

Tremor, fasciculations, and movement disorders

Michael Podell, MSc, DVM^{a,b,c}

^a*Animal Emergency and Critical Care Center, 1810 Frontage Road, Northbrook, IL 60089, USA*

^b*Department of Veterinary Clinical Medicine, College of Veterinary Medicine, University of Illinois, Champaign, IL, USA*

^c*Department of Veterinary Biosciences, College of Veterinary Medicine, The Ohio State University, Columbus, OH, USA*

Cats and dogs can develop a variety of unusual movement disorders that bewilder even the most seasoned clinicians because of the difficulty in determining their neuroanatomic origin and etiology. From life-altering tremors to benign sleep-related muscle twitches, these movements are representative of a range of underlying neuropathology, toxicology, neurodegeneration, or even normal behaviors. In general, the study of movement disorders encompasses a wide range of neurologic disturbances characterized by excess (hyperkinesia) or reduced (bradykinesia) movements. These abnormal involuntary movements (AIMs) refer to a number of muscle jerks, twitches, postures, and oscillations that have been classified in human neurology with official terms, such as tic, chorea, tremor, dystonia, and myoclonus [1]. Uncontrolled muscle contractions may be of muscle or neuronal origin [2]. Many of these disorders are the result of neurodegenerative changes of the basal ganglia in people, a condition not well documented in nonprimate species. Many small animals exhibit a number of AIMs that merit further investigation and possible therapy, however. The purpose of this article is to review and discuss the clinical presentation of movement disorders with emphasis on tremors and fasciculations in small animals (Box 1).

Box 1. Summary of abnormal involuntary movements in small animals

Hyperkinetic abnormal involuntary movements

Neuromuscular disorders

- Myotonia
- Tetany and tremor
 - Hypocalcemia
- Fasciculations
 - Benign
 - Exercise
 - Stress
 - Toxicity
 - Metabolic: hypercalcemia
 - Other causes of neuropathy

Myokymia

- Environmental (hypothermia)

Central nervous system disorders

Noncerebellar

- Myoclonus
 - Spinal
 - Proprioceptive
 - Epileptic
 - Toxicity
 - Tetanus
 - Tremor
 - Essential
 - Toxicity
 - Idiosyncratic drug-induced
 - Metabolic
 - Hypoglycemia
 - Hepatic or uremic encephalopathy
 - Degenerative disease

Cerebellar-related tremor disorders

Congenital

- Neonatal syndromes
 - Hypoplasia
 - Malformation
 - Granuloprival degeneration
 - Hypodysmyelinogenesis
 - Axonopathy

Postnatal syndromes

- Abiotrophy

Lysosomal storage diseases**Acquired****Inflammatory****Infectious****Immune-mediated****Neoplasm****Vascular/traumatic****Toxin****Idiopathic****Hypokinetic abnormal involuntary movements: parkinsonian syndromes****Primary****Secondary: drug reaction****Paroxysmal abnormal involuntary movements****Epileptic seizures****Nonepileptic seizures****Sleep-related movements****Clinical history**

The saying “a picture is worth a thousand words” is made for movement disorders. The ability to visualize the characteristics of AIMs should be supplemented with a detailed history to characterize the nature of the movement disorder. Information regarding anatomic distribution, rhythmicity, amplitude, frequency, speed of onset and offset of the movement, relation to posture and activity, situations that alleviate or exacerbate the movement, presence or absence during sleep, and affected littermates are all essential to help determine the neuroanatomic localization and potential etiology. If the movement disorder is not present at the time of the examination, owners should be encouraged to videotape the events for future review. Many times, the initial few minutes of observation solidify the clinical perspective, allowing an accurate diagnostic and therapeutic course of action to proceed.

Without doubt, dealing with movement disorders is a challenging diagnostic prospect. There are three diagnostic methods of approach for movement disorders [3]. The first is pattern recognition. This method is available to a select group of experienced and highly trained senior neurologists who can recognize the underlying disease just by history and evaluation. This method is by no means “foolproof.” The second method is the irrational method. Here, the clinician relies on as many diagnostic tests as possible to try to screen out as many underlying diseases as possible. This method is neither cost-efficient nor practical for the patient or the client. The last, and most acceptable method, is a rational diagnostic approach. The

goal for this method is to identify the type of movement disorder, to neurolocalize the lesion as to whether the signs are more suggestive of peripheral nervous system (PNS) or central nervous system (CNS) disease, to perform the proper diagnostic testing for this neurolocalization, and then to implement the associated treatment plan. Many movement disorders are early hallmark signs of diseases that can potentially progress to life-threatening situations, emphasizing the importance of proper identification of an underlying cause.

Review of voluntary control of motor unit activity

Most movement disorders are the outcome of loss of normal voluntary muscle control. Review of normal voluntary control of the motor unit is important to an understanding of the origin of movement disorders. The neuromuscular system consists of an efferent component and an afferent component. The efferent neuron of the PNS connecting the PNS with the CNS is known as the lower motor neuron (LMN). The afferent neuron is the first sensory neuron in the ascending spinal cord pathways, or the dorsal root ganglion. There are three divisions of the LMN system [2]: (1) the general somatic efferent (GSE) system, which innervates striated voluntary muscle of the tongue, extraocular apparatus, and limbs; (2) the special visceral efferent (SVE) system, which innervates striated voluntary muscle associated with the respiratory and digestive systems; and (3) the general visceral efferent (GVE) system, which innervates the involuntary smooth muscle associated with autonomic function. The SVE system cell bodies are located in cranial nerve nuclei V, VII, IX, X, and XI. The GVE system is divided into sympathetic and parasympathetic autonomic systems with a thoracolumbar and craniospinal location, respectively. The GSE cell bodies are located in cranial nerve nuclei III, IV, VI, and XII along with spinal motor neurons that innervate appendicular and axial skeletal muscles. The motor unit is composed of the LMN (GSE cell body, its axon, and neuromuscular junction) and the muscle innervated (Fig. 1).

