Effects of MK-329 on Gastric Emptying of Solids in Cats

TO THE EDITOR: We have read the article by Gould et al. (*1*) on the effects of MK-329 on gastric emptying of solids in cats and are concerned with the validity of the study and the conclusions drawn. Figure 1 is a radiograph of a normal cat in the prone position taken after oral administration of barium. Figure 2 is a ventral image of a normal cat acquired after intravenous administration of pertechnetate which, as in humans, is trapped by the gastric mucosa. By comparing these figures with the authors' Figure 1, it is obvious that the regions of interest chosen by the authors excluded the body and pylorus of the stomach. Since only the fundic portion of the stomach was used to determine gastric emptying, the results could represent redistribution of gastric contents within the stomach rather than actual alteration in global gastric emptying.

We have further concerns about the methods of curve normalization and fitting used. In the Materials and Methods section, the authors state that all subjects were imaged 15 min after the beginning of ingestion regardless of the type of meal, and that liquid meals were subsequently imaged every 15 min, while solid meals were imaged every 30 min. Since, in Figure 2 of the manuscript, only the liquid meal data points are shown at t = 15 min, we conclude that all four of the initial data points must be superimposed at 100% at t = 0. This means the authors have used the gastric counts in the first image as the starting dose and have also set the time of the first image to zero. Normalizing the data to a single image weights any error in that image. The fact that the solid-phase data points in Figure 2 at t = 30 are in excess of 100% proves that error is present. When using a model which forces the fit through 100% at t = 0, setting the time of the first image to zero further weights the first image and its error. Elashoff et al. (*2*) were careful to state that t = 0 should be the time of the beginning of ingestion, when they proposed the power exponential model for gastric emptying, but did not address what parameters should be used for curve normalization. The use of a partial gastric region that diminishes confidence in all points including the first, combined with grossly overweighting the first point by first normalizing to it and then forcing the fit through that point, make the results suspect.

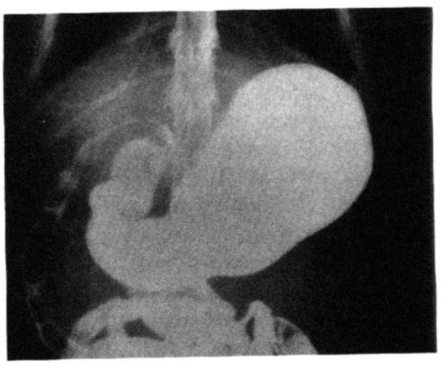

FIGURE 1
Dorsoventral radiograph of a cat subsequent to oral administration of liquid barium.

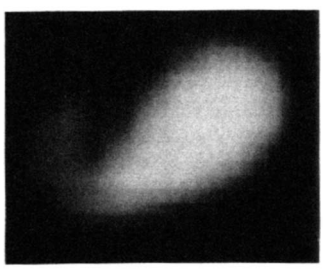

FIGURE 2
Ventral abdominal image of a cat after intravenous administration of pertechnetate.

In addition, from the data presented, we have concerns about the statistical conclusions. Given the day-to-day variability in the calculated half-lives shown in Table 1 of the manuscript, one would expect half of the individuals in any group to show a "significant" increase (and half a decrease) in gastric emptying rate between any two randomly paired determinations. After administration of 3 mg/kg, only one more than half (four of six) showed an increase in gastric emptying, and of the two nonresponders who were repeated with 10 mg/kg, only one showed an increase.

Our concern can be exemplified by examining the data conveniently provided by the authors in Table 1, which tabulates the results of two to three repeated gastric emptying studies in six cats. If any drug was administered to each cat between the first and second solid-phase half-life determinations, we would find that cats 1 and 4 decreased the rate of emptying, whereas the rest increased (we could conclude 4/6 responded). Since cat 4 had a third study that showed an increased rate of emptying and if the drug had been administered in a higher dose before the third study, we could have concluded it too responded. Cat 1 did not have a third study, but even if no response was seen, we have just duplicated the results that the authors have concluded should occur with a probability of only 0.014. We do not feel this study was sufficient to "...elucidate the role of CCK in the normal regulation of gastric function..." (*3*).

REFERENCES

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William J. Hornof
Philip D. Koblik
Veterinary Medical Teaching Hospital
University of California
Davis, California