SECTION 4. DISEASES

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4.1 Degenerative and stenotic changes in the cervical spine of mammals

About the degenerative-dystrophic process present in mammals, there are many publications and scientific articles, but the etiology and pathogenesis of the disease are still largely undefined at present. Although there are many similarities in this disease between humans and small domestic animals, there are also some differences. In our study, we compared the etiopathogenetic, morphological, clinical symptoms, and syndromes of degenerative spondyloarthrosis, intervertebral osteochondrosis, deformative spondylosis, and spondylolisthesis, which are the main manifestations of the degenerative-dystrophic process in the cervical spine structures. The processes occurring in the vertebrae, intervertebral joints, discs, ligamentous apparatus significantly affect clinical signs, comfort, and full-fledged life. It is advisable to take a comprehensive approach to each individual patient: apply one or several visualization methods during examination, carefully study clinical symptoms and syndromes, medical and life history, objective data, laboratory diagnostics, additional examination methods such as CT/MRI, radiography, radioscopy, etc. The degenerative-dystrophic process is associated with pain syndrome of varying intensity, both in humans and in certain groups of animals. More often, intervertebral osteochondrosis and deformative spondylosis affect both people and large dog breeds weighing over 20 kg. There is also a fraction of patients who, radiologically, are diagnosed with stenotic changes in the spinal canal during CT or MRI examination, but clinical data, complaints, paraplegia, or paresthesia are not detected. In our study "Asymptomatic degenerative disc disease and spondylosis of the cervical spine. MRI" by Teresi LM, Lufkin RB, Reicher MA et al. (1987), it is noted that the frequency of asymptomatic stenosis in old age is at least 25%, as argued by German scientists, including Andreas Raabe [129]. It is a well-known fact that humans have bipedal locomotion, while animals have quadrupedal locomotion. Therefore, they bear different axial loads on the spine, internal organs, etc.

It is impossible to assess posture in animals. Different groups and species of animals and humans do not have similar physical loads, especially on the cervical spine, but they have a similar anatomical and simultaneously functionally different body structure, skeleton, etc. Degenerative-dystrophic processes in the cervical spine are an urgent problem for them. In our research, we have noticed that the degenerative process in the cervical spine, both in animals and in humans, can affect gait and balance: symptoms of dizziness, vertigo, hearing or vision impairment may appear in humans and may require significant correction in some cases. For animals, especially large dog breeds, characteristic signs include walking in circles, tilting their head to the floor, limping on their front or hind legs. Subjectively, both humans and animals complain of pain, which is almost the main symptom, as well as various types of paresthesia and numbness of one or several fingers, partial or generalized numbness in the upper limbs, and possible balance disturbances. In small domestic animals, behavioral changes are characteristic, reduced activity during walks, whining, which is interpreted as a manifestation of pain syndrome, leaning to one side, which is interpreted as a balance disturbance. During objective examination by veterinarians, changes in superficial and deep sensitivity, reflex changes are detected. Depending on the manifestations, similar symptoms may be present in the legs in humans and in the hind limbs in animals. Spanish neurosurgeons-practitioners, studying clinically significant criteria for stenotic changes in the cervical spine by John Shim, MD, FACS, Orthopedic Surgeon (2016) and Brian McHugh (2017), symptomatology, clinical and syndromic picture, diagnostics, propose modern methods and ways of diagnosing and treating degenerative changes in the cervical spine. It is important for Ukrainian doctors and the global medical community to exchange modern methods and ways of diagnosing degenerative changes in the cervical spine, as this pathology affects many people worldwide and is not endemic. The multifactorial nature of pathology in the cervical spine, the diversity of syndromes and symptoms, insufficiently studied etiopathogenic factors of the development of degenerative changes, progression and unstable remissions of the pathology present a challenge for doctors and veterinary doctors in the search for new etiopathogenetic mechanisms of the disease, prevention, and

treatment. To support Ukrainian doctors, BMJ Publishing Group Ltd provides free access to the online edition of the British Medical Journal, specifically to two online resources - BMJ Best Practice and BMJ Learning [130]. Also, in the cervical spine, there is degenerative disease of the cervical spine (cervical spondylosis)-this is the osteoarthritis of the spine, which includes spontaneous degeneration of disc or facet joints. Manifestations include axial pain in the neck and neurological complications [131]. To search for new etiopathogenetic factors in the development of degenerative-dystrophic process, to determine groups of patients and small animals, and criteria for including patients in the study were: pain syndrome in the upper part of the torso, disturbances of segmental innervation of the hands, characteristic conductive disorders, and the presence of degenerative-dystrophic processes in the cervical spine. Similar clinical disorders and neurovisualization data in animals also served as criteria for their inclusion in the study.

