Sporadic anecdotal reports of ceftiofur-induced diarrhea continue to be voiced by equine practitioners. Whereas some practitioners apparently use doses higher than the label-approved 1–2 mg/lb (≈0.45 kg) IM q 24 h, the use of ceftiofur at the lower label dose (1 mg/lb IM q 24 h) in adult horses in dose confirmation and clinical studies was not associated with increased diarrhea compared with controls. Safety studies with higher doses resulted in mild anorexia (3 and 5 mg/lb IM q 24 h for 30 days) and diarrhea, dehydration, depression, and colic (10 and 25 mg/lb IV q 24 h for 10 days). An experimental perioperative use of ceftiofur (1 mg/lb IM q 12 h) in ponies undergoing laparotomies resulted in an increased prevalence of postoperative diarrhea. Author’s address: Dept. of Veterinary Clinical Medicine, College of Veterinary Medicine, University of Illinois at Urbana-Champaign, 1008 W. Hazelwood Dr., Urbana, IL 61802. © 1998 AAEP.

1. Introduction
Previously we cited anecdotal reports from practitioners that ceftiofur administration resulted in diarrhea in some horses. Since that time, we have retrospectively investigated our earlier experimental data and have also continued a prospective study on the possible adverse effects of the perioperative use of ceftiofur. Continuing anecdotal reports of the possible diarrheogenic effect of ceftiofur have prompted this brief report for equine practitioners concerned about possible ceftiofur toxicity.

2. Materials and Methods
In all experiments, treatments were administered randomly in a blinded manner. Ceftiofur sodium was reconstituted with bacteriostatic water to a concentration of 50 mg/ml and was administered intramuscularly. Horses were observed in a blinded manner at least twice daily for at least 1 h/session. The presence of abnormal feces was recorded.

A. Experiment 1: Negative Control
Thirty pairs of recently transported, young mixed-breed horses with respiratory infections were treated with either isotonic saline (1 ml/50 lb IM q 24 h) or ceftiofur sodium [1 mg/lb (≈0.45 kg) IM q 24 h] for no more than 10 days.

B. Experiment 2: Positive Control
Sixteen pairs of recently transported, young mixed-breed horses with respiratory infections were treated with either ampicillin sodium (3 mg/lb IM q 12 h) or ceftiofur sodium (1 mg/lb IM q 24 h) for no more than 10 days.

C. Experiment 3: Strangles
Eighteen young mixed-breed horses with strangles were treated with either procaine penicillin G (10,000 IU/lb IM q 12 h) or ceftiofur sodium (1 mg/lb IM q 24 h) for up to 30 days.
D. Experiment 4: Perioperative Use

Thirty-six junior surgery ponies undergoing ventral midline laparotomies were treated with either isotonic saline (1 mL/50 lb IM q 12 h) or ceftiofur sodium (1 mg/lb IM q 12 h), beginning 1–2 h prior to surgery and continuing for a total of 5 days.

3. Results

A. Experiments 1 and 2

Ceftiofur-treated horses from Experiments 1 and 2 were pooled and compared with control horses. Ceftiofur-treated horses had a higher prevalence of diarrhea (2.9% of total treatment days) than did either saline-treated (1.5%) or ampicillin-treated (1.5%) horses. However, ceftiofur-treated horses also had a higher prevalence of diarrhea immediately after transport and before receiving ceftiofur than they did after ceftiofur therapy began.

B. Experiment 3: Strangles

There was no greater prevalence of diarrhea in ceftiofur-treated horses than in penicillin-treated horses.

C. Experiment 4: Perioperative Use

There was a higher prevalence of diarrhea (chi-square, p < 0.05) in ceftiofur-treated ponies (25% of the treated ponies; 7.5% of the total treatment days) than in saline-treated ponies (16.7% of the ponies; 6.7% of total treatment days).

4. Discussion

In Experiments 1–3, we did not observe a dramatic diarrheogenic effect from ceftiofur. The data are equivocal because they show either (a) no association between ceftiofur and diarrhea (Experiment 3) or (b) that ceftiofur horses actually had less diarrhea while being treated than they did before treatment (Experiments 1 and 2). In none of these horses did the diarrhea require adjunctive therapy.

The results of the perioperative study (Experiment 4) are disturbing because of the high prevalence of diarrhea in ceftiofur-treated ponies. Because of these data and because of a few postoperative surgical cases that developed diarrhea while being treated with ceftiofur in our hospital, we are concerned about toxicity from the perioperative use of ceftiofur. One must ask first whether this is a use that is indicated by the label (it is not), and second whether perioperative antibiotics are indicated in a given procedure. A sterile arthroscopy performed quickly in a well-designed operating theater may not require prophylactic antibiotics compared with a deep, septic wound debridement performed in a barn aisle. It is likely that the stress of general anesthesia contributes to the potential diarrheogenic effect of perioperative ceftiofur or any other gram-negative effective antibiotic. At this time, we do not recommend ceftiofur as a perioperative antibiotic unless specifically indicated by a documented sensitivity pattern.

Our FDA-approved dose confirmation and clinical efficacy trials were performed with a dose of 1 mg/lb IM q 24 h.1–3 Toxicity studies performed at 10× and 25× the original dose for 10 days resulted in depression, diarrhea, dehydration, and colic.e Safety studies at 1, 3, and 5 mg/lb IM q 24 h for 30 days documented injection site irritation and transient decreased pelleted feed consumption at the higher doses but not at 1 mg/lbe. Pharmacokinetic studies have shown good tissue penetration (except for the central nervous system and endometrium) at 1 mg/lb IM given either once4 or twice5 daily. Whereas some practitioners apparently use doses higher than the flexible label-approved 1–2 mg/lb IM q 24 h, the continued use of ceftiofur at that label dose in adults should minimize toxicity problems. If a greater antibiotic effect is required to kill some of the more resistant bacteria (e.g., Klebsiella, Enterobacter), then we advise the use of aminoglycosides such as gentamicin or other gram-negative effective antibiotics to minimize ceftiofur toxicity documented at higher doses.

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References and Footnotes


aNaxcel (USA) and Excenel (Europe) Sterile Powder, The Upjohn Company, Kalamazoo, MI 49001.
bBacteriostatic water for injection, USP, Elkins-Sinn, Inc., Cherry Hill, NJ 08034.
cAmp-Equine, Beecham Laboratories, Bristol, TN 37620.