Megaesophagus

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Abstract: Megaesophagus is a disorder of the esophagus characterized by diffuse dilation and decreased peristalsis. It is classified into congenital and acquired forms. Gastrointestinal, endocrine, immune-mediated, neuromuscular, paraneoplastic, and toxic disorders have been associated with acquired megaesophagus. Common clinical signs of megaesophagus are regurgitation, weight loss, coughing, and halitosis. Most cases of megaesophagus can be diagnosed using thoracic radiography; however, diagnosing the underlying cause requires a thorough history and additional diagnostics. The treatment, management, and prognosis of megaesophagus vary greatly depending on the underlying cause.

Megaesophagus is defined as a disorder of the esophagus characterized by diffuse esophageal dilation and decreased peristalsis.1 It may be congenital or acquired;1 acquired megaesophagus is subclassified into idiopathic and secondary forms. Congenital and idiopathic acquired megaesophagus disorders are suspected to be due to a combination of neurologic dysfunction within the afferent arm of the swallowing reflex, altered esophageal viscoelastic properties, and poor vagal responsiveness to intraluminal esophageal distention.1,2 Secondary acquired megaesophagus can be caused by any disease that inhibits esophageal peristalsis by disrupting central, efferent, or afferent nerve pathways or by any disease of the esophageal musculature, including immune-mediated, infectious, and preneoplastic etiologies.3

Clinical Signs
In uncomplicated cases of megaesophagus, patients may present with only regurgitation and weight loss. Other patients may present with additional clinical signs that hint at the underlying cause of megaesophagus.1 The most common complication of megaesophagus is aspiration pneumonia; often, these patients present with a moist cough, dyspnea, or fever.1

History
The index of suspicion for megaesophagus should be high when a patient presents for regurgitation. Regurgitation that occurs in a young patient at the time of weaning and conversion to solid food is likely due to congenital megaesophagus. In older patients, the frequency of regurgitation and timing may be more variable.

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condition in Parson Russell terriers, springer spaniels, and smooth fox terriers that results in a deficiency or functional abnormality of acetylcholine receptors (AChRs) at the neuromuscular junction. The long-term prognosis for congenital MG is poor because of the mechanism of the condition, lack of a specific treatment, and high complication rate of aspiration pneumonia. Congenital MG patients usually present with generalized weakness in addition to megaesophagus. Congenital MG patients generally succumb within 1 year; however, there are reports of some cats and Parson Russell terriers that have survived for several years.

**Acquired Megaesophagus**

The etiology for acquired idiopathic megaesophagus is unknown. The current theory is that a defect in the afferent neural pathway causes reduced responsiveness to esophageal distention.

The diffuse neuromuscular dysfunction of acquired secondary megaesophagus can be caused by a variety of neuromuscular, immune-mediated, endocrine, gastrointestinal, paraneoplastic, and toxic diseases. Generalized inflammatory myopathies can have immune-mediated, endocrine, gastrointestinal, paraneoplastic, and toxic diseases.

**Neuromuscular and Immune-Mediated Causes**

The most common neuromuscular disorders associated with megaesophagus include MG and generalized inflammatory myopathies such as polymyositis and those associated with infectious diseases. Less common neuromuscular disorders associated with megaesophagus include myopathies such as muscular dystrophies, dysautonomia, storage diseases, and neurogenic muscular atrophy. Because the canine esophagus is composed predominantly of striated muscle, any neuromuscular disease that affects limb muscles can affect the esophagus.

Of all acquired megaesophagus cases, approximately 25% are secondary to MG. Acquired MG is a disorder of neuromuscular transmission due to immune-mediated destruction of postsynaptic AChRs in skeletal muscle by AChR antibodies. Acquired MG can present in focal, generalized, and acute fulminating forms. Focal MG can present with various degrees of esophageal, facial, laryngeal, or pharyngeal dysfunction. Ninety percent of dogs with generalized MG have megaesophagus. Although acquired MG can affect dogs of any age older than a couple of months, most affected dogs are between 2 and 3 years of age or older than 9 years. Acquired MG occurs most often in German shepherds and golden retrievers. Akitas and Scottish terriers have an increased relative risk for MG. Familial and breed-associated forms have been described in Newfoundlands and Great Danes. Affected feline breeds include the Abyssinian, Somali, and Siamese.

