Lesions in Bovine Progressive Degenerative Myeloencephalopathy ("Weaver") of Brown Swiss Cattle

L. D. Stuart and H. W. Leipold

Department of Pathology, College of Veterinary Medicine, Kansas Agricultural Experiment Station, Kansas State University, Manhattan, KS

Abstract. Gross changes and other necropsy findings in 36 purebred Brown Swiss cattle affected with bovine progressive degenerative myeloencephalopathy were nonspecific. Primary microscopic lesions were confined to the central nervous system, specifically the white matter of the spinal cord, axons in some brainstem nuclei, and Purkinje cells of the cerebellar cortex. Spinal cord lesions involved only the white matter and consisted of axonal degeneration, loss of axons and myelin, and status spongiosus. Axonal degeneration was characterized by swelling and fragmentation of the axoplasm or formation of large, discontinuous swellings referred to as spheroids. Lesions were qualitatively similar at all levels, but quantitatively dissimilar in the same funiculi at different levels. Both ascending and descending fibers were involved but correlation to specific fasciculi was not evident. Lesions always were most severe in thoracic spinal cord segments. Little or no astroglial response, no inflammatory response, and no involvement of gray matter were observed in the spinal cord. Cerebellar lesions were limited to selective degeneration and loss of Purkinje cells and occasional swelling of Purkinje cell axons (torpedos) in the granular layer of the cerebellar cortex. Brainstem lesions were inconsistent and limited to occasional axonal swelling in brainstem nuclei. The pathogenesis of bovine progressive degenerative myeloencephalopathy is unknown and possible mechanisms were discussed. The disease exhibits a familial pattern in Brown Swiss cattle and may be hereditary. Extraneural lesions were considered secondary to central nervous system lesions.

Bovine progressive degenerative myeloencephalopathy of purebred Brown Swiss cattle is a progressive disease with clinical signs that implicate central nervous system involvement. Epidemiology, clinical signs, and other clinical and laboratory findings have been described. Briefly, bovine progressive degenerative myeloencephalopathy has an onset at five to eight months of age, affects both sexes, and is characterized clinically by hind leg weakness, ataxia, and dysmetria in the absence of other significant clinical abnormalities. A familial relationship has been suggested. The disease occurs throughout the United States and has been reported only in Brown Swiss cattle. The purpose of this study was to characterize the morphologic lesions and to examine the distribution and nature by light microscopy.

Forty-three cattle were necropsied in this study, including 36 Brown Swiss cattle, 28 females and 8 males, affected with bovine progressive degenerative myeloencephalopathy. A fetus in the last trimester of gestation from an affected cow (number 16) was not affected. Additional control animals free of bovine progressive degenerative myeloencephalopathy included three other Brown Swiss affected with other conditions and two Jersey cows and one Brown Swiss calf which were all neurologically normal. Animal numbers, sex, age at death, manner of fixation, and final diagnoses are summarized in table I. Cattle were obtained and handled as described previously.

Different necropsy methods were used in various phases of this study and different fixatives were employed to correspond with subsequent procedures. The standard necropsy procedure for this study was designed for fixation in situ or to permit removal of brain and spinal cord tissue as rapidly and accurately as possible without causing trauma to the delicate central nervous system tissues. Critical tissues were removed and placed in fixative within 10 to 15 minutes following euthanasia, and no more than 30 minutes ever elapsed between death and fixation.

All non-perfused cattle were given T-61 euthanasia solution (American Hoechst Corp., Sommerville, NJ) intravenously via the jugular vein. All tissues were fixed by immersion in Trump's solution of 1% glutaraldehyde and 4% phosphate buffered formalin or a 10% buffered neutral formalin solution. Central nervous system tissues were either fixed in situ or after careful dissection from their bony encasements. In either method the dura mater was incised to allow rapid penetration of fixatives. After 24 hours fixation, coronal sec-
Table I. Data for necropsied affected, unaffected, and control cattle

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1 All tissues were fixed by immersion except those with an asterisk which were fixed by perfusion.
2 Fetus of animal 16.
3 BPDME = bovine progressive degenerative myelonecephalopathy.
4 Abattoir specimen.

