inflammation.



ADAPTIVE PAIN (ACUTE)

Adaptive pain prevents us from doing things that are harmful—like touching a hot stove. In this case, mediators cause afferent nerves in the peripheral nervous system to fire signals which are then picked up by the spinal cord and relayed to the brain—potentially leading to a change in behavior and a subsequent reduction in the concentration of pain mediators and neural firing. This is the case in reflex reactions: neural pathways that process input via a connection in the spinal cord and provide a nearly immediate response without the need for conscious thought. The animal then can quickly change its behavior so that it is able to withdraw and heal.



MALADAPTIVE PAIN (CHRONIC)

Maladaptive pain has no clear biological value. It occurs when the source of pain is ongoing (e.g. osteoarthritis), and the mediators persistently bombard the peripheral neuron. In the case of ongoing NGF release, the combined effects of upregulating receptors and potentiating inflammation after NGF release amplify peripheral input into the central nervous system (CNS). In turn, this ongoing nociceptive input drives central changes (central sensitization).¹

1. Enomoto, M. Antinerve growth factor mono-clonal antibodies for the control of pain in dogs and cats. *Vet. Record*, Vol. 2018: 184 (1).

NERVOUS SYSTEM SENSITIZATION



Neural plasticity describes changes in the nervous system in response to input. An increase in peripheral input increases sensitivity; a decrease in peripheral input decreases sensitivity. When effective analgesia is not provided, central sensitization sets in, making the pain it is contributing to increasingly more difficult to manage.

The primary result is abnormal signals that cause spontaneous firing without a pain stimulus, and exaggerated pain responses to what would normally be painless or mildly painful stimuli. All of this is the manifestation of maladaptive pain.

NEURAL PLASTICITY OCCURS IN TWO WAYS

1. PHENOTYPICALLY ALTERS NEURONS

Mediator binding to the peripheral neuron alters expression of certain cell surface receptors that increase sensitivity to nociceptive input.

2. FUNCTIONALLY ALTERS NEURONAL COMMUNICATION

OA signaling molecules lead to transcription changes that results in higher expression of pronociceptive neurotransmitters.



THE HORIZON OF OA PAIN

TREATMENT: NERVE GROWTH FACTOR (NGF)

In veterinary medicine, new approaches and targets are being studied for the treatment of chronic pain. One target in particular, Nerve Growth Factor (NGF), is showing promise in providing long-lasting OA pain relief for dogs and cats. New scientific innovations allow for the creation of monoclonal antibody therapy (mAbs) designed specifically for feline and canine use. Clinical researchers have found that it is now possible to block NGFs' negative influence in the joint with anti-NGF antibody therapies.¹

Dr. Margaret Gruen: *"I think it's become very clear that NGF is a potent driver of pain in osteoarthritis. And in the studies that we did with cats, we found that when you effectively block NGF you can profoundly improve cats' quality of life, and decrease their pain."*

TALKING OA PAIN WITH PET OWNERS

Educating pet owners about pain can help manage client expectations for treatment outcomes and underscore the importance of compliance to effective treatment outcomes.

RECOGNIZING PAIN IN EVERYDAY BEHAVIORS

USE CHECKLISTS TO TRANSLATE PET OWNER'S OBSERVATIONS

Pet owners are highly attuned to their pet's behaviors, moods, and activity level. They understand their pet's behavior in the context of their life and their experience. However, they may not know when behavior changes are indicators of OA pain.

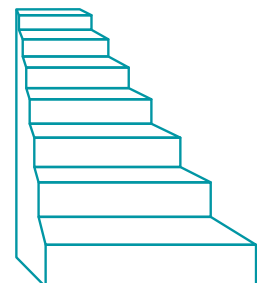
How owners interpret changes in their pets behaviors:	What may be really happening
My dog is getting older and slowing down is natural	<ul style="list-style-type: none">• Dog is likely showing signs of lameness due to pain
Great! My cat has finally learned to stop jumping up on the counter	<ul style="list-style-type: none">• Cat may have lost mobility due to the pain of OA and now it hurts to jump
My cat has developed a behavioral issue (e.g. not using the litter box, hiding more)	<ul style="list-style-type: none">• Cat may be experiencing the effects of chronic pain, such as inability to get to, or climb into the litter box
My cat/dog has outgrown their playfulness; lost their inner kitten/puppy	<ul style="list-style-type: none">• Chronic pain is impacting the cat's/dog's emotional well-being

Simple and easy to use checklists can be a great way to help clients identify pain and keep them engaged by monitoring the efficacy of treatment.

