Polybrominated Biphenyl (PBB) Problems in Michigan

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After attending the Bovine Practitioners meeting in St. Louis, December, 1977, I would like to present a somewhat different point of view and findings than Dr. Hellend presented in his paper on polybrominated biphenyl or PBB. Let me state that I have been in dairy cattle practice since December, 1943, and in no way am I employed nor do I receive any pay from Farm Bureau, Michigan Chemical Company, or any attorney.

I have contacted many bovine practitioners in Michigan and we would like to present our findings in regard to our experience in a number of herds that we personally have had the care of veterinary problems in which PBB was diagnosed either in the milk or by fat biopsy.

I would first like to state that I subscribe to the cardinal rule of toxicology that all substances are toxic at some level, it is only the dose relationship that makes a substance toxic.

I believe a very brief history of the PBB problem in Michigan might be in order. The first indication that there was a problem came to attention in a herd in the fall of 1973. Listed are some of the symptoms noted in the herd, such as inappetence, lowered milk production, skin disorders, some abortions, and calves hard to raise. In the spring of 1974 (April) the definite identification of the problems was identified as polybrominated biphenyl (PBB). It had been mistakenly mixed in the feed by the elevator thinking it was magnesium oxide. The level mixed in the food was 8 to 10 lbs. per ton of grain ration or 4,000 parts per million.

In controlled experiments at the Ohio experimental station in Wooster, in cattle fed over 25 grams in the ration for 60 days, toxic symptoms were observed. In rations containing 250 mg a day, no toxic symptoms were observed.

After the toxic substance was identified, the Michigan Department of Agriculture secured a list of all the farms that had purchased Farm Bureau feed. The milk was sampled from each of the above herds and any herd where the milk showed contamination above the Federal guidelines, was quarantined. The next step was the testing of individual cows. The guideline set by the Food and Drug Administration was 1 ppm on a fat basis, which was also adopted by the Michigan Department of Agriculture. I would like to mention that PBB was first identified on April 29, 1974, and the first herd was quarantined on May 2, 1974, which I feel is not much time lag when one considers the tremendous job that was encountered. After a time, as more sophisticated equipment to test samples in larger quantities was available, the level was lowered to 0.3 ppm. In the herds tested and found above this level, cattle, sheep, swine, goats, rabbits, and poultry were sent to a burial ground established at Kalkaska, Michigan. I have listed below the number destroyed and buried at Kalkaska.

Cattle	23,715
Goats	2
Horses	2
Poultry	1,511,938
Rabbits	32
Sheep	15,000
Swine	4,646

Food Products Destroyed

Feed	865 tons
Cheese	17,944 pounds
Butter	2,634 pounds
Dried milk	34,000 pounds
Eggs	403,936 dozen

The total number of herds quarantined from 1974 to 1976 was 576.

A great majority of the animals destroyed and buried were not destroyed because of ill health, but because of being over the FDA guideline. To emphasize my pount, I would like to list one of several herds.

When the owner first discovered that this herd was contaminated, the running herd average of DHIA was 17,600 lbs. of milk. This was early 1974. By fall, when the majority of the herd's 100 head was sent to Kalkaska, the running herd average was 18,300 lbs. of milk.

The owner stated that there were no herd health problems except the usual kind that occurs in a herd of this size. He also stated that he had fewer veterinary calls during this period than for previous comparable periods of time. He now has 148 cows in the herd with a running herd average of 18,200 lbs. of milk and 675 lbs. of fat. He has retained some of the original herd.

I would like to devote the rest of my paper to herds that are below the federal guidelines of 0.3 ppm. I have two such herds, and Dr. Hekhuis has twelve herds, and in no way have we encountered problems like Dr. Hellend described and attributed to low levels of PBB. I have several herds that would fit the symptoms Dr. Hellend described, but on milk tests

BRIEF SUMMARY
(For full prescribing information, see package insert.)

Lasix® (furosemide)* Bol-O-Tabs® (2g)

A diuretic-saluretic for prompt relief of edema.

CAUTION: Federal law restricts this drug to use by or on the order of a licensed veterinarian.

INDICATIONS
Cattle:
Lasix® (furosemide) is indicated for the treatment of physiologic parturient edema of the mammary gland and associated structures.

CONTRAINDICATIONS – PRECAUTIONS
Lasix® (furosemide) is a highly effective diuretic-saluretic which, if given in excessive amounts, may result in dehydration and electrolyte imbalance. Therefore, the dosage and schedule may have to be adjusted to the patient's needs. The animal should be observed for early signs of electrolyte imbalance, and corrective measures administered. Early signs of electrolyte imbalance are: increased thirst, lethargy, drowsiness or restlessness, fatigue, oliguria, gastrointestinal disturbances and tachycardia. Special attention should be given to potassium levels. Lasix® (furosemide) may lower serum calcium levels and cause tetany in rare cases of animals having an existing hypocalcemic tendency.