The spinal cord was smaller than normal in all affected cattle. No significant gross lesions were observed in the brain.

Results

The spinal cord was smaller than normal in all affected cattle. No significant gross lesions were observed in the brain.

There was frequently atrophy of muscles of the hind leg, especially in long-standing cases of bovine progressive degenerative myelonecephalopathy. Extensors of the hip and stifle, such as the biceps femoris, muscles of the quadriceps group, and semimembranosus were involved more commonly. More striking changes were
inconsistently noted in these and other muscles and included focal hemorrhagic and necrotic lesions up to 4 to 6 cm in diameter or focal areas of fibrosis and replacement by adipose tissue (up to 3 to 5 cm in diameter) (fig. 1).

In cattle severely affected for a longer duration, or cachectic cattle, long bones of the hind legs had soft, thin cortices, and the marrow cavity was replaced by adipose tissue.

Ovaries of heifers and cows were smaller than normal. Frequently there were multiple, small or single, large fluid-filled cysts present. Otherwise, the parenchyma was dense, firm and white. Corpora lutea or other evidence of follicular activity were observed infrequently.

The uterus in most cows examined was smaller than normal, turgid and thick-walled. One cow (number 16) was pregnant—carrying a fetus in the last trimester.

Three mature bulls and one younger bull were examined. Testicles in each were small, soft and flabby, and pale on cut surface. Testicular weights for the largest bull were 170 and 165 g, right and left, respectively. Testicular weights for the other bulls were not recorded. Average single testicular weight for mature dairy bulls is 351 g.

Lymph nodes draining the hind legs were often moderately enlarged, especially popliteal, prefemoral, and inguinal nodes. The medullary region of enlarged nodes was red-brown to gray-brown on cut surface, with a shiny, moist appearance. Other body lymph nodes were grossly normal.

No significant macroscopic lesions were observed in

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Fig. 1: Diffuse, severe fibrosis in an extensor muscle of stifle joint. Animal 19.
Fig. 2: Thoracic spinal cord; wallarian degeneration and a large axonal swelling (spheroid) at arrow. Animal 13. HE. Bar = 20 μm.
Fig. 3: Section of cervical spinal cord; large granular axonal spheroid and compression of peripheral white matter. Animal 13. HE. Bar = 20 μm.
Fig. 4: Cervical spinal cord section; large empty vacuole and several smaller vacuoles. Animal 13. HE. Bar = 20 μm.
other tissues, with the exception of a single cow which had multiple esophageal, buccal and lingual ulcers, abomasal erosions, interlobular pulmonary emphysema, and slight emphysema in pericardial tissues. Fluorescent antibody studies of small intestine, lymph node, esophagus and soft palate for bovine virus diarrhea virus were positive in this cow (number 31) of two cattle studied. Virus isolation and fluorescent antibody studies for bovine virus diarrhea virus were negative in the second cow (number 19). No virus isolation was attempted on cow number 31.

Central nervous system lesions were observed in all cattle affected with bovine progressive degenerative myeloencephalopathy. No significant differences were observed in the quantity or quality of lesions between cattle perfused and those fixed by immersion following rapid necropsy. Control cattle had no microscopic central nervous system lesions.

The white matter of the spinal cord was the most consistently and severely affected portion of the central nervous system in every affected animal. Active axonal degeneration, loss of axons and myelin, status spongiosus of the white matter, and voluminous axonal swelling (spheroids) were present at all levels. No significant changes were observed in the gray matter, spinal motor nerve cell bodies, or spinal ganglia at any level.

