Susceptibility to Drug Toxicity: A Gene Deletion

P-glycoprotein works in concert with cytochrome P450 3A in enterocytes to prevent the oral absorption of many drugs. It is also expressed on renal tubular cells, bile canalicular cells, and brain capillary endothelial cells, functioning as part of the blood–brain barrier and apparently playing a role in renal and biliary drug excretion. A deletion mutation of the mdr (multidrug-resistant) gene, which codes for a P-glycoprotein, has been demonstrated in ivermectin-sensitive collie dogs. This may contribute to the susceptibility to toxicity of collie dogs and related breeds from chemotherapy drugs and digoxin. Dogs with this gene deletion also have increased brain concentrations of ivermectin, moxidectin, loperamide, and corticosteroids. The mdr gene deletion has been documented in 10 dog breeds, being widespread in collie dogs (30% homozygous and 40% heterozygous) and present at a much lower frequency in herding breeds of collie lineage (eg, Shetland sheepdog, Old English sheepdog, and Australian shepherd). It has not been found in border collie, bearded collie, or Australian cattle dogs. Adverse effects from ivermectin and other P-glycoprotein substrate drugs at dosages that are safe in normal dogs are seen in dogs homozygous for the gene deletion. In heterozygous dogs, toxicity may be seen when substrate drugs are given at increased dosages (eg, daily ivermectin for treatment of demodicosis). Rather than adhering to the old adage “White feet, don’t treat,” thereby withholding drugs that might be ideal for the situation, it is recommended that the genotype of dogs from affected breeds be determined via a simple test to see instead whether it is safe to treat the individual dog.

COMMENTARY: This article describes one of the true “ah-ha” moments in scientific discovery—the gene-deletion mutation responsible for drug hypersensitivities in collies and other herding breeds. A simple and available genetic test can now screen for the mutation and provide veterinarians and owners the peace of mind of knowing whether they can administer macrolides and other drugs to an individual dog. Visit www.vetmed.wsu.edu/depts-vcpl for further information on submitting test samples, susceptible breeds, and problem drug lists.—Bess J. Pierce, MZS, DVM, Diplomate ABVP & ACVIM


The Role of Trainers & Lay Personnel in Behavioral Issues

The American College of Veterinary Behaviorists (ACVB) outlines the following guidelines on the role and limitations of nonspecialized technicians, dog trainers, and lay personnel with respect to providing behavior-related medicine to the public. In general, nonveterinary professionals or lay persons should not be making decisions about or treating behavior problems. Clients should be referred to their veterinarian, who can decide whether a referral to a behaviorist is needed. General tasks that fall under the purview of dog trainers include general training of dogs, including that aimed at preventing behavior problems, treatment of a problem in a specific situation, and recognition of problems that require referral because humans and other animals are at risk for injury. Animals with refractory problems should be referred. Dog trainers should be able to address an acute problem with appropriate behavior modification. Examples are dogs barking at one another in class and dogs showing fear of someone in the room. If problems are ongoing in the home, dog trainers should refer clients to veterinarians. In a veterinary practice, lay staff can address problems that occur only in the veterinary clinic, with the intent of training the dog, owner, or other staff on how to make the dog more comfortable and tractable. Lay trainers can assist veterinarians with behavior modification techniques prescribed by veterinarians. The ACVB considers it inappropriate for lay personnel to diagnose and treat behavior disorders independent of a veterinarian: “We should not encourage the practice of medicine without a license.”

COMMENTARY: After the diagnosis and treatment plan is made for a patient with behavior issues by a veterinarian, having a trainer help the owner implement the prescribed program can be one of the keys to success. It is important to recognize the limitations of a trainer with the management of behavior cases in the veterinary practice setting, and this article helps to clarify that.—Sandra A. Sawchuk, DVM, MS