CLINICAL APPLICATION
Switching Medicines Produces Seizures

A 10-pound, 7-year-old, FS (female spay) miniature poodle (Jackie) presented with a history of increased seizure activity. The dog had been diagnosed with idiopathic epilepsy 2 years previously. Idiopathic means "cause unknown"; idiopathic epilepsy is a common default diagnosis for recurrent seizure activity. Jackie had been placed on phenobarbital, a common anticonvulsant medication used to control seizures, at a dose of 15 mg every 12 hours. Jackie's veterinarian drew blood every 6 months from Jackie to determine the concentration of phenobarbital in the blood (plasma) and to verify that the dose given was achieving concentrations in the blood sufficient to control seizures. The plasma concentrations of phenobarbital were always within acceptable concentrations. Jackie did well for 16 months but then started to show signs of seizure activity again. The veterinarian checked another plasma concentration of phenobarbital and found it significantly lower than the previously checked concentrations. The veterinarian increased the dose to 30 mg every 12 hours, based on the new plasma concentrations. Doubling the dose kept Jackie's seizures well under control for 4 months. Then Jackie's owners reported that Jackie was acting more sedated and lethargic and would occasionally be ataxic (wobble a bit in the hind end). The veterinarian examined Jackie and took another plasma concentration of phenobarbital. To his surprise, the plasma concentration of phenobarbital was significantly higher than previous concentrations and sufficiently high enough to produce signs of sedation and ataxia. He ordered Jackie's owners to skip a dose of phenobarbital (to allow concentrations to drop lower) and reduce the dose to the original 15 mg every 12 hours. The sedation and ataxia resolved by the next day. A recheck of plasma concentrations revealed drug levels had returned to the normal, acceptable range. What had happened?

Careful questioning of Jackie's owners and review of inventory records of the veterinary hospital revealed that the increase in seizure activity occurred 2 weeks after Jackie's owners had picked up a new refill of phenobarbital tablets from the hospital. The onset of sedation 4 months later had occurred 2 days after Jackie's owners had picked up another refill. Examination of inventory records revealed that the hospital had switched from one generic phenobarbital drug to another manufacturer because the second generic was cheaper. The second generic was likely dispensed to Jackie's owners at the refill that occurred just before the return of the seizure activity. The plasma concentrations at that time confirmed that less drug was present in the body despite Jackie's owners' strict adherence to the dose schedule. Adjustment of the dose of the second generic temporarily solved the problem. However, when the hospital inventory of the second generic ran out, the hospital ordered more of the first generic that it had always carried. The first generic was then dispensed to Jackie's owners and, when dosed at the higher adjusted dose, caused the sedation and ataxia associated with phenobarbital overdose. Confirmation of higher phenobarbital concentrations was verified, indicating more of the drug was entering the body. The only explanation was the generic drug's form. The first generic drug was apparently better absorbed by Jackie than the second, even though both tablets contained the identical amount of phenobarbital.

What should be learned from this situation: For animals on long-term treatments such as seizure control, thyroid supplementation, or long-term chronic disease, selecting the correct generic is not as important as consistently providing the same generic drug. Switching brands based on whatever is the most inexpensive at the time may invite problems. For many animals switching does not cause a clinically apparent change; however, many more do show some significant variability between generic brands, as Jackie did.