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cold medicine, over-the-counter, dextromethorphan, environmental exposure

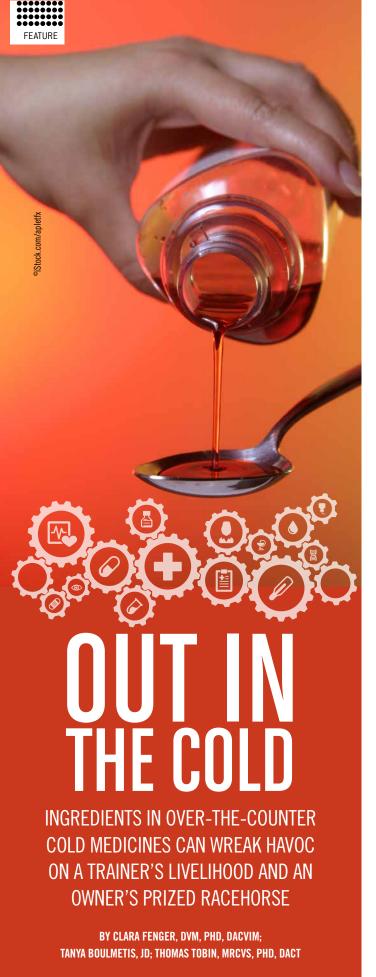
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The percussive beat of the groom's morning alarm was slightly out of rhythm with the ringing in his ears, a cacophony of sound in perfect cadence to intensify the throbbing of his head and sinuses. A well-timed dose of NyQuil before bed had drowned out the influence of the respiratory virus on his system through the night, but for grooms in most stables across the country, there are no sick days in horse racing. Most outfits run a skeleton crew, and there is no backup, no temp agencies to fill the gap when a key member of the team is under the weather.

So, with help from a little DayQuil and more than one cup of coffee, the groom was up with the sun to tend to his precious charges. It was a big day, with which no sub-microscopic virus would be able to interfere, because the stable's big filly was racing beneath the fabled twin spires. Little did the groom know that his valiant effort to soldier on in the face of a respiratory snuffle was a good deed that would not go unpunished.

The 2-year-old filly was firing on all cylinders, and despite her being guaranteed to go off at steep odds, the groom and trainer knew she had a shot to hit the board, maybe even win, if everything went her way. And win she did, in a maiden special weight at a prestigious track in a major jurisdiction.

As her breeder, the filly's owner always knew she was destined for big things, and this win was affirmation of even bigger things to come. The owner, trainer and a contingent of friends and associates had come to the track that day to witness the big event. There is no greater joy than standing in the winner's circle with a few dozen of your closest friends to share in the highest high that the Sport of Kings has to offer.

After an afternoon and evening of celebration, nothing could bring the owner down. The groom had almost forgotten about his rough start to the day. A great win for a deserving filly provided enough adrenaline to overcome any respiratory virus. Along with a little more medicine that night.

DEXTROMETHORPHAN (

Dextromethorphan is one of the principal ingredients of both NyQuil and DayQuil (and similar products), a structure related to codeine included in the popular over-the-counter medications as a cough suppressant. In humans, the liver converts dextromethorphan into dextrorphan by removal of a methyl group, which, along with the parent compound, contributes to its cough suppressant effects. The horse's liver is very efficient at this rapid conversion of the consumed dextromethorphan to dextrorphan, and recent research has shown that horses, like people, are widely variable in how efficiently they accomplish this conversion. The next step is the inactivation of the metabolite by adding a sugar or glucuronide, which increases the water solubility allowing the glucuronidated dextrorphan to pass out of the horse in the urine. Horses are highly efficient at this glucuronidation step, such that many drugs are rendered inactive almost immediately, markedly limiting the number of medications available to effectively treat medical conditions of horses.

Outside its use as a cough suppressant in humans, dextromethorphan has also been implicated as a drug of abuse, representing the most common drug abused by adolescents in the United States and abroad. Substances of human abuse, including cocaine, methamphetamine, morphine (heroin) and "bath salts" (cathinone), have all been implicated in very low concentration positive tests in postrace samples in horses, such that some jurisdictions have established screening levels for these substances, below which they will not call a positive test.

In horses, dextromethorphan has been investigated as a treatment for cribbing at a dose of 1 milligram per kilogram intravenously, and it is very effective for stopping the stereotypic behavior for up to an hour. This suppressive effect on cribbing occurs at blood levels in the range of 200 to 600 nanograms per milliliter (ng/ml) of dextromethorphan, while the active metabolite, dextrorphan, is well below 1 ng/ml. During this time, the inactive glucuronidated metabolite is in the range of 200 to 600 ng/ml, demonstrating the efficiency of the horse's liver to render drugs inactive. Based on the studies of the pharmacokinetics of dextromethorphan in horses, during the time that any effect of the drug is evident on the horse, the urinary concentrations would be expected to be in thousands of nanograms per milliliter.