Axonal degeneration in HE-stained sections was manifested by selective, but widespread, axonal swelling accompanied by increased basophilia (fig. 2), fragmentation of axoplasm and the formation of large, ovoid to elliptical structures designated as spheroids. Axonal spheroids were present throughout the white matter and were characteristically well-delineated and varied from 25 µm up to 75 to 100 µm in diameter in transverse sections. The internal structure of characteristic spheroids was lightly eosinophilic and lacy to finely granular and amorphous (fig. 3). Occasional spheroids were more homogeneous to hyaline-like and stained lightly basophilic to deeply eosinophilic, respectively. Numerous empty spaces were observed where axons would have normally been present; this resulted in a status spongiosus in affected white matter (fig. 3). The empty spaces varied in size from 10 to 15 µm up to 75 µm in diameter. Open spaces were usually devoid of stainable material (fig. 4), however, a few spaces contained single, foamy microglial macrophages (gitter cells) or unidentifiable tissue fragments (figs. 5, 6). All spaces had distinct boundaries that separated them from adjacent white matter and sometimes slightly displaced adjacent tissue. Some open spaces were considered to be remaining areas which had been previously occupied by large axonal spheroids lost when spinal cord sections were cut and stained.

Although myelin sheaths are not well-demonstrated in routine HE-stained sections, the openness of the white matter and overall appearance of areas associated with axonal degeneration indicated some loss or lack of myelin. Myelin wrappings may have been disrupted or distended (fig. 2).

Glial response was notably unremarkable in the spinal cord. An occasional microglial phagocyte (gitter cell) was observed in association with a degenerating axon, and rare, focal microglial accumulations were seen in the white matter. Microglial accumulations consisted of less than 10 to 15 cells and were usually unrelated to blood vessels in areas of severe degeneration.

Luxol fast blue-cresyl echt violet-stained sections confirmed the observation in HE-stained sections that a lack or loss of myelin was present. In affected funiculi a general pallor was present at low magnification; it varied in degree with the area and segment examined. At higher magnification, myelin sheaths, where present, were often stained poorly. Axonal spheroids and debris in open spaces were not stained or poorly stained by Luxol fast blue-cresyl violet. Myelin sheaths of degenerating axons were poorly stained by Luxol fast blue-cresyl violet and often were partially separated or otherwise disrupted.

Bodian’s method confirmed the HE findings of nerve fiber degeneration and loss in affected portions of spinal cord white matter. Spheroids were stained a light brown with Bodian’s method, and most debris in open spaces also stained light brown—indicating axonal debris.

The Marchi technique for degenerating myelin confirmed the selective, widespread degeneration of nerve fibers in spinal cord white matter. The degree of positive staining varied with the funiculus and segment of spinal cord examined.

Topographically, lesions were present at all levels of the spinal cord; they were consistently more widespread and severe in thoracic segments. However, in some more severe cases, lesions were nearly equal in all anatomical divisions. Larger, more heavily myelinated axons were more frequently affected than smaller diameter, thinly myelinated or unmyelinated axons. The extent and degree of involvement of separate funiculi or tracts within funiculi varied in different anatomic locations. The peripheral portions of lateral and ventral funiculi were more severely affected than portions closer to the gray matter. Dorsal funiculi, in general, exhibited more uniform involvement throughout.
In thoracic spinal segments the most severe changes were in the ventral funiculi, and generally were more prevalent in the periphery and extended dorsally along the ventral median septum. Degenerating axons, loss of axons and myelin, and extensive status spongiosus were commonly seen. Axonal spheroids were observed less frequently. Lateral funiculi had a less spongiform appearance overall, but more axonal spheroid formation. Wallerian degeneration was qualitatively and quantitatively similar to that in the ventral funiculi, and again was more severe in the peripheral one-third to one-half of each funiculus. Dorsal funiculi contained even fewer large, empty spaces, however, spheroids and axonal degeneration were comparable to that in affected areas of lateral and ventral funiculi—though more evenly dispersed throughout the funiculus.