Approximately 14% of dogs with diagnosed generalized inflammatory myopathies present with megaesophagus. Patients presenting with generalized weakness, stiff gait, dysphagia, or diffuse muscle atrophy may have myositis. Serum creatine kinase (CK) activities may or may not be elevated, so a normal CK activity does not rule out myositis. Generalized inflammatory myopathy is a comprehensive term used to group causes of diffuse myositis. Generalized inflammatory myopathies can have immune-mediated (polymyositis), infectious, or paraneoplastic etiologies. Protozoal, rickettsial, spirochetal, and fungal infections can be associated with myositis. Paraneoplastic syndromes differ from paraneoplastic syndromes in timing. Paraneoplastic syndromes occur with occult cancer. Paraneoplastic syndromes that can cause myositis include bronchogenic carcinoma, lymphoma, myeloid leukemia, and tonsillar carcinoma.

Megaesophagus associated with distemper is due to demyelination. Neurologic signs can develop 1 to 3 weeks or even months after initial recovery. The nerve damage is due to an inflammatory response to the viral antigens in neurons and glial cells. This results in gray matter damage and demyelination. Dogs with clinical signs of nasal and footpad hyperkeratosis are more likely to develop central nervous system disease.

Generalized tetanus is known to cause esophageal dysfunction in dogs and humans. Classic clinical signs in dogs include a stiff gait, an outstretched or dorsally curved tail, the “joker’s smile” (erect ears, drawn-back lips, wrinkled forehead), protrusion of the third eyelids, enophthalmos, trismus, increased salivation, and a strong response to stimuli.

Although dysautonomia is rare, megaesophagus is a common finding in these patients. Dysautonomia is an idiopathic autonomic nerve disorder of cats and dogs that is suspected to be immune-mediated. All ganglia and sympathetic and parasympathetic nerves are affected, with neuronal cell body damage and axonal degeneration. Within 1 to 7 days, patients experience a fulminating loss of autonomic nervous system function, followed by constipation, dry mucous membranes, pupillary dilation, prolapsed nictitating membranes, diminished pupillary light response, bradycardia, areflexic anus, and bladder atony.

Glycogen storage diseases (GSDs) are inborn errors of glycogen metabolism. Of the eight human GSD types, small animal equivalents have been published for GSD I A (glucose-6-phosphatase deficiency), GSD II (α-glucosidase deficiency), GSD III (debrancher enzyme amylo-1,6-glucosidase deficiency), GSD IV (branching enzyme α-1,4-D-glucan), and GSD VII (phosphofructokinase deficiency). Only GSD II, which is documented in Swedish Lapland dogs, has been associated with megaesophagus.

A clinical presentation of megaesophagus associated with gait abnormalities and laryngeal paralysis is suggestive of laryngeal paralysis–polyneuropathy complex (LP-PNC). Megaesophagus is documented in most dogs that are affected with LP-PNC, which is due to neurogenic muscular atrophy. The intrinsic laryngeal and appendicular skeletal muscles are affected. LP-PNC is documented in Dalmatians, Leonbergers, Pyrenean mountain dogs, and rottweilers. Puppies usually present between 2 and 6 years.
months of age\(^1\); however, in Leonbergers, onset is delayed to 1 to 9 years of age.\(^1\) A demyelinating polyneuropathy has been reported in a family of miniature schnauzer dogs presenting with predominantly respiratory dysfunction associated with laryngeal paralysis and esophageal dilatation.\(^{27}\)

**Endocrine Causes**

Hypoadrenocorticism and hypothyroidism are associated with reversible megaesophagus. Patients with hypoadrenocorticism may have megaesophagus due to electrolyte imbalances and a cortisol deficiency. Electrolyte imbalances cause altered membrane potentials, which results in decreased neuromuscular function. In addition, muscle weakness is a consequence of deficient cortisol.\(^{28}\)