SHARE PERSONAL OBSERVATIONS OR EXPERIENCES

For animals suffering from OA pain, some everyday tasks can become enormous hurdles. Sharing personal stories about animals with OA pain and solutions developed to improve the pet's quality of life can lead pet owners to their own 'eureka moment' with their pets.

Dr. Stacy McVicker: "When I talk with families who have older cats, I often share a Eureka moment that I had with my own cat, Nero. When he was around 17, I noticed he was reluctant to go down the stairs to the litter box. Nero was struggling with getting up and down and I was essentially asking a 90-year old man go down a flight of stairs every time he had to go to the bathroom. I thought to myself, 'this is ridiculous!' So we added litter boxes upstairs and Nero never went down the stairs again. That was my Eureka moment!"



EXPLAINING 'PAIN GONE WRONG'

Dr. Mike Petty: *"Animals are non-verbal beings. They can't tell us that they hurt in a verbal way. They can only tell us by their behavior, their unwillingness to socialize, their unwillingness to play ball and so forth. And if we don't treat that pain of arthritis, we're taking all of that away from them. And that's really sad, because then they're not going to have a fuller life that they really deserve."*

Pet owners are highly motivated to treat their pet's OA pain when it is first detected. Too often they stop giving pain medications when the signs disappear, thinking that the problem has been solved. OA pain is progressive in nature, therefore explaining the importance of compliance is key.

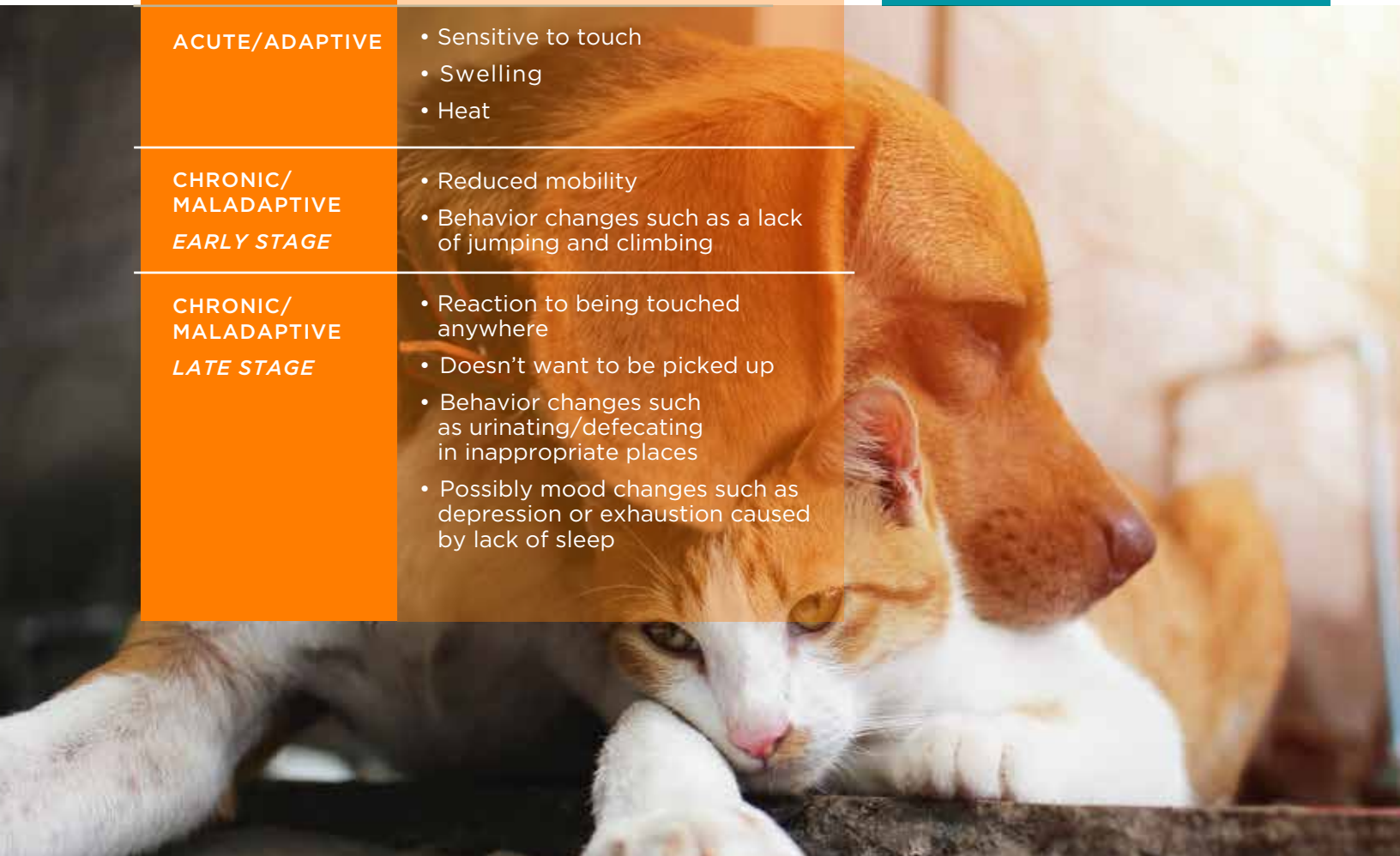
We can help pet owners anticipate the consequences of untreated pain by providing them with specific observations they might see, or using a metaphor to explain what is going on in the body to manifest those observations. And because a picture is worth a thousand words, a schematic can help illustrate these points.

