ABSTRACT

Key words: respiratory disorders, radiography, computed tomography, cytology, microbiology, dog, cat.

The respiratory system represents, along with the central nervous system and the cardio-vascular system, one of the three major vital functions of any mammal body. The absence of this function causes the death of the patient.

In human medicine, the pneumology represents a major field of specialization, just as the cardiology and the neurology, completing with these last two the emergency medicine and intensive therapy. Keeping under control the respiratory and heart functions means keeping patients alive and gives doctors time to investigate the causes of a pathology.

In veterinary medicine, synchronizing the scientific level with the one in the human medicine became necessary. These last years, various directions of specialization became available, from imaging diagnosis to cytological diagnosis, specializations that allow a faster and more accurate respiratory conditions diagnosing. Worldwide performant medical equipment and dedicated software development brought an increased utilization trend in veterinary medicine as well.

Respiratory conditions are closely connected to the thoraco-pleuro-pulmonary pathology, that is to all those structures involved in the respiratory act, and with a direct effect on the respiratory pathology: the thoracic cage and the diaphragm that shelter the respiratory system and are responsible of the respiratory mechanics, the pleurae and the pleural space that play a major part in respiration, the mediastinum that displays a respiratory reflective pathology and finally the trachea, the bronchial tree and the pulmonary parenchyma with their specific pathology.

Because we are talking here about a complex Whole displaying a plethora of pathologies, the diagnosis is never simple, and even when it appears to be so, we need to be aware of the possible complications. One thing is certain: the respiratory segments disorders are in a continued interdependence and evolution, and the respiratory symptomatology is somehow limited.

As a consequence, pathologies of very different etiology display a resembling clinical picture, while one single pathology can display extremely diverse aspects, depending on the evolution stage and on the affected segment. This is why differentiate diagnosing must follow a specific procedure.

A sore spot in veterinary pneumology is handling the patient which, as opposed to the human medicine, is more often than not reluctant and therefore subject to stress. This can endanger the patient's life, which makes careful monitoring a necessity, during the examination procedures and the sample collection.

The aim of this thesis was to study the applicability, patient tolerance and diagnostic value of imaging and laboratory diagnosis methods in the respiratory pathology, using advanced paraclinical methods and establishing correlations between them in order to optimise the diagnostic protocols. These methods are in an ongoing evolution, in accordance with two principal coordinates: obtaining a maximum of information through a minimum of interventions, potentially stressful to the patient. Thus an important role was given to the careful evaluation of the patient's status, the knowledge of the diagnosing methods availability and limitations and their appropriate use in order to obtain a firm diagnosis wihin the shortest time possible.

The study concerning "*The diagnosis of pleuro-pulmonary disorders in dog and cat*" theme was completed in three institutions: the Faculty of Veterinary Medicine of the University of Agricultural Sciences and Veterinary Medicine – Ion Ionescu de la Brad Iassy, the Clinical Veterinary Hospital of the Veterinary Medicine Faculty at the University of Cordoba, Spain and in the Interdepartmental Imaging Center of the Veterinary Medicine Faculty Federico II in Naples, Italy, for a total duration of four years, from September 1st, 2010 to September 1st 2014. The thesis is structured in two parts – the first part being named "*Current state of knowledge*" and the second part named "*Personal contribution*".

The first part is structured in three chapters and represents a synthesis of bibliographical data from literature concerning the main theme, and it represents the foundation on which the studies from the second part of the doctoral thesis took place.

For a better understanding of the respiratory pathology, it is essential to have a very good knowledge of the anatomy, physiology and physiopathology of the structures involved in the respiration, of the way they interconnect and of the species particularities. This is the reason why the first chapter is named "*Bibliographical data concerning the anatomy and physiology of the respiratory system in dog and cat*" and it refers to the morphological and physiological aspects

of the respiratory system and the adjacent structures, and their implication in specific pathology.

Chapter II is called "*Thoraco-pleuro-pulmonary pathology in domestic carnivores*" and it briefly describes the disorders in these segments. In this chapter there are described the thoracic, diaphragmatic, mediastinal, pleural and pulmonary affections and more specifically both bronchial tree and pulmonary parenchyma, using a unitary etiologic classification system.

Chapter III describes from a technical point of view the present diagnostic methods and sampling methods. This chapter is named "*Imagistic and laboratory diagnostic techniques in toraco-pleuro-pulmonary disorders in dog and cat* " and concludes the bibliographical part of the thesis.