The association between megaesophagus and hypothyroidism has yet to be understood. Hypothyroidism is prevalent in some breeds that are predisposed to megaesophagus and laryngeal paralysis.\(^{2,29,30}\) Megaesophagus occurs in 3% of hypothyroid dogs.\(^{29}\) Resolution of megaesophagus once the thyroid is regulated has been reported.\(^{31}\) Aspiration pneumonia may cause a sick euthyroid syndrome that may be misdiagnosed as hypothyroidism.\(^{29}\)

**Gastrointestinal Causes**

Gastrointestinal disorders associated with acquired megaesophagus include esophagitis, esophageal obstruction, gastric dilatation–volvulus, and hiatal hernia. In cats, acquired secondary megaesophagus is due to pyloric dysfunction.\(^1\)

Esophagitis is a common finding associated with megaesophagus.\(^1\) It may or may not precede megaesophagus. In patients with esophagitis, secondary megaesophagus develops due to chemical or obstructive irritation. Gastric reflux contains gastric acid, pepsin, bile salts, and trypsin, all of which cause esophageal inflammation and ultimately decrease esophageal motility\(^7\) (FIGURE 1).

Esophageal obstructions can be caused by esophageal foreign bodies, neoplasia, strictures, or vascular ring anomalies. Foreign bodies can cause a partial or complete mechanical obstruction. Peristaltic spasms over the retained foreign object cause tissue edema and mucosal abrasions. Although possible in any small dog, there seems to be a higher incidence of esophageal foreign bodies in young terriers. Because these terriers are young, this may be a condition of delayed esophageal maturation.\(^7\)

Foreign bodies or chronic gastroesophageal reflux (GER) can cause esophageal strictures, which occur secondary to mucosal healing attempts.\(^{27,28}\) Esophageal damage that penetrates the submucosa and muscularis layers causes inflammation resulting in collagen deposition and fibrous connective tissue stricture.\(^{32,33}\)

Extraluminal esophageal obstruction is most commonly associated with vascular anomalies. In 95% of patients with secondary megaesophagus due to a vascular ring anomaly, the cause is a persistent right aortic arch.\(^{30}\) Other vascular anomalies associated with secondary megaesophagus include persistent right or left subclavian arteries, double aortic arch, persistent right dorsal aorta, left aortic arch, right ligamentum arteriosum, aberrant intercostal arteries, and persistent left cranial vena cava.\(^{34,35}\)

Dogs with chronic or recurrent gastric dilatation with or without volvulus have an increased risk of developing megaesophagus.\(^{28}\) In these dogs, megaesophagus is due to decreased lower esophageal sphincter (LES) tone caused by a combination of esophagitis from chronic GER or vomiting; chronic intermittent obstruction of the LES; increased intragastric and intraabdominal pressures; and delayed gastric emptying.\(^{2,28}\)

In patients with hiatal hernia, the esophagus is essentially obstructed. Four types of hiatal hernias have been described in humans.\(^{10}\) Two of these types are applicable to animals. Type I is the “sliding” hernia, defined as intermittent cranial displacement of the abdominal esophagus, LES, and gastric cardia through the hiatus.\(^{36}\) Type II is the paraesophageal hernia, in which the gastroesophageal junction remains in its normal anatomic position; however, the stomach and abdominal organs enter the caudal mediastinum through a defect adjacent to the esophageal hiatus.\(^{10}\)

**Paraneoplastic Causes**

According to one study, megaesophagus was present in 40% of dogs with thymoma.\(^{36}\) The incidence of thymoma in dogs with MG is 3%; in cats with MG, the incidence is 26%.\(^{16,18}\) In humans, thymomas have increased production of CD4+CD8+ T cells and lack antigen-presenting cells that function for negative selection. This combination results in autoimmune disease.\(^{37}\) The prognosis for nonresectable thymoma in a dog with MG and megaesophagus is poor. However, complete thymic resection can result in resolution of megaesophageus and a decrease in AChR antibody titer.\(^{8,38}\)

