A Therapeutic Regimen for Purging Dieldrin from Adulterated Individuals

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SUMMARY

In four feedlots 1013 steers had become contaminated by being fed over 50% of their diet as cull seed potatoes containing 0.1 to 0.2 ppm dieldrin (dry weight basis), developing residues of up to 0.76 ppm (rendered fat). These residues were in excess of federal guidelines (0.30 ppm, rendered fat), but considered non-pathological and without physiological effect. Application of a therapeutic regimen, consisting of an initial injection of testosterone propionate and vitamins A, D and E and of daily oral doses of phenobarbital (first 20 days only) and activated charcoal in a finishing ration, resulted in marked reductions in dieldrin residues within 30 days. The rate of dieldrin loss was increased six-fold and the residual half-life reduced from a reported 150 to 250 days to about 25 to 80 days. The effectiveness of individual components or combinations was not evaluated, but the rate of charcoal feeding appeared most important.

The Problem

The Meat Inspection Division (MID) of the Consumer Market Service (CMS) of the United States Department of Agriculture (USDA), through a selective testing program in slaughter establishments, identified a fat sample from a beef submitted for slaughter in a Portland, Oregon, meat-packing plant to be adulterated with dieldrin[1] (760 ppb). This concentration exceeds the federal administrative guidelines of 300 ppb (ng/gm rendered fat) set for compliance with the "zero tolerance" for dieldrin in food and feedstuff. Subsequent investigation by MID established that cattle in four feedlots in a restricted geographical region of central Oregon

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[1] Dieldrin is used to indicate 1,2,3,4,10,10-hexachloro-6,7-epoxy-1,4,4a,5,6,7,8,8a-octahydro-1,4:5,8-*endo-exo*-dimethanonapthalene.

Bulletin of Environmental Contamination & Toxicology,
Vol. 12, No. 4

contained 140 to 670 ppb dieldrin in rendered fat. The average dieldrin concentration in the rendered fat of 82 steers from these four herds was 330 ± 69 ppb.

The affected herds contained 2600 steers, of which about one-third were dairy-types (predominantly Holstein averaging 1750 lbs) and the remainder beef animals (Hereford, Angus, and black-white faces averaging 1300 lbs). Sampling procedures and brand records cleared 1587 head of contamination, and they were released for slaughter. The remaining 1013 head were to be retained in the feedlots until the average dieldrin concentration in rendered body fat samples taken from 30 randomly-selected steers was at least one standard deviation less than 300 ppb.

Source of Contamination

Investigation of husbandry procedures and medication records and analysis of feedstuffs established that the most likely source of dieldrin exposure was from consumption of cull potatoes raised on soil treated with aldrin[2], a chlorinated hydrocarbon insecticide and a chemical precurser to dieldrin.

In central Oregon cull potatoes comprised a major portion of the rations fed by both cattle feedlot operators and ranchers. This practice was developed and encouraged by a federal diversionary marketing agreement. In addition, ranchers allowed cattle to grub harvested potato fields which contained an average of 1.5 tons of cull potatoes per acre. An estimated 500 pounds of soil was consumed per acre foraged.

Dieldrin/aldrin residues as determined from analysis of washed cull potatoes from the 1970 crop were 10 to 50 ppb (CLAEYS 1971). Potatoes scrubbed with a mechanical brush contained 45% less dieldrin + aldrin than those that were simply washed. Thus, a large portion of the dieldrin associated with cull potatoes was attributed to the soil which remained on the potato. There was less than 1 ppb dieldrin + aldrin residue in any other feedstuff or associated materials (i.e., water, grain, concentrate, roughage, and bedding).

Feedlot operators fed 50 to 65% of the total dry matter of the ration as potatoes. Twenty percent of the total ration was dry matter. The typical feedlot ratio of feedstuffs was 10:1:1/2, respectively, for washed or scrubbed cull potatoes, pelleted concentrate and poor quality roughage. Adulteration of the steers was due to the large amount of potatoes (and soil) consumed. The concentration of dieldrin in the total ration on a dry matter basis was 70 to 100 ppb or approximately one-third the dieldrin concentration in the adipose tissue.

