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Association of phenylbutazone usage with horses bought for slaughter: A public health risk

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ABSTRACT

Sixty-seven million pounds of horsemeat derived from American horses were sent abroad for human consumption last year. Horses are not raised as food animals in the United States and, mechanisms to ensure the removal of horses treated with banned substances from the food chain are inadequate at best. Phenylbutazone (PBZ) is the most commonly used non-steroidal anti-inflammatory drug (NSAID) in equine practice. Thoroughbred (TB) race horses like other horse breeds are slaughtered for human consumption. Phenylbutazone is banned for use in any animal intended for human consumption because it causes serious and lethal idiosyncratic adverse effects in humans. The number of horses that have received phenylbutazone prior to being sent to slaughter for human consumption is unknown but its presence in some is highly likely. We identified eighteen TB race horses that were given PBZ on race day and sent for intended slaughter by matching their registered name to their race track drug record over a five year period. Sixteen rescued TB race horses were given PBZ on race day. Thus, PBZ residues may be present in some horsemeat derived from American horses. The permissive allowance of such horsemeat used for human consumption poses a serious public health risk.

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1. Introduction

Phenylbutazone (PBZ) was marketed in the United States for the treatment of rheumatoid arthritis and gout in 1952. Serious and often fatal adverse effects such as aplastic anemia and agranulocytosis appeared in the literature within three years of its use (Benjamin et al., 1981; Böttiger and Westerhom, 1973; Cameron et al., 1966; Chaplin, 1986; Deaths due to butazolidin, 1952; Dunn, 1972; Etess and Jacobson, 1953; Hale and DeGruchy, 1960; Leonard, 1953; Mauer, 1995; McCombs, 1958; Nelson et al., 1995; Ramsey and Golde, 1976; Risks of agranulocytosis and aplastic anemia, 1986; Steinberg et al., 1953). The serious adverse effects of PBZ culminated in its unavailability for human use in the United States.

Because of the bone marrow toxicity caused by PBZ in humans, the Food and Drug Administration (FDA) has set no safe levels of PBZ in animals intended for food and bans the administration of this drug in any horse sent to slaughter for human consumption (http://www.fda.gov/cvm/CVM_Updates/buteup.htm).

By 1990, over a dozen foreign-owned slaughter houses in the United States were slaughtering approximately 350,000 horses per year (weekly United States Department of Agriculture statistics up to 2007 when all of the slaughter plants were closed by state statutes: http://www.ams.usda.gov/mnreports/SJ_LS711.txt), and the United States was exporting another 70,000 live horses per year for slaughter to Canada (monthly United States Department of Agriculture statistics: http://www.fas.usda.gov/ustrade/USTExFatus.asp?QI=).

Veterinary records from American horses sent to slaughter for human consumption are not available to the public. Moreover, horses are not raised as food animals in the United States and there appears to be inadequate testing to ensure that horses given banned substances such as PBZ do not enter the slaughter pipeline.

Thoroughbred race horses may have a higher rate of PBZ exposure because of their intense training and racing schedule. Thoroughbred race horses frequently develop training- or race-related musculoskeletal injuries that require treatment with a non-steroidal anti-inflammatory drug (NSAID). Phenylbutazone is the most widely used NSAID in horses because of its availability and cost (Hopes, 1972; Goodrich and Nixon, 2006).

The method of identifying TB race horses by lip tattoo and PBZ administration from race track records makes it possible to determine PBZ exposure in horses that have raced at certain tracks that permit race day PBZ and record its administration.

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In our study, the objective is to show that TB race horses are given PBZ prior to being bought for intended slaughter for human consumption. We present data which shows that some TB race horses sent to intended slaughter for human consumption were given PBZ on race day. The data show that the FDA ban on PBZ usage in horses intended for human consumption is ignored by some members of the race track community and that this ignorance in addition to the fact that approximately one-half of all TBs that are born are slaughtered for human consumption abroad portends a potentially serious health hazard.

2. Methods

We contacted individuals who rescued TB race horses from the slaughter pipeline over a five year study period. Through these individuals, we identified 50 TB horses rescued from slaughter and an additional 18 TB horses that were sent for intended slaughter. Each of the 68 horses could be identified by a lip tattoo registered with the Jockey Club of America and all of the 68 horses have Lifetime Past Performance records that are available on the public database.

