Cardiorespiratory syndrome (also called lung-heart syndrome) among common foxes was described for the first time in mid 1980s in Poland and Canada and has been reported as a cause of significant losses in fox farms (3, 9). However, despite extensive research, the etiology of the disease still remains elusive. Usually, the disease affects young, 2- to 6-month-old, animals. The most characteristic clinical symptom of the cardiorespiratory syndrome in foxes is severe dyspnea; furthermore, the animals present with increased heart rate and complete loss of appetite. Elevating the fox and holding it by the tail with head down causes massive foamy bloody nasal discharge, exacerbation of dyspnea and even death. The symptoms are present suddenly and persist for several hours to several days. Eventually, the animal dies with the symptoms of exacerbating dyspnea, and sometimes also progressive cachexia. Postmortem examination usually reveals variable volume of fluid in pleural and pericardial cavities and an enlargement of the heart. Also pulmonary edema can be observed, sometimes with signs of pneumonia. Moreover, some authors documented pathological changes corresponding to dilated cardiomyopathy (6). Motz et al. (7) observed typical signs of hypoxia on histopathological examination of the myocardial specimens; only few specimens showed discrete infiltration with mononuclear cells. Based on the results of many studies, the involvement of infectious factors in etiopathogenesis of the cardiorespiratory syndrome can be virtually excluded (2, 11, 14, 15). Also the role of taurine deficiency was studied extensively, as involvement of this amino acid in the etiopathogenesis of cardiorespiratory syndrome was suspected, similarly as in the case of feline cardiomyopathy. However, this hypothesis was not confirmed experimentally; moreover, administration of taurine did not influence the therapeutic outcomes of the
cardiorespiratory syndrome (3, 12). Our previous study conducted on foxes without signs of cardiorespiratory syndrome revealed that over half of the animals from three farms in Poland had valve dysplasia (8).

The aim of the study was to examine the frequency of heart valve dysplasia among foxes dying with symptoms of cardiorespiratory syndrome to evaluate its role in the pathogenesis of the disease.

**Material and methods**

The deaths of common foxes (*Vulpes vulpes*) due to cardiorespiratory syndrome were observed during two breeding seasons (2012-2013) on a farm located in Central Poland. A total of 500 females and 150 males are kept at the farm, and the average yearly production amounts to 1900 cubs. Previously, cardiorespiratory syndrome was observed at this farm in 2002 and caused fatal outcomes in 20% of the young. In 2012, the cases of cardiorespiratory syndrome were observed between July and October; a total of 96 fatal outcomes were recorded, which corresponded to 5.32% of new young. The number of fatal outcomes due to cardiorespiratory syndrome documented in 2013 was smaller (n = 38, 2.14% of new young).

The study included 38 cadaveric specimens of foxes that died in 2013 with the typical clinical signs of cardiorespiratory syndrome, as well as 12 hearts of foxes that died in 2012, obtained during postmortem examination and frozen until analysis.

Cadavers underwent standard postmortem examination with a detailed analysis of gross pathology of the hearts (including 12 specimens from 2012). The heart examination included: (a) changes in heart shape and size, (b) analysis of ventricular internal diameter and wall thickness, (c) detailed analysis of the morphology of mitral and tricuspid valve, papillary muscles and tendinous chords.

Myocardial sections were fixed for 24 hours in 7% buffered formaldehyde, processed routinely, embedded in paraffin and cut into 4 µm-thick slices. Microscopic slides were stained with hematoxylin and eosin and subjected to histopathological examination. The examination included: morphology of cardiomyocyte (presence of absence of signs of cardiomyocyte and nuclei degeneration), amount of interstitial tissue and presence of inflammatory infiltrates. Microphotographs of the sections were subjected to a computer image analysis on a computer connected to Olympus BX53 light microscope equipped with ColorView IIIu digital camera (Olympus, Japan). The digital analysis was conducted with cell^A^ software (Olympus Soft Imaging Solution GmbH, Germany).

According to the Polish law studies conducted on animal tissue (including organs collected post-mortem) do not require permission from the Ethical Board.

**Results and discussion**

The postmortem examination of foxes that died in 2013 revealed pulmonary congestion and edema, and the presence of foamy bloody fluid in large bronchi and trachea. Additionally, 20-140 ml of straw-yellow or straw-bloody fluid were revealed in pleural cavities of 35 (92.1%) of the foxes. Moreover, 17 animals (44.7%) had fluid in the pericardium, and 11 (28.9%) in the abdominal cavity.

