Effect of siRNA on Virus Shedding, Viremia, and Clinical Disease in Experimental EHV-1 Infection

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Metaphylactic, intranasal administration of equine herpes virus-targeted siRNA decreased severity of fever and neurological signs relative to controls in experimentally infected animals. Author’s address: Department of Microbiology and Immunology, College of Veterinary Medicine, Cornell University, Ithaca, New York 14853; e-mail: mmb263@cornell.edu. © 2009 AAEP.

1. Introduction
Available vaccines fail to induce lasting immunity to all diseases associated with equine herpes virus (EHV-1). RNA interference is a novel technology showing promise for use in outbreak situations. This study examined the effect of siRNA on nasal shedding, viremia, and clinical signs in experimentally infected horses.

2. Materials and Methods
siRNA-targeting EHV-1 genes (glycoprotein B, origin binding protein helicase) was administered 12 h before and 12 h after intranasal infection with neuropathic EHV-1. Control horses received siRNA-targeting firefly luciferase.

3. Results
There was no significant difference in viral shedding, viremia, or initial fever between the two groups. Within the control group, there was a significant difference between mean baseline temperature and temperatures on days 6 and 7 (p = 0.005–0.02). Temperature in the treated group differed from baseline only on day 6 (p = 0.01). Neurologic signs developed in 3 of 4 control horses and 2 of 10 horses receiving EHV-1–targeted siRNA. Neurologic scores were significantly lower in the horses administered EHV-1–targeted siRNA from day 9 (p = 0.03) onward.

4. Discussion
Neurologic disease was decreased in horses receiving EHV-1–targeted siRNA. However, the etiology of EHV-1 neurological disease is complex. Further research is necessary to define the relative contributions of host and virus factors and to determine an optimal dosing regimen for siRNA metaphylaxis.