RECOGNIZE STAGES OF OA PAIN

STAGE OF OA PAIN	WHAT YOU WILL OBSERVE
ACUTE/ADAPTIVE	<ul style="list-style-type: none">• Sensitive to touch• Swelling• Heat
CHRONIC/ MALADAPTIVE EARLY STAGE	<ul style="list-style-type: none">• Reduced mobility• Behavior changes such as a lack of jumping and climbing
CHRONIC/ MALADAPTIVE LATE STAGE	<ul style="list-style-type: none">• Reaction to being touched anywhere• Doesn't want to be picked up• Behavior changes such as urinating/defecating in inappropriate places• Possibly mood changes such as depression or exhaustion caused by lack of sleep

"If you can get to the understanding that chronic pain becomes a life of its own regardless of the initiator, then they can understand that you have to manage it."

Dr. Steve Budberg



CREATE A METAPHOR USING A TANGIBLE EXAMPLE

For some pet owners, a metaphor relating the pain pathway to a concept they are already familiar with may work best. Dr. Sheilah Robertson has used the electrical system as an effective metaphor for distinguishing maladaptive from adaptive pain.

MALADAPTIVE PAIN IS LIKE A MISFIRING ELECTRICAL SYSTEM

As described by Dr. Sheilah Robertson, the effect of untreated chronic pain has a similar effect on the nervous system as someone who opens a junction wiring box and switches a couple of white wires around.

“All the lights start flickering and going out, because somebody messed with the complex wiring box. And I often like to show a photograph of an open wiring box, and just ask, ‘What would happen if you just switched two of those cords?’ Everyone’s like ‘Wow!’”