The second part, "*Personal contribution",* is formed of seven chapters (IV-X), and it focuses on the personal research made in the institutions mentionned above by personal examination of the cases through the methods that were available and accepted by the owners, as per the guiding principle stated at the beginning of the thesis, "*Primum non nocere*". We would like to take this opportunity to mention that when examining each case we considered first and foremost the wellbeing of the patient and the scientific interest was followed according to the professional ethics.

Chapter IV is named *„Aim and objectives of the research"* and, according to its title, it enunciated the major objective of this thesis, as well as the activities accomplished in order to achieve it. The main interest of this thesis was directed towards the unique purpose of refreshing the current knowledge level when it comes to diagnosing the respiratory pathologies in domestic carnivores, more exactly to optimize the existing diagnosis procedures and to finally obtain a diagnosis and to apply an adequate therapy as fast as possible. We observed the thoraco-pleuro-pulmonary pathologies that were correlated with clinical, imaging and laboratory exams results. An important objective was to determine the diagnosing value of the imaging techniques, first and foremost the radiography (knowing that in the human medicine, the thoracic radiography is critically important in the respiratory pathology), the thoracic non-cardiac ultrasound, and the CT - advanced high resolution imaging method. Another objective was to evaluate the risk implied by the pathologic materials samples collection and by the diagnosis value of the laboratory methods such as cytology, microbiology and antibiogram. In order to achieve this we evaluated the utility, the feasibility, the tolerability and the risk of applying these methods to the thoracic cage and diaphragm pathology, as well as to the mediastinal and pleural pathology, and finally to the pulmonary pathology.

Chapter V is named *"Considerations concerning the simple and associated thoraco-pleuro-pulmonary pathology epidemiology in dog and cat".* In this chapter, we evaluated the frequency of the different diagnosed disorders, for both studied species, first by lesion type and then by case and primary etiology type. Because we are mostly talking of associated disorders, that affected several segments at the same time, the total number of diagnosed lesions was bigger than the total number of cases. Thus, classifications followed several criteria: by species, by lesion type (five categories were identified: congenital anomalies, inflammatory, circulatory, traumatic pathologies and neoplasia) by affected respiratory segment (thoracic cage and diaphragm, trachea, mediastinum, lung and pleurae). Therefore, the 416 studied cases (272 dogs and 144 cats) were centralized first from a lesion perspective and then from a case number perspective. Out of the total number of cases, 25 cases (17 dogs and 8 cats) didn't receive a primary pathology diagnosis, 46 cases (25 dogs and 21 cats) were oncologic patients with a normal thoracic image (negative result on the pulmonary metastases verification) and the rest of 345 patients presented a total of 459 diagnosed lesions located on different segments. Following these classifications, we noticed an increase of almost 100% of the congenital anomalies and of the circulatory disorders in dogs compared to cats (8,8 % in dogs compared to 4,8 % in cats in terms of anomalies; and 18,75 % in dogs compared to 9,02 % in cats for the circulatory pathologies, with differences of 4 and 9 percents respectively). In other words, dogs present a predisposition for the mentioned pathologies. As far as the cats were concerned, they presented a predisposition for the inflammatory and traumatic pathologies, as well as for neoplasia. (19,48% in dogs compared to 24,30 % in cats for the inflammatory pathologies; 12,86 % in dogs compared to 15,97 % in cats for the traumatic pathologies; and 23,16 % in dogs compared to 28,47 % in cats for neoplasia, the differences being always of 3-5 percents). In addition, we noticed that neoplasia represented 25 % of pathologies, with 104 cases and 167 lesions, and a 23,16 % in dogs and 28,47 % in cats. When adding these percentages to the oncologic patients with a normal thoracic image (9,19% in dogs and 14,5 % in cats) we obtained a very high percentage - 32,35 % of the dogs 42,97 % of the cats suffering from tumoral processes, which represents the dominating pathology of our study.

Chapter VI is named „*Results concerning the thoracic cage and diaphragm pathologies diagnosis"*, and it correlates the thoracic radiography with the CT, with special sample collection methods such as the fine needle aspiration, the microbiological exam, the antibiogram and the cytological exam. The radiographic exam was performed on all the cases and it was the most important criteria when it came to including the cases in this study. A total of 39 cases