Cervical spinal segments had more quantitative homogeneity with respect to lesion distribution than other segments. Ventral funiculi remained somewhat more severely affected while dorsal funiculi were qualitatively more markedly affected than lateral funiculi. Spheroid formation and axonal degeneration with formation of large, empty spaces were all observed in dorsal funiculi, while milder axonal swelling and less vacuolar appearance were observed in lateral funiculi. Lesions in the brachial enlargement of the cervical portion of spinal cord were not remarkably different from the remainder of cervical segments.
In lumbar segments, lesions were quantitatively and qualitatively more severe in the ventral funiculi than in other funiculi. Degeneration in lumbar ventral funiculi was equal to and in some cases exceeded that described in thoracic segments. Axonal degeneration, loss of axons and myelin, and vacuolation of white matter were much the same quality, but quantitatively less severe in lateral funiculi of lumbar segments than in thoracic segments. Dorsal funiculi were overall less severely affected than lateral and ventral funiculi, although in some cattle, focal changes in dorsal funiculi were equal to those in lateral and ventral funiculi, and were often comparable to those in dorsal funiculi at higher levels.

This was the most frequently observed pattern of lesion distribution in the spinal cord of cattle affected with bovine progressive degenerative myelonecephalopathy. Minor differences from case to case were not unusual, however.

Changes in the brainstem were focal and involved only the medulla oblongata. Lesions were observed most frequently in the pyramids and less so in the inferior olives. In both regions occasional axonal degeneration and axon loss (small empty spaces) were noted (fig. 7). In the pyramids there were infrequently observed spheroids of the lacy eosinophilic form as described in the spinal cord. They were not always observed bilaterally, when present. Degenerative changes were rarely observed in any other nuclei or elsewhere in the brainstem.

Changes observed in the cerebellum were restricted to the Purkinje cell layer, and to a lesser degree, to the granular layer of the cerebellar cortex. A selective degeneration with occasional complete segmental loss of Purkinje cells was consistently observed. Degenerating Purkinje cells were greatly shrunken, deeply eosinophilic remnants of the perikaryon surrounded by an open space. Nuclei were either absent or fragmented. This continued to complete Purkinje cell loss with only an empty space remaining where a Purkinje cell would have been. Morphologically normal Purkinje cells were frequently observed immediately adjacent to degenerating Purkinje cells or empty spaces.

In the cortical granular layer, occasional swollen Purkinje cell axons (torpedos) were seen (fig. 8). An occasional reactive astrocyte was also seen in the granular layer as swollen, pale, lacy eosinophilic cells with eccentrically placed nuclei.

No changes were observed in the cerebrum or elsewhere in the neuraxis, nor in peripheral nerves of the hind legs, or any other peripheral nerves examined. No changes were observed in the optic nerve, retinal layers, or elsewhere in ocular tissues.

Skeletal muscle lesions were focal, but frequently locally extensive. Microscopic lesions were observed only in muscles with macroscopic lesions.

Hemorrhage and muscle fiber necrosis were most frequently observed. Affected fibers were swollen and eosinophilic—typical of Zenker's necrosis—to fragmented, pale and occasionally mineralized. Hemorrhage was severe and extended between fibers and groups of fibers. In long-standing lesions there was fibrous connective tissue replacement, and less frequently, replacement by adipose tissue. The only reactive cells observed were occasional, small clusters of mononuclear cells, and in long-standing cases, a few macrophages laden with hemosiderin.

Ovarian atrophy, present in all affected heifers and cows, was characterized by diffuse increase in fibrous connective tissue and diminished or absent oogenesis. This was bilateral in all cattle except a pregnant cow which had a unilateral corpus luteum of normal morphology. Other changes observed in the ovaries of affected cows were multiple, small or single, large fluid-filled cysts lined by a thin layer of follicular epithelium. Corpora lutea were observed infrequently in other cows. No estimate as to when ovarian changes occurred was made and no fertility studies were done.

Uteri were consistently in a state of physiological inactivity, except for the single pregnant cow. There was little evidence of glandular activity, a mild to moderate increase in fibrous connective tissue of the lamina propria and submucosa, and a condensation of the muscular layers, characterized by decreased fiber size and increased nuclear prominence. The epithelial lining was invariably thin and inactive.

Bilateral testicular degeneration was present in all affected bulls examined. Seminiferous tubular atrophy with absence of spermatogenesis and severe vacuolation of spermatogonia along with a mild increase in interstitial fibrous connective tissue were the most frequent microscopic findings. Spermatid giant cells with multiple nuclei, degenerating spermatogonia, and amorphous debris were occasionally observed in the tubular lumina. Semen quality in affected bulls steadily decreased from the onset of clinical signs.