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[2]Aldrin is used to indicate 1,2,3,4,10,10-hexachloro-1,4,4a,5,8,8a-hexahydro-1,4:5,8-*endo-exo*-dimethanonapthalene.

The estimated ratio of the concentration of dieldrin in whole cull potatoes to rendered fat from adulterated steers was 1:12. However, on a dry matter basis, cull potatoes contained 100 to 200 ppb dieldrin. On a whole tissue basis, fat contained 220 to 350 ppb dieldrin, approximately twice as much as the potatoes.

Addition of cull potatoes to the feedlot rations and grubbing of harvested potato fields were discontinued when it was determined that this was the most probable source of contamination. The cattle were then fed a high concentrate feedlot ration, consisting mainly of barley and pelleted concentrate, to maintain or increase weight and finish.

Therapy

Rationale. Without intervention other than to remove the source of dieldrin, the half-life of dieldrin in cattle tissue is estimated to be between 100 and 250 days (assuming first-order loss rate) (STREET et al. 1966a; HUNTER and ROBINSON 1967; HIRONAKA 1968; GARRETTSON and CURLEY 1969). Since 80 to 200 days would be required in this instance for sufficient dieldrin to be metabolized and excreted to permit the cattle to be marketed, and because of the high per diem costs of maintaining beef animals beyond a finished condition, this method of decontamination was economically unsatisfactory to the feedlot owners. Various methods for successful intervention in reducing residues of persistent pesticides in dairy cattle have been reviewed by COOK (1971). Thus, after consultation with Drs. R. W. Cook of Michigan State University and J. C. Street of Utah State University, a therapeutic regimen[3] was devised and initiated to purge dieldrin from these animals.

Three methods have demonstrated degrees of efficacy in hastening loss of persistent pesticides (DDT, dieldrin) from cattle: a) dietary charcoal treatment to prevent adsorption and resorption of dieldrin in the enterohepatic cycle (BRAUND et al. 1968b; WILSON and COOK 1970); b) dietary barbiturate to induce hepatic microsomal detoxication of dieldrin (STREET et al. 1968a,b; BRAUND et al. 1968b; COOK and WILSON 1970); and c) injections of vitamins A, D and E (HIRONAKA 1968). Reported absorption of dieldrin from the intestine of the rat (HARR et al. 1970), dog and man (SOTO and DEICHMANN 1967), and cattle (BRAUND et al. 1968a) suggests that 95 to 98% of dieldrin ingested at the low concentration found in the cull potatoes would be absorbed. Subsequently dieldrin is recycled into the

[3]The authors make no claims explicit or implied as to the safety and acceptability of this regimen for use in purging animals or human beings contaminated with chlorinated hydrocarbon pesticides. Use of tradenames does not constitute an endorsement of any particular product necessarily to the exclusion of any other and is included for the convenience of the reader.

gastrointestinal tract by release into bile (HEATH and VANDEKAR 1964), saliva, and gastric juices (WILSON and COOK 1970). Binding to charcoal, the dieldrin would pass on out in the feces.

The metabolic pathways for the breakdown and excretion of dieldrin are not completely understood, but it is known that both dieldrin and phenobarbital are slowly metabolized by hepatic microsomal mixed function oxidases which may be induced (i.e., increased in amount) by exposure to a number of drugs, pesticides, and natural products, including both dieldrin and phenobarbital (CONNEY 1967). Induction by phenobarbital results in increased urinary excretion of dieldrin metabolites and increased biliary excretion of dieldrin into the intestine (CUETO and HAYES 1965; STREET et al. 1966a; BRAUND et al. 1968b; COOK and WILSON 1970). STREET et al. (1966b) reported that male rats excrete dieldrin and its metabolites more rapidly than females or castrates. HIRONAKA (1968) found that heifers excrete dieldrin more rapidly than steers.