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While a positive test obviously affects the owner and trainer, it can also affect the breeder as the value of a broodmare can be negatively affected when the status of a victory is still undetermined.

Our trainer was planning the campaign for the winning filly, while the owner/breeder was relieved to know that the first hurdle had been overcome. One of the most important achievements for a filly is the maiden win, because her offspring would then be out of a winning dam. Further, when the breeder still owns the filly's dam, it is another box checked on the pedigree: another winner for the mare. Each of these milestones represents incremental value and translates into real dollars for a breeder. More important, many horses only win one race.

The next condition for the filly would be a race against other winners, representing a big step up as she tried to replicate her maiden performance.

Then came the phone call. The stewards notified our trainer of a positive test. Dextrorphan.

"What?" she asked, unsure if she could pronounce the drug name or spell it. The positive test came with the requisite barn search, a graceless procedure in which every nook and cranny of the training barn is searched for contraband. All this while the trainer wracked her brain, trying to piece together what might have happened. The owner was in shock.

In some cases, a positive test spurs owners to desert their trainer, reeling from what they feel is betrayal: a trainer who gave "something" to the horse for an edge, with callous disregard for the feelings, beliefs and standards of the owner. For some trainers, the positive test spells financial ruin as owners pull their horses because of the stain of impropriety. In this case, the owner had complete faith and confidence in her trainer, full belief that no rules had been breached and no lines crossed.

The level of dextrorphan in the filly's urine was 15 ng/ml. This result could be associated with the administration four or five days earlier (three or four days and 23 hours after any possible effect had expired) of the same amount used in the aforementioned cribbing study or a much smaller amount only hours before the race. Perhaps the amount left on the hands of a groom who had been taking NyQuil or DayQuil for a minor respiratory infection. Perhaps the amount that splashed onto some hay in the stall, as could have happened

if a dedicated groom urinated in the corner, rather than leave his precious racehorse unattended to run to the restroom.

Noted expert Dr. Steven Barker, director emeritus of the Louisiana Drug Testing Laboratory, was called in by attorneys for our trainer and owner, and he evaluated the laboratory data. He concluded that "it is unfortunate that such insignificant findings result in a prosecution. The mere presence of a drug does not necessarily imply nefarious actions and the calling of positives for insignificant concentrations of a [Association of Racing Commissioners International] Category 4 drug serves no one. Rather than protect the integrity of the sport, such prosecutions continue to damage the image of the industry and the reputations of trainers, owners and horses."

INADVERTENT ENVIRONMENTAL EXPOSURE TO MEDICATIONS



It's impossible to know when exposure to a substance on a groom's or barn visitor's hands or anything in the stall could lead to a positive test.

The increasing sensitivity of testing laboratories to identify substances in infinitesimal concentrations has begun to paint the racing industry in a dark light. The blind calling of positives for substances that are clearly present in the animal but at completely inconsequential trace concentrations has become almost a daily event, confusing the public and racing participants alike. Fielding a horse in a race is becoming a game of Russian roulette: one never knows when some unforeseen event could trigger a positive test.

Dextromethorphan and its primary metabolite are commonly present at trace levels in human wastewater, with a spike identified in the winter months, coincident with cold and flu season. The wastewater enters water treatment facilities, where bacteria are removed, but substances like medications and their metabolites remain dissolved in the water that is then discharged into waterways. Other common human therapeutics that are metabolized using the same liver pathways and are similarly stable in the environment include the pain reliever tramadol and the antidepressant venlafaxine.

Our trainer was not alone in Kentucky with a positive for dextrorphan. She was joined by two other trainers for a total of three positives from November 2015 to April 2016. Other dextrorphan positive tests among trainers included one in California in October 2013, one in New Jersey in April 2016, one in Ohio in September 2015 and one in Illinois in November 2015. These positives follow the same pattern of dextromethorphan and dextrorphan found in waterways following the cold and flu season.

CONSEQUENCES OF BAD REGULATIONS

A second trainer receives a call from the stewards. It seems that the winner of a certain maiden special weight for 2-year-olds in which this trainer



sent out the second-place finisher has a positive test. For the foreseeable future, while this issue is adjudicated, the runner-up filly must compete as a winner. The trainer sighs deeply. Many horses can never win against the next condition, a fact that is so well accepted in the industry that a maiden win is also known as "the loss of the horse's best friend." Never again will that horse face competitors that have never crossed the wire first. The filly does eventually win a race but not before the horse has been dropped in for a claiming tag and taken by another owner. This positive test, like many others, has far-reaching consequences and even penalizes the second-place horse and its trainer and owner. This scenario is being repeated over and over across the country as positives that shouldn't qualify as such are called from coast to coast.