Although diabetes mellitus is a rarely reported disease in animals, active or latent diabetes mellitus may on rare occasions be exacerbated by Lasix® (furosemide).

Electrolyte balance should be monitored prior to surgery in patients receiving Lasix® (furosemide). Imbalances must be corrected by administration of suitable fluid therapy.

Lasix® (furosemide) is contraindicated in anuria. Therapy should be discontinued in cases of progressive renal disease if increasing azotemia and oliguria occur during the treatment. Sudden alterations of fluid and electrolyte imbalance in an animal with cirrhosis may precipitate hepatic coma; therefore, observation during period of therapy is necessary. In hepatic coma and in states of electrolyte depletion, therapy should not be instituted until the basic condition is improved or corrected. Potassium supplementation may be necessary in cases routinely treated with potassium-depleting steroids.

WARNINGS
Lasix® (furosemide) is a highly effective diuretic and, as with any diuretic, if given in excessive amounts may lead to excessive diuresis that could result in electrolyte imbalance, dehydration and reduction of plasma volume, enhancing the risk of circulatory collapse, thrombosis and embolism. Therefore, the animal should be observed for early signs of fluid depletion with electrolyte imbalance, and corrective measures administered. Excessive loss of potassium in patients receiving digitalis or its glycosides may precipitate digitalis toxicity. Caution should be exercised in animals administered potassium-depleting steroids.

Sulfonamide diuretics have been reported to decrease arterial responsiveness to pressor amines and to enhance the effect of tubocurarine. Caution should be exercised in administering curare or its derivatives to patients undergoing therapy with Lasix® (furosemide) and it is advisable to discontinue Lasix® (furosemide) for one day prior to any elective surgery.

CATTLE: Milk taken from animals during treatment and for 48 hours (four milkings) after the last treatment must not be used for food. Cattle must not be slaughtered for food within 48 hours following last treatment.

Lasix® (furosemide) is not indicated during the second trimester of pregnancy.

DOSAGE AND ADMINISTRATION
The usual dose of Lasix® (furosemide) is 1 to 2 mg/lb body weight (approximately 2.5 to 5 mg/kg). A prompt diuresis usually ensues from the initial treatment. Diuresis may be initiated with Lasix® (furosemide) Injection 5% and maintained by oral treatment following a 12-hour interval.

DOSAGE:
Oral: CATTLE
One 2g bolus daily.
Treatment not to exceed 48 hours postparturition.

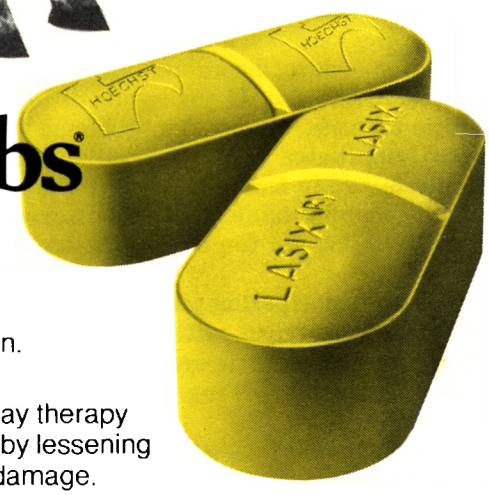
Parenteral: CATTLE
The individual dose administered intramuscularly or intravenously is 500 mg (10 ml) once daily or 250 mg (5 ml) twice daily at 12-hour intervals. **Treatment not to exceed 48 hours postparturition.**

HOW SUPPLIED
Parenteral:
Lasix® (furosemide) Injection 5% (50 mg/ml)
Each ml contains: 50 mg furosemide as a diethanolamine salt preserved and stabilized with myristyl-gamma-picolinium chloride 0.02%, EDTA sodium 0.1%, sodium sulfite 0.1% with sodium chloride 0.2% in distilled water, pH adjusted with sodium hydroxide.
Available in 50 ml multidose vials.

Oral:
Lasix® (furosemide) 2g Bol-O-Tabs®
Each bolus contains 2g of furosemide: 4-chloro-N-furfuryl-5-sulfamoylanthranilic acid.
Available in boxes with 12 Bol-O-Tabs® each.

Now Treat Udder Edema Before Calving

Lasix® (furosemide) Bol-O-Tabs® (2g)



Safe- no risk of abortion.

Effective- two-day therapy rapidly relieves edema, thereby lessening the risk of permanent udder damage.

Convenient- simplified dosage regimen (generally one Bol-O-Tab a day for two days).

Economical- no adverse effect on feeding habits means no loss in milk production following "milk-out" period.

AVAILABLE ONLY FROM LICENSED VETERINARIANS

Lasix® (furosemide) 2g Bol-O-Tabs®
Manufactured By:
Hoechst-Roussel Pharmaceuticals Inc.
Somerville, N.J. 08876

Lasix® (furosemide) Injection 5%
Manufactured By:
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Decatur, Illinois 62525

Manufactured expressly for:
National Laboratories Corp.
Subsidiary of American Hoechst Corporation
Somerville, New Jersey 08876
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*U.S. Patent 3,058,882

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and fat biopsy, we have been unable to confirm PBB present at any detectable levels. In one herd, the perihepatic fat was sent for biopsy (which is supposed to carry the highest level of any fat) and it came back non-detectable.