Lesions of these LMN systems could include involvement of any component of the motor unit: neuronal cell bodies in the spinal cord or cranial nerve nuclei, spinal or cranial nerve roots, spinal or cranial nerves, peripheral nerves, neuromuscular junction, and muscle. In the spinal cord, these cell bodies are located in the ventral gray column, with the axial musculature arranged medially and the appendicular musculature located laterally. Proximal limb muscles are arranged along the ventral aspect, whereas the distal limb neurons are in the dorsal aspect of the lateral ventral gray column. The respective axons course from the dendritic zone in the gray matter to course distally as the ventral root, spinal nerve, and peripheral nerve to innervate the appropriate muscle. Each axon divides into branches to terminate on a motor end plate at the muscle cell. The final branching occurs at the neuromuscular junction. The number of muscle cells

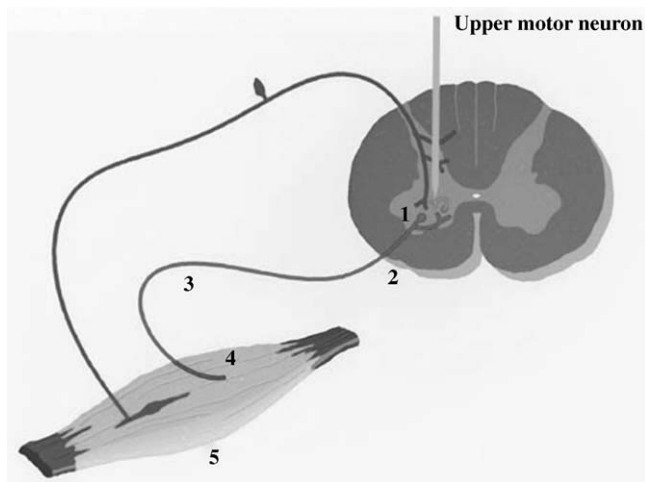


Fig. 1. Schematic diagram of the motor unit. 1, motor neuron in the spinal gray matter; 2, spinal nerve root; 3, peripheral nerve; 4, neuromuscular junction; 5, muscle; and 6, descending upper motor neuron tracts.

innervated by one motor neuron varies according to the muscle group. In general, the greater the degree of coordination involved, the smaller is the motor unit.

Voluntary movement is finalized with the coordinated firing of the motor neuron, which produces depolarization of all muscle fibers within a motor unit [4]. The initial information for excitation of the motor neuron derives from input from the upper motor neurons in the brain, which descends via white matter pathways in the spinal cord to terminate at either the cervical (C6–T2) or lumbosacral (L4–S1) spinal segment. The depolarization then spreads throughout the muscle fiber, followed by release of calcium, and culminates in the contraction of myofibrils. Muscle fibers are composed of myofibrils that contain the myofilaments actin (thin) and myosin (thick), which are attached to the muscle cell membrane (sarcolemma) by cytoskeletal proteins. Cytoskeletal proteins give muscle fibers their shape and transmit the force of muscle contraction to the sarcolemma. Muscle contraction and relaxation are active energy-dependent processes that result from either shortening or lengthening of the myofibrils, respectively. Calcium acts as a “security” system and must be released for muscle contraction. Free fatty acids are the major energy substrate for muscle metabolism. These free fatty acids enter muscle mitochondria via a carnitine-dependent transport process for oxidative phosphorylation to take place (for an in-depth discussion of muscle metabolism, see the article by Platt and Garosi in this issue).

Thus, the process of initiation and completion of voluntary movement is a complex one that relies on coordination of serial communications between

multiple components of the CNS and PNS. Failure of any of these components to complete their assigned tasks can result in loss of the desired movement or excessive abnormal movements.

Hyperkinetic movement disorders

Myotonia

Myotonia is a sustained muscle contraction with delayed relaxation. Myotonia congenita has been reported in the Chow Chow [5] and Miniature Schnauzer [6] breeds and seen sporadically in a number of other breeds. The disease is caused by a failure of normal myocyte chloride conductance, resulting in delayed muscle hyperpolarization, and thus delayed relaxation [7]. As an inherited autosomal recessive disease, puppies are affected from birth. Clinical signs are seen within the first few months of life and are characterized by a stiff “sawhorse” stance on ambulation, with improvement in gait as exercise time increases. Some dogs may suffer from dysphagia and respiratory problems caused by contraction of the tongue and oropharyngeal muscles. Affected dogs have hypertrophied glossal and proximal appendicular muscles that exhibit percussion dimpling on being struck with a percussion hammer (Fig. 2). Electromyography (EMG) recordings demonstrate the classic myotonic discharge of a high-frequency waxing-waning spontaneous discharge that produces a “dive-bomber” or revving motorcycle sound (see Fig. 2). Muscle biopsy is usually normal, although a type I fiber predominance or fiber hypertrophy may be found. Treatment consists of trial with an antiarrhythmic drug, such as mexiletine (2 mg/kg administered two or three times daily) or procainamide, but it may not alleviate the clinical signs. Many dogs can have a good quality of life by avoiding excessive exercise in the cold and maintaining a normal exercise routine.