Lymph nodes draining the upper parts of the hind legs were frequently hyperplastic, with increased numbers of germinal centers in the cortex. Macrophages were increased in number in the medullary region associated with moderate to marked hemosiderosis.
Hemosiderin was both free and within macrophages. Other changes observed less consistently were edema and mild to moderate hemorrhage. All other lymph nodes were within normal limits.

No significant lesions were observed in other tissues, except cow 19 had multifocal, ulcerative stomatitis and esophagitis, along with an erosive abomasitis and moderate, interlobular pulmonary emphysema and mild interstitial pneumonia. This was also the single animal that was fluorescent antibody-positive for the presence of bovine virus diarrhea viral antigen.

**Discussion**

Bovine progressive degenerative myeloencephalopathy of purebred Brown Swiss cattle is considered to be a familial degenerative central nervous system disease. Clinical signs and epidemiological analysis clearly support this hypothesis. The degenerative changes observed in the spinal cord are considered to be the primary lesions of the disease and the overall pattern of all central nervous system lesions in bovine progressive degenerative myeloencephalopathy is consistent with that of a spinocerebellar degeneration. Both afferent and efferent systems responsible for controlled movement were affected; lesions involved not only the spinal cord, but also the cerebellum and brainstem.

Axonal lesions in the spinal cord were present in both the ascending and descending tracts of the white matter, and were considered degenerative in nature. Changes were consistently more severe and occurred earlier in thoracic spinal segments; furthermore, all thoracic funiculi were more equally affected than funiculi in lumbar or cervical segments. It is suggested then, that initial axonal changes were neither completely proximal nor completely distal, but were probably multicentric in origin in the long axons. Proximal axonal lesions would be observed in the spinal cord gray matter while distal axonal lesions would first appear in either ventral lumbar or dorsolateral cervical segments. Neither was true in bovine progressive degenerative myeloencephalopathy. Furthermore, it is presumed that both anterograde and retrograde axonal degeneration occurs in bovine progressive degenerative myeloencephalopathy. With an initial locus of axonal degeneration in the thoracic segments and involvement of both ascending and descending tracts in more cranial and caudal spinal cord segments, neither a pure dying back process or simple Wallerian degeneration would be compatible with the lesions described in bovine progressive degenerative myeloencephalopathy.

Lesions, when observed, were inconsistent and mild in the brainstem. Specific fiber tracts were not consistently affected, nor were changes consistent at sequential levels in the same case. Axonal degeneration was not consistently observed in the same brainstem nuclei.

No cerebellar lesions were observed outside the Purkinje cell layer, except for occasional axonal swellings (torpedos) of Purkinje cell processes in the granular layer. Empty spaces (baskets) observed where Purkinje cells would normally be located were felt to be due to loss of the nerve cell body following degeneration and atrophy (Gudden's atrophy). Selective degeneration and loss of Purkinje cells without other significant alterations in the cerebellar cortex are frequently reported in other bovine central nervous system disorders.

Degenerative lesions in the brainstem and cerebellum in bovine progressive degenerative myeloencephalopathy existed without demonstrable continuity with axonal degeneration in the spinal cord. Systemic central nervous system degeneration may involve neuronal degeneration in one or several related systems, while other related systems remain unaffected. This transneuronal degeneration is common and may occur with either retrograde or anterograde processes. This is thought to be related to trophic influences in associated systems and has been documented in the spinocerebellar degenerations in man. Presumably, this phenomenon explains the lack of morphological continuity between the spinal cord and the higher central nervous system lesions in bovine progressive degenerative myeloencephalopathy.

Pathogenesis of central nervous system lesions of bovine progressive degenerative myeloencephalopathy is unknown at this time. Numerous avenues have been investigated, however no consistent significant findings have been made. Other mechanisms await future investigation but will be discussed briefly. In all cases it is assumed that degeneration of nerve fibers is the primary lesion.