Another case is a herd from the upper peninsula, which was listed as having all the typical symptoms of a PBB herd and was mentioned as having excellent management as Dr. Hellend stated of the herds he visited. This herd was designated to be sold for beef at the St. Louis, Michigan, Livestock Sale. The beef buyers who purchased the cows returned them, due to adverse publicity, and the possibility of PBB contamination. The ownership was transferred back to the Michigan Livestock Exchange. At this time the Michigan Department of Agriculture and Michigan State University's College of Veterinary Medicine and College of Agriculture and Natural Resources worked out an agreement to move the herd to a farm near Mason, Michigan, for study. Shortly after the herd arrived the cattle were weighed, the milk production recorded, a complete blood profile taken, and a PBB test was run as well as other toxic substances as pesticides and the like. A decision to check for internal and external parasites was made and required treatment. A balanced feed ration was instituted; below is the weight gain.

30 calves and yearling, 137 days, gained 238 lbs.
34 lactating and dry cows, 137 days, gained 238 lbs.
24 open cows, 137 days, gained an average of 337 lbs.

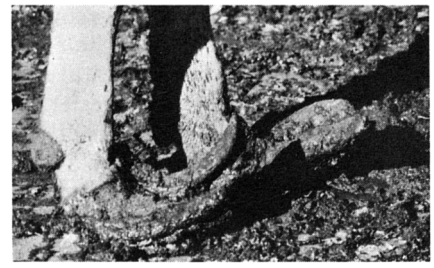
Later on, these cows were sold to a dairyman whom Dr. Hekhuis and I visited in November, 1976. Our comment was that the cattle were too fat.

In regard to calf losses in the one herd I have under my direct supervision, that had PBB the first year after the contamination was discovered, he raised 36 calves from 36 cows, and it has not dropped significantly since. In some other herds that were negative to PBB, and that have never been fed contaminated feed, the calf losses may range from 50% to 60% mortality, and this will continue until some changes are made in management and diet.

Research has been carried out at MSU on a cow from a contaminated herd revealing the following: 1) Holstein cow calved June 3, 1974, and on June 6, 1974, a diagnosis of metritis, mastitis and a left displaced abomasum. The cow was treated for the above-mentioned problems and retained for experimental work. 2) This cow has never been milked or bred back. The biopsy levels taken at different times are as follows:

6-28-74	870 ppm
3-23-76	118 ppm
4- 6-76	98 ppm
7-12-77	64 ppm

During this period of time this cow has been exposed to several experiments which consisted of nine laparotomies, teat fistulas, two partial udder ligations, as well as having 20 gallons of blood drawn from her. I observed this cow in September of 1977 and she would have graded choice. Her hooves were normal. All of the above stress did not appear to affect her immune system to any degree. In regard to long curled up hooves, I would like to show a picture of a cow in a herd of 250 head (Figure 1). We have biopsied her along with 52 other cows and no detectable level has been found. I can recall in my 34 years of practice seeing these same symptoms long before PBB was ever manufactured. I have a feeling that rations, confinement, housing, and possibility inheritance are some of the most contributing causes.



Governor Milliken appointed a committee of toxicologists to study the problem of PBB. Members of the panel were: Dr. Isadore A. Bernstein, Ph.D., University of Michigan; Dr. M. Lloyd Hopwood, Ph.D., Colorado State University; Dr. Nelson S. Irey, M.D., Armed Forces Institute of Pathology; Dr. Frederick W. Oehme, D.V.M., Ph.D., Kansas State University; Dr. B. L. VanDuuren, Sc.D., New York University Medical Center; and Dr. Thomas Tephly, M.D., Ph.D., University of Iowa.

Here is a part of the report from the Scientific Advisory Panel on PBB. "No specific disease of symptomology in animals or man can presently be associated with exposure to low levels of PBB."

I feel that PBB is toxic at high levels, but that it is not a problem at the levels that are now present in Michigan. From the last report of June 29, 1978, there have been 67,627 tissue samples tested and only 1,082 were above the new guideline that the Michigan legislature established, which is 20 parts per billion. The FDA guideline remains at 300 parts per billion. From this group above the allowable levels many were from farms where PBB was not known to exist, and no herd health problems have been reported.

I would like to close with an observation of Paracelsus who lived from 1493 to 1541. He said, "All things are poisonous, for there is nothing without poisonous qualities. It is only the dose which makes things a poison." There have been no exceptions to the rule that compounds whether natural or synthetic follow a dose response relationship with respect to their biological activity. In fact, this is one of the basic biochemical criteria for deciding if one is looking at an effect of a substance in a biological system or just observing an unrelated process. From our experience I am wondering if in some of the herds where PBB is blamed, that an unrelated process is being observed.