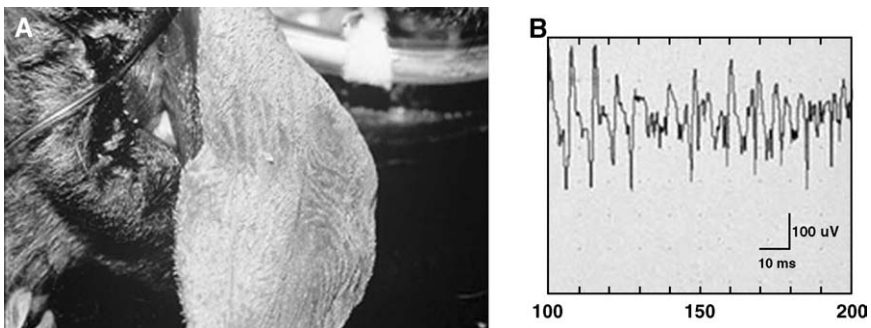


Fig. 2. (A) Percussion dimpling of the tongue of a 6-month-old Chow Chow dog with myotonia. Note the contraction of the muscle despite the dog being under general anesthesia. (B) The diagnosis is confirmed with the presence of myotonic discharges obtained with electromyography.

Acquired myotonic myopathy has been reported secondary to exposure to herbicides containing 2,4-dichlorophenoxyacetic acid (2,4-D) or 2-methoxy-3,6-dichlorobenzoic acid (dicamba) [8–10] and as an idiopathic condition associated with a myotonic dystrophy-like disorder in a Rhodesian Ridgeback dog [11]. The clinical signs are similar to those of the congenital form of myotonia.

Tetanus and tetany

Tetanus is a continuous sustained extensor muscle contraction. The cause is the tetanus toxin released by *Clostridium tetani* bacterial infection of domestic animals. The disease occurs when the tetanus spores localized to an anaerobic environment, such as a necrotic wound, transform into the toxin-producing form. The exotoxin, tetanospasmin, travels from the infected site via peripheral nerves to the CNS [12]. The toxin prevents the release of the inhibitory neurotransmitter glycine from interneurons in the spinal cord and brain, resulting in excessive excitation of brain stem and motor neurons.

Cats and dogs are fairly resistant to tetanus; however, when infected, they can exhibit an extreme stiffness progressing to extensor rigidity of all limbs, spastic facial muscles, and trismus within 5 to 10 days of infection (Fig. 3) [13,14]. A “grimacing” expression with the ears pulled back is usually seen. Occasionally, localized tetanus may affect only a single limb or be confined to the facial muscles. Many animals are hypersensitive to external stimuli. The diagnosis is based predominantly on a history of recent wounds and clinical signs. Initial treatment consists of aggressive wound debridement, parenteral penicillin or metronidazole treatment, muscle relaxant therapy (diazepam continuous rate infusion at 0.3 mg/kg/h or pentobarbital, 3–10 mg/kg, administered intravenously [IV] to effect), and nutritional support. Tetanus antitoxin (100–1000 IU/kg administered IV) has been reported useful to reduce the duration of clinical effects [15]. A test dose of 0.2 mL administered subcutaneously (SC) should be given first, with observation for anaphylactic reaction. Careful attention should be given to hydration and nutritional support, because the trismus can prevent adequate fluid and food intake. Complete remission of clinical signs usually occurs within several weeks to months.

Tetany is a variable and intermittent extensor muscle contraction. It may accompany CNS and PNS diseases. In dogs, tetany is most commonly seen with hypocalcemia-associated parturition or hypoparathyroidism [16]. Total calcium is typically below 7.0 mg/dL. Dogs often suffer from an inability to rise, extensor muscle contractions, and hyperthermia (from muscle contractions). Secondary hypoglycemia may also be seen because of the excessive muscle movements. Treatment is focused on initial muscle relaxation with benzodiazepines, followed by calcium and vitamin D supplementation.



Fig. 3. Generalized tetanus in a 2-year-old Boxer dog. Note the extreme and constant extensor muscle rigidity characteristic of tetanus. The dog developed tetanus after an infection from an untreated wound of the pelvic limb paw (shown bandaged).

Myoclonus

Myoclonus is defined as a sudden, rapid, involuntary muscle movement of short duration caused by active muscle contractions (positive myoclonus) or pauses in muscle activity (negative myoclonus) [17]. Classification can be based on clinical presentation, site of origin, or etiology. Reflex myoclonus to auditory stimuli has been reported in the retriever dog breeds [18]. Spinal myoclonus arises from abnormal neuronal discharges originating in the spinal cord and is of two main types: segmental and propriospinal. Segmental myoclonus can occur in dogs infected with canine distemper, producing a repetitive myoclonic jerk motion of one or more limbs, even during sleep [19,20]. Epileptic myoclonus [21,22] and drug-induced myoclonus [23] in dogs are examples of etiologic classification.