A DEXTRORPHAN "POSITIVE" ↔



A picogram is equivalent to a single drop of water in 1,000 Olympic-sized pools.

As with most postrace tests that return with a finding of a drug or a metabolite of a drug, the consequences depend on the jurisdiction in which the test was taken. The identical finding could lead to a fine with or without a loss of purse, with or without suspensions, or no repercussions at all for the trainer or owner. If the drug does not have a defined threshold, the threshold becomes the "limit of detection." Dextromethorphan falls in this category.

"Limit of detection" is defined exactly as it sounds. If the lab is able to find any drug at all, then it is "prima facie" evidence that the drug was given to the horse. When these rules were crafted more than 15 years ago, it was very rare to have a positive test as a result of inadvertent environmental exposure. That's because at that time, if the lab was able to find it, there was a good chance the drug had a pharmacological effect. However, today's advanced drug testing techniques are light-years ahead of what they were a decade or two ago. Labs can now detect at the picogram and even femtogram level. To put it into perspective, the nanogram level is "only" one in a billion grams, or approximately one drop of water in an Olympic-sized swimming pool. A picogram is one in a trillion grams. This is the equivalent of one drop of water in 1,000 Olympic-sized swimming pools.

States have three levels of trainer responsibility. The most reasonable are states like New York and Indiana. While the trainer is the absolute insurer, there is a rebuttable presumption of guilt. The trainer shall be held responsible for any positive test unless the trainer can show by substantial evidence that the trainer, employee or agent was not responsible for the administration of the drug or other restricted substance. That means, if the trainer is able to provide evidence that they had nothing to do with a very low-level positive test, such as in the case of inadvertent environmental exposure, the stewards have the authority to include this evidence in deliberations about the accountability of

the trainer. Unfortunately, it usually requires great expense on the part of the trainer or owner to prove cases of inadvertent environmental exposure.

Other states have a "failure to guard" regulation. For dextrorphan, a trainer would have to provide the same evidence as above—that they had nothing to do with the horse receiving the medication—and then prove there was no way they could have prevented it from occurring. For example, if a trainer was taking NyQuil at bedtime the night before going to the barn and could prove no one in the barn could have given it to the horse, his failure to protect his horse from inadvertent environmental exposure may still leave him with a positive.

Illinois has an absolute insurer rule with a safety valve. A trainer may be sanctioned without fault if the positive falls under the "Foreign Substances and Pharmaceutical Aids Banned" section, which covers dextrorphan at a low level. Because dextrorphan is categorized as not having any pharmacodynamic or chemotherapeutic action at ultra-low levels, stewards have the option of only fining the trainer, without it being a violation of the trainer responsibility rule. This is what occurred in 2015, but again, it required the trainer hiring an attorney at great expense.

Most states follow the most stringent variation of the absolute insurer rule: the trainer is responsible, regardless of the acts of third parties. With the current level of sensitivity of drug testing technology, limit of detection combined with absolute fault on behalf of the trainer is a formidable combination. In these states, unless the commission recognizes there is no scientific basis for the infraction or penalty and unless the trainer is in a position to hire legal counsel and dig in for a long, expensive fight, it usually means the trainer takes his fine, purse redistribution and days, not to mention a potential big hit to their career and future.

In Kentucky, the trainers with the dextrorphan positives were in a position to challenge the findings and access the latest scientific findings showing the disposition of dextrorphan has great variance in horses. The Kentucky Horse Racing Commission (KHRC) took a strong stand for innocent trainers everywhere stating had the commission known about the study prior to the stewards' rulings, the tests would not have been considered positives.

Horsemen applaud this result by the KHRC, but we should be thanking the horsemen who had the positives and were fortunate to have the resources to challenge the rulings both legally and scientifically. Had they not been in a position to do so, going forward there would have been more trainers on days, more purses lost and a larger black eye on the sport we love.

CONCLUSION

Over a year after that race beneath the twin spires, our owner has received her vindication and her filly has retained her win. After her good performance, the filly remained in training for several months, but the uncertainty of whether she would race again as a maiden or would have to step up against winners hung over the barn. The owner decided to retire the filly and breed her, with hopes that the situation would be resolved by the time she could be offered for sale. The filly's value as a broodmare exceeded the value of the claiming tag for which she could compete as a winner. However, as the sale dates loomed, the case had not yet been fully adjudicated and the decision by the KHRC had not been made. Legal counsel advised the owner not to offer the filly for sale without a significant disclaimer about her race record, a clear knock on the value of the filly.

In the end, the KHRC made the right decision, although why it took so many months is anyone's guess. Hopefully, other jurisdictions will follow suit and the problem of hypersensitive testing methodology spurring penalties and their unending unintended consequences will begin to be solved. in