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Scoping Out Doping:

*Penn Vet Researchers Put the Brakes on
Performance-Enhancing Drugs in Racehorses*



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about the cover:

Penn Vet researchers at Pennsylvania's Equine Toxicology Laboratory have developed the premier program for effective testing for artificial substances such as steroids. Read about their work starting on page 4.

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scoping out doping



HOW PENN VET RESEARCHERS PUT THE BRAKES ON PERFORMANCE-ENHANCING DRUGS IN RACEHORSES

By Susan I. Finkelstein

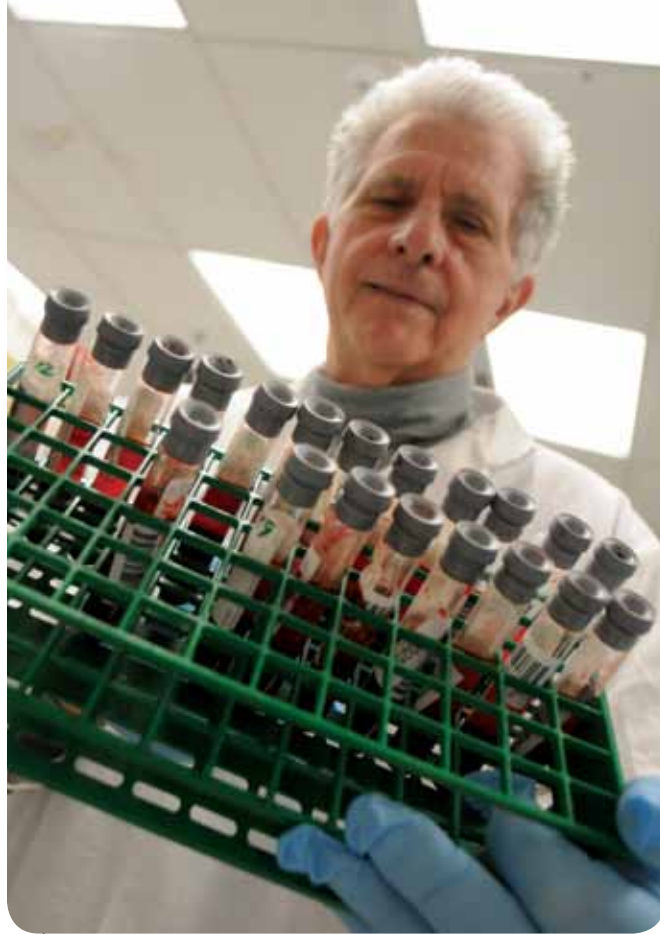
Building a faster racehorse: the dream of horsemen for hundreds of years, back to the days when horseracing was considered the sport of kings. As early as 1140, Henry I tried to make his “hobby horses” faster and stronger by breeding them with Arab stallions brought from the Crusades. Obviously, selective breeding has come a long way in the intervening centuries toward increasing a horse’s natural speed and endurance, but a modern phenomenon called “doping”—illegal application of a substance to improve a horse’s natural capacities at the time of a race—famously used by human athletes, has become a shortcut of choice to create a winning horse. Traditionally, the most commonly abused substances in horseracing have included anabolic steroids, etorphine, narcotic analgesics, erythropoietin (EPO), caffeine, beta blockers, butazolidin, bicarb and propantheline bromide. All these (along with hundreds of others) have been banned, and even substances not on the prohibited list of the Association of Racing Commissioners International cannot be administered on race day, or sometimes for up to even 30 days before a race. Enforcement of the ban requires effective monitoring, detection, identification and confirmation methods. Enter **Dr. Lawrence R. Soma, V’57**, Marilyn M. Simpson Professor of Large Animal Veterinary Medicine, and **Dr. Cornelius E. Uboh**, adjunct associate professor of pharmacy and pharmacology and director of the Pennsylvania Equine Toxicology and Research Laboratory (PETRL) in West Chester, Pa.

{ THE 411 ON EPO }

In 2006, Drs. Soma and Uboh and their colleagues at Penn Vet and PETRL became the first in the world to develop a method for confirming blood-doping agents—recombinant human erythropoietin (rhEPO) and darbepoetin-alfa (DPO)—in equine athletes by testing plasma through liquid chromatography (separation) and mass spectrometry (identification). Previously, only the antibodies caused by the drug—not the drug itself—were detectable in the blood. Used in human and small animal veterinary medicine to treat conditions that produce anemia such as cancer, and renal disease, EPO is a natural hormone protein produced in the kidneys that stimulates red blood cell production; rhEPO and DPO are genetically engineered versions of EPO. These synthetic agents have been abused in human endurance sports and horseracing because they are difficult to detect and they increase hemoglobin, hematocrit concentration (the ratio of the volume of packed red blood cells to that of whole blood) and maximal oxygen uptake (since red blood cells carry oxygen)—hence improving speed and endurance time. Not only does use of these agents violate rules of fair competition, but deaths in equine and human athletes also have been linked to them. The potential harmful effects they may have on the health of horses are still being investigated, but because they are made from human EPO they are foreign proteins being administered to animals. In other words, they do not naturally belong there.