Fasciculations and myokymia

Muscle fasciculations are spontaneous contractions of muscle fibers within a motor unit and arise from ectopic electrical activity in the distal axon [24]. Fasciculations typically are the manifestation of irritability of the neuronal cell body (motor neuron) or its accompanying axons [25]. As such, they are most often associated with motor neuron disease and peripheral nerve disorders. Fasciculations can be more readily observed in the distal appendicular muscles and the tongue but can be difficult to detect in more obese animals. One can usually detect a fine “rippling” movement of the muscle as a sign of fasciculation.

The differential diagnoses of muscle fasciculations range from benign to more severe neuromuscular disease. Benign contraction fasciculations can

be seen after strenuous exercise and possibly in tense animals [26]. Other transient muscle fasciculations can be associated with hypercalcemia, hypomagnesemia, and certain toxic drug reactions to theophylline, terbutaline, caffeine, and methylxanthine (chocolate toxicity), for example, as well as with reactions to anticholinesterase agents (ie, pyridostigmine and neostigmine used for the treatment of myasthenia gravis). Fasciculations associated with neuromuscular disease are most likely to be present after the onset of clinical signs of weakness. Degenerative feline and canine motor unit disease and more advanced cases of distal axonopathy in the dog are conditions that are more likely to be associated with muscle fasciculations [3,27].

Myokymia is a pattern of abnormal muscle contraction that produces a rippling or “writhing” appearance of the area involved. The change is the result of spontaneous discharges of large motor units. Myokymia is an indication of neuronal disease, followed by sprouting of the motor unit territory in response to the denervation [28]. Myokymia or myokymia-like syndrome has been described in Jack Russell Terriers and is associated with hyperthermia and collapse [29,30].

Tremor syndromes

A number of tremor syndromes that have been described in human beings are also seen in small animals. Tremor is classified according to its anatomic distribution as well as frequency and amplitude during rest, postural maintenance, movement, intention, and the performance of specific tasks. The degree of tremor (amplitude) is often variable and can be exacerbated with emotional (anxiety) and physical activity. The two main types of tremor are known to occur at rest or with action [1]. Resting tremor describes an involuntary rhythmic oscillation of a body part completely supported against gravity. This tremor can be seen in a leg, with the animal lying down and not supporting weight. Action tremor occurs during voluntary contraction of skeletal muscle and is classified as postural, kinetic, isometric, or task specific. Postural tremor describes oscillation of a body part that is voluntarily maintained against gravity. This tremor type is rare in small animals. Kinetic tremor describes oscillation during guided voluntary movement. This intentional tremor is the most common type seen with cerebellar disease in small animals. Isometric tremors and task-specific tremors are seen with primate species that can hold objects and initiate specific movements of the hands and arms.

Essential tremors

Physiologic and essential tremor syndromes are the most common syndromes in people [31] and can occur in older dogs, particularly in aging terrier breeds. In affected people, such a syndrome is believed to be an autosomal dominant inherited trait with variable penetrance [31]. It is a pure

clinical syndrome characterized by progressive action tremor of pelvic limbs that worsens with activity and excitement. Severity can range from barely perceptible tremor to altered gait and balance problems. Signs can progress as the dog ages.

Tremor associated with neuromuscular disease

Tremor attributed to weakness is almost always associated with underlying nerve disease [3]. Most likely, this type of tremor is an exaggeration of the normal physiologic tremor that results from the synchronized discharge of enlarged motor units in patients that have a reduced number of surviving motor neurons [32]. Dogs with advanced peripheral neuropathies can present with this type of tremor in the pelvic limbs. The tremor is exaggerated after exercise and while standing. Other conditions that directly affect nerve function with this type of tremor include compressive neuropathy from lumbosacral disk disease or stenosis, nerve sheath tumors, and other mass effects or entrapment syndromes involving the nerve.

Drug-induced tremors

Drug-induced tremor has been reported in the cat and dog. Predictable tremor can be seen with stimulant toxicity (eg, caffeine, amphetamines, cocaine). Other potential drugs that have induced tremor in human beings include valproic acid, amiodarone, procainamide, and lithium [1]. Tardive dyskinesia represents a wide variety of involuntary movements in human beings, including chorea, dystonia, akathisia, myoclonus, tremor, and stereotypies. Stereotypy, or rhythmic involuntary movement, is the most common manifestation resulting from exposure to dopamine receptor–blocking agents, such as phenothiazine (eg, acepromazine) or antiemetic drugs (eg, metoclopramide) [33]. Loss of D₂ receptors in the neostriatum is postulated to contribute to the pathophysiology [34].

Cerebellar-related tremors

By far, the most common cause of tremor in small animals is cerebellar syndromes and disease. Cerebellar diseases are often associated with a conglomeration of signs related to abnormal motor activity to include any or all of the following: tremors, bilaterally symmetric ataxia without paresis, dysmetria, vestibular signs (eg, head tilt, nystagmus, falling), absent menace with preservation of vision, and pupillary changes [2]. An altered resting posture is often present, with affected animals demonstrating truncal ataxia (swaying of the body back and forth or side to side) and a compensatory broad-based stance for balance. Cerebellar tremors are associated with diffuse cerebellar cortical diseases. These intention tremors are characterized by a fine head tremor that worsens with initiation of voluntary head movements. “Titubation” is a cerebellar postural tremor that affects the head and trunk. The more acute-onset diseases affecting the

cerebellar cortex usually result in more pronounced tremor disturbances. Severe tremors may affect the entire body, with complete loss of all muscular coordination, failure to posture, and failure to prehend food. Ensuing hyperthermia, rhabdomyolysis, and related complications from continuous muscle activity require that these patients be aggressively treated on an emergency basis (see below). Fortunately, many “pure” cerebellar diseases can be treated or compensated for by the patient.