Problem Statement: The exclusion criteria for patients in the study included the presence of comorbidities such as developmental defects, dysplasia, and dysraphism of vertebral bodies and intervertebral joints, cystic changes in vertebral bodies, oncopathology, diagnosed osteoporosis, and systemic connective tissue diseases. Animals were excluded from the study if they exhibited pathological processes similar to those observed in humans and if they belonged to chondrodystrophic dog breeds. For the objectivity of the study and the analytical process, a retrospective analysis of medical histories was conducted after CT scans of the cervical spine in 65 patients (human subjects). Clinical-morphometric and CT examinations were performed on 75 small domestic animals: 14 cats, 42 dogs weighing up to 20 kg, and 19 dogs weighing over 20 kg, with the participation of owners at the "Favorit" Veterinary Center, License No. 571, issued on July 19, 2017. The study was conducted due to pain reactions in animals, including neck tenderness, acquired neurological deficits, and characteristic motor disorders. Computer tomography was used for neurovisualization of pathology in animals, utilizing the Philips MX 8000 CT scanner (Amsterdam, Netherlands, 2002). Neurovisualization and examination of human subjects were performed at the "MEDCORUG" Medical Center, License No. 565755, series AB, on the Siemens

SOMATOM Definition AS CT scanner (Munich, Germany, 2017). The age of dogs was converted to human age using the formula: human age = 16 x (natural logarithm of dog age) + 31 [132]. The average age of dogs compared to the age of humans was 43.4 ± 7.0 years, which was identical to the data in examined humans - 41.5 ± 5.2 years ($p < 0.001$). The intensity of pain in humans was recorded using a 10-point visual analog scale, while in animals, it was assessed using a 5-point scale with evaluation of physique, gait, behavior, response to palpation, and body tension. Morphometric-densitometric measurements of vertebral density were performed in Hounsfield units according to scanning protocols for both humans and animals in line with commonly accepted recommendations. The Pavlov-Torg index was used to study the dimensions of the human spinal canal to detect cervical canal stenosis. All veterinary examinations were conducted with the permission of animal owners. Instrumental examinations and clinical procedures were painless, non-invasive, taking into account the individual condition of each patient and animal. All studies were conducted in accordance with existing bioethical standards. The obtained data were presented as the mean (x) and standard error of the mean (SE). One-way analysis of variance (ANOVA) with subsequent Neuman-Keuls post-test was used to identify significant differences between the study groups. The non-parametric Kruskal-Wallis test was used to identify significant differences when using untreated absolute indices. A value of $p < 0.05$ was considered a statistically significant difference. In the course of the work, the data on the leading manifestations of degenerative-dystrophic changes in the cervical spine, such as neck or upper back pain radiating to the arms, of moderate intensity according to the visual analog scale, and characteristic tension headaches, combined with the above-mentioned painful manifestations, were obtained. Like the pain syndrome, frequent systemic dizziness intensified with head and neck movements. Clinical neurological symptoms were characteristic of disorders of segmental innervation, which are typical for secondary myelopathy, radicular, and other syndromes due to degenerative changes in the bone-cartilaginous apparatus of the neck. In this case, the above clinical picture was associated with stenotic changes in the spinal canal in the cervical spine, which appeared on CT scans against the background of degenerative