were diagnosed as follows: *5 congenital anomalies* (2 cases of *Pectus excavatum* and 3 cases of rib anomalies), 3 *circulatory pathologies* – pectoral edema in cardiac insufficiency, *18 traumatic pathologies* (2 pathologic fractures, 8 traumatic rib fractures, 3 bite or shut gun wounds, 5 diaphragmatic ruptures, 13 neoplasia represented by 1 mastocytoma, 4 lymphoma, 2 vaccinal fibrosarcoma, 5 osteosarcoma and a feline ventral hemangiosarcoma). For proper diagnosis, radiography was used every time. Congenital anomalies, cardiac declive edema and traumas – with one exception – were diagnosed using the radiography. The ultrasound was used to diagnose the migrated foreign bodies (aristae) presence within the muscles. The CT was necessary in 5 of the cases, one for the evaluation of one patient poly-traumatised by shooting, and 4 for the evaluation of thoracic masses (2 cases of vaccinal fibrosarcoma and 2 cases of rib osteosarcoma). Five of the cases of parietal masses required a fine needle aspiration, as well as a cytological exam; two of them required an additional microbiological exam. The radiologic exam proved to have a high diagnosis value in the thoracic cage congenital anomalies, in the circulatory pathologies as well as in the traumatic ones. As for the neoplasia, the radiography had an orientative role mostly. The thoracic ultrasound proved to be useful in finding migrated foreign bodies. The CT played a major part in finding and characterising the thoracic cage neoplasic lesions, as well as in estimating their size and the affected adjacent tissues, which is very important for surgery planning. Multiplanar and volumetric reconstruction allow the exact lesion visualization - especially for the tumoral ones, the adjacent tissue infiltrates evaluation, measuring the tumoral dimensions and volume and monitoring it for the entire duration of the pathology. The cytology establishes the final diagnosis of the neoplasia type and of a parietal abscess. The microbiological exam confirmed the parietal abscess.

Chapter VII is named „*Results regarding the diagnosis of pleural and mediastinal pathologies"* and it is divided in 2 subchapters. The first subchapter analyses the „*Results regarding the mediastinal disorders"*. We discussed the actual mediastinal pathologies of the lymphnodes, the oesophagus and the trachea. A total of 83 cases were identified. The mediastinal affections included: traumatic pathologies (5 pneumomediastinums, 8 mediastinal effusions – 5 circulatory and 3 neoplasia related) and 9 mediastinal masses (1 extraskeletal osteosarcoma, 1 neuroendocrine tumor, 1 heart-base tumor and 6 lymphosarcoma). The oesophagus pathologies were 13 congenital anomalies (5 vascular ring anomalies with segmental megaoesophagus, one o them being doubled by a general meaoesophagus and 8 congenital megaoesophagus), 3 oesophagitis și 4 foreign bodies blocked in the oesophagus. As for the lymphnodes, in 3 cases they were reactive as an answer to lung inflammation, and in 20 cases

their hypertrophy was a response of a tumoral processes distance metastasis. The tracheal pathology was constituted of 21 cases, as follows: 11 tracheal collapses, 2 tracheal hypoplasya, 3 tracheitis and 5 traumatisms with consecutive mediastinum.

To diagnose these pathologies, several methods were utilized. The radiography was used in all cases, and it had a diagnosing role in the mediastinal traumatic pathologies (pneumomediastinum), in the anomalies and the oesophagus foreign bodies, in the tracheal collapse, the tracheal hypoplasya and the tracheal traumatisms. For all these conditions, the radiography was necessary and in the same time a sufficient method. Mediastinal neoplasia are only sometimes diagnosed by radiography; the recommendation is they are studied with the mediastinal ultrasound as well, because it brings additional data on the mass echostructure and location. The ultrasound also provides assistance when it comes to performing interventional manoeuvres for cytology samples collection. The non-cardiac thoracic ultrasound was utilised in 4 cases for guiding the fine needle aspiration process. The CT is the preferred method when it comes to the evaluation of the mediastinal liquid and masses; it has a high capacity of spotting the details of the tracheal or mediastinal lesions, and when performed with contrast, it indicates the vascularised neoplasia zones and the surrounding invaded territories, as well as small local or distance metastases. Advanced imaging was utilized on 8 cases of mediastinal and tracheal pathology.

Virtual bronchoscopy is a true help in appreciating the degree and the location of the tracheal collapse, the tracheal deviations due to extrinsic mediastinal masses and to prominent nodules in the tracheal and bronchial lumen. It is also utilized in the bronchial collapse (the only way to detect it) as well as in the lung lobe torsion.

Imaging methods can be utilized as stand alone ones or as complementary methods. They can detect a neoplasia suspicion, but the diagnosis is only possible through laboratory exams such as the cytological or the microbiologic exams. Three mediastinal masses cytological exams and 3 pharyngeal exudates microbiologic exams were performed for the mediastinal pathology. Mediastinal and tracheobronchial lymphnodes reactivity were correlated with the inflammatory pathology in the case of the pneumonias, or with neoplasia in the case of the abcedated external tumors with metastases.