Cerebellar syndromes associated with tremor can be divided into congenital and acquired diseases (see Box 1). Congenital neonatal syndromes represent diseases of the newborn animal in which the clinical signs are present from birth and are nonprogressive. In contrast, the clinical signs of congenital postnatal diseases begin in the pediatric animal after birth and are slowly progressive. Acquired cerebellar diseases can be acute or chronic in onset, with rapid progression most commonly seen with inflammatory diseases [35] and toxic exposures (eg, mycotoxins, metaldehyde, macadamia nuts) [36].

Hypokinetic movement disorders: Parkinson syndromes

Parkinson disease is a neurodegenerative disease of the nigrostriatal dopaminergic system in human beings. A parallel naturally occurring disease has not been reported in nonprimate species. Secondary parkinsonism, however, can occur in a number of species. Potential causes of secondary disruption of normal dopaminergic function can be classified as drug induced, toxin induced, associated with a metabolic disorder, vascular-related disease, postencephalitic/postinfectious disease, and posttraumatic events [37]. Drug-induced parkinsonism is the most common cause of symptomatic parkinsonism in human beings and can occur in animals. Because of the ability of neuroleptics (eg, haloperidol, droperidol) to block dopamine receptors, a higher prevalence is reported with longer treatment. Doberman Pinschers seem to be sensitive to an acute-onset type of secondary parkinsonism with tremor that is reversible. Other potential drugs include metoclopramide, prochlorperazine, calcium channel blockers, fluoxetine, pyridostigmine, and meperidine.

Paroxysmal movement disorders

Paroxysmal movement disorders can be classified as seizure disorders that can be caused by an associated epileptic change in brain activity (epileptic seizures) or can occur without such a change (nonepileptic seizures). These sudden changes take the form of many manifestations of body position, motion, ability to stand, facial expressions, and limb movements, for example. Severity varies from involvement of the whole body to movement of only a single muscle group. It is important for the

clinician to recognize the presence of these movements as benign or suggestive of more serious underlying neurologic problem.

Epileptic seizures

Epileptic seizure types can be classified into two major categories: partial and generalized [38]. Partial seizures are the manifestation of a focal epileptogenic event in the cerebral cortex. With simple partial seizures, there are usually asymmetric motor or sensory signs without a change in consciousness. Examples include facial focal seizures or excessive pawing or biting of a body part. Animals with complex partial seizures, also termed *psychomotor seizures*, have impaired consciousness, often with bizarre behavioral activity and possible motor disturbances. Generalized seizures are subdivided into convulsive (“grand mal”) and nonconvulsive (“petit mal”) seizures. These seizures are characterized by impaired consciousness coupled with bilateral motor signs of a tonic-clonic, tonic, myoclonic, or even atonic nature. The major form of nonconvulsive seizure is the “absence” variety manifested as impaired consciousness only. This seizure type is poorly documented in animals.

Nonepileptic seizures

Many events may mimic epileptic seizures. Two major categories of nonepileptic seizures in people are psychologic and organic. Veterinarians are fortunate in not having to determine the presence of hysterical seizures in cats and dogs. Behavioral disorders, however, may obscure this distinction. In particular, obsessive-compulsive behaviors, such as tail-chasing and repetitive licking, can occur and end suddenly. The organic nonepileptic seizures can be broken down into nonneurologic and neurologic causes. More common causes of nonneurologic and nonepileptic seizures are syncope of cardiac origin, metabolic disturbances (eg, transient hypoglycemia, endocrine diseases), and toxicities. Two major neurologic causes of nonepileptic seizures are acute vestibular attacks (often peripheral in nature) and narcolepsy. In practically all instances, dogs with nonepileptic seizures do not exhibit postictal effects.

Diagnostic approach

The diagnostic approach to an animal with AIMs starts with an evaluation of whether the movement disorder is hyperkinetic, hypokinetic, or paroxysmal (Fig. 4). The next step is to determine if the animal exhibits any signs of tremor of the head, neck, or other areas of the body. Animals without tremor should then be evaluated for signs of excessive rigidity or stiffness. Constant extensor muscle rigidity is more likely to be a sign of tetanus, whereas variable extensor muscle rigidity is associated with tetany.

