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The Demyelinating Encephalomyelitis of Canine Distemper

by
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Dr. R. W. Carithers†

The pathogenesis of canine distemper was well described by Max Appel (1969). Upon infection by inhalation or ingestion, the virus first invades the tonsils and bronchial lymph nodes. During the first week, the virus spreads to the rest of the lymphoid tissues, including the spleen, thymus, and bone marrow, causing a leukopenia and a transient fever. After about nine days, the infected dogs will follow one of two courses. Approximately fifty percent of the animals develop protective titers greater than 1:100 and are able to overcome the disease, with a gradual decline in both virus levels and the leukopenia. The other fifty percent of the dogs are not able to develop a protective titer and suffer widespread invasion of epithelial and central nervous system tissue. The clinical illness then occurs, often including anorexia, diarrhea, conjunctivitis, pneumonia, and finally terminal convulsions.

The virus disappears in the dogs that develop antibodies and survive, except for a few cases with virus remaining in the neurons and epidermal cells of the foot pads, which may explain the central nervous system syndromes and hardened foot pads after apparent recovery.

During the course of distemper, the specific clinical signs seen depend on the degree of involvement of each tissue. An individual may show primarily respiratory involvement, or blindness, or possibly only convulsions without previous recognized illness. The most common situation, however, is the syndrome involving multiple systems as described above. In the past, different forms of the disease, such as systemic distemper, systemic nervous distemper, and nervous distemper were recognized, but in reality were different manifestations of the same disease. Secondary bacterial infections are extremely important in the development of the clinical signs, since the viral destruction of the lymphoid tissues affects the cells responsible for antibody formation.

The survival of a given dog seems dependent on its ability to form antibodies early in infection, that is, within 14 days. This development of antibodies also influences the severity of the clinical signs.

The cerebral tissues are invaded at the same time as the epithelium but the lesions develop slower, are cumulative, and tend to be progressive while the epithelial changes are reparable. Encephalomyelitis invariably occurs if an affected dog lives three weeks or so.

The central nervous system involvement is particularly significant since it is this aspect that prevents recovery. The particular form depends on the area of the brain affected. The basic syndromes are as follows: (1) petit mal or grand mal seizures (epileptiform syndrome), (2) ataxia and head tilt (cerebellar or vestibular syndrome), (3) animal oblivious to the environment with forced locomotion and a circling tendency (frontal lobe syndrome), (4) hyperesthesia and rigidity of muscles, especially the neck (meningeal syndrome), (5) ascending spinal paralysis without cerebral irritation, (6) paresthesia with self-mutilation, and (7) tremor syndrome.3,10

The epileptic syndrome usually accompanies the acute or subsiding systemic disease whereas the other neurological syndromes usually occur after the systemic phase has subsided, or with no history of any clinical signs.10,17

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The tremor syndrome of canine distemper is often incorrectly called chorea. The two conditions differ because the tremors are regular, rhythmic, and persist during sleep, while the human syndrome of chorea consists of irregular, jerking movements which disappear during sleep. The tremor syndrome, or flexor spasm syndrome, is usually accompanied by a history of systemic distemper signs. The nerves affected are usually the cranial or spinal nerves to the face, neck, or limbs. Affected muscle groups exhibit short, forceful contractions occurring about one second apart, and persist during sleep. The syndrome can be acute or chronic—the animal may die within a few days or weeks, while chronic cases may survive, and some do recover.

During the course of experimentation, in a group of 62 dogs that did develop protective titers greater than 1:100 within 14 days and had shown a rapid disappearance of virus from the lymphatic tissues, two developed convulsions 41 and 60 days post-exposure and were euthanized. Fluorescent antibody tests on the tissues showed viral antigen in neurons of the white matter, the pituitary gland, and foot pads. A few fluorescing cells were also found in the bladder epithelium and stomach epithelium. Both suffered demyelinating encephalitis. This finding supports the fact that even dogs that have been properly vaccinated and subsequently attain a "protective" antibody level can develop neurological signs. Dr. Appel suggests that natural infections are often of a more chronic form in which encephalomyelitis or hardpad does not develop for weeks or months following the acute illness.

