

SHINING A LIGHT ON

Scopolamine and Environmental Contamination

A commonsense examination of the circumstances is in order given the recent news about Justify

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On September 11 of this year, news broke that 2018 Triple Crown winner Justify, trained by Bob Baffert, had tested positive for a little-known substance called scopolamine in a post-race drug test from the Santa Anita Derby. Worth 100 Kentucky Derby points, the Santa Anita Derby amounts to a “win and you’re in” event for America’s most famous horse race. Once the news hit, social media blew up with wild accusations of cover-up and corruption, despite very few facts being available. Horse racing media, from traditional outlets to all sorts of online blogs, and even mainstream media weighed in before any facts had come to light.

The dust still has not yet settled in the case. However, some of the details are now known, and with the benefit of time, reflection and actual facts, the circumstances can now be laid out and conclusions drawn. There is a message for the entire racing industry hidden in the details that extend far beyond the particulars of any one case.

JUSTIFY MADE THE HEADLINES AS A TRIPLE CROWN WINNER IN 2018, AND NOW HE’S IN THE NEWS AGAIN AFTER A POSITIVE TEST FROM THE SANTA ANITA DERBY WAS REVEALED EVEN THOUGH SOME DETAILS REMAIN UNKNOWN.



WHAT IS SCOPOLAMINE?

Scopolamine is a plant alkaloid and prescription medication used for nausea in humans. A closely related synthetic compound, N-butylscopolamine (Buscopan), is approved for use for spasmodic colic in horses. Scopolamine slows intestinal motility by blocking a neurotransmitter called acetylcholine, but such anticholinergic drugs also may be used for bronchodilation, or relaxing the smooth muscles of the airways and improving air flow in the lungs. It is this latter action that puts this class of drug among the banned substances in horse racing. Theoretically, such drugs could improve performance by improving air flow. Of course, there is actually no evidence that such an effect is achieved in racehorses, but most banned drugs are classified by their theoretical mechanism of action and not their actual effect on the animal.

WHERE DOES SCOPOLAMINE COME FROM?

Alkaloids are substances produced by plants that are typically highly toxic and bitter-tasting, which generally deters consumption by grazing animals. Scopolamine is produced by jimsonweed (*Datura stramonium*), a weed with a worldwide distribution and a common invader of hay, straw and cereal grain. While horses rarely seek out such plants as forage, when jimsonweed is dried as a component of hay or straw or if the seeds are mixed with grain, they can readily consume it.

Scopolamine is also a component of an old-time treatment called "Bell Drops" or "Bells," which was a tincture of belladonna. This remedy is still available on the internet but is not an approved formulation. Other plant alkaloids that can be consumed by horses in the same fashion are morphine, barbarin (the precursor of aminorex) from the plant yellow rocket and glaucine from poplar shavings.

SCOPOLAMINE TOXICITY

Scopolamine toxicity in humans has been reported throughout the world in the medical literature. Typically, it results from the ingestion of *Datura spp.* plants that are consumed by accident, such as their inclusion in prepared meals in which plants are harvested from a garden. In other cases, toxicity has resulted from the ingestion of herbal or homeopathic medicines in India and China. There are even reports of severe toxicity and death from their intentional exposure as recreational substances. Scopolamine at high doses causes hallucinations, restlessness and aggression, and even convulsions, coma and death.

Toxicity also has been reported in horses from either contamination of hay or grain with *Datura* seeds or the whole plants. Clinical signs include dilated pupils, colic, muscle cramps and abnormal locomotion.

SCOPOLAMINE IN RACING

Scopolamine has not been a significant source of positive tests in many years. A review of Association of Racing Commissioners International (RCI) records shows that only 28 scopolamine identifications and rulings occurred between 1982 and 2011. The positives have tended to cluster over time, a not uncommon phenomenon for plant substances. A number of these clusters have been identified in South Africa, and racing authorities use clusters to aid them in determining if penalties should be called. When hay is in short supply due to drought conditions, trainers have fewer choices for providing forage to their horses, and with jimsonweed being drought-resistant, it is more likely to contaminate the hay.

Like in South Africa, California appears to have a jimsonweed problem. Of the 28 positive scopolamine tests over the 30 years that RCI tracked positive tests, 22 of them were in California. The California Horse Racing Board (CHRB)



SCOPOLAMINE IS PRODUCED BY JIMSONWEED (*DATURA STRAMONIUM*), A WEED WITH A WORLDWIDE DISTRIBUTION AND A COMMON INVADER OF HAY, STRAW AND CEREAL GRAIN.

clearly recognizes this fact, as Dr. Rick Arthur, the CHRB equine medical director, released a statement on November 14, 2016, to horsemen at Del Mar warning of the presence of jimsonweed in straw.

Despite the intermittent positive reports from 1982 to 2011, after that period there seemed to be an abrupt stop to the RCI-reported positive tests for scopolamine in horse racing. As most of the positives had been in California, the assumption can readily be made that an in-house cutoff or screening level was identified and put in place. Such screening levels are in place already, such as the International Federation of Horseracing Authority level of 60 ng/ml (nanograms per milliliter) in urine and the Louisiana screening limit of 75 ng/ml. The levels associated with the identifications in South Africa have not been reported.

THE “LEVEL”

Justify's post-race urine level has been reported to be approximately 300 ng/ml of scopolamine. While jurisdictional standards place a threshold between 60 ng/ml and 75 ng/ml as a cutoff point, it has been suggested that, because of its unique climate leading to a larger jimsonweed problem, California's unpublished cutoff is much higher than this level. However, as with many substances in California racing, the CHRB does not report or publish what it considers a positive for scopolamine.