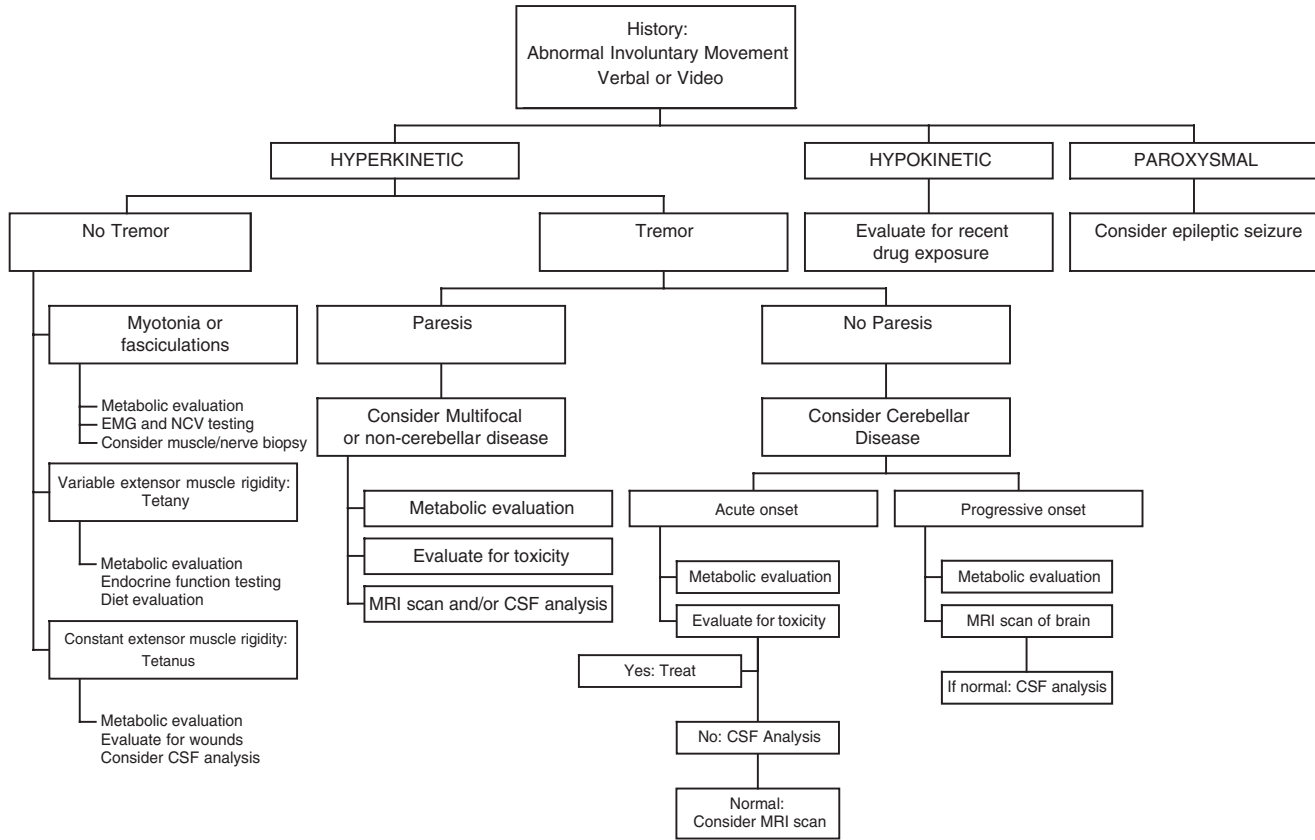


Fig. 4. Algorithm for the diagnostic approach to abnormal involuntary movements in small animals.

An initial metabolic evaluation, including a complete blood cell count, serum chemistry panel, ionized calcium measurement, and creatine kinase measurement, should be performed. Tetanus is diagnosed based predominantly on clinical signs and history, whereas tetany is typically diagnosed based on the presence of hypocalcemia or another metabolic disorder.

If no extensor muscle rigidity is detected, signs of abnormal muscle movement, including myotonia, fasciculation, and myokymia, should be suspected. These signs are all indicators of underlying neuromuscular disease; as such, they merit further specific diagnostic testing for peripheral neuropathy or myopathy. Again, an initial metabolic evaluation, including a complete blood cell count, serum chemistry panel, ionized calcium measurement, and creatine kinase measurement, should be performed. The next level of testing is electrodiagnostic evaluation with EMG and nerve conduction testing. EMG tests the stability of the muscle membrane. Major causes for muscle membrane instability resulting in spontaneous firing, or activity of muscle cells, are denervation, inflammation, or intrinsic or extrinsic metabolic abnormalities. The type of activity pattern is useful in categorizing the etiology. Motor and sensory nerve conduction velocity testing is often done in conjunction with EMG to evaluate peripheral nerve function. Reduced velocity is more indicative of a demyelinating process, whereas decreased amplitude of evoked motor or sensory action potentials is more representative of a primary axonopathy.

If tremor is present as part of the history or clinical examination, the next step is to determine if any paresis is present. Care must be taken not to confuse weakness with falling from incoordination. A reliable test is to hop an animal on each leg individually to see if it collapses on that leg during the testing. A weak animal cannot support weight on that limb, whereas an incoordinated one can. If paresis is present, one should consider a multifocal or noncerebellar CNS disease. A history of possible toxic exposure should be ruled out before pursuing more advanced testing. If the metabolic evaluation is normal as stated previously, an MRI scan of the brain or spinal cord, with possible cerebrospinal fluid (CSF) analysis, is warranted to evaluate for the underlying etiology.

If paresis is not present with the tremor syndrome, it is most likely that the animal is suffering from a pure cerebellar disease process. An acute onset of clinical signs is more suggestive of a toxic reaction or inflammatory disease process. If toxicity is documented, no further diagnostic testing may be needed and symptomatic therapy can be instituted. If toxicity cannot be documented, CSF analysis is recommended. If the CSF is normal, MRI scanning of the brain may be necessary. If the disease process is more chronic and progressive in nature, the patient should be evaluated for a possible mass lesion of the cerebellum with a MRI scan before collection of CSF for analysis.

