Increased total duration of penile prolapse during trazodone treatment in horses
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### Introduction

Trazodone is an anxiolytic with mild sedative properties that has been widely used in humans and pet animals. Despite almost no study of its safety and efficacy in horses, in recent years it has rapidly become widely prescribed, particularly for hospitalized patients and stall-bound lay-ups. As an example, 2017 was the first year that trazodone was dispensed in our equine hospital and ambulatory veterinary service. The number of tablets dispensed has gone from 1000 per month in 2017 to over 28,000 per month in 2024. While trazodone treatment is anecdotally reported to have beneficial calming effects for the majority of nervous or anxious horses, it is not uncommon for caretakers to report either no apparent beneficial calming effect or paradoxical adverse side-effects (hyperreactivity). Certainly, further study in horses is needed.

Due to the nature of their husbandry conditions, stallions are one segment of the domestic equine population for which anxiolytics are commonly considered. When considering any medication in a breeding stallion, safety and potential adverse effects on breeding behavior and/or fertility are especially important. Accordingly, we are exploring the efficacy and safety of oral trazodone treatment of stallions. In this regard, one of the reported side effects of trazodone treatment in humans is priapism (persistent penile erection) [1]. In the stallion, because of the dependent nature of the prolapsed penis, priapism typically progresses rapidly to paraphimosis (inability to retract the penis). Even when the paraphimosis is found early and can be effectively reduced, within only a couple hours of prolapse, fibrosis of the delicate erectile tissues can lead to permanent penile paralysis and inability to achieve erection sufficient for breeding or semen collection [2]. Accordingly, there is a pressing need to evaluate the effects of trazodone treatment on penile function in stallions. Here we report a repeated-measures within-subjects evaluation of penile prolapse in geldings, comparing each of two commonly prescribed low and medium dose levels of oral trazodone with placebo control treatment.

# Methods

Archived video recordings of 5 geldings from a recently published study of effects of trazodone treatment on footsteps and recumbent rest [3] were viewed to record all occurrences of penile prolapse. Horses at rest in their stalls had been videotaped for 48 consecutive hours during each of three treatment periods with either oral trazodone treatment at 2.5 mg/kg, or 7.5 mg/kg, or placebo Q12 for 48 hours. Order of treatment was counterbalanced among subjects, with a 14-day washout period between treatments. The total duration of prolapse (fully dropped, erect or flaccid) was calculated as a percentage of the portion of the 48-hour video sample during which view of the caudal abdomen was sufficient to visualize penile prolapse. Behavior recording was done without knowledge of the treatment involved or purpose of the study.

### Results

The mean (sd) percentage of time of penile prolapse was 1.3 (0.76) during control, 2.4 (2.2) during low dose, and 4.2 (1.5) during medium dose trazodone treatment, with medium dose significantly greater than control (dependent t-test, P < 0.005). Of note, for one of the geldings, penile prolapse time was 5 times greater during trazodone treatment than during control treatment, both with low and medium doses. [Additional detailed results are being analyzed and will be available at the time of proceedings abstract and presentation].

# Discussion

In these geldings, penile prolapse time was considerably greater during trazodone treatment at a medium dose level. These results clearly support the need for similar evaluation of effects of trazodone treatment on penile function of intact stallions, where the risk of priapism and paraphimosis is greater than in geldings, and resulting compromised penile function can end a breeding career. Further planned work

includes similar evaluation of penile activity as well as semen measures and breeding behavior in a large number of stallions. Until these and other potential side-effects are better understood, treatment of male horses with trazodone should be carefully considered.

### References

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Acknowledgments: This is a Dorothy Russell Havemeyer Foundation project. Partial funding for Rebecca Turner was provided through a grant from Fear Free veterinary student research training grant. The authors are grateful to Drs. Daniella Luethy and Kallie Hobbs for providing archived video recordings.