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CONTENTS

THE PAST AND FUTURE OF EQUINE DRUG TESTING AND MEDICATION REGULATION

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In Greek mythology Diomedes fed his mares human flesh to make them savage and unbeatable. In Roman times hydromel was believed to be effective and authorities banned it. Irish mythology had the Salmon of Knowledge. Victorian mythology had Alice in Wonderland. American Mythology had Popeye and spinach. The concept of very powerful effects from minute quantities of drugs is woven into the human psyche.

In the mid 1800s there was no drug testing or other regulatory controls. The concept of 'hay, oats and water' was apparently not a concern. Contemporary prints suggest open medication of horses right before post. Oral administration of medications so soon before racing during this era however, were unlikely to be effective. In the late 1800s morphine and cocaine were purified, making acute stimulant medication a reality. These developments caused no concern in the US, but a significant concern in Europe, where American trainers were highly successful and were called 'The Yankee Alchemists'. In 1903, in England, the Hon. George Lambton, concerned about American medications, announced that he would medicate certain horses in certain races, thereby forcing the English Jockey Club to take note of the problem. That year, the Jockey Club made medication of a racing horse an offence. Punishment was to be 'warned off the turf'.

In Europe, from 1903 to 1910, drug testing began. Following introduction of drug testing in France, Bourbon Rose tested positive in the 1910 Maisons Lafitte. The courts later supported this finding. Drug testing at this time was based on saliva testing, and the test barn was called 'The Spit Box'. Post race urine testing was begun in 1910.

In North America in the 1930s, there was widespread use of medication in racing. An editorial from a 1931 edition of The Blood Horse denounced the widespread doping and the 'unmitigated curse' of heroin. In 1932 legal betting expanded. Federal authorities raided trainer's barns and 100 horsemen were arrested for breach of the narcotics regulations. The Florida Racing Commission sent Drs Catlett and Morgan to France to learn the French testing techniques. The Commission then introduced analytical chemistry. By the 1970s testing contracts began to be given to university-based laboratories. Ohio State began testing in about 1965, Cornell in about 1971 and The University of Kentucky in about 1975. Screening was based on Thin Layer Chromatography (TLC) with Mass Spectrophotometry as the confirmation technique.

Enzyme Linked Immunosorbent Assay (ELISA):

By 1985, equine drug testing was based on thin layer chromatography. This had limited sensitivity and high potency narcotics and stimulants were being used with relative impunity. Any drug given to a horse at a dose of less than 10mg/horse, including etorphine, fentanyl, acepromazine, buprenorphine, cocaine, oxymorphone and detomidine, was not being reliably detected and was being used at will by some horsemen. In 1985, the University of Kentucky started a research project that rapidly evolved into the ELISA testing program. The sensitivity of testing increased 100-1000 fold, virtually overnight, for more than 20 drugs. There were subsequently multiple identifications of narcotics, stimulants, tranquillisers and bronchodilators. In the autumn of 1987, ELISA was used to test frozen post-race samples in New Mexico. The

first panel of tests put down more than 40 trainers in that state. A problem that had existed, in one form or another, for 100 years, had been controlled.

ELISA provided simple fast testing which was about 1000 times more sensitive than TLC and is the current basis for equine drug testing. Tests are performed on post-race urine samples and about 10% of runners or approximately 500.000 samples are tested per year worldwide. The technology involved allows for inexpensive, high throughput, automated systems and is highly adaptable. The scope for testing is very broad, at between 250 to 2500 agents.

Medications: Effects on Racing:

Acute stimulant medication:
Classic stimulants:
These include cocaine, caffeine, amphetamine, methylphenidate, methamphetamine and mazindol.

Opiates:
These include etorphine, fentanyl, morphine and buprenorphine. They are used as a locomotor stimulant, to suppress pain and prolong endurance and they are potentiated by stimulants. This is reliable, stimulant medication, which was widely used pre ELISA.

Tranquillisers:
These drugs are used to treat 'washy' horses (running the race in the paddock) and also used to allow the jockey to 'rate' a horse in a race. They include detomidine, reserpine, acepromazine and promazine. All are legitimate therapeutic agents, so it can be difficult to assess the rate of improper use.