For hypokinetic movement disorders, the most likely scenario is a possible reaction to recent drug therapy or exposure. Owners should be

questioned about any possible accidental exposure to their own medications. Paroxysmal movement disorders have a history of an animal going from a normal state to a sudden change of body movement for a finite period of time, followed by either an immediate return to normalcy or a period of postictal changes for epileptic seizures.

Treatment approaches

The goal for the control of tremors in small animals is to determine the etiology, remove any inciting cause (toxin or iatrogenic), and provide immediate and prolonged symptomatic relief for acquired diseases. A number of treatments for essential chronic tremor disorders have been proposed for people, with varying results. First-line treatments useful in the dog include phenobarbital, 2.5 mg/kg, administered orally (PO) twice daily or a β -adrenergic antagonist (eg, propranolol, 2.5–10 mg, administered PO two to three times daily). Benzodiazepines do not seem to be effective in human beings [39] or dogs (personal experience). Clozapine, a D₂ dopamine receptor antagonist, significantly reduced tremor severity in human patients with essential tremor with chronic dosing between 18 and 36 mg/d [40]. Topiramate, a new antiepileptic drug, has recently been shown to be efficacious in refractory essential tremor cases in human beings at a dose range between 100 and 200 mg/d [41]. Documentation of the success of these therapies in animals is not currently available.

Recommended emergency treatment for acute onset of suspected acquired tremor disease (ie, steroid-responsive tremor syndrome or toxicity) is listed in **Box 2**. This situation can be a life-threatening disease; as such, it requires a rapid therapeutic approach. Care should be given to avoid the use of corticosteroid therapy, because this treatment can alter the ability to obtain a diagnosis of an inflammatory disease with CSF analysis.

Summary

AIM disorders are common neurologic problems in small animals. Most animals exhibit hyperkinetic uncontrolled movements that are the result of underlying cerebellar or neuromuscular diseases. Using precise historical and examination information, a well-planned diagnostic approach can be formulated. Most important for the clinician is the ability to discern if a primary brain or neuromuscular disease is present. The use of a guiding algorithm has been presented to aid in this decision-making process. Advanced diagnostic testing with electrodiagnostic testing or biopsy of the PNS or imaging or CSF fluid analysis of the CNS is critical in the definitive diagnosis of many of the diseases associated with AIMs in small animals. Fortunately, with proper diagnostic testing that leads to appropriate treatment strategies, many animals suffering from these often unusual problems can go on to lead quality lives.

Box 2. Emergency treatments for acute-onset tremors in the dog

1. Intravenous bolus injection of diazepam, 0.5 mg/kg, administered intravenously. If an intravenous route is not possible immediately, a per rectal injection at a rate of 1 mg/kg can be given.
2. If tremors continue or return, start diazepam at a continuous rate intravenous infusion of 0.25 mg/kg/h in 0.9% saline at a maintenance fluid rate. This rate can be increased to 0.5 mg/kg/h.
3. If the tremors are not controlled, give an intravenous bolus of phenobarbital, 20 mg/kg, followed by 2 mg/kg administered orally every 12 hours.
4. If the tremors continue, a continuous intravenous infusion of a barbiturate should be used.
 - a. Propofol intravenous continuous rate infusion at a rate of 5 to 10 mg/kg/h to effect to stop tremors, **or**
 - b. Pentobarbital administered intravenously at a rate of 2 to 5 mg/kg/h to effect to stop tremors
 - c. Continue a balanced electrolyte solution for fluid therapy to avoid hypotension
5. Monitoring and supportive care
 - a. Maintain normal ventilation and blood oxygenation
 - b. Maintain normal body temperature
 - c. Provide proper intravenous fluid therapy to avoid hypotension and dehydration
 - d. Maintain normoglycemia
 - e. Maintain normotension

References

- [1] Zesiewicz TA, Hauser RA. Phenomenology and treatment of tremor disorders. *Neurol Clin* 2001;19:651–80.
- [2] DeLahunta A. *Veterinary neuroanatomy and clinical neurology*. 2nd edition. Philadelphia: WB Saunders; 1983.
- [3] Mendall JR, Kissel JT, Cornblath DR. Clues to the diagnosis of peripheral neuropathy: history and examination of the patients. In: *Diagnosis and management of peripheral nerve disorders*, vol. 59. New York: Oxford University Press; 2001. p. 10–29.
- [4] Griggs RC, Mendall JR, Miller RG. *Evaluation and treatment of myopathies*. Philadelphia: FA Davis; 1995. p. 3–14.
- [5] Farrow BRH, Malik R. Hereditary myotonia in the chow chow. *J Small Anim Pract* 1981; 22:451–65.
- [6] Vite CH, Melniczek J, Patterson D, et al. Congenital myotonic myopathy in the miniature schnauzer: an autosomal recessive trait. *J Hered* 1999;90:578–80.

