A Review of Possible Environmental Sources of Drug Positives

Cynthia Kollias-Baker, DVM, PhD

Environmental sources of drugs and medications exist, but at the current time, many are not well defined and may not be accepted by regulatory officials as mitigating circumstances. Veterinarians and trainers need to understand the risks and take whatever measures possible to prevent environmental contamination from causing positive drug tests in horses in their care. Author’s address: KL Maddy Equine Analytical Chemistry Laboratory, West Health Sciences Drive, University of California, Davis, CA 95617. © 2002 AAEP.

1. Introduction
Since the 1980s, the racing community has accepted that the horse’s environment can serve as a source of non-permitted substances. For example, salicylates have long been recognized as natural components of some grass hays, and arsenic has been shown to be a contaminant in a number of different types of feedstuffs. As the methodology of analytical drug testing has improved, however, smaller and smaller quantities of drugs and medications can be detected in urine samples collected after races and other athletic events. This has led to a new awareness that some positive drug tests could be the result of inadvertent contamination of the horse with drugs or medications that are present in its environment.

2. Cocaine
Cocaine is a naturally occurring substance that has both local anesthetic and psychostimulatory effects. It is a highly addictive drug of abuse in society and is consumed in a number of different forms, including snorting, smoking, and intravenous injection. Once in the body, cocaine is extensively metabolized with little or none of the parent compound excreted in the urine. Benzoylecgonine (BZE) and ecgonine methyl ester (EME) are the major urinary metabolites produced from cocaine in both humans and horses.

Recent studies completed at University of California (UC) Davis demonstrate just how sensitive current drug testing methods are for the metabolites of cocaine. When four horses were administered 2.5 mg of cocaine sublingually, urine samples contained detectable concentrations of BZE for up to 24 h post-administration (Fig. 1). This very small amount of cocaine could easily be transferred from a cocaine abuser’s hands to the mouth or muzzle of a horse. In addition, the peak concentrations of BZE associated with the 2.5-mg dose of cocaine ranged from 19 to 83 ng/ml. These concentrations are similar to those that are occasionnally found in urine samples collected from show and race horses. Of course, it is possible that these analytical findings are the result of cocaine that was purposely administered in attempts to alter the horses’ performances. It is important to note, however, that in the same UC Davis study referred to above, doses of cocaine of up
to 50 mg administered intravenously produced no detectable central nervous system (CNS) or cardiovascular effects, but did produce urinary concentrations of BZE and EME that were, in general, far in excess of those found in urine samples collected after races or other athletic events.

3. Morphine

Although commonly used as analgesics and pre-anesthetic drugs in many species, opiate agents, with the exception of butorphanol, are only used occasionally in horses because they can cause CNS stimulation. Morphine, however, has been occasionally detected in urine samples collected from horses after racing. Typically, the concentrations of morphine found in these post-race urine samples are <50 ng/ml, and in most cases, morphine is not present in detectable concentrations in the corresponding plasma samples. The presence of any opiate at any concentration in post-race urine samples, however, is of concern to racing authorities, because in the past these drugs have been administered to horses in illicit attempts to enhance their racing performances.

The opiate morphine is derived from the opium poppy *Papaver somniferum*, a plant native to the Far and Middle East but widely cultivated throughout the world. In addition, seeds of the plant are commonly imported into many countries for use in baking. The poppy plant and seeds contain variable amounts of naturally occurring opiates, such as morphine, codeine, and thebaine. It has been well documented that the consumption of poppy seeds by human subjects, generally in the form of baked goods, can result in the excretion of detectable concentrations of morphine in urine. There are several ways in which horses could inadvertently consume poppy seeds. For example, bakery byproducts, which may contain poppy seeds, are occasionally used in the preparation of animal feeds. In addition, bakery products, such as bagels and muffins, are sometimes fed to horses as treats.

In one study that used gas chromatography/mass spectrometry (GC/MS) methodology, morphine was present in detectable concentrations for up to 24 h in urine samples collected from horses after administration of 1, 5, and 10 g of poppy seeds that contained approximately 73 μg of morphine per gram of seed (Fig. 2). In a different study, morphine was detected in urine samples collected from horses administered 2 g of poppy seeds that contained a total dose of approximately 3 μg of morphine. In this study, maximum urinary concentrations of morphine were in the range of 80–120 ng/ml.