**Toxic Causes**

Toxic substances that can cause megaesophageus include lead, organophosphates, and snake venom.\(^{3,29}\) Low-level lead exposure causes severe abdominal pain, vomiting, diarrhea, and megaesophageus.\(^{39}\) Lead intoxication can occur from ingestion of batteries,
fishing line weights, lead-based paint, linoleum, and plumbing or solder supplies. Organophosphate toxicosis should be suspected if a patient presents with concurrent weakness and cerebellar signs. They irreversibly bind to acetylcholinesterase, causing a cholinergic crisis (salivation, lacrimation, urination, defecation). Australian tiger snake envenomation causes a rapidly progressing myopathy of skeletal muscle. If not lethal, Australian tiger snake envenomation has a 75% recovery rate for normal esophageal function.

**Diagnosis**

**Diagnostic Imaging**

Thoracic radiography is diagnostic for most cases of megaesophagus. Common findings include a prominent, dilated esophagus that can be filled with air or ingesta (Figure 2). The degree of esophageal dilation has no diagnostic value in determining the etiology. Underlying causes of megaesophagus that may be revealed by radiography include neoplasia, foreign body, vascular ring anomaly, gastric dilatation–volvulus, and hiatal hernia. Normal midline tracheal location does not exclude a vascular ring anomaly; however, focal leftward deviation of the trachea near the cranial border of the heart on a dorsoventral or ventrodorsal view is a reliable sign of persistent right aortic arch in young dogs that regurgitate after eating solid food. Radiographic findings of megaesophagus with concurrent aspiration pneumonia or a distended stomach, small bowel, or urinary bladder should raise suspicion for dysautonomia. Incidental esophageal dilation does occur and is associated with excitement, aerophagia, general anesthesia, and vomiting.

If thoracic radiographic findings of megaesophagus are questionable, a barium contrast esophagram can confirm dilation and mechanical obstruction. Barium accumulates within the distended esophagus. Focal narrowing of the esophagus at the cardiac base is suggestive of a vascular ring anomaly. However, the diagnostic benefit of a contrast study should be weighed against the potential for aspiration of contrast agent.

Fluoroscopy evaluates pharyngeal motility and the presence and intensity of esophageal peristalsis. However, this diagnostic modality is not essential for diagnosis of megaesophagus and may not be readily available. It can be helpful in cases of MG or esophagitis. MG can selectively affect only the pharyngeal and esophageal musculature without more overt clinical signs. Also, in cases of mild esophagitis, fluoroscopy may be of greater diagnostic value than a contrast esophagram in detecting hypomotility.

Esophagoscopy is rarely indicated for a diagnosis of megaesophagus, but it can be helpful for suspected cases of obstructive disease or reflux esophagitis (Figure 3). Esophagoscopy may identify an esophageal stricture due to a vascular ring anomaly, but it cannot differentiate the type of vascular ring anomaly.

**Laboratory Testing**

A complete blood count (CBC), serum chemistry panel that includes CK activity, and urinalysis should be performed for all regurgitating patients and those in which megaesophagus is suspected. In addition, an AChR antibody titer test should be performed in all cases of acquired megaesophagus. AChR antibody testing is performed by the Comparative Neuromuscular Laboratory in the School of Medicine at the University of California, San Diego. Information regarding sample submission can be obtained at http://vetneuromuscular.ucsd.edu/. Corticosteroid therapy at immunosuppressive dosages for longer than 7 to 10 days lowers AChR antibody levels, so a pre-corticosteroid serum sample is
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Nutrition

Preventive measures include frequent small meals with the patient in a cranially elevated position. This helps minimize regurgitation, a common complication associated with megaesophagus. It is important to maintain a postprandial upright position to reduce the risk of aspiration pneumonia. Special feeding chairs designed for megaesophagus patients can also be beneficial. These chairs are often elevated to help maintain an upright position during feeding. Additionally, it is essential to ensure that the food consistency is optimal for each patient, as recommended by veterinary professionals. For some patients, the optimal food consistency might require a liquid diet or the use of special feeding aids. Regular recheck exams are necessary to monitor the patient’s condition and adjust treatment accordingly. Early detection and intervention can significantly improve the prognosis for patients with megaesophagus. 

