

# Increased incidence of megaesophagus in dogs in Latvia 2014-2016

## Preliminary results

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### What is esophageal dilatation; what are the causes and the incidence of this disease?

Megaesophagus (ME) is the generalized dilatation of the esophagus with decreased or absent motility. It is the most common cause of regurgitation in dogs and cats. Food fails to enter the stomach, remains in the esophagus, and is eventually regurgitated.

The disease can be congenital (clinical signs appears shortly after weaning) or acquired. Acquired ME affects dogs of various ages (mean age 7 – 15 years). There are numerous causes of ME – the most common is a neuromuscular disease *myasthenia gravis* (25% of cases). ME can also be one of the clinical signs in a wide range of diseases: neurological, muscular diseases (polymyopathy, polyneuropathy, dysautonomia); hormonal diseases (hypoadrenocorticism, hypothyroidism); esophageal inflammation – esophagitis; toxins – botulism, lead, organic phosphates etc; anatomical changes of esophagus – pathology of vascular ring; neoplasia; infectious diseases – canine distemper, neosporosis, tick born paralysis. If the cause of ME is not identified, it is classified as idiopathic ME. Most cases (50%) of ME in adult dogs are considered idiopathic.

Due to the diverse causes of this disease, the incidence of ME is rarely reported. The incidence of ME at the University of Missouri over an eight year period was reported to be approximately 1 per 1000 admissions (Guilford et al., 1990). Data about overall ME incidence in Latvia is not readily available. Only 4 dogs were diagnosed with ME at the Small Animal Hospital of Faculty of Veterinary Medicine in Latvia between 2008 and 2012 (5 year period) therefore ME in Latvia before 2014 was considered to be a rare diagnosis.

### The situation in Latvia in 2015: an unusual increase of ME cases

During spring of 2015 small animal practitioners began noticing and reporting on the unusual increase of meagesopahgus (ME) patients in their practices. The Latvian Association of Veterinarians (LAV) together with the Latvian University of Agriculture Faculty of Veterinary Medicine (LUA FVM) started to gather information about these cases. In the period from April 2014 until May 2015 there were at least 70 dogs diagnosed with ME in Latvia (all confirmed by X-ray). Such an increase had not been observed or reported in any other country during this period (information from FECAVA directors).

In May 2015 the Ministry of Agriculture of Latvia funded the study investigating the cause of the ME outbreak in Latvia. The research was led by Dr. Ilze Matise, USA Board Certified

veterinary pathologist (Diplomate, ACVP). Other researchers contributing were from the Veterinary faculty ( LUA FVM): Dr. Ivars Lusis, an epidemiologist, Dr. Kristine Drevinska, a small animal veterinarian; and Dr. Inga Piginka, a veterinary pathologist from the Latvian State Research Institute BIOR and pathologist at LUA FVM. The research was carried out by BIOR. A 6 month research plan was developed after consultations with various specialists in Europe and the USA representing a variety of disciplines: small animal internal medicine, neurology, toxicology and epidemiology.

The most important goal of this study was to identify the cause of the sudden increase of ME cases. There also existed the serious concern of the underlying possibility that any “contaminant” that was affecting the health and/or killing of dogs may also have the potential to infiltrate the environment or food supply causing human disease.

A retrospective study done in May 2015 was used to assess the epidemiological situation before the research plan for prospective study was designed. Locally made dog food was identified as one of potential risk factors; thus, the differential diagnoses included: acrylamide toxicity (toxic compound formed if carbohydrates are processed at high temperatures), botulism, dysautonomia, heavy metals (lead etc.), thallium, organic phosphates, toxicity of unknown substances, as well as *myasthenia gravis*.

## Plan of the study

1. To identify the characteristics of the affected dogs – predisposing factors (age, breed, weight, gender, place of living, indoors/outdoors, feeding, health prophylactic measures, other diseases); to compare ME dogs with a control group (any other dog without ME). In order to gather data, a questionnaire was designed in consultation with foreign specialists. According to the request from the dog food manufacturer some questions were added to questionnaire.
2. To understand and describe the pathology of the disease. Only dogs with a diagnosis confirmed by radiography (x-rays) were included in the study.
  - a. Clinical signs of the disease, appearance, progress, response to treatment
  - b. Blood tests – changes in the complete blood count ( CBC) and biochemistry tests
  - c. Tissue changes in dead or euthanized dogs
3. Tests for toxins as possible causes of ME (test of tissues, blood and food samples)
  - a. Botulinum toxins
  - b. Acrylamide
  - c. Heavy metals, thallium
  - d. Organic phosphates
  - e. Other unknown substances
4. Tests on dog food
  - a. Bacteriological, chemical and toxin tests
  - b. Quantitative analysis of food (microelements, supplements, vitamins)

## Current results and conclusions

Currently, only the first half of the research plan has been completed. The Control group of healthy dogs must be formed and similar information gathered and compared. Part of the planned tests have been completed and the botulinum toxin tests are nearly finished. However, the test for organophosphates and other unknown substances must still be done. The analysis of the dog food is also partly completed but the quantitative analysis still must be performed.