The lip tattoo allowed us to find the registered name of each TB horse by submitting the horse's tattoo into the Jockey Club of America database and thus to obtain the race track drug records.

The race track drug record was acquired from two national sources: (1) the Lifetime Past Performance record and (2) individual race track records. Both sources are available to the public. The Lifetime Past Performance record is obtained by entering the registered name of the TB horse into the Equibase database at the following web site: http://www.equibase.com/premium/eqpHorseLookup.cfm?SAP=HLN&PID=50214.

These records reveal a great deal of information about an individual TB horse including all race tracks at which the TB horse raced over its lifetime. TB race horses that raced at one or more race tracks where PBZ given on race day is allowed were documented in the Lifetime Past Performance record. At least three individual race track drug racing records were obtained from eight out of the thirty-four TB race horses that were randomly selected from the study population to ensure that the drug record from the specific race track matched the drug record from the same race track listed in the Lifetime Past Performance record. Individual race track records from a TB race horse that was given race day PBZ were obtained by entering the registered name of the TB horse at the following Equibase web site: http://www.equibase.com/premium/eqpVchartSearch.cfm.

We were able to obtain records (track records and Lifetime Past Performance record) to determine whether PBZ was administered on race day or given within 24 h of a race on 32 horses: all 18 of the non-rescued TB horses and 16 of the 50 rescued horses. National databases were used to determine the number of TB race horses sent to slaughter for human consumption during the five year study window.

The thirty-four TB race horses described in this study came from the West coast, the Midwest and the Northeast of the United States.

3. Results

All eighteen horses sent to intended slaughter for human consumption and 16/16 of the 50 identified rescued TB horses had a positive history of PBZ administration (Table 1). One of the 18 non-rescued horses was not given PBZ on race day but was documented to have been given the drug by a licensed veterinarian prior to being sent to slaughter for human consumption. Another TB race horse that was sent to slaughter for human consumption had documented PBZ in its blood. This horse won at a race track in the United States where all winners must be tested for PBZ blood levels by law. Approximately 91,000 TB race horses were sent to slaughter over the five years that we examined the data.

Table 1
TB horses given PBZ and sent to slaughter or rescue.

TB race horse category	*N*	Positive PBZ track record review (*N*)	Other positive information (*N*)	Positive (%)
Not rescued	18	16	2	100
Rescued	50	–	–	–
Records examined	16	16	–	100
Records not examined	34	–	–	–

The PBZ profile of TB horses bought for intended slaughter is presented in Table 2. The time interval from the last known PBZ administration to intended slaughter ranged from 0.25 to 48 months. It should be emphasized that it is unknown whether additional PBZ was given to any of the horses from the time they left they left the race track to the time the horse was bought for slaughter. It is common for old race track injuries to require additional NSAID treatment after their racing career is over.

4. Discussion

In February 2007, a federal appeals court ruled that the two slaughter houses in Texas were in violation of a 1949 law against selling horsemeat for human consumption (Empacadora de Carnes de Fresnillo vs Tim Curry, 2007), and by March the Texas plants were closed. By September of 2007, a new state law in Illinois (Illinois HB 1711) resulted in the closure of the third and final horse slaughter facility in the United States.

The foreign owners of the three slaughter plants relocated their operations to Canada and Mexico. By the first quarter of 2008, the increased export of American horses to slaughter in Canada and Mexico had replaced the reductions in slaughter within the United States and the total slaughter of American horses had recovered to its 2006 level (Fig. 1). It is normally the case that once a horse ends

Table 2
Data on PBZ administration and slaughter date.