Supportive and Symptomatic Care

Aspiration pneumonia and regurgitation can be detrimental to the health of patients with megaesophagus, so preventive measures such as frequent feeding, special feeding chairs, and diet modifications are crucial. Early detection and treatment of complications can improve the patient's overall prognosis.
with each patient, so experimentation is encouraged. The use of enteral feeding may be needed in weak patients or in patients in which regurgitation cannot be controlled by other methods. In these cases, a gastrostomy tube should be placed. In our clinical experience, a percutaneous endoscopic gastrostomy tube or low-profile gastrostomy tube is effective. Nasoesophageal or esophageal tubes are not advised because they increase regurgitant volume, raising the risk of aspiration pneumonia.

**Treatment of Secondary Complications**

Aspiration pneumonia and esophagitis are the most common complications of megaesophagus. For aspiration pneumonia, administration of a broad-spectrum antibiotic is advised. Culture and sensitivity testing of a transtracheal wash or bronchoalveolar lavage sample can be helpful in choosing an antibiotic; however, the risk of obtaining the sample should be considered.

Esophagitis can result in esophageal stricture within 1 to 3 weeks; therefore, eliminating further mucosal damage and allowing the mucosa to heal are important considerations. Liquid sucralfate is advised because it binds to eroded mucosa, allowing it to heal. For megaesophagus secondary to esophagitis, addressing the underlying cause of GER is the key to improvement. Antacids (e.g., calcium carbonate), H2-blockers, and proton-pump inhibitors are all used to lower gastric acidity and may prevent esophagitis due to GER.

Promotility drugs (e.g., metoclopramide, cisapride) have no current documented benefit in managing canine megaesophagus but may have a role in managing feline megaesophagus. This is due to the differences in feline and canine anatomy and the mechanism of action of these drugs. Metoclopramide and cisapride act on smooth muscle. They have no effect on striated muscle. The canine esophagus has striated muscle its entire length. Cats have smooth muscle within the distal esophagus, so cisapride may improve lower esophageal smooth muscle motility in cats. Metoclopramide and cisapride are not advised in canine megaesophagus patients because these drugs increase the LES tone, which slows esophageal emptying and contributes to further regurgitation. Bethanecol may be a better option for dogs as it is documented to stimulate esophageal propagating contractions in skeletal muscle by stimulating cholinergic receptors.

**Acquired Secondary Megaesophagus**

Treatment for acquired secondary megaesophagus is based on a definitive diagnosis. For example, the cornerstone of treatment for this form of MG is anticholinesterase drugs. If an animal is confirmed by positive AChR antibody titer as having MG and pyridostigmine alone does not control the clinical signs, then other agents are indicated. These can include either low-dose prednisone (not an immunosuppressive dosage, which can worsen the weakness) or immunosuppressants such as azathioprine, mycophenolate mofetil, or cyclosporine. Although anticholinesterase therapy does not decrease the AChR antibody titer, many dogs with acquired MG (if they do not develop severe megaesophagus and aspiration pneumonia and expire) go into spontaneous remission in the absence of immunosuppression. Before immunosuppressive therapy is used, pneumonia or any other infectious disease should be completely resolved.

**Prognosis**

The prognosis for megaesophagus varies with the underlying etiology and presence of secondary complications. Aspiration pneumonia, dehydration, and malnutrition can significantly worsen the prognosis. Congenital megaesophagus has a guarded to poor prognosis; however, there is potential for improvement of esophageal motility with maturity up to 1 year of age. The prognosis for congenital MG is poor due to the mechanism of the condition, lack of a specific treatment, and high complication rate of aspiration pneumonia. Acquired idiopathic megaesophagus in general has a guarded to poor prognosis due to the common occurrence of aspiration pneumonia and malnutrition. Morbidity and mortality depend on the degree and nature of the underlying disease and client compliance. In the absence of severe aspiration pneumonia or thymoma, the success rate for acquired MG can be good with early diagnosis and appropriate management. Spontaneous remission of acquired MG with resolution of megaesophagus can also occur within an average of 6 months. However, many myasthenic dogs die of aspiration pneumonia during the first month after diagnosis, so the overall prognosis is still guarded. With the exception of the acute fulminating form of myasthenia, there is no association between the severity of MG and the possibility of remission.