One result? “The horses make antibodies against the drug. There have been a number of deaths because they have been given multiple doses,” said Dr. Soma. “Multiple doses in one animal seem to build up a resistance that suppresses its own naturally occurring [equine] EPO, and produces antibodies that can be identified, so when you take it away, the horse suddenly can become very anemic and crashes. There have been some DNA changes, genetic changes in the proteins, some amino acid changes, endogenous changes, but we haven’t been able to figure that out completely yet.”

Although long-term deleterious effects of the administration of the human-protein-based drugs on horses are still being determined, the immediate impact of a positive banned-substance test on the winners’ purses are very much known. In Pennsylvania, blood and urine



Dr. Lawrence R. Soma, V57. Photo by Sabina Louise Pierce.

from all first-place winners and horses randomly selected at the commonwealth’s six racetracks are drawn automatically. The laboratory also receives anonymous samples for testing. If a horse tests positive, its race victory is voided, and the winning purse—which can range from \$5,000 to \$500,000 or more—is awarded to the next finisher. In addition to affecting the bottom line, violators can also face fines, suspension and even license revocation. Inevitably, with such high stakes come increasingly sophisticated methods by cheaters to beat the system.

“We call them ‘basement chemists.’ They are advising the horsemen on what to do,” explained Dr. Uboh. “Yes, it is a great challenge for us to keep up with the new designer drugs being illegally developed. We are working within the legal system, meaning that we are looking for drugs approved for use; those are the standards we have. We can go to the market and buy those, but the ones synthesized in basements are not publicized, are not out there on the market. We can’t buy them. So that’s a challenge we face.”

{ THE DECLINE OF STEROIDS }

Because anabolic steroids have become very easy to detect via today’s testing protocols, their abuse in horseracing has rendered them largely a thing



of the past. Anabolic and androgenic steroids, synthetic forms of the male hormone testosterone, have been used to create fitter, powerful and more aggressive horses. Corticosteroids (e.g., prednisone and dexamethasone), on the other hand, generally are used to relieve inflammation in joints and in the airways of racehorses. Equine athletes are not allowed to receive either type of steroid within 24 hours of a race (the exception is in Florida, where horses can receive the corticosteroid prednisolone on race day). The Racing Medication and Testing Consortium (RMTC), founded in 2000 and governed by a board of directors consisting of 23 racing-industry stakeholder groups (including the American Association of Equine Practitioners and the National Thoroughbred Racing Association), has developed a model rule regulating use of anabolic steroids in racehorses. To date, 24 states (including Pennsylvania, the first to go steroid free) have adopted the model rule, and nine states are in the process of doing so.

Again a pioneer, PETRL was the first laboratory in the world to develop a method of screening, quantifying and confirming the anabolic steroids in plasma. Making the switch from urine to plasma for screening and confirming the presence of anabolic steroids made it more rapid and cost effective. “Everyone was testing urine because it’s a lot easier to get a lot more urine from the horse,” said Dr. Uboh. “But if you’re really looking for the action of the drug, it’s not what is in urine; what it is in plasma matters. If it is in urine, the body is sending it out, it doesn’t want it. If it’s in plasma—in the blood—then it most likely had an effect on the horse.

“Plasma is also cleaner,” Dr. Uboh continued. “When you look at the urine result, there are so many peaks/signals, so many other naturally occurring substances represented by the many signals observed. With plasma, it’s very clean. If a drug is present, you see one single signal. And then you tackle that signal and find an

answer or identify that peak instead of wasting time on so many irrelevant peaks or signals.”

Dr. Soma believes most horsemen are glad about the ban. “I think if you talk to the average trainer now, he is happy with the ban because he says, ‘Now, it’s a level playing field. I know my neighbor. He doesn’t have a competitive edge on me because he can give an anabolic steroid and I don’t want to.’ Some trainers didn’t want to give steroids but felt forced to because they wouldn’t have had that same competitive edge.”

Aside from the unfair impact anabolic steroids had on racing, the chemicals also seemed to have negative effects on the animals’ behavior, akin to the “roid rage” that can occur in people using the substances. “That’s why they’ve been banned, finally—because they caused behavioral changes,” Dr. Soma explained. “We started looking at anabolic steroids about six years ago now. The racing commission veterinarians were saying, ‘I’ve got horses I can’t handle.’ They were having females act like males. If you give testosterone to a female, put her out in the pasture and there’s another female out there, she’s going to act like a stud. And if a gelding is given testosterone, he’s going to act like a stud.”