The hearts of all the animals were round-shaped and enlarged (Fig. 1), mostly due to dilatation of the right ventricle and right atrium. The lumen of the right ventricle was enlarged (up to 6.5 cm in diameter below the tricuspid valve fibrous ring), and its wall was thinned down to 2 mm. Moreover, a dilatation of the right atrioventricular opening and abnormal structure of the tricuspid valve were documented in all cases. The septal cusp was shortened, thickened, and immobilized due to fusion with the interventricular septum (Fig. 2). The tendinous chords of the septal cusp were completely absent in 29
In some cases, the presence of the defect leads to the development of right ventricular heart failure, manifesting itself as accumulation of fluid in body cavities, dyspnea, lack of appetite, and cachexia resulting from the loss of protein (transudate); i.e. the symptoms that are also observed in the cardiorespiratory syndrome in foxes. Left ventricular overload and secondary left ventricular heart failure, typically with resultant pulmonary edema, develop at more advanced stages. Clinical manifestation of mitral valve dysplasia is predominated by the signs of left ventricular heart failure and pulmonary edema, which can progress rapidly in some cases. The clinical signs and anatomicopathological lesions of cardiorespiratory syndrome among foxes, previously described by many authors (2, 3, 7, 9), resemble those documented in the case of atrioventricular valve dysplasia.

The fact that our postmortem examination revealed tricuspid valve dysplasia in all those animals that died with the symptoms of cardiorespiratory syndrome indicates the potential involvement of congenital heart defects in the etiology of this condition.

**References**

1. Diman N. V., Remacle S., Bertrand N., Picard J. J., Zaffran S., Rezzoahazy R.: A retinoic acid responsive Hoxa3 transgene expressed in embryonic pharyngeal endoderm, cardiac neural crest and a subdomain of the second heart field. PloS One 2011, 6, e27624, doi: 10.1371/journal.pone.0027624.
2. Jaśko J.: Is the cardiopulmonary insufficiency syndrome of foxes a distemper virus infection? Veterinářství 1990, 40, 34-35.
3. Kopczewski A., Saba L., Biz-Wencel H., Slawoj I., Strażakowski L., Ulewicz W.: Influence of taurine on the prevention and treatment of cardio-pulmonary syndrome in foxes. Med. Weter. 1998, 54, 325-330.
4. Lisowska A., Sobkowicz B., Maslaj W. J., Skibitaska E.: Congenital tricuspid valve dysplasia in a patient with advanced heart failure. Kardiol. Pol. 2006, 63, 201-203.
5. Liu S. K., Tilley L. P.: Dysplasia of the tricuspid valve in the dog and cat. J. Am. Vet. Med. Assoc. 1976, 169, 623-630.
6. Martino P. E., Gimeno E. J., Parma A., Stanchi N. O., Bautista E., Petrucelli M. A.: Congestive cardiomyopathy in a fox colony. Revue Med. Vet. 2007, 158, 40-45.
7. Motz J., Rabaj B., Saba L., Slawoj I., Biz-Wencel H., Nozdróm-Plotnicki Z.: The anatomic and histopathological examination in the chronic cor pulmonale syndrome of foxes (Valves vulpes). Med. Weter. 1995, 51, 618-620.
8. Noszczyk-Nowak A., Piasecki T., Cepeli A., Nowak M., Janus I., Pasławsk A.: Atrioventricular valvar anomalies and their role in etiopathogenesis of cardiorespiratory syndrome in farmed common foxes (Vulpes vulpes). Vet. Quart. 2016, 36, 16-21.
9. Onderka D. K.: Congestive heart failure in juvenile foxes, [in:] Biology, pathol- ogy and genetics of fur bearing animals. Proceedings of the IV International Congress of Fur Animal Production. (Murphy BD, Hunter DB, eds.) Aug 21-24 Rexdale (ON): Hudson’s Bay Auctions House 1988.
10. Pasławsk A., Noszczyk-Nowak A., Janiszewski A., Nicpoń J.: Congestive tricuspid dysplasia in dogs. Bull Vet. Inst. Pulawy 2013, 57, 123-126.
11. Saba L., Kopczewski A., Biz-Wencel H., Tymczyna L., Nowakowicz-Dębek B.: Indices of blood metabolic profile in foxes with lung-heart syndrome. Scientifur 1998, 22, 55-58.
12. Saba L., Kopczewski A., Slawoj I., Biz-Wencel H., Tymczyna L.: Taurine in serum, bile and feed of foxes with lung-heart syndrome. Scientifur 1998, 22, 59-61.
13. Snavre B. S., Kern C. B., Wessels A.: Origin and fate of cardiac mesenchyme. Dev. Dyn. 2008, 237, 2804-2819.
14. Wójcik J., Miziak B., Chrobocińska M., Kopczewski A., Saba L.: Attempts at evaluating the role of the viral agent in the etiology of cardiopulmonar syndrome in foxes. Med. Weter. 1996, 52, 647-648.
15. Wójcik J., Miziak B., Chrobocińska M., Saba L.: Virusiological examination of foxes which died of a lung heart syndrome. Anim. Prod. Rev. 1996, 28, 177-178.

Corresponding author: Prof. dr hab. Agnieszka Noszczyk-Nowak, Department of Internal and Diseases with Clinic for Horses, Dogs and Cats, Faculty of Veterinary Medicine, Wrocław University of Environmental and Life Sciences, Grunwaldzki Sq. 47, 50-366 Wrocław, Poland