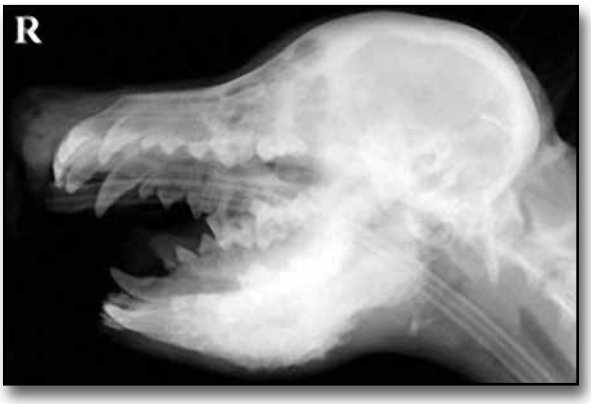
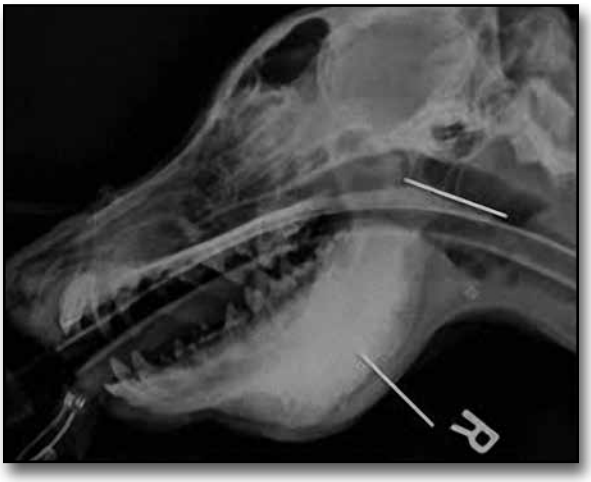
Craniomandibular Osteopathy (CMO) and a DNA-Based Test for the Recently Identified CMO Mutation

By Patrick Venta, PhD





Craniomandibular osteopathy, or CMO, is generally known to most breeders of West Highland White Terriers, Scottish Terriers, and Cairn Terriers. It is an inherited condition that affects the formation of bones in young dogs, most notably those of the jaw. Clinically affected dogs can have periodic jaw pain and very often they also have a noticeable lump of extra bone on the mandible. X-rays are often used by veterinarians to confirm a diagnosis. The condition is first noticed in the first month or two after birth and generally spontaneously disappears after about a year's time.

The laboratories of Dr. Hannes Lohi (Finland) and Dr. Cord Drogemüller (Switzerland) recently identified the causative gene and mutation, thus permitting the development of a DNA-based test to determine carrier status of terriers for this mutation. A manuscript is being prepared by the members of these labs for publication in a scientific journal.

An early report by Drs. George Padgett and Ulreh Mostosky suggested that CMO is inherited as a simple recessive gene (American Journal of Medical Genetics, volume 25, pages 9-13, 1986). However, the data produced by the European labs suggest that the mode of inheritance may be slightly more complicated. A few Westies that were reported by their owners to be affected have turned out to have only one copy of the mutant gene, with the other copy not having the discovered mutation. The meaning of this result is still under investigation. Breeders should be aware that there may be some possibility that dogs that are heterozygotes for this mutation have some chance of showing CMO signs (perhaps ~15%, based upon the European sample – see the web link below for details). Results for Westies, Cairns Terriers, and Scottish Terriers can also be found on Dr. Drogemüller's website.

On the other hand, some dogs that are homozygous for the mutation did not appear to show clinical signs of CMO. This result has been predominantly seen in West Highland White Terriers, for which nearly as many homozygotes have been reported to be clinically normal as those that are clinically affected. It is possible that some of the clinically unaffected dogs actually had very mild cases of CMO that were unnoticed by the owners. Alternatively, it is also possible that the gene truly did

not express itself. Either way, the result would indicate that the mutant gene has a characteristic called "incomplete penetrance."

Penetrance is a term used by geneticists to describe the non-expression of some condition in individuals that have the genetic constitution that should cause the expression of the condition. For example, if, among 100 dogs that were homozygous for the mutation (that is, that have two copies of the mutant gene) and only 57 showed the clinical signs of expected for homozygotes, the condition would be said to be only 57% penetrant rather than 100% (complete penetrance). Incomplete penetrance in the case of CMO might be caused by the nature of the mutation (some normal function might still be produced from the mutant gene) and/or the effect of other variable genes that influence the function of the CMO gene might cause CMO not be expressed in some dogs.

The frequency of the mutant gene may be higher than has been predicted from health surveys. For example, a recent health survey for West Highland White Terriers (Westie) in the United States (http://offa.org/surveys/survey_westie.html) suggests that only about 1% of Westies were CMO-affected, which would indicate that the frequency of carriers among all Westies should be about 10%. The data from Dr. Drogemüller's website indicates that the carrier frequency is about 36%. The disparity might be explained by real frequency differences in the European vs. North American Westie populations, by the reduced penetrance mentioned above, by some unknown bias in the health surveys, or by some combination of these things. A relatively small sample (36 Westies) from early testing in the United States testing lab (see below) suggests that frequency of the mutant gene may be significantly higher than the recent health surveys would otherwise indicate.

The test is available in Europe through the two labs that discovered the mutation. The test is available in North America through a lab at Michigan State University. The cost of the test was set by the European labs at $110 (85 Euros) per test, and the same price will be used in the United States. Those breeders who would like to have a dog or dogs tested should contact Dr. Patrick Venta by e-mail. He will send cheek-swab collection kits, instructions on how to perform the collections, and reporting forms. Dr. Venta's e-mail address is venta@cvm.msu.edu. [copy and past this email to contact Dr. Venta]