Besides poppy seeds, it is also possible that analytical findings of morphine in post-race urine samples could result from contamination of the horse with either illegal opiates, such as heroin, or prescription medications, such as codeine, which are metabolized to morphine. In humans, a unique minor metabolite of heroin, 6-monoacetylmorphine, has been identified, but it has not been determined whether horses also produce this metabolite. In addition, in most regulatory situations, the urinary concentrations of morphine and its major metabolites are quite small, and it would be unlikely that minor metabolites would be present in detectable concentrations. As with cocaine, it is also possible that analytical findings of morphine in post-race urine samples are the result of the purposeful administration of morphine or other opiates to the horse. Thus, although there is growing evidence that there may be multiple sources of morphine in a horse’s environment, at this time it is not possible to...
distinguish the source of low-level morphine positives in post-race urine samples.

4. Therapeutic Medications
The results of recently published studies indicate that environmental sources of nonsteroidal anti-inflammatory drugs (NSAIDs) may result in detectable concentrations of those agents in equine urine samples. For example, in one study, ibuprofen was present in urine samples collected from a horse that consumed feed that had been prepared by someone with ibuprofen gel on their hands. In another study, untreated horses, housed in stalls previously occupied by horses treated with therapeutic doses of flunixin, had detectable concentrations of that NSAID in their urine for up to 14 days. Other therapeutic agents, especially those requiring long durations of therapy, may also be present in the horse’s environment in fairly high concentrations. For example, in one horse, after a 10-wk treatment period with isoxsuprine, the drug was detected in various parts of the stall and grooming materials, including a plastic feed bucket, wood samples, and brushes, for weeks after the last treatment was administered. The results of these studies emphasize the importance of good barn hygiene. After administering any medication, barn workers should wash their hands thoroughly. If at all possible, horses being administered medications should be segregated from non-treated horses, and stalls should be stripped and re-bedded once treatment is terminated.

5. Nutraceuticals
In terms of drug testing, the world of human sport provides numerous examples of the hazards of nutraceuticals. For example, multiple athletes in the 2002 Winter Olympics claimed that positive tests for nandrolone resulted from consumption of nutraceuticals contaminated with the steroid. These same hazards exist for competitive equine athletes subjected to drug testing. For example, in California in 2000, our laboratory identified an herbal supplement, which contained small amounts of ephedrine and pseudoephedrine, as the source of exposure for numerous positive post-race analytical findings for norpseudoephedrine and phenylpropanolamine. The label for the product did not indicate that it contained any nonpermitted medications. In several cases, trainers and veterinarians have submitted samples of herbal supplements and nutraceuticals to our laboratory for analysis to determine whether they contain nonpermitted substances. Unfortunately, quality control for many of these products is lacking, and the presence or absence of contaminating nonpermitted substances may vary from batch to batch.

6. Methylxanthines
Caffeine, theobromine, and theophylline are all examples of methylxanthine agents. Best known for their mild stimulatory effects on the CNS, these agents also have a number of other systemic effects including bronchodilation, diuresis, and in humans, an increase in the skeletal muscle workload capacity. The results of several studies indicate that caffeine, in particular, may enhance certain types of athletic performances in humans. For this reason, regulators have often viewed the finding of even small amounts of methylxanthines in post-race urine samples as a serious infraction of drug and medication rules. These agents, however, are pervasive in the horse’s environment, and opportunities for inadvertent contamination abound. Sodas, chocolate, coffee, and tea all contain varying amounts of caffeine and theobromine. In one study, horse’s administered 10 peanut M&Ms had detectable concentrations of theobromine and caffeine in their urine samples for up to 48 h.

In some situations trainers may not be aware that they are administering caffeine-containing substances. For example, in California in the 1990s, a number of caffeine positives were traced to administration of an electrolyte supplement. The supplement contained guarana extract, which is a plant that naturally contains caffeine. Trainers and veterinarians need to be especially wary of any supplement that claims to have energizing effects, because these often contain nonpermitted substances, such as caffeine, even though the label may not indicate its presence.

7. Summary
Although environmental sources of drugs and medications exist, at the current time many are not well defined and may not be accepted by regulatory officials as mitigating circumstances. Veterinarians and trainers need to be aware of the risks to avoid inadvertent contamination of the horse. For example, accurate records should be kept for every horse that is being treated with any type of medication. In addition, grooms and handlers should wash their hands between treating one horse and handling another. Stalls and feed buckets should be cleaned thoroughly whenever occupants change and after therapy with non-permitted medications. In addition, human food items, such as candy, coffee, sodas, and bakery goods, should not be fed to horses that are subject to drug testing. Finally, herbal remedies may contain numerous substances, which, while all natural, are still considered to be non-permitted substances in many drug-testing programs. Horsemen and veterinarians need to be cognizant of this fact and use these products with great care in horses that are competing in sanctioned athletic events.

References