- [7] Vite CH. Myotonia and disorders of altered cell membrane excitability. *Vet Clin N Am Small Anim Pract* 2002;32:169–87.
- [8] Beasley VR, Arnold E, Lovell RA, et al. 2,4-D toxicosis: a pilot study of 2,4-dichlorophenoxyacetic acid and dicamba myotonia in experimental dogs. *Vet Hum Toxicol* 1991;33:435–40.
- [9] Dickow L, Podell M, Gerken DF. Clinical effects and plasma concentration determination after 200 mg 2,4-dichlorophenoxyacetic acid/kg administration in the dog. *J Toxicol Clin Toxicol* 2000;38:747–53.
- [10] Steiss JE, Braund KG, Clark EG. Neuromuscular effects of acute 2,4-dichlorophenoxyacetic acid (2,4-D) exposure in dogs. *J Neurol Sci* 1987;78:295–301.
- [11] Simpson ST, Braund KG. Myotonic dystrophy-like disease in a dog. *J Am Vet Med Assoc* 1985;186:495–8.
- [12] Price DL, Griffin JW, Young A, et al. Tetanus toxin: direct evidence for retrograde intraaxonal transport. *Science* 1975;188:945–7.
- [13] Baker JL, Waters DJ, de Lahunta A. Tetanus in two cats. *J Am Anim Hosp Assoc* 1988;24:159–64.
- [14] Ratcliff J. Tetanus in a dog. *Vet Rec* 1989;124:666.
- [15] Greene CE. Tetanus. In: *Infectious diseases of the dog and cat*. Philadelphia: WB Saunders; 1990. p. 521–9.
- [16] Bruyette DS, Feldman EC. Primary hypoparathyroidism in the dog. Report of 15 cases and review of 13 previously reported cases. *J Vet Intern Med* 1988;2:7–14.
- [17] Fahn S, Marsden CD, Van Woert MH. Definition and classification of myoclonus. *Adv Neurol* 1986;43:1–5.
- [18] Fox JG, Averill DR, Hallett M, et al. Familial reflex myoclonus in Labrador Retrievers. *Am J Vet Res* 1984;45:2367–70.
- [19] Inada S, Nomoto H, Kawasaki Y. Canine distemper myoclonus and sleep: observation of a case. *Electromyogr Clin Neurophysiol* 1993;33:137–41.
- [20] McGovern VJ. Canine encephalitis causing a syndrome characterized by tremor. *Aust J Exp Biol Med Sci* 1950;28:433–47.
- [21] Genton P, Van Vleymen B. Piracetam and levetiracetam: close structural similarities but different pharmacological and clinical profiles. *Epileptic Disord* 2000;2:99–105.
- [22] Holland JM, Davis WC, Prieur DJ, et al. Lafora's disease in the dog. A comparative study. *Am J Pathol* 1970;58:509–30.
- [23] Muir WW, Mason DE. Side effects of etomidate in dogs. *J Am Vet Med Assoc* 1989;194:1430–4.
- [24] Roth G. The origin of fasciculations. *Ann Neurol* 1982;12:542–7.
- [25] Wettstein A. The origin of fasciculations in motor neuron disease. *Ann Neurol* 1979;5:295–302.
- [26] Fleet WS, Watson RT. From benign fasciculations and cramps to motor neuron disease. *Neurology* 1986;36:997–1002.
- [27] Cuddon PA. Acquired canine peripheral neuropathies. In: Shelton GD, editor. *Neuromuscular diseases*, vol. 32. Philadelphia: WB Saunders; 2002. p. 207–49.
- [28] Albers JW, Allen AA, Bastron JA, et al. Limb myokymia. *Muscle Nerve* 1981;4:494–504.
- [29] Reading MJ, McKerrell RE. Suspected myokymia in a Yorkshire Terrier. *Vet Rec* 1993;132:587–8.
- [30] Van Ham L. Suspected neuromyotonia in 12 Jack Russell terriers. *Eur Soc Vet Neurol* 1998;26–7.
- [31] Brin MF, Koller W. Epidemiology and genetics of essential tremor. *Mov Disord* 1998;13(Suppl 3):55–63.
- [32] Adams RD, Shahani BT, Yound RR. Tremor in association with polyneuropathy. *Trans Am Neurol Assoc* 1972;97:97–102.
- [33] Stacy M, Cardoso F, Jankovic J. Tardive dyskinesia. *Curr Opin Neurol Neurosurg* 1993;4:343–9.

- [34] DeKosky ST, Palmer AM. Neurochemistry of aging. In: Albert ML, Knoefel JE, editors. *Clinical neurology of aging*. New York: Oxford University Press; 1994. p. 79–101.
- [35] Wagner SO, Podell M, Fenner WR. Generalized tremor in dogs: 24 cases. *J Am Vet Med Assoc* 1997;211:731–5.
- [36] Hansen SR, Buck WB, Meerdink G, et al. Weakness, tremors, and depression associated with macadamia nuts in dogs. *Vet Hum Toxicol* 2000;42:18–21.
- [37] Colcher A, Simuni T. Other Parkinson syndromes. In: Hurtig HI, Stern MB, editors. *Movement disorders*, vol. 19. Philadelphia: WB Saunders; 2001. p. 629–49.
- [38] Podell M. Seizures in dogs. *Vet Clin N Am Small Anim Pract* 1996;26:779–809.
- [39] Thompson C, Lang A, Parker JD. A double-blind trial of clonazepam in benign essential tremor. *Clin Neuropharmacol* 1984;7:83–8.
- [40] Ceravolo R, Salvetti S, Piccini A, et al. Acute and chronic effects of clozapine in essential tremor. *Mov Disorder* 1999;14:468–72.
- [41] Galvez-Jimenez N, Hargreave M. Topiramate and essential tremor. *Ann Neurol* 2000;47:837–8.