The one lesion of the central nervous system that distinguishes canine distemper from most other viral infections of this tissue is demyelination. This involves degeneration of the myelin sheath and therefore loss of the insulation influencing the impulse transmission. The mechanism of demyelination has been difficult to prove since it has been hard to reproduce experimentally. Lately, however, consistent demyelination has been attributed to certain mutants of canine distemper virus which are better able to persist in the brain and induce an antimyelin response.

There are two broad theories as to the mechanism of demyelination: (1) The virus exerts a direct toxic effect during active replication on the myelin tissue, and (2) tissue is destroyed by interaction of virus and immune factors such as antibody and complement. Hence, the damaged myelin may act as an antigen to further destroy myelin.

Dogs that develop demyelination often have chronic illness that may last several weeks, or they may have few or no signs but then develop sudden and severe neurologic signs some time later. Yet some individuals with demyelination never show clinical signs.

There is one interesting characteristic of dogs with demylinating encephalomyelitis. These animals develop higher serum and cerebral spinal fluid antibody titers than dogs that die early in the disease. This may be explained by the theory that antibody levels were not high enough initially to prevent entry to the central nervous system, and once there, most cells are infected and remain a long time, causing extended stimulation of antibodies. This explanation supports both the virus and immunologic theories.

At the same time as the invasion of epithelial tissues, the virus spreads hematogenously to the vascular endothelium of the brain. It then moves on to the nervous tissue to proliferate in the nuclei and cytoplasm of neurons. The virus is distributed diffusely in the brain, but the predominant location is the cerebellum near the fourth ventricle.

The encephalomyelitis of canine distemper is non-suppurative with demyelination as the outstanding feature. The earliest tissue change is meningitis, which is always present to mild degrees with distemper. A diffuse astrocytic reaction begins early. As they swell and withdraw their processes, the astrocytes appear as plump cells in the areas of demyelination or necrosis. The acidophilic intranuclear inclusion bodies are best seen in the astrocytes because they are more numerous and persist longer here than in other cells. The microglia are very sensitive to neural injury, and with myelin necrosis, they become phagocytic and are then called...
"gitter cells." Eventually the gitter cells disappear, leaving vacuolated tissue. One of the primary histological changes of encephalomyelitis, perivascular cuffing, is a late development in distemper, occurring secondary to the demyelination. In fully mature lesions, with the myelin debris cleared, the lace-like demyelinated areas are invaded by fibrous astrocytes in an attempt to repair the defect.

The diagnosis of canine distemper is usually made clinically and then may or may not be supported by the clinical pathology laboratory. Final confirmation is usually done by histopathological examination, but other methods include fluorescent antibody test, virus isolation, paired serum samples, and conjunctival smears positive for intracytoplasmic inclusion bodies. An EEG can be run to detect focal brain damage. Kirk's *Current Therapy V* reports that a greatly accelerated erythrocyte sedimentation rate is quite suggestive of canine distemper.

Treatment of acute canine distemper is aimed toward (1) controlling the secondary bacterial infection, and (2) improving the animal's general condition to increase natural resistance. This is attempted by the administration of fluids, vitamins, antibiotics, and applying good nursing care. As far as the advanced cases of encephalomyelitis, no effective treatment has yet been substantiated.

In summary, the neurological aspect of canine distemper is not one type of the disease, it is ordinarily present as the final stage of the disease if the dog lives long enough. And, the virus is able to survive for long periods of time in the central nervous system and epithelium. In addition, secondary bacterial invasion is very important in the severity and the outcome of the disease and can be treated, unlike the virus. It is also a major factor in determining the predominant systems affected clinically, whether respiratory or gastrointestinal, etc. Finally, animals properly vaccinated for canine distemper can still develop the disease. The possibility must be realized in considering differential diagnoses.

**BIBLIOGRAPHY**