

Cerebellar Abiotrophy: A Review

Cerebellar abiotrophy (CA), also referred to as cerebellar cortical abiotrophy (CCA), is a genetic neurological disease in animals best known to affect the Arabian horse and over a dozen breeds of dog. In addition to dogs and horses, there also have been cases of cerebellar abiotrophy in Siamese and Domestic Shorthair cats; in Angus, Polled Hereford, Charolais and Holstein Friesian cattle; Merino and Wiltshire sheep; and Yorkshire pigs.

CA is believed to follow a monogenic autosomal recessive inheritance. This means it is not sex-linked, and the mutant allele has to be carried and passed on by both parents in order for an affected animal to be born. Horses that only carry one copy of the allele may pass it on to their offspring, but themselves are perfectly healthy--without clinical signs of the disease.

CA cannot be prevented, other than by selective breeding to avoid the concurrence of two alleles for CA, and it cannot be cured. In horses, the condition is most commonly seen in Arabian and part-Arabians, but a few cases have been observed in the Miniature Horse, the Gotland Pony, and possibly the Oldenburg. Most foals appear normal at birth, with clinical signs noticeable at an average age of four months, though there have been cases where the condition is first seen shortly after birth and other cases where the onset is gradual and clinical signs are first recognized in horses over one year of age.

The condition develops when a set of neurons located in the cerebellum of the brain, known as Purkinje cells, begin to degenerate. These cells affect balance and coordination. They have a critical role to play in the brain. The Purkinje layer allows communication between the granular and molecular cortical layers in the cerebellum. Put simply, without Purkinje cells, an animal loses its sense of space and distance, making balance and coordination difficult.

Cerebellar abiotrophy in horses was originally thought to be a form of cerebellar hypoplasia, a condition where the Purkinje cells fail to develop in the embryo before the animal is born, and cases were described as such in older research literature. However, it was discovered that in horses, the decline of Purkinje cells usually began after the animal was born.

CLINICAL SIGNS

Clinical signs of CA are, when taken as a group, fairly unique and not easily mimicked by other illnesses, though certain types of neurological injury and inflammation due to infection do need to be ruled out. Though distinguishable from other neurological conditions, many local veterinarians have never seen a case, or are not familiar with the clinical signs, and thus CA has been confused with Wobbler's syndrome, Equine Protozoal Myeloencephalitis (EPM), and head injury.

However, the combination of clinical signs and lack of neurological damage to other areas of the brain or spine is sufficiently unique that CA can be clearly distinguished from other neurological problems in a living animal. Verifying the diagnosis in a laboratory setting is only possible by examining the brain post-mortem to determine if there has been a loss of Purkinje cells. While some other diseases exist that lead to neural degeneration; in horses, the loss of Purkinje cells is unique to CA. Clinical signs of cerebellar abiotrophy include ataxia or lack of balance, an awkward

wide-legged stance, a head tremor (intention tremor), hyperreactivity, lack of menace reflex or blink response, a stiff, excessively high-stepping gait in the forelimbs known as hypermetric action, a stiff, abrupt, bursty quality of the gait in all limbs, coarse or jerky head bob when in motion (or in very young animals, when attempting to nurse, known as intention tremor), apparent lack of awareness of where the feet are (sometimes standing or trying to walk with a foot knuckled over), poor depth perception, and a general inability to determine space and distance. There is a marked tendency to rear up and occasionally fall over backwards when a handler reaches for the halter or pulls abruptly on a lead shank. Clinical signs of CA may become exacerbated when the horse is excited.

Signs may worsen from the time of onset for six to 12 months, but if not severe enough to mandate euthanasia, they gradually stabilize over a period of one or two years. Most affected animals have normal intelligence and mildly affected animals can, in theory, live out a normal lifespan. However, they are quite accident-prone. Horses may experience difficulty stepping up and over objects, run into fences, fall easily, and even if allowed to mature to full growth, are generally considered unsafe to ride. Thus, many horses that develop CA are euthanized for humane reasons. There is anecdotal evidence that affected animals partially compensate for the condition by cognitively learning alternative methods for moving or to determine distance. Thus, they appear to improve because they become less accident-prone and may learn to control levels of activity when anxious.

WHAT CAN BE DONE?

There currently is no DNA test for CA. However research is taking place at the Veterinary Genetics Laboratory at the UC Davis School of Veterinary Medicine, <http://www.vgl.ucdavis.edu> and at the Institute of Genetics at the University of Bern. http://www.genetics.unibe.ch/content/index_eng.html Researchers working on this problem include Dr. Cecelia Penedo, PhD, Veterinary Genetics Laboratory, University of California, Davis; Prof. Dr. Tosso Leeb, Molecular Geneticist, Institute of Genetics, and PD Dr. med. vet. Vinzenz Gerber, PhD, DACVIM, DECEIM, FVH, Head of Equine Internal Medicine, Vetsuisse-Fakulty, both at the University of Bern, Switzerland. <http://www.unibe.ch/unitel/ergebnis.html?name=Tosso+Leeb>
<http://www.unibe.ch/unitel/ergebnis.html?name=Vinzenz+Gerber>

The late Dr. Ann T. Bowling also made significant contributions to the genetics research on CA at UC Davis, performing breeding experiments, including an F1 test-cross, that supported an autosomal mode of inheritance.

If you should have an affected horse or have knowledge of an affected horse please support the CA research by donating samples to the researchers at UC Davis and the University of Bern.

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Web links:

<http://www.vgl.ucdavis.edu/research/equine/CA.html> Information from the University of California-Davis on Cerebellar Abiotrophy in horses

<http://www.foal.org/> F.O.A.L., an organization dedicated to fighting lethal genetic conditions in Arabian horses.

http://www.vetsuisse.unibe.ch/genetic/content/e2353/e2734/index_eng.html Information from the University of Bern on Cerebellar Abiotrophy in horses (in English)

http://www.vetsuisse.unibe.ch/genetic/content/e2353/e2734/index_ger.html Information from the University of Bern on Cerebellar Abiotrophy in horses (German version)

http://www.genetics.unibe.ch/content/index_eng.html Institute of Genetics at the University of Bern

http://www.dkv.unibe.ch/content/pferdeklunik/index_ger.html Equine Clinic at the University of Bern (in German)