ACUTE PAIN

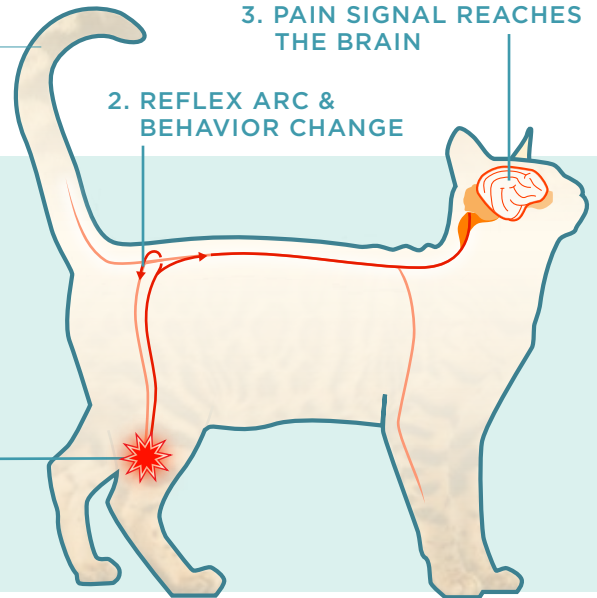
ADAPTIVE PAIN

Acute pain helps us avoid behaviors that can harm us, like touching a hot stove. Responses usually lead to a change in behavior in order to get away from the thing that hurts and stop any more damage. Sometimes this is a reflex that happens before the brain even knows about the pain.

1. SOURCE OF ACUTE PAIN

2. REFLEX ARC & BEHAVIOR CHANGE

3. PAIN SIGNAL REACHES THE BRAIN



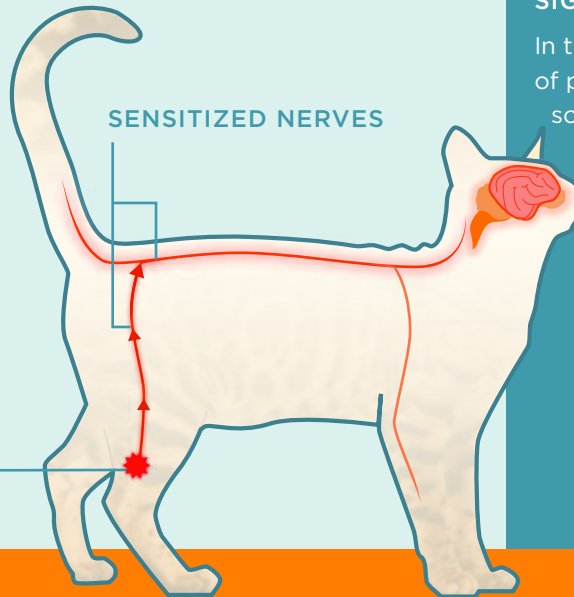
CHRONIC PAIN UNTREATED

MALADAPTIVE PAIN

Chronic pain happens when the pain signal doesn't go away. It keeps bombarding the nervous system until the nervous system actually changes. It becomes even more sensitive to pain signals and can severely impact the cat's quality of life.

SENSITIZED NERVES

CONTINUOUS SOURCE OF PAIN



SIGNS OF OA PAIN IN CATS

In the wild cats need to hide any signs of pain or weakness, that is why it's so hard to tell when they are in pain.

Look for these behaviors to identify pain in your cat:

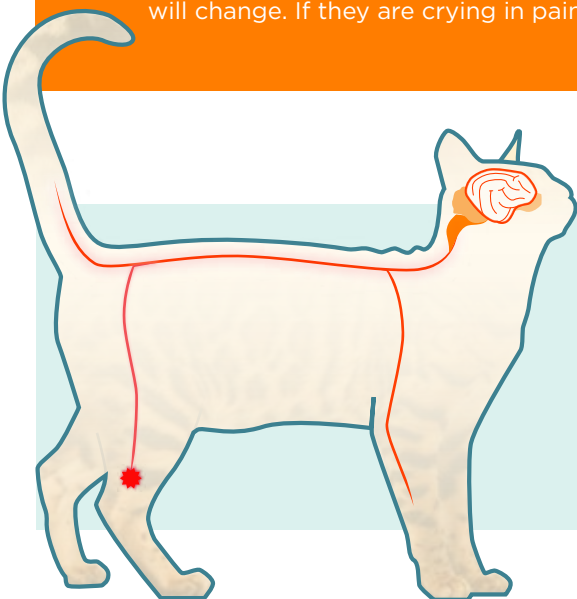
- No longer running or chasing toys
- Hesitant to jump up or down
- Breaks up jumps into small jumps
- Difficulty with stairs
- Less energetic or enthusiastic
- Not using the litter box
- Less social or interactive

CRYING

When people hurt, they usually complain or cry out. Cats don't typically do this: instead, their behavior will change. If they are crying in pain, you need to pay attention!