spondyloarthrosis, intervertebral foramen narrowing, degenerative spondylolisthesis, hypertrophy of the longitudinal and yellow ligaments, and was additionally determined by disc protrusion, the presence of vertebral outgrowths, and intervertebral joints. Such damage influenced the further formation of acquired spinal stenosis and also involved the vascular structures of the neck, ganglia, and nerve roots and the closely located vegetative structures in the pathological process. Early diagnosis and preventive treatment are key to preventing complications such as radicular neurological manifestations of the upper extremities, neck, occipital area, myelopathy due to complications of cervical osteochondrosis, such as protrusions and intervertebral disc herniations, circulatory disturbances, vertebrobasilar symptoms, and visual impairments. For the examination of patients, computer tomography, compared to the prototype of magnetic resonance imaging and other radiological and functional examination methods, will allow for the early objective diagnosis and objective assessment of acute and chronic pain in cervical osteochondrosis in humans and domestic animals, improving the somatic condition of patients, reducing the number of relapses, complications, and enhancing the quality of life for people. According to the literature and our data, large and giant dog breeds are more likely to suffer from intervertebral osteochondrosis. Computer tomography and magnetic resonance imaging of dogs of both sexes and such breeds as the Labrador Retriever, Rottweiler, Golden Retriever, English Mastiff, and English Bulldog revealed combined pathology: damage, degeneration, calcification of the intervertebral disc, marginal bone osteophytes, calcification of the ligamentous apparatus, displacement of vertebrae relative to the axis of physiological lordosis, narrowing of intervertebral foramen, as a result, root syndromes, and structural spinal canal changes and signs of compressive myelopathy. The cervical spine (CVS) is the most complex joint system in the human body, containing thirty-seven individual joints that facilitate numerous movements of the head and neck. The seven cervical vertebrae, with their capsular, ligamentous, tendinous, and muscular attachments, offer relatively poor protection for their connections compared to the skull and rib cage [133]. The contents of this anatomical cylinder, located between the skull and rib cage, include the vertebral and carotid

arteries, the spinal cord, nerve roots, and the brainstem [134]. Another pressing issue is the tendency for "rejuvenation" of degenerative-dystrophic processes in the CVS. The peak incidence occurs in middle-aged and adolescent individuals. In the young population, this pathology is more common than alcoholism, drug addiction, and asthma [135]. Among the most prevalent progressive chronic pathological conditions in the cervical spine are acquired spinal canal stenosis, which, in cases with clinical symptoms, can reach up to 80% [136]. The frequency of spinal canal stenosis increases with age, and the rate of disability cases also rises (Galbusera & Wilke, 2018; Davison et al., 2020). It is necessary to clarify and optimize the etiopathogenesis and diagnostic factors of stenosis in humans. This issue is particularly relevant and practically unexplored in veterinary medicine (Pavlov et al., 1987; Amadu et al., 2017). Furthermore, anatomical indicators may not always align with clinical manifestations in both humans and animals, necessitating further clinical-morphometric clarification [137]. The determination of the causes of acute and chronic pain in degenerative-dystrophic processes in the cervical spine and its complications, such as organic stenotic changes in the structures of the spinal canal, intervertebral disc protrusion, marginal bony outgrowths of vertebral bodies, degenerative changes in intervertebral joints, etc., is crucial. Neck pain significantly affects the quality of life for humans and small domestic animals. In the clinical picture of cervical disc degeneration, neck and back pain dominate, affecting more than half of the global population, with a prevalence rate of 60-80%, which has increased by 21% over the past 10 years. Chronic pain ranks fourth in the causes of disability (Yemecz, O.T. 2020) [134, 136, 138]. Objective tomographic diagnostics, along with other instrumental and differential diagnostics of degenerative-dystrophic processes in the cervical spine in mammals, is one of the leading methods in the clinical practice of neurologists, neurosurgeons, orthopedists, traumatologists, rehabilitators, veterinarians, therapists, cardiologists, and physical rehabilitation specialists. Patients often experience pain, paresthesia, and upper limb dysfunction in humans, and similar syndromes in the forelimbs of animals. Pain, in combination with other neurological symptoms, may require surgical intervention. Treatment options range from non-surgical measures to decompression,