Thoroughbred horse	Date of last known PBZ administration	Date horse sent to slaughter	Approximate time interval (months)
1	6/17/2006	4/18/2008	10
2	6/28/2007	4/18/2008	10
3	9/2004[a]	9/2004	1
4	2/09/2008	4/21/2008	2
5	3/2/2003	3/2003	1
6	12/13/2006	4/18/2008	16
7	6/03/2008	10/17/2008	4
8	9/17/2007	9/2007	0.5
9	–[b]	6/20/2008	0.25
10	10/14/2007	4/11/2008	6
11	03/01/2007	4/18/2008	13
12	10/07/2004	7/2008	45
13	10/30/2004	1/2005	3
14	5/07/2008	10/17/2008	5
15	9/06/2003	4/22/2004	7
16	3/24/1993	3/1993	0.25
17	10/29/2004	11/2004	0.25
18	11/17/2004	2008	48

[a] This thoroughbred race horse was not given PBZ as indicated in the Past Performance Record. A licensed veterinarian provided documentation of PBZ administration prior to being sent to slaughter.

[b] This thoroughbred race horse was not given PBZ according to its Past Performance Record. PBZ was documented in blood via drug testing after winning a race. All winning horses are required by law to have drug testing.

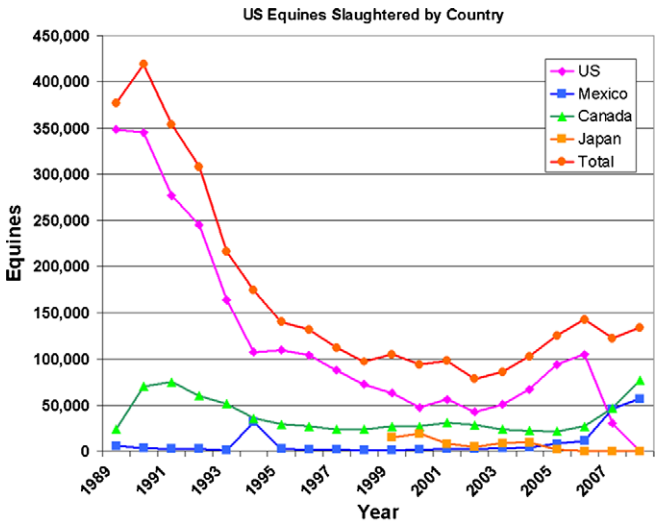

Fig. 1. Equines slaughtered by country and year. The number of equines (horses, ponies, donkeys and mules) slaughtered is plotted against the year slaughtered. The data were obtained from the USDA (http://www.nass.usda.gov:8080/QuickStats/Index2.jsp).

up on a slaughter truck, the next stop is a feed lot associated with a slaughter plant.

Currently, three Mexican horse slaughter facilities are known to export horsemeat to the European market while a large number of small provincial plants provide meat for local consumption. In the wake of the closing of plants in the United States, Canadian horsemeat production has approximately doubled (http://www.atssea.agr.gc.ca/stats/5034x-eng.pdf). There is a limited market for horsemeat in French speaking areas of Canada, with the bulk of the meat produced being exported to Europe.

This is the first report to show that many TB race horses bought for human consumption may have residual PBZ; over 30% of the TB horses were given PBZ within six months of being sent to slaughter for human consumption. Winning TB horses have PBZ blood levels determined to ensure they are within the range and allowed by law (<5 μg ml^{-1}). According to Dr. Lawrence Soma, the racing commissioner's equine research director at the New Bolton Center of the University of Pennsylvania School of Veterinary Medicine, the mean PBZ concentration in the blood of a horse that tests "negative" (horses that have a legally permissible level of PBZ) is about 2 μg ml^{-1} (personal communication). One of the slaughter bound horses listed in Table 1 had a documented PBZ level after winning a race at a race track in the United States. The total number of winning TB race horses with documented PBZ blood levels bought for slaughter for human consumption is unknown. This is an important point because this horse's Lifetime Performance Record did not indicate race day PBZ administration. A second TB race horse presented in this study had PBZ administration documented by a licensed veterinarian. Again, the Lifetime Performance Record of this horse did not indicate race day PBZ administration. These results support the view that TB race horses can and do receive PBZ at times other than on race day.

It is disturbing to note that a documented 9000 lb of horsemeat (500 lb of dressed horsemeat per horse × 18 contaminated horses) taken from horses with known exposure to PBZ was sent abroad for human consumption over the five year study period. This estimate of the amount of contaminated horsemeat may be at the low end because our sample size is small and the records indicate a high likelihood of exposure in this cohort.