In one study, 39% of dogs with immune-mediated polymyositis had clinical improvement of their megaesophagus with continued medical management. However, early diagnosis and initiation of appropriate therapy are key to a good clinical outcome. Evaluation of muscle biopsy samples early in the course of the disease to establish a diagnosis is critical. The prognosis for pre- and paraneoplastic myositis is poor due to the underlying cancer. Dysautonomia is progressive, with a survival rate of <25% in cats over 18 months. Prognostic indicators include showing response to therapy (e.g., maintenance of body weight with oral feedings, fecal and urinary continence) within 7 to 10 days.

**Conclusion**

Megaesophagus is common in dogs and less common in cats. Regurgitation is the most common clinical sign of megaesophagus at presentation. Diagnosis of megaesophagus is made radiographically, and the primary cause should be evaluated with appropriate diagnostic testing. Idiopathic megaesophagus is a diagnosis of exclusion. Management of megaesophagus is supportive unless an underlying cause is identified. The prognosis for megaesophagus depends on the presence of aspiration pneumonia and the underlying condition.

**References**

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1. __________ is not a clinical sign of megaesophagus.
   a. Regurgitation
   b. Halitosis
   c. Weight gain
   d. Coughing

2. Which condition is matched with the wrong clinical signs?
   a. congenital megaesophagus: regurgitation at time of weaning
   b. pneumonia: moist cough, dyspnea, and fever
   c. myositis: generalized weakness, stiff gait, and dysphagia
   d. organophosphate toxicosis: stiff gait, erect ears, and strong response to stimuli

3. In which breed is congenital megaesophagus not commonly documented?
   a. Parson Russell terrier
   b. Malinois
   c. Newfoundland
   d. Samoyed

4. Which statement regarding feline megaesophagus is false?
   a. Congenital and acquired megaesophagus occur in cats.
   b. Abyssinian, Somali, and Siamese cats may have a familial predisposition for megaesophagus.
   c. In cats, acquired secondary megaesophagus is not due to pyloric dysfunction.
   d. Metoclopramide may have a role in managing feline megaesophagus.

5. Which statement is true regarding diagnosing megaesophagus?
   a. Thoracic radiography is diagnostic for most cases of megaesophagus.
   b. Radiography is never useful in revealing underlying causes of megaesophagus.
   c. Normal midline tracheal location excludes a vascular ring anomaly.
   d. Incidental esophageal dilation does not occur.

6. Which statement regarding MG is true?
   a. All dogs with generalized MG have megaesophagus.
   b. Acquired MG occurs more often in German shepherds and golden retrievers than in other canine breeds.
   c. Definitive diagnosis of congenital MG requires an AChR antibody test.
   d. Dogs with acquired MG do not have measurable circulating anti-AChR antibodies.

7. Which CBC/serum chemistry result is not correctly matched with an appropriate etiology?
   a. hypercholesterolemia and hyponatremia: hypothyroidism
   b. hyperkalemia and hyponatremia: hyperadrenocorticism
   c. normochromic, normocytic, nonregenerative anemia: hypothyroidism
   d. nucleated erythrocytes without anemia: lead poisoning

8. Which therapy is not recommended as supportive care for megaesophagus?
   a. enteral feeding with an esophageal tube
   b. broad-spectrum antibiotics
   c. liquid sucralfate
   d. antacids and H₂ blockers

9. Which statement is true regarding medication administration for a patient with diagnosed megaesophagus?
   a. Formulation (liquid or pill) does not matter.
   b. Pills cannot result in subtherapeutic medication levels.
   c. Pills cannot result in overdose.
   d. Pills can lead to esophageal irritation.

10. Which statement regarding megaesophagus prognosis is true?
    a. The prognosis for congenital MG is good.
    b. Aspiration pneumonia contributes to a poor prognosis.
    c. Malnutrition does not contribute to the prognosis.
    d. Congenital idiopathic megaesophagus has a good prognosis.