A defect in axonal transport mechanisms necessary to carry essential nutrients synthesized under direction of nuclei of the long nerve fibers of the spinal cord could theoretically produce lesions similar to those observed in bovine progressive degenerative myeloencephalopathy. Failure of transport of essential nutrients or a local metabolic dysfunction at any point in the fiber would result in degeneration of the nerve fiber distally, probably to its terminus, and proximally, for some unknown distance, toward the cell body of origin. These theories regard the primary defect to
be an inhibition of enzymes required for axonal transport of metabolites or alternatively, a disruption of normal ionic gradients for transmembrane transport. Axonal transport disturbances of 'cytoskeletal constituents' (e.g., neurofilaments) have been suggested as a cause of axonal (and nerve cell body) degeneration in central nervous system disease of animals.

A genetic or familial predisposition to drug influences, such as organophosphorus pesticides, can be ruled out in the pathogenesis of bovine progressive degenerative myeloencephalopathy, unless a specific enzymatic or metabolic defect and a common toxic agent could be identified. Laboratory studies for bovine virus diarrhea or other virus infection were insufficient to make a definite conclusion, but tended to indicate no involvement of this virus. Further studies should be undertaken to rule out any possibility of a viral etiology.

In affected cattle with severe ataxia or recumbency for prolonged periods, lesions were consistently observed in skeletal muscles of the hind legs above the stifte joint, and in peripheral lymph nodes draining these areas. Muscle lesions were always focal and frequently associated with bony prominences or laterally located muscles of the thigh. Microscopic findings in skeletal muscles were consistent with acute, localized trauma (bruising) and associated fiber degeneration induced secondary to primary neural lesions. Areas of fibrosis and adipose tissue replacement of muscle resulted subsequent to healing. Lymph node changes were limited to cases with acute traumatic muscle lesions and were consistent with acute inflammatory and circulatory disturbances in a field of lymphatic drainage associated with skeletal muscle damage or localized stasis from prolonged recumbency.

Microscopic findings in reproductive organs; both males and females had macroscopic and microscopic gonadal changes, and cows showed changes in the tubular genitalia. In bulls, testicular changes were considered primarily degenerative, however secondary sex characteristics were unaltered. In man, testicular atrophy has been reported to occur with traumatic spinal cord lesions and with degenerative lesions in the spinal cord. Cows and heifers had no specific degenerative changes in the gonads, other than atrophy, with an increase in fibrous connective tissues, and disturbance of cyclic follicular activity—suggesting a hormonal disturbance. Although tubular genitalia were atrophic, external genitalia were normally developed. Only one cow was pregnant. The fetus from this cow was normal and uterine changes were consistent with estimated time of gestation. Women afflicted with degenerative cerebellar ataxia have exhibited uterine hypoplasia, failure of development of external genitalia, and failure of menstruation. These findings were suggested to be due to a failure of gonadotropin production, possibly because of a hypophyseal lesion. Pituitary glands were histologically normal in cattle affected with bovine progressive degenerative myeloencephalopathy. Other mechanisms of hormonal dysfunction require further study.

A significant number of heredofamilial neurodegenerative diseases have been described in several breeds of cattle. These diseases have been grouped according to anatomic location of lesions; clinical differentiation may be difficult and has been discussed elsewhere. Distinctive pathological features characterize these diseases.

Primary cerebellar cortical diseases in cattle are characterized by selective Purkinje cell degeneration, mineralization, or abiotrophy of both Purkinje and granular cell layers. These diseases are considered intrinsic abnormalities that cause premature aging or degeneration of neurons or, in the latter, both hypoplasia and in utero abiotrophy of Purkinje and granular cells.

Inherited bovine storage diseases, including mannosidosis, GM1 gangliosidosis, generalized glycogenosis, and neuronal lipodystrophy, are characterized by abnormal cellular metabolism that results in accumulation of 'storage' material within nerve cell bodies. Absolute or relative enzyme deficiencies have been discovered in most of these diseases.

Hereditary neuraxial edema and congenital brain edema are characterized by status spongiosus in the brain and the spinal cord white matter or white and gray matter, respectively. The spongy state in these diseases has been correlated with accumulation of fluid within glial cells and between myelin lamellae, possibly due to ionic pump failure leading to chronic edema.