The scope of the amount of horsemeat that may be contaminated with PBZ can be inferred from the number of rescued horses given race day PBZ. All sixteen of the rescued TB horses on which we obtained Lifetime Past Performance records were given PBZ on race day or within 24 h of a race. If rescue organizations did not outbid horse dealers that buy for the slaughterhouses, more horsemeat would be expected to be contaminated with PBZ.

The data presented in Table 2 shows that the time interval from the last known dose of PBZ to the animal being bought for slaughter varies from about one week to four years. In our study, four years may be a safe withdrawal time since a horse was given PBZ prior to being sent to slaughter. However, the FDA does not allow any use of PBZ in horses destined for human consumption and neither does the United Kingdom (UK) or the European Union (EU) regardless of withdrawal time. In addition, we did not have access to veterinary records prior to, during racing or after retirement from racing. Therefore, we do not know whether any of the horses sent to slaughter for human consumption were given PBZ during the interval between the last known PBZ dose and the time they were bought by horse dealers that buy horses for the slaughterhouses. Thus, it is possible that horses given race day PBZ four years ago could have been given more of this drug at times other than racing and prior to being sent to slaughter.

In 2008, three TB horses whose records we examined were bought for slaughter and given PBZ on the same day. These TB horses were rescued from slaughter (http://tuesdayshorse.wordpress.com/2008/11/11/five-banned-in-suffolk-downs-no-slaughter-policy-mass/). A fourth TB horse, given race day PBZ six weeks prior to being taken off a slaughter truck, was also rescued (http://www.horsetalk.co.nz/news/2008/09/019.shtml). This information underscores the fact that recent administration of PBZ given to horses destined for slaughter for human consumption is a current and immediate problem.

In horses, phenylbutazone is metabolized in the liver where it is converted to oxyphenbutazone, γ-hydroxyphenylbutazone and probably γ-hydroxy-phenbutazone and follows a bi-exponential model of decay. The plasma half-life of PBZ is 5.46 h in young horses but is longer in horses older than ten years and those with impaired liver function. In addition, PBZ uptake into the bloodstream is delayed by food in the stomach (Lees et al., 1985, 1986, 1987, Maitho et al., 1986, McConnico et al., 2008). Oxyphenbutazone is a major metabolite of PBZ and remains elevated up to at least 72 h (Lees et al., 1985, 1986, 1987, McConnico et al., 2008). Tissue levels of phenylbutazone and oxyphenbutazone were highest in kidney. In one study, high levels were also found in liver, lung and heart whereas the lowest levels were found in muscle (gluteus and biceps) and tendon (Lees et al., 1987). Since the elimination of PBZ follows exponential decay, traces of PBZ will remain as a contaminant of horsemeat in previously treated horses for a very long and as yet undetermined period of time.

Oxyphenbutazone has NSAID properties and at one time was thought to be less toxic that PBZ. However, oxyphenbutazone also has serious adverse effects in humans including those of producing aplastic anemia, agranulocytosis, thrombocytopenia, leucopenia, pancytopenia, and hemolytic anemia (Chaplin, 1986). The mortality rate of PBZ- and oxyphenbutazone-induced aplastic anemia was 94% and 71%, respectively (Benjamin et al., 1981; Böttiger and Westerhom, 1973; Cameron et al., 1966; Chaplin, 1986; Deaths due to butazolidin, 1952; Dunn, 1972; Etess and Jacobson, 1953; Hale and DeGruchy, 1960). Overall, the data suggest that the risk for the development of the lethal adverse effects in humans by PBZ and oxyphenbutazone are not always dose-dependent indicating an idiosyncratic effect. In addition to its well-known bone marrow suppression effects, PBZ is also associated with a hypersensitivity reaction in the liver which can cause death (Benjamin and Ishak, 1981). Taken together, it is clear why phenylbutazone is currently unavailable for human use in the United States and is banned in animals destined for human consumption.

