Inherited Neurologic Disorders in the Dog

The Science Behind the Solutions

Cathryn Mellersh, BSc, PhD

KEYWORDS

• Inherited disorder • DNA testing • Genetic mutation

KEY POINTS

- Inherited neurologic diseases are varied and can be congenital, neonatal, or late onset as well as progressive or stationary.
- Modern genetic technologies are revolutionizing the speed and efficiency with which mutations responsible for inherited neurologic disease are being identified.
- Clinically similar disorders can be caused by different mutations, even within a single breed, and are thus genetically distinct.
- DNA tests can be used by dog breeders to reduce the prevalence of inherited neurologic disorders in specific breeds and help the veterinarian diagnose disease.

BROAD CHARACTERISTICS OF INHERITED DISEASE—WHEN SHOULD A VETERINARIAN SUSPECT A DISEASE IS INHERITED?

There is no definitive or trademark characteristic of an inherited disorder, and the veterinarian should always be open minded about the possibility that a patient may be suffering from an inherited condition. A variety of inherited neurologic diseases has been described in the dog, including examples that are congenital, neonatal, and late onset as well as those that are progressive and stationary, so potentially any neurologic patient could be suffering from an inherited disorder.

It is not possible to tell whether a disease is inherited from a single case; the only indication a disease might be inherited is whether other dogs of the same breed or from the same extended pedigree have also been reported with the same or similar clinical presentation. Mutations that cause inherited disorders arise at random in founder animals and are passed to offspring and subsequent generations if the founder reproduces. If the mutation is recessive, clinically affected animals are only produced when inbreeding has occurred and a dog inherits an identical

Centre for Preventive Medicine, Animal Health Trust, Lanwades Park, Kentford, Newmarket, Suffolk CB8 7UU, UK
E-mail address: cathryn.mellersh@aht.org.uk

Vet Clin Small Anim 44 (2014) 1223–1234
http://dx.doi.org/10.1016/j.cvsm.2014.07.011 **vetsmall.theclinics.com**
0195-5616/14/$ – see front matter

copy of the mutation from both parents. For this reason, specific inherited diseases are nearly always associated with particular breeds or several closely related breeds.

Sources of Data Regarding Inherited Diseases in Domestic Animals

A literature review might reveal whether a specific disorder has been reported previously. PubMed[1] is a free search engine accessing primarily the MEDLINE database of references and abstracts on life sciences and biomedical topics and is a sensible place to initiate a search for evidence a disease might be inherited.

Another source of evidence that a disorder may be inherited in a domestic species is Online Mendelian Inheritance in Animals (OMIA), which is a catalog/compendium of inherited disorders, other (single-locus) traits, and genes in 214 animal species (other than human and mouse and rats, which have their own resources) authored by Professor Frank Nicholas of the University of Sydney, Australia.[2] OMIA information is stored in a database that contains textual information and references as well as links to relevant PubMed (described above) records at the National Center for Biotechnology Information and to the equivalent database for human inherited disorders, Online Inheritance in Man,[3] and to Ensembl,[4] a software system that produces and maintains automatic annotation on selected eukaryotic genomes.

A database that compiles information specifically about diseases/conditions of pure-bred dogs that are likely to have a genetic component is the Inherited Diseases in Dogs database compiled by Dr David Sargan at Cambridge University.[5]

In addition to online sources of information, an excellent text describing canine and feline disorders that are potentially breed associated is Breed Predispositions to Disease in Dogs and Cats, 2nd Edition by Alex Gough and Alison Thomas,[6] which includes reference to a peer-reviewed publication for each disorder described.

However, not all inherited diseases will have been described in the scientific literature, although considerable anecdotal evidence might still exist to suggest a disease has an inherited component. Breed clubs and breed societies as well as individual breeders are frequently knowledgeable regarding conditions that segregate in their breed, often well before they have been formally recognized by the veterinary profession, so making contact with a breed health coordinator or the equivalent might also yield useful information.

IDENTIFYING THE UNDERLYING CAUSE OF AN INHERITED DISORDER

Once it has been established that a specific disorder is likely to be inherited, by virtue of the fact that it is more prevalent in certain breeds than others, it becomes desirable to identify the mutation(s) or genetic variant(s). Once the causal mutation is known, a DNA test can be developed that breeders can use to guide their breeding decisions and reduce the prevalence of the condition in their breed. The opportunity to minimize the risk of producing clinically affected puppies is particularly desirable when the disorder is challenging to treat effectively or is particularly debilitating—as is frequently the case for diseases of the nervous system.

Over the last decade, the tools available to dissect the genetic basis of canine inherited traits have become increasingly sophisticated since the canine genome was sequenced in its entirety in 2004. The current rapid rate at which disease mutations are identified can be expected to increase further in coming years as next-generation sequencing techniques become increasingly cost effective and therefore within the reach of even the most modestly sized research groups.