Bronchodilators:
These include clenbuterol, terbutaline, atropine and albuterol. These are presumably used to improve oxygen delivery to blood and musculature. They were widely used close to race start time prior to the advent of ELISA, but their use cut back dramatically after it's introduction.

Chronic stimulant medication:
These include the anabolic steroids, growth hormone and erythropoietin (EPO). With the exception of the anabolic steroids, this is not currently a very active area.

Medication to restore 'normal' performance:
It is thought that a horse can be medicated to restore 'normal' performance, without the use of drugs with stimulant or depressant actions, but particularly with the use of non-steroidal anti-inflammatory agents. It is possible that corticosteroids may also be used for this purpose. Prophylaxis of EIPH with furosemide also comes under this heading.

Medication to lose races:
'Stopping' or 'nobbling' a horse is the oldest form of illegal medication. In principle, it is always possible to medicate a horse so that it will lose, the challenge is to treat a horse so that he is able to start the race but does not win. The horse is medicated with a tranquilliser or depressant to slow or stop it and it is usually done to a heavily backed horse, but may also be done to a horse to allow another favoured horse to win.

Medication to dilute out other drugs:
This is the administration of a drug that dilutes drugs or metabolites and makes them more difficult to detect. Diuretics generally do not affect blood levels of drugs but they do dilute drugs and metabolites in equine urine. The effect is generally up to, but not greater than, the diluting effect. In the US, there are rules, which specify the dose and time of administration of furosemide.

Medication to 'mask' other agents:
This is where agents are administered which interfere with testing. As testing techniques improve, this becomes a less likely scenario. Examples include use of furosemide for dilution, polyethylene glycol which causes smearing of TLC plates and thiamine which interferes with UV analysis.

ARCI Classification:
The 'Uniform Classification Guidelines for Foreign Substances and Recommended Penalties and Model Rule', published by the Association of Racing Commissioners International, are available at their website: www.arci.com, where they are regularly updated. These classes are intended as guidelines only, to assist racing officials to evaluate the seriousness of alleged violations of prohibited substance rules.

The RCI Drug Classification Scheme is based on:

1. Pharmacology:
Drugs that are known to be potent stimulants or depressants are placed in higher classes, while those that have (or would be expected to have) little effect on the outcome of a race are placed in lower classes.

2. Drug Use Patterns:
Consideration is given to the practical use of drugs eg. Procaine is placed into class 3 instead of class 2 because of its usual association with penicillin use.

3. Appropriateness of Drug Use:
Drugs clearly intended for use in equine therapeutics are placed in lower classes, while those clearly not intended for use in the horse are placed in higher classes, particularly if they might affect the outcome of a race. Drugs intended for therapeutic use, but which could affect the outcome of a race, are placed in intermediate classes.
The list does not include drugs, which do not seem to have an effect on performance or drug detectability, such as antibiotics and anthelmintics.

Classification:
Class 1: Stimulant and depressant drugs that have the highest potential to affect performance and that have no generally accepted medical use in the racing horse. Includes opiates, synthetic opioids, psychoactive drugs and amphetamines.

Class 2: Drugs with a high potential to affect the outcome of a race, but less of a potential than drugs in class 1. Most are generally accepted as therapeutic agents in the horse. These include, psychotropic drugs, certain CNS stimulants and depressants, CVS stimulants and neuromuscular blocking agents. Injectable local anaesthetics (except procaine) are included here.

Class 3: Drugs that may or may not have a therapeutic use in the horse, which have a lower potential to affect the outcome of a race than those in class 2. These include bronchodilators, and other drugs with primary effects on the autonomic nervous system, procaine, antihistamines with sedative properties and the more potent diuretics.

Class 4: Therapeutic medications that could be expected to have less potential to affect performance than those in class 3. These include less potent diuretics, anabolic steroids, corticosteroids, antihistamines and skeletal muscle relaxants without prominent CNS effects, expectorants and mucolytics, haemostatics, cardiac glycosides and antiarrhythmics, topical anaesthetics, antidiarrhoeals, mild analgesics and also NSAIDs at concentrations greater than established limits.