In response to a letter under the Freedom of Information (FOIA) act, the United States Department of Agriculture (USDA) indicated that during an "exploratory project" they found two of twenty-four horse carcasses tested (8.3%) that were violative for PBZ in 2004–2005. The USDA also stated that they determined PBZ levels in equine fat samples in 2002 and 2003 and none was detected. Horse carcasses were not among those animal carcasses tested for PBZ during the year of 2006, the year that horses were under Federal Inspection by the Food Safety and Inspection Service (FSIS), the USDA's Public Health Regulatory Agency. This agency works with the Environmental Protection Agency (EPA) and FDA "to control veterinary drug, pesticide, and environmental contaminant residues in meat, poultry, and egg products. Residue control is a cooperative effort. EPA and FDA have statutory authority for establishing residue tolerances or action levels, and FSIS, through the National Residue Program (NRP), tests animal tissues and egg products to verify that tolerances or action levels are not violated" (http://www.fsis.usda.gov/science/2006_Red_Book/index.asp). The FDA has set no safe residue limits of PBZ in animal carcasses. If PBZ is found to be present in food animal tissue, it is considered a violation. Given that musculoskeletal injuries are frequent in horses and are treated commonly with PBZ to ameliorate the pain associated with these injuries, it is unclear why none of the horse carcasses were tested for PBZ in 2006 (http://www.fsis.usda.gov/science/2006_Red_Book/index.asp). Moreover, it is unclear why FSIS would analyze fat to determine PBZ levels because the volume of distribution indicates that almost the entire drug stays in the bloodstream. In fact, the FSIS directive requires that PBZ levels be determined in kidney. Kidney is the organ that exhibits the highest levels of PBZ (Lees et al., 1987).

PBZ is used in equines of all ages and while most of the horses sent to slaughter are young and sound, old equines are also sent to slaughter. Slaughter bound horses are either bought directly by dealers or purchased at auction houses. There is limited information on how the horses are handled at dealer feedlots and there are no laws of governance. Clearly, the longer horses are kept on dealer feedlots the lower the profit. Whether horses on dealer's feedlots are given any medications is unknown. Domestic horses may need medications to treat bacterial or viral infections. Moreover, domestic horses need drug treatment to control parasitic infections and certain vaccines are also required by law. Many of the drugs used to treat bacterial, parasitic and viral illnesses are also banned if the animal is sent to slaughter for human consumption. Banned drugs given to horses such as PBZ are not tracked for human consumption purposes.

As stated above, almost all of the PBZ remains in the bloodstream. The blood is drained from horses but its level of completeness is unknown. There are 100 ml of blood/kg of thoroughbred horse. Thus, there are fifty quarts or 12.5 gallons for a horse that weighs 1000 lb. This is confirmed at: http://www.thehorse.com/ViewArticle.aspx?ID=5491. So, a horse has about 1.25 gallons per 100 lbs of body weight. To provide a point of comparison, a 1400 lb cow has 60 ml/kg body weight or almost 10 gallons (http://www.milkproduction.com/Library/article_series/bovine_biology/14_Blood.htm) or 0.71 gallons per 100 lbs of cow. The ratio is 1.25/.71 = 1.76:1. Thus, a horse has 1.76 times as much blood per pound of body weight compared to a cow. The owner of a horse slaughter house in Canada that was shut down by the Canadian Food Inspection Agency for food safety issues stated publicly that they were slaughtering more than 100 horses a day. Thus, the blood may not be completely drained from muscle increasing the likelihood of contamination.

The FDA, like the EU and UK, specifically bans the use of PBZ in any horse destined for slaughter for human consumption. Yet, this ban is being circumvented because there is no pre-slaughter mechanism to determine and remove horses that receive PBZ during their lifetime. This is because horses are not regarded as or treated as food-producing animals in the United States and there are no USDA regulations to prevent them from being given banned substances like PBZ.

The lack of oversight to prevent horses given PBZ from being sent to slaughter for human consumption as ordered by the FDA indicates a serious gap in food safety and constitutes a significant public health risk, a fact that has been recently highlighted by the Department of Animal and Food Science at the University of Delaware (http://copland.udel.edu/~kniel/VirtualFarm/Templates/horses.htm). We recommend that the FDA and USDA join forces to track the administration of PBZ to horses and stop the slaughter or exportation for slaughter of horses with a positive history of PBZ treatment. If such a process cannot be put in place expeditiously, both agencies should ensure that horse carcasses only be used for non-human purposes.

Conflict of interest statement

The authors declare that there are no conflicts of interest.

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