**From May 2015 until December 2015, 70 new ME dog cases have been diagnosed – these are cases confirmed by X-ray and enrolled in the prospective study (samples collected and survey completed). The average number of ME cases is 8-9 per month.** Thirteen of the 70 dogs in prospective study have died or have been euthanized due to poor health. Twenty veterinary clinics were involved in this study. The ME cases were found in 28 various counties. The greatest number of dogs (13) lived in Riga or its proximity. **Affected dogs were from all regions of Latvia – both from urban and rural territories. In 30% of the cases more than one dog in the household was affected suggesting a common cause of the disease.**

Results of the detailed questionnaire have been summarized. There were 54 complete questionnaires from 60 dogs. The affected dogs were adults, 1-12 years old (mean age 6 years), mostly male (76%). 17 different breeds have been identified, predominantly: Bernese mountain dogs, Golden retrievers, Labradors, German Shepherds, Doberman pinchers. Only a few dogs represented small breeds – Toy terriers, Dachshunds. Most dogs were medium to large breed dogs with a median weight of 25 – 55kg. The age and breed profile of the dogs confirms that this disease is not a congenital form of ME. **In Latvia's dogs, ME is an acquired disease.**

The first ME cases were observed early in 2014 and some of the cases enrolled in the study had symptoms long before diagnosis of ME was made. The most common clinical sign reported was regurgitation and/or vomiting (94%). Regurgitation occurred soon after the meal (67%) or during the meal (50%). Other common clinical signs were a changed voice or loss of voice – dysphonia (72%), difficulty breathing and coughing. Weight loss was observed in more than 60% of the dogs and fatigue in 52%. 64% of the dogs improved after treatment but 17% were too sick and died during the study.

A greater number of ME affected dogs (53%) lived in restricted areas with rare access to chemicals (4%) or household waste (15%). Food supplements were used in 11% of dogs. Information about use of parasite control was as follows: 45% of dogs received tick treatment, 59% flea treatment and 70% internal parasite treatment. 72% of dogs were vaccinated during the last 3 years. Esophageal trauma or chronic disease were diagnosed in 2% suggesting that the ME disease affected previously healthy dogs.

**The most common factor for ME affected dogs was the consumption of one particular, locally made dry dog food. 94% of all dogs were fed Brand A dog food. In most cases (86%) the food was stored in its original packaging which in 50% of cases was a combination of paper and polyethylene. In order to compare the incidence of the above mentioned factors in the whole dog population of Latvia, a control group will be formed**

**and assessed.** However, dog food remains under high suspicion since it is highly unlikely that 94% of dogs in Latvia are consuming one and the same food.

Blood tests show mild inflammation – possibly associated with the ME complication -- aspiration pneumonia. *Dirofilaria repens* (a larval parasite transferred by mosquitoes, usually without any clinical signs) was observed in the blood more often than is typical (15% of cases). Serum chemistry tests showed mild muscle damage. Muscle atrophy was observed on post-mortem examination of dogs. Another post-mortem histological finding was abnormalities in the nerves – a polyneuropathy and a loss of ganglion cells in the esophageal tissues. Anaerobic bacteria *Clostridium baratii* possibly capable of producing *botulinum toxin F* was discovered in the stomach of 33% dogs, however these isolates were negative for all botulinum toxin genes by PCR (A, B, C, D, E, F). Botulinum toxin was assayed for all blood samples and these results were negative. One more test remains for botulism – assessment of fecal samples of sick dogs for botulinum toxins (testing in progress in Sweden).

The analyses of blood (20 samples) and food (17 samples) for acrylamide, heavy metals and thallium were performed at BIOR. None of these substances were above normal limits. In addition, 16 dog food samples were analyzed for bacterial, chemical and mycotoxin contamination at BIOR. No significant deviations were observed, including no anaerobic, botulinum toxin-producing bacteria were found. Due to ruling out these toxins other differential diagnoses must be considered for evaluation – see below. However, these results do not rule out food as the possible cause of the ME outbreak. Tests for organophosphates, levels of specific microelements, supplements and vitamins, as well as testing for unknown substances will be done in blood and tissues of sick dogs and in Brand A pet food. In addition to this further plans for this study include establishing a control group to evaluate risk factors, completing testing for botulinum toxins in feces. Meanwhile we are continuing to register new ME cases to follow the incidence of ME in Latvia. Specialists from Europe and USA are regularly contacted to discuss results and to provide guidance for the study.

## Importance of research

The increase of ME cases is unique to Latvia – we are facing an emerging disease. During the last 6 months 4 researchers and many veterinarians in Latvia have donated their time to investigate this disease, to find its cause, and to identify any risk factors. Due to this research and the increased public awareness, ME cases are being diagnosed faster and the proportion of lethal cases have decreased from 30% in the first half of 2015 to 17% in second half of 2015.

The significance of this research may be far reaching:

1. New cases may be prevented alleviating suffering and death of dogs.
2. Similar situations may be prevented from occurring in other countries.
3. A new cause of ME may be discovered and controlled/eradicated.
4. Understanding the cause of this degenerative muscle/nerve pathology may help in the understanding of similar human diseases.

If you have any comments and suggestion that could contribute to our study, please contact Dr. Ilze Matisē [imatise.vh@gmail.com](mailto:imatise.vh@gmail.com).

*Information about ME – **Everything the veterinarian and the dog owner should know** has been available at LAV website [www.lvb.lv](http://www.lvb.lv) since June 2015. The information was compiled by researchers and practicing veterinarians. Information in English about retrospective study is available here <http://lvb.lv/lv/veterinararstiem/pasakumi/about-megaesophagus-in-english>*