instrumental spondylodesis, or a combination of both laminoplasty, instrumentation, or a combination of both [139]. In diagnostic search and clinical diagnosis formation, magnetic resonance imaging (MRI) is used, selecting the optimal scanning parameters [140]. Computed tomography (CT) for domestic animals is a visualization method based on measuring and computer processing the difference in X-ray attenuation by tissues with varying densities. Despite being based on X-ray radiation, CT has significant advantages over standard radiological diagnostics and is often used in cases such as trauma or lung examinations before MRI. To understand the difference between MRI and CT, it is necessary to know the fundamental differences between these types of imaging. Magnetic resonance imaging obtains data on the condition of internal organs and systems by using a strong magnetic field, while CT relies on X-ray radiation. Both methods are effective for examining the abdominal cavity, soft tissues of the head, bones, and other body parts. Different scanning methods are prescribed depending on the individual patient's needs [137, 141]. The higher the sensitivity and specificity of the CT method and the technical capabilities of the CT machine, the better tissues that even slightly differ in morphological structure are differentiated. CT provides precise information about the size and density of individual organs and tissues. The imaging obtained in the plane of the investigated cross-section eliminates the overlaying of "shadows" and allows for assessing the localization, nature, and extent of the disease focus [142].

CT with intravenous contrast for cats and dogs, as well as all exotic animals and rodents, is a highly informative diagnostic procedure. It involves performing a CT after introducing a contrast agent into the mammal's body. The substance is transported by the blood, accumulates in areas with active blood supply, and reflects X-rays. Using contrast enhancement can make CT scans clearer, visualize soft tissues, blood vessels, areas of inflammation, and oncology, as stated by veterinarians at the Zoolex Clinic [139, 140, 145]. Post-processing of tomographic images performed with CT allows for qualitative and quantitative CT analysis. Quantitative CT analysis (Q-CTA) is a set of tools that help make quantitative measurements in anatomical structures [135, 140, 143]. By changing the brightness and contrast, i.e., shading surfaces from different

sides, you can significantly improve the visualization of the area of interest. Additionally, real-scale manipulations with three-dimensional images include scaling, rotation around any axis, and "cutting out" organs to demonstrate structures located beneath the tissues. By making tissues transparent, the organs are exposed. It is easy to measure distances, three-dimensional volumes, and angles [144]. If necessary, under the same anesthesia, a material can be taken for cytological examination (the location of the biopsy needle can be monitored on the tomograph). This allows viewing native scans (scanning "as is," without additional contrasting) [145]. Before performing a CT examination, thorough anesthesia planning is required, which includes evaluation by an anesthesiologist and patient stabilization, premedication, induction and maintenance of anesthesia, monitoring, and post-anesthesia recovery [143,144, 146]. The care of animals until their full recovery is the responsibility of a veterinarian. According to available open sources, such clinical symptoms were observed in more than 80% of human patients and more than 65% in large and giant dog breeds. Perhaps such changes in the cervical spine are key factors in acute and chronic pain in mammals. The relevance of the Pavlov-Torg index for CT of the CVS for an objective assessment of stenosis of spinal canal structures in all groups of young and middle-aged mammals, taking into account the formula (human_age = 16ln (dog_age) + 31) [146]. Measurements of the Pavlov-Torg index on X-rays and on magnetic resonance images of the CVS reflect the same result: stenosis [147]. Researchers, Danika Bannas from the University of California at Davis and Elaine Ostrander from the National Institutes of Health, compared changes in the methylation pattern with humans, studied 104 Labrador Retrievers, from puppies a few weeks old to 16-year-old dogs, and studied age-related problems and aging of the body as a whole and individual organs and systems. The calculation of the dog's age to human age was carried out according to the formula and data of Christian Yates et al. (2020) [148]. Degenerative and dystrophic lesions of the spine significantly affect the quality of life of humans and mammals, leading to the development of neurological deficit, restricted mobility, and pain syndrome. The most clinically significant consequence of the progression of degenerative-dystrophic changes, mainly in the form of stenosis at the CVS level, is