CHRONIC PAIN TREATED

The pain signal doesn't ever go away in certain chronic pain conditions like arthritis, so it's important to decrease the signal in order to get relief from pain. This is why you need to keep giving pain treatments as directed by your veterinarian.



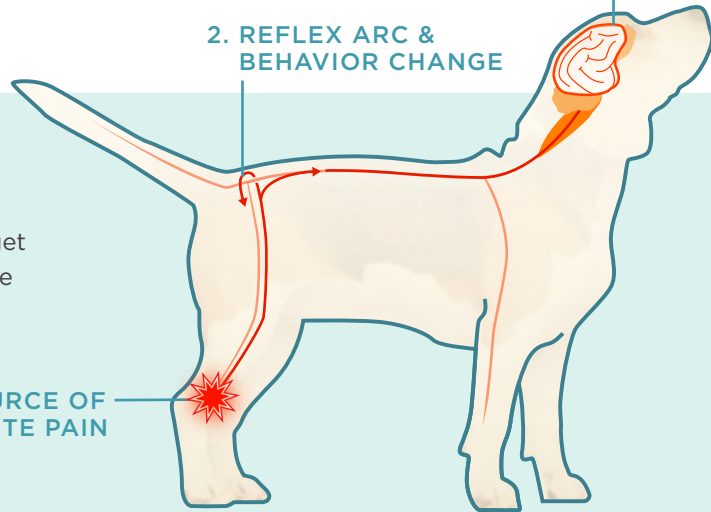
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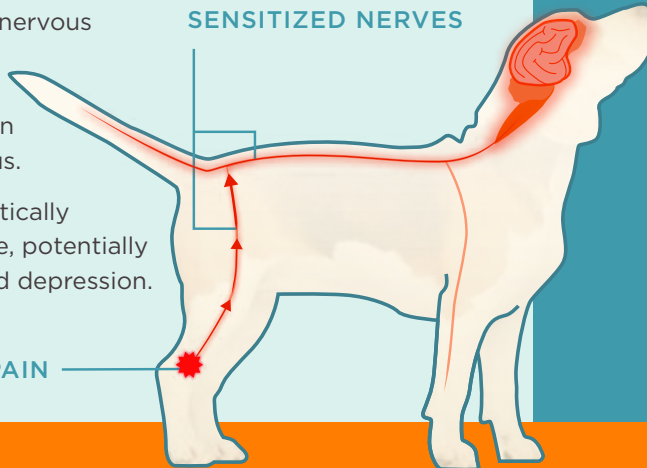
MALADAPTIVE PAIN

Chronic pain can alter the nervous system of your pet so that the peripheral nerves are firing painful signals even in the absence of any stimulus.

Long term pain can dramatically affect a dog's quality of life, potentially leading to loss of sleep and depression.

CONTINUOUS SOURCE OF PAIN

SENSITIZED NERVES



SIGNS OF OA PAIN IN DOGS

If dogs have chronic pain, the signs may be subtle, or they will creep up slowly so you may not notice them.

- Limping
- Lagging behind on walks
- Slower getting up or laying down
- Difficulty jumping
- Difficulty with stairs

VOCALIZATION

When humans experience acute pain they cry out, and when they have chronic pain they often complain. Animals sometimes vocalize due to sudden, intense acute pain. However, it would be an uncommon behavior for a pet who is suffering long term. The absence of vocalization should not be seen as an absence of pain.

CHRONIC PAIN TREATED

Relieving chronic pain at the joint may slow or prevent the worsening of chronic, maladaptive pain. Pain medications give the nervous system a chance to recover. This is why it's important to comply and follow through with your dog's pain treatment.

The logo for Zoetis Petcare is centered on the page. It consists of the word "ZOETIS" in a bold, orange, sans-serif font, positioned above the word "PETCARE" in a bold, blue, sans-serif font. The background of the page is a blurred photograph of a wooden deck railing with a dog's paw resting on it, set against a backdrop of green foliage. An orange horizontal bar is at the top of the page.

ZOETIS PETCARE