Regimen. Based on the principles of the above approaches, a regimen (Table 1) was devised consisting of a single, initial intramuscular injection of testosterone propionate and vitamins A, D and E, and then daily oral doses (as a top dressing mixed with concentrate) of phenobarbital for 20 days and activated charcoal for 30 days.

It was estimated that 10 mg of testosterone propionate per head would provide about the equivalent hormonal level of an uncastrated animal. The vitamin dosages given by HIRONAKA (1968) were 10^6 IU of vitamin A, 10^5 IU of vitamin D_2, and 100 IU of vitamin E in 2 ml per steer (800 lbs/head) three times at two-week intervals. Since reductions in tissue dieldrin were not significant at that dosage, the recommended dosage herein was increased to the same dose per 500 lbs of steer. However, due to the large numbers of animals and the short time of treatment, the recommendation was for only a single, initial dose.

A daily dosage of between 5 and 10 g of phenobarbital/1000 lbs of steer was estimated (STREET et al. 1966a; BRAUND et al. 1968b; COOK and WILSON 1970) to be necessary in inducing a two- to fourfold increase in dieldrin metabolism and excretion. Because of anticipated adverse clinical effects on fattened steers in the dry, hot (42°C) climate of the region, the recommended dosage was reduced to 2 g/1000 lbs/day. The chemical treatment would be stopped 10 days prior to termination of treatment to permit a feed-off period and avoid contamination with phenobarbital residues.

The dosage of activated charcoal reported in the literature is 2.5 lbs/1000 lbs of steer/day (BRAUND et al. 1968b; WILSON and COOK 1970). The 160-mesh fine powder form employed provides optimal surface area relative to the increasing difficulty of handling and mixing finer material. Charcoal is expensive and tends to settle out when mixed with feed concentrates, so the recommended dosage was reduced to 0.25 lbs/1000 lbs/day.

TABLE 1

THERAPEUTIC REGIMEN FOR REDUCING DIELDRIN RESIDUES IN BEEF CATTLE

Agent	Treatment	Recommended Dosage	Actual Dosage Used	Comments
Activated charcoal, 160 mesh (Aqua-NuChar, Sears Roebuck & Co., Portland)	Fed as top dressing for 30 days	2.5 lbs per 1000 lbs per day	0.1 to 0.25 lbs/1000 lbs/day	Difficult to mix and handle, settles out; expensive at rec. rate
Phenobarbital Sodium, USP (American Chem. Co., Portland)	Fed as top dressing for 20 days	5 to 10 g/1000 lbs/day for max. effect; 2 g 1000 lbs/day for min. effect	0.9 to 1.2 g/1000 lbs/day	Cattle not adversely affected, some reported mild sedation
Vitamins A, D, and E (Burns Pharmaceutical Co.)	Intramuscular injection	Single dose of $2x10^6$ IU of A, $2x10^5$ IU of D_2, and 100 IU of E/1000 lbs at start treatment	Same	Effect not proven
Testosterone propionate (Burns Pharmaceutical Co.)	Intramuscular injection	10 mg/head, single dose at start of treatment	Same	Effect not proven

Procedures. Samples of back fat were collected by biopsy on May 15-21 (initial), June 21 (pre-treatment) and July 21, 1971, (post-treatment). The steers were detained in a dehorning chute under a spinal block while a 1 to 3 g sample of back fat was removed surgically from the tail head area between the spinal ridge and the crest of the illium.

At the time of pre-treatment and post-treatment sampling and at an intermediate period (July 1) 50-ml samples of oxalated whole blood and 20-ml samples of serum were taken from the same series of steers biopsied for back fat, in an attempt to establish a ratio between dieldrin concentrations in body fat and blood lipid as reported for rats (HARR et al. 1970) and human beings (HUNTER and ROBINSON 1967). Fat, blood, and serum samples were analyzed by either the MID Laboratory or by Dr. R. D. Rateliff of VTL-USDA. The former reported dieldrin residues in adipose tissue on the basis of rendered (extracted) fat, whereas the latter reported on the basis of whole fat (wet weight, fresh adipose tissue). Eleven samples of fat collected July 21 were divided and analyzed at both laboratories, forming a basis for conversion of all data to ppm rendered fat.