Class 5: Drugs in this category are therapeutic medications for which concentration limits have been established by the racing jurisdictions, as well as certain miscellaneous agents such as DMSO. Also included are agents with very localised actions such as anti-ulcer drugs and certain antiallergic drugs, Anticoagulants are also in this class.

The Future of Equine Drug Testing and Medication Control:

ELISA offers virtually complete control of the abuse of high potency medications, however it also offers super-sensitive testing for therapeutic medications. This has accentuated a long-standing problem in medication control: detection of trace residues of therapeutic medications and environmental and endogenous substances.

Therapeutic Medications:

In 1991 the McKinsey Report, a definitive review of medication control commissioned by the Jockey Club, assigned high priority to the establishment of 'threshold levels' for therapeutic medications permitted in animals on race day.
In 1995, the Association of Racing Commissioners International (ARCI) adopted a resolution, which reads in part: "the ARCI recommends that its members specifically implement procedures to have an official veterinarian or veterinary consultant review findings for ARCI class 4 and 5 substances to address 'trace' level detection so as not to lead to disciplinary action based on pharmacologically insignificant 'traces' of these substances."

The European Horseracing Scientific Liaison Committee (EHSLC) in its 1997 'Veterinary Drug Detection Times' booklet points out that: "three central reasons for having rules to control the use of drugs in horse racing are:

1. To ensure fair competition
2. To protect the welfare of horses
3. To protect the breed from becoming debased"

And then goes on to say: that "The rules of racing are not intended to discourage the proper veterinary care of racehorses if such treatment would not threaten any of these important objectives."

Clearly, if horses are not to be deprived of proper veterinary care, then suitable information on the detection time post administration of therapeutic agents and their metabolites must be made available to the veterinary profession.The problem of equine medication has not been easy to approach and proposed solutions have included:

1. The 'threshold' approach:
This is where there is a defined drug or metabolite concentration in a biological fluid that determines whether regulation should take place or not. The advantage of this approach is that it allows for standardised testing for an agent in all jurisdictions adhering to that threshold. The disadvantage is that the information is not directly useful to horsemen and needs to be translated into withdrawal time guidelines to be readily utilised by them.

2. The 'detection time' approach:
These are times post administration during which particular agents can be detected. The problem with these is that they are method- or laboratory-specific and are therefore local solutions to the problem. In addition, they have often been developed in a small number of horses.

3. The 'official withdrawal time' approach:
At least one racing jurisdiction expresses its medication rules in terms of the number of days pre-race that a certain medication should not be administered

4. Suggested 'withdrawal time' approach:
A jurisdiction may suggest a withdrawal time, which is the suggested period before an event to cease medication to minimise the risk of post race detection. Withdrawal time estimates are almost always significantly longer than the longest detection time for an agent and can vary between jurisdictions depending on methodology.

5. The 'zero-tolerance' approach:
Some jurisdictions maintain that they have a 'zero-tolerance' policy for certain drugs, taking the position that no amount whatsoever of these drugs are permitted in horses in their jurisdiction. 'Zero-tolerance' is a myth; no chemist can detect down to zero. Racing chemists can quantify down to about 1 quadrillion molecules (10^15). Professional chemists never declare a sample negative, but say that a substance was not detected and then specify the limit of detection of the method used.
Problems arise with this approach when there is detection of irrelevant traces, resulting from environmental contaminants, of politically sensitive substances. It is not unusual for example, to find traces of morphine and its metabolites in equine urine of about 50-100ng/ml. Reported sources of morphine in horse urine are poppy seeds from human foodstuffs and bakery waste, wild poppies contaminating equine foodstuffs (Australia) and, in Europe, contamination of hay dried in a commercial dryer following the drying of opium poppies grown under licence.

6. Unofficial or 'practitioners withdrawal times':
This is where veterinarians and those involved in racing pool their historical information on the sensitivity of testing in a certain jurisdiction.

7. Published 'performance specifications':
The Association of Official Racing Chemists (AORC) and the International Federation of Horseracing Authorities (IFHA) have developed a set of performance specifications.

Summary:
During this century, equine drug testing has grown from 'nothing' to a very sophisticated technology and we are now closer to 'hay, oats and water' than we have ever been. We still need new techniques for certain agents and we urgently need better guidelines for our therapeutic medications.