Progressive ataxia in Charolais cattle and the shaker calf syndrome in horned Hereford calves are two diseases characterized by abnormal accumulation of neuronal structural components. Hallmarks of progressive ataxia are eosinophilic plaques in white matter of the cerebellum, brainstem and spinal cord. These plaques are composed of distorted myelin lamellae and hypertrophied or hyperplastic oligodendroglial processes and are thought to be related to a form of oligodendrogial dystrophy. Shaker calf syndrome in Hereford calves is characterized by excessive accumulation.
of neurofilaments within nerve cell bodies of the central, peripheral and autonomic divisions of the nervous system. A neuronal transport defect is suspected.\textsuperscript{33} Toddler cattle are characterized by degenerative changes and calcification of neurons and small vessels.\textsuperscript{32}

Comparatively, then, most other heredofamilial central nervous system diseases in cattle differ considerably from bovine progressive degenerative myelonecephalopathy from a pathological standpoint. Pathogenetically, a defect in neuronal transport mechanisms, as suggested in shaker calf syndrome in Herefords, may be usefully employed in attempting to understand the lesions in bovine progressive degenerative myelonecephalopathy. Mechanistically, however, the localization of accumulated neurofilaments within nerve cell bodies in shaker calf syndrome contrasts with the suggested multicentric axonal locus in bovine progressive degenerative myelonecephalopathy.

In other domestic animals similar heredofamilial degenerative central nervous system diseases have been documented, however few compare entirely with bovine progressive degenerative myelonecephalopathy. Feline hereditary neuroaxonal dystrophy exhibits axonal degeneration primarily in the brainstem and cerebellum with Purkinje cell degeneration in the cerebellar vermis.\textsuperscript{62} Systemic neuroaxonal dystrophy in Suffolk sheep is characterized by axonal spheroids and open spaces, primarily in the spinal cord gray matter. Axonal lesions were thought to be distal.\textsuperscript{20} Cerebellar neuroaxonal dystrophy in Collie sheep dogs is characterized by axonal degeneration only in the white matter of the cerebellum and associated cerebellar and brainstem nuclei.\textsuperscript{17} Canine giant axonal neuropathy in Alsatians is a distal axonopathy, but affects both peripheral and central nervous system structures.\textsuperscript{30} Hereditary canine spinal muscular atrophy in Brittany spaniels, shown to be due to a defect in transport of neurofilament triplet protein,\textsuperscript{28} is characterized by motor neuron degeneration and loss and axonal degeneration of associated motor axons in the spinal cord gray matter and brainstem nuclei.\textsuperscript{22, 23} Progressive axonopathy in boxer dogs is manifested by axonal lesions in both peripheral and central nervous system locations, and is thought to involve both anterograde and retrograde degeneration.\textsuperscript{29} Equine degenerative myelonecephalopathy is characterized by axonal degeneration in spinal cord white matter tracts, spinal gray matter and specific brainstem nuclei; pigmentedary changes and necrobiosis are described in nerve cell bodies in the same sites.\textsuperscript{46}

Heredofamilial central nervous system diseases in man that involve changes primarily in the spinal cord, cerebellum and/or brainstem include motor neuron disease, neuroaxonal dystrophy and spinocerebellar degeneration.\textsuperscript{12, 13, 24, 27, 40, 52, 54, 55} Motor neuron diseases are characterized by degeneration and loss of nerve cell bodies, principally in the ventral horns of the spinal cord; and neurogenic muscular atrophy.\textsuperscript{12, 52} Axonal degeneration may be either distal or proximal.\textsuperscript{12, 13} In neuroaxonal dystrophy the primary disturbance is in the axon, while nerve cell bodies remain relatively unaffected morphologically. Axonal changes in neuroaxonal dystrophy usually begin distally but may be observed proximally, even reaching the nerve cell body.\textsuperscript{54}

Bovine progressive degenerative myelonecephalopathy shares common features with some of the heredofamilial neurodegenerative diseases in man.

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