cervical spondylotic myelopathy, the predominant cause of all myelopathies in adults [149]. In her work (2017), I. K. Bakumenko studied the features of the formation, clinical picture, and developed an algorithm of vestibular dysfunctions in degenerative changes in the cervical spine in humans with signs of vertebral artery compression on the background of intervertebral osteochondrosis [150]. Additionally, the author (Bakumenko I. K., 2017) conducted experimental studies on laboratory rats dynamically, after bilateral occlusion of vertebral arteries. As a result of the experiment, it was found that in animals with impaired blood circulation, specifically occlusion of vertebral arteries, the same symptoms appeared as in humans - akinesia and hypokinesia. Neurological deficit is a clinically significant pathology. It is well known that intervertebral discs of the cervical spine at the C2-C7 level, which make up the vertebral-mobility segments, perform a cushioning function between the vertebrae, and participate in providing full head and neck movements. Intervertebral discs that have not undergone degenerative changes, retain the pulpy core, without signs of dehydration and sequestration, withstand intensive and everyday loads. When the muscular apparatus is exhausted by stress, and the pulpy core of the intervertebral disc begins to change its structure (dehydration, degeneration, sequestration), this leads to pathologically altered vertebral mobility in these areas [151]. In her research, O. Ye. Yurik [133,152,153] based on long-term clinical-functional, biochemical, and immunohistological studies found that the formation of CVS damage and neurological manifestations, primarily depends on disturbances in the activity of the autonomic nervous system (ANS) in the form of subclinical systemic autonomic dysfunction. Along with neuro-dystrophic changes in the structures and tissues of the spine, vascular dysfunctions, a large number of reflex syndromes activation (mainly sympathetic-adrenal reactions) of the ANS affects the hormonal status, especially in women, which, in turn, is reflected in the disruption of the structures of the musculoskeletal system in the CVS, and even more triggers ANS dysfunctions, launching a series of somatic disorders, including metabolic diseases in mammals."

Key words: *degenerative-dystrophic changes, cervical spine in mammals, intervertebral osteochondrosis*.

Objective: Differentiation and determination of clinical, etiopathogenetic factors with CT data in humans and animals. The CT method is objective and informative in diagnosing intervertebral osteochondrosis in all mammals. Morphometric analysis of CT results and their correlation with objective clinical syndromes and subjective data.

Research methods: Determination of objective and subjective clinical data of human patients, morphometric, syndromal, anatomical-physiological, statistical data, computer tomographic diagnostics of the cervical spine in humans and small domestic animals.

Tasks: To determine the clinical significance of the occurrence and features of the clinical manifestations of degenerative-dystrophic and stenotic changes in the cervical spine in mammals. Determine models for clinical trials.

Research object: Humans, small domestic animals of various breeds and weight categories, the significance of the degenerative-dystrophic process of the cervical vertebrae.

Research subject: People with discomfort and pain of varying intensity in the neck, upper limbs, proximal chest area; domestic animals with a corresponding clinical picture, pain in the neck, and gait disturbances in the front limbs, paresthesias.

Materials and Methods:

During the period of 2017-2021, examination of domestic animals was conducted at the veterinary center "Favorit", located at 4v Artillery Street, Odessa. For retrospective analysis of degenerative-dystrophic changes, computed tomographic examination with painful and radicular neck syndrome was studied in humans (65 individuals) and small animals (75 animals). Clinical and visualization examinations of animals were performed at the veterinary center, using computer tomography for animals "Favorit" by veterinary doctors. Animals with dysraphic pathology of the spine and intervertebral joints, other developmental anomalies, acute traumas, and oncological pathology were excluded from the study. The identification of the cause of pain syndrome in the cervical spine and front limbs, clinical syndromes, and paresthesias in small animals is an important aspect in the differential diagnosis

between the degenerative-dystrophic process of the cervical spine and local lesions of the shoulder-blade and elbow joints, as these pathologies have many similar features, although there are clinical and morphological differences. A symptom such as lameness in the front limbs of animals can be a complication of intervertebral osteochondrosis in medium, large, and giant breeds, as well as joint changes [154]. In small breeds and cats, similar symptoms may be present in dysraphias of various anatomical structures of the cervical spine and are not associated with complications of intervertebral osteochondrosis, as in such species of animals, minimal degenerative-dystrophic changes were found in intervertebral discs during CT examination, and this was observed in a small number of mammals, and there were also no changes in the bodies of the vertebrae and intervertebral joints. Additionally, a retrospective analysis of computed tomographic examination of humans was conducted, analyzing changes in the cervical spine against the background of degenerative-dystrophic processes. The age range of all patients included in the sample was: men from 29 to 65 years old, women from 20 to 65 years old. The average age in men was 41.5±5.4 years, in women - 41.5±4.9 years. The age of all examined animals ranged from 1 to 14 years. The age of dogs was converted to human age using the developed formula: human age = 16 x ln (natural logarithm of the dog's age) + 31. The calculation of the formula is based on the quantitative translation of aging from a dog to a human through conservative remodeling of epigenetic networks. (Wang T, Ma J, Hogan AN, Fong et al., 2020; Yates K., 2021) [140, 142, 155]. For grouping cats by age, 6 categories were distinguished. Infant 0-6 months; youth lasts up to 2 years; young age - from 2 to 6 years; maturity - from 7 to 10 years; old age - from 10 to 14 years; elderly - over 14 [135, 138, 156]. The average age was: in cats 6.2±2.6 years (43.4±6.3 years when converted to human age); dogs weighing up to 20 kg - 5.8±2.8 years (40.6±5.2 years); dogs weighing over 20 kg - 6.5±4.8 years (45.5±7.0 years). Signs of spinal cord involvement, syndromal signs of myelopathy, painful and radicular syndromes, morphologically interpreted as narrowing of the intervertebral foramina with degeneratively changed intervertebral disc and manifestations of degenerative spondyloarthrosis, were observed in most adult dogs (6-14 years), large breeds, n=19,