On its face, the 300 ng/ml of scopolamine in urine seems high—four times higher than the highest accepted urinary threshold for the substance. There are several critical points that need to be understood before any conclusion can be drawn about whether Justify is undeserving of his place in history as a result of this urine test.

First, urinary concentrations of drugs are drugs in the urine. They may lend a clue as to the amount in the horse, but drugs in urine are already out of the horse's bloodstream. It is the job of the kidneys to eliminate drugs, and the amount in the urine is typically at least an order of magnitude higher than the level in the blood. It is the level in the blood that determines whether or not the substance has any effect on the horse.

Second, the urine levels change depending on the acidity and specific gravity of the urine, as well as recent exercise. None of these details regarding Justify's case have been disclosed to the general public. Finally, where cutoffs have been set either internationally or in local jurisdictions, those levels are well below the level at which an effect can be expected, usually from 1/100th to 1/500th the effective concentration. This huge “safety factor” is adopted by regulators on the off chance that there may be some unidentified effect at lower concentrations. To date, no such effect has been identified for any substance, but it is a philosophical position and not a scientific one.

SCOPOLAMINE IN CALIFORNIA

Six horses at Santa Anita tested positive for scopolamine in the days surrounding the 2018 Santa Anita Derby. This brings us back to the cluster discussion, as clusters of positives often serve as a hallmark signal of environmental contamination. Jimsonweed, the presumed environmental contaminant in this case, can occur sporadically in bales of hay and straw. It is not in every bale, nor is it spread uniformly through a flake of hay or straw.

All horses identified with scopolamine in this recent cluster also contained the substance atropine. This is significant because jimsonweed contains not only scopolamine but also another anticholinergic alkaloid—atropine, at a much lower concentration. Intentional administration of a pharmacological preparation of scopolamine would lead to a positive test for scopolamine without the co-identification of atropine. While not all jimsonweed positives lead to both scopolamine and atropine identification, no pharmacological preparation administrations would result in the identification of atropine. This simple forensic fact makes any intentional administration to six horses highly unlikely. For these horses to be subjected to “doping,” they all would have had to receive both atropine and scopolamine.

LEGAL RAMIFICATIONS

The CHRB has been criticized and questioned for failing to file complaints and for deliberating and making decisions in private sessions regarding

Justify's scopolamine positive, as well as for the other horses that tested positive. Further criticism has been leveled at the CHRB for its actions of amending and modifying its rules regarding scopolamine after the substance was detected in Justify's samples and those of three of the other horses that tested positive. While that criticism and questioning may well be warranted, the regulator's actions and inactions have far-reaching ramifications on the future of those participating in the sport both in California and beyond.

How will the CHRB respond when the next scopolamine positive is detected, either above or below the 300 ng/ml level? Will an administrative complaint be filed or penalty imposed, or is the "Justify scopolamine rule" to be followed? Similarly, what action, if any, is taken when a nonperformance-enhancing substance, which is prohibited but not assigned a threshold, is detected in the equine athlete and subject to an argument of environmental contamination? If no action is taken, why? If action is taken, the licensee will have a strong argument based on the arbitrary and capricious nature of the enforcement.

State agencies must uniformly and fairly enforce the rules and regulations—to do otherwise is arbitrary and capricious. A licensee facing an administrative complaint or seeking judicial review of an administrative ruling now has precedent to argue that any penalty imposed against them is arbitrary and capricious compared to and based on the Justify case. As such, there is now precedent that, even absent a published threshold, 300 ng/ml of scopolamine is not an actionable level for pursuing an administrative complaint or penalty against a licensee. Licensees faced with positive test results for therapeutic substances with unpublished thresholds such as scopolamine are often presented with a difficult choice—take the deal offered by the regulators or face a lengthy and expensive defense that is often fought in an uneven playing field. However, the action/inaction and decisions of the CHRB may well have leveled that playing field for licensees—perhaps not in the controlled environment of administrative proceedings before the state agency but certainly in a courtroom on appeal before a state judge.

Licensees seeking review or judicial review of the state agency's actions/inactions must establish that they were prejudiced for the reason that the agency's actions were arbitrary and capricious, an abuse of discretion or otherwise not in accordance with the law. Additional prejudice may be established by proving that the agency's actions were in excess of its statutory jurisdiction, authority or limitation, or without observance of procedure required by law. Finally, a licensee may prove prejudice by showing that the agency's actions are contrary to the licensee's constitutionally protected rights.

Fair, uniform and consistent enforcement of defined rules is the legislative intent and directive in establishing and empowering state regulators. Failure to do so and operating without transparency will, at best, result in future suspicion, distrust and decline of our industry. The absence of thresholds, the modification of rules during an ongoing meet and the lack or refusal to provide the basis for the decision of no action—whether that be environmental contamination, cluster effect or otherwise—are damaging to the agency as well as to those in the industry.

CONCLUSIONS

The final chapter has not yet been written in the Justify scopolamine case. The scientific evidence pointing to environmental contaminants in the form of weeds in forage or actual drug contamination from the urine of humans or horses is overwhelming. The regulatory response to the ever-increasing sensitivity of drug testing technology has failed to keep pace with the reality of environmental contamination. Many in racing continue to ignore the need for regulatory screening limits accounting for the presence of naturally occurring substances and environmental contaminants in racehorses.

Clear protections for horsemen need to be sought, investigated and implemented for horse racing. Many substances, such as scopolamine, may



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require regulation on a local level, because some jurisdictions are at greater risk than others. Other substances, such as common human prescriptions, need universal cut-off levels. Common sense must prevail in the penalty structure for all substances that may contaminate a racehorse.

Finally, thresholds should be published and the procedure by which they are determined should be clearly in place in the regulations. If thresholds are to be identified after the race in which the substance is identified, the process needs to be clearly laid out in the rules. **HJ**