The second subchapter is named „*Results regarding the diagnosis of pleural affections"* and it covers the pneumothorax, the pleurisy and the pleurites, the pleural tumors and the associated pleural effusions. A total of 87 pleural lesions were diagnosed as follows: 10 septic exudative pleurisies, 4 aseptic exudative pleurisies, 25 modified transsudates (2 iritative and 23

of neoplasic etiology), 7 circulatory transsudates, 5 cases of chylothorax (1 of traumatic etiology – also causing a pneumothorax), 9 cases of traumatic pneumothorax, 7 hemothorax, 20 suspected neoplasic effusion (associated to a cancerous pathology with multiple metastases at the pulmonary level).

Pleural affections required an intense utilization of the imaging techniques, but also the use of thoracocentesis and of the cytological and microbiological exams. The left and dorso-ventral view radiography played a diagnosing part in pneumothorax and in identifying the pleural effusions, especially those in significant quantity. The thoracic ultrasound was utilized in 13 cases, to characterise the effusion and its cellularity, as well as to highlight the subpleural nodules and to accomplish the fine needle aspiraton echoguided manoeuvres, for the loculated or small pleural effusions. The CT was preferred when it came to evaluating the pleural thickening, the pleural effusions as well as for finding the source of intrapleural hemorrhages.

Thoracocentesis played a major diagnosing and therapeutic part, allowing the evaluation of the macroscopic characteristics of the collected liquid samples and facilitating their analysis from a cytological and microbiologic point of view, which offered the possibility of a firm diagnosis. This is an important step of the therapeutic approach and it influences the life expectancy.

Chapter VIII is named „*Results regarding the diagnosis of the pulmonary pathology"* and it analyses the diagnosis of the 250 cases of lung lobes pathologies, as follows: 89 inflammatory affections (17 acute brochitis, 19 chronic bronchitis in dogs, 9 feline asthmatic bronchitis, 44 cases of bronchopneumony: 7 interstitial, 16 multifocal lobular, 21 lobar of which 6 lung abscesses and 15 aspiration pneumoniae), 44 diagnosed circulatory affections (non-cardiogenic and cardiogenic pulmonary edema), 35 traumatic pathologies (lung contusions) and 82 pulmonary neoplasia (5 primary and 77 metastases). The diagnosing methods were the radiology, which permits locating the inflammatory lesions and identifying the metastatic nodules. The ultrasound can only be utilized for lesions on the surface of the lungs. The CT was used in 23 cases, to diagnose bronchial collapse, chronic bronchitis, all types of pneumonia, inhaled foreign bodies and small dimensions lung masses. MIP și MinIP visualisation facilitated the identification of up to 1 mm lesions, and differentiated them from other normal physiological structures within the pulmonary parenchyma. The collection of the pharyngeal exudate (19 cases) and the fine needle aspiration (3 cases) facilitated 3 cytological exams and 20 microbiological exams.

Chapter IX of the doctoral thesis is named *"General discussions regarding the diagnosis methods applied in the thoraco-pleuro-pulmonary disorders in dogs and cats"* and it evaluates, in 3 different subchapters, the utility of the diagnosis methods, correlating them with the results obtained. Each method is evaluated based on a necessity point of view and on a sufficiency point of view, compared to the pathology type, the affected segment, and the necessity of using additional methods. Thus, the first subchapter develops the necessity and sufficiency of the imaging methods. The radiography was necessary in all thoraco-pleuro-pulmonary pathologies, but sufficient only in the cases of the tracheal, oesophagus an thoracic anomalies, and in the cases of pleural, pulmonary, mediastinal and thoracic traumatisms, without topographic nor circulatory complications. The remaining pathologies required the use of more specific methods. The ultrasound was successfully used in describing extra- and intrathoracic soft tissue lesions, in contact with the thoracic cage, with increased specificity for the pleural and mediastinal affections. The CT is an advanced method utilized for complicated cases, and as far as the thoracic pathology is concerned, it has an increased sensibility for neoplasic lesions, especially for small dimensions metastases (31 cases, representing 75% of the CT exams).

The second subchapter presents the utilisation of the cytological method, with a high specificity for neoplasia (51 % of the cytological exams) and therefore with a high sensibility for the inflammatory affections as well, especially for the aseptic and circulatory ones.

The last subchapter presents the sensibility of the microbiologic exams and their specificity when it comes to the infectious pathologies of the thorax and of the respiratory system. It also provides significant details on the pathogen flora that can be found in the respiratory system and continues with a study on the common-use antibiotics efficiency on isolated germs.

Chapter X is named *"General conclusions"* and it reviews the most important conclusions of this thesis, along with a few recommendations regarding the projection of the diagnosis protocol in the respiratory pathologies in dog and cat.