{ PETRL NEVER SLEEPS }

PETRL scientists process 60,000 samples a year—equine samples for research, post-race and pre-race, as well as from human drivers and trainers and occasional “specials” (e.g., if a horse expected to win loses, and vice versa, or retesting positives from other laboratories). Each positive result helps build PETRL’s own database of specific drug “fingerprints,” which now numbers in the hundreds. Truly, Dr. Uboh and his laboratory colleagues have almost single-handedly rescued the integrity of the horseracing industry—in Pennsylvania and beyond.



“We did some screening in 2005, and 60 percent of the horses running in Pennsylvania had an anabolic steroid in them; some had two or three different anabolic steroids,” Dr. Soma remembered. In 2008, the Pennsylvania Horse Racing Commission and Pennsylvania Harness Racing Commission collected 2,061 samples during the first two months of the year 2008; results showed 98.8 percent of the samples were negative, according to the governor’s office. Currently all horses in Pennsylvania are competing anabolic-steroid-free.

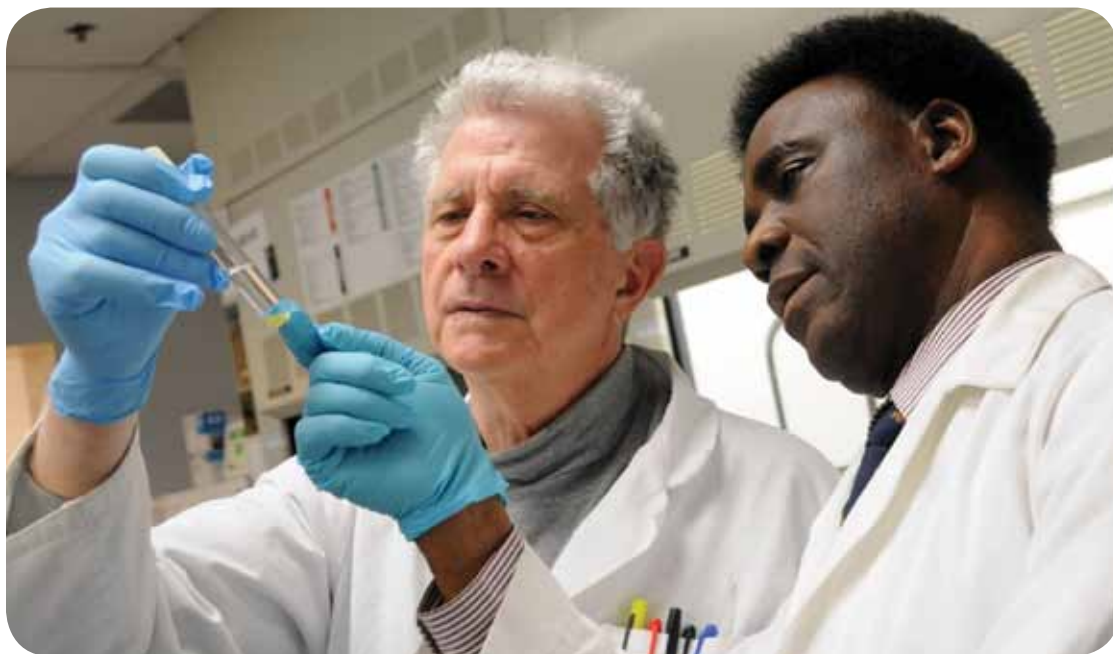
“People think [horseracing] is a very dirty industry, nothing but drugs, but that’s not true,” said Dr. Uboh. “We know that only about 0.1 percent test positive. It’s a very clean industry. Very well regulated, believe me. Horses are very intensely tested. We don’t leave stones unturned. Whenever we see something, we pursue it down.”

It is only fitting that such groundbreaking work takes place in this commonwealth. “Pennsylvania has a proud history of horseracing reaching back to the earliest colonists,” said

Dr. Corinne R. Sweeney, associate dean of Penn Vet’s New Bolton Center campus and chief operating officer and executive director for the George D. Widener Hospital for Large Animals. She currently serves as chair of the Pennsylvania Horse Racing Commission.

“Pennsylvania’s horse- and harness-racing industries are the backbone of our state’s \$1.5-billion equine industry,” Dr. Sweeney continued. “In 1967, the Pennsylvania Horse Racing Commission was established, and since then Penn Vet has been there, advising the commission on issues associated with generating a healthier racehorse and implementing a safer racing product.

“Because of the work of Drs. Soma and Uboh, the Pennsylvania Horse Racing Commission implemented the first ban on anabolic steroids in the country, which soon was followed by other major racing jurisdictions,” said Dr. Sweeney. “The commission continues to turn to these Penn scientists to guide us as we eliminate the future use of other drugs in the hope to reduce catastrophic and lesser racing injuries.”



Dr. Soma with Dr. Cornelius E. Uboh. Photo by Sabina Louise Pierce.