with the presence of stenosis (15-78.9%). Slight weakness of one (6-31.5%) or both (3-15.8%) hind limbs; one (3-15.7%) or both (2-10.5%) front limbs were registered. In some cases, "scratching of claws" on asphalt could be heard (6–18.2%). Inconvenience when rising from the "sitting" or "lying" position (10–52.6%), changes in posture (4–21.1%), ataxia of the hind limbs (5–15.1%), disorders of pelvic reservoirs (3- In 21 animals (84.0%), a pain syndrome was detected upon palpation of the cervical spine. The results of our work indicate that complications in the form of stenotic changes in the intervertebral foramina, structures of the spinal canal of the cervical spine arise not only in the elderly mammals but are also characteristic for young and middle-aged individuals (the average age of the examined patients was 43.4±6.7 years and 41.5±5.2 years (when converted to human age) respectively). Acquired (secondary) spinal stenosis of non-traumatic origin develops against the background of degenerative-dystrophic changes in the neck ($p<0.05$) in 87.7% of humans and 78.9% of dogs with clinical manifestations of cervical myelopathy ($p<0.05$) with predominant persistent pain syndrome (3.1±0.3 points in humans and 2.6±0.4 points in animals according to the VAS scale). This type of pathological process in the studied groups mainly developed at the level of C6 ($p<0.05$). The mass fraction of stenotic changes in the cervical spine according to the Pavlov-Torg stenosis index in large breed dogs was 78.9% and likely coincided with clinical manifestations ($p<0.05$). Similar clinico-morphometric indicators were obtained in humans (87.7%, $p<0.05$). The use of standardized scanning parameters, depending on the size of the field of view (FOV) window; patient's weight, Voltage [KV] intensity, and Current [mA] x-ray rigidity, examination area Length (mm); filters Filter [C, D]: for soft tissues-[C] and bone structures-[D] for better tissue detailing. The radioresistance of tissues is directly proportional to proliferative activity and inversely proportional to the degree of differentiation of its cellular components (Bergonie-Tribondeau rule) [157,158]. The observed difference in densitometric indicators of trabecular bone tissue (at the level of C3-C6 bodies) in the central parts of the bodies on the right and left [159]. Measurements on simple X-rays overestimate the canal diameter. The average diameter of the lower cervical spine is approximately 14 mm. [160].

Perspectives of Research on this Issue:

Computer tomographic examinations of small domestic animals and their analysis will assist medical professionals in diagnosing and treating humans, taking into account new etiopathogenetic factors. This will provide valuable insights into the diagnosis and treatment of cervical osteochondrosis and its complications, allowing specialists to choose the optimal method and approach to manage pain and prevent complications of degenerative-dystrophic disorders of the cervical spine. This research has the potential to improve the quality of life for both humans and animals.

Conclusion:

CT scanning is an objective and morphometrically reliable method for assessing the degree of stenosis and stenotic changes in the cervical spinal canal, root canals, and intervertebral foramina in the context of degenerative-dystrophic processes. These findings can enhance our understanding of the underlying causes of neck pain and neurological deficits in both humans and small animals, leading to more effective treatments and preventive measures. CT examinations serve as a key tool in objectively assessing patients' conditions and guiding treatment decisions, which underscores the significance of this research.