Additionally, at each of the feedlots at the pre-treatment, intermediate, and post-treatment sampling times a sample of premix and three samples of the mixed barley ration were taken and assayed by R. R. Claeys to monitor the extent of contamination of the diet during therapy.

Results and Discussion

The data and results are summarized in Table 2. Due to mixing errors in administration of phenobarbital, the dosage was reduced by feedlot owners to 0.8 to 1.2 g/1000 lbs of steer/day. Problems in handling the charcoal resulted in variable dosage between feedlots, ranging from 0.1 to 0.25 lbs/1000 lbs of steer/day. The cattle were not depressed by the phenobarbital and no adverse effect of the regimen was observed.

Comparison of analyses by the two laboratories was good, with rendered fat values being about 1.38 times the fresh tissue values; the average variation of the ratio of the comparable samples was about 10%. Since the adipose tissue of finished cattle would be expected to contain about 0.8 to 0.9 g lipid/g tissue, yielding a lipid concentration to tissue concentration ratio of 1.1 to 1.25, the recovery by MID may have been low for either dieldrin and/or lipid. Lacking measurement of lipid content of each tissue sample, it is not possible to derive more than the effect of the overall treatment from the data, notably because the pre-treatment mean concentration (determined by VTL) averaged higher after conversion to a rendered fat basis than the initial levels for two of the feedlots and the overall average. Alternatively, if the adipose tissue is assumed to be 90% lipid and recoveries by MID to be 85%, the

TABLE 2

SUMMARY OF DATA

Item	Feedlot 1	Feedlot 2	Feedlot 3	Feedlot 4	Mean (Total)
No. of cattle treated	66	134	500	313	(1013)
Phenobarbital consumed (g/1000 lbs b.w./day)	1.2	1.1	0.9	1.0	1.1
Charcoal consumed (g/1000 lbs b.w./day)	45	117	90	78	82
Dieldrin residues[a] (ug/g rendered fat in adipose tissue)					
Initial (May 15-21)	0.36±0.02(5)	0.38±0.02(13)	0.44±0.01(19)	0.42±0.02(13)	0.40±0.01 (50)
Pre-treat (June 21)	0.32±0.05(2)	0.40±0.04(7)	0.56±0.07(9)	0.40±0.03(10)	0.44±0.03(28)
Post-treat (July 21)	0.21±0.05(2)	0.31±0.05(6)	0.24±0.02(10)	0.21±0.03(9)	0.28±0.01(27)
Percent loss of dieldrin residues[b]					
Pre-treatment	11	(+5)	(+27)	5	(+4)
During treatment	34	22.5	57	47	40

[a]Mean ± s.e., numbers of samples in parentheses; values for fresh adipose (all pre-treatment samples and some post-treatment samples) multiplied by 1.384 g adipose/g lipid.

[b]Values in parentheses indicate dieldrin residue increases; calculated only for animals sampled at all periods.

adjusted means would be 0.48 ppm lipid (initial), 0.36 ppm lipid (pre-treatment), and 0.21 ppm lipid (post-treatment). In any case, the residues were significantly reduced ($P<0.01$) during the 30-day treatment. Ratios of blood or serum to adipose were too variable to permit estimation of tissue residues from blood analyses. All but 1 of the 1013 cattle were released for slaughter as non-adulterated after a 15-day post-treatment feed-off period.

The effect of each component of the treatment regimen is not clear. There appears to be a linear correlation between the charcoal consumption and the extent of dieldrin reduction for three of the feedlots, in agreement with WILSON and COOK (1970), COOK and WILSON (1970), and BRAUND et al. (1968a, 1968b, 1970) and contrary to FRIES et al. (1970). Depending upon the basis for the analytical results discussed earlier, the pre-treatment rate of loss of dieldrin was increased two- to six-fold, shortening the biological half-life from 150-250 days to 25-80 days. Since the regimen was designed only to purge dieldrin from tissues of adulterated cattle to allow their sale as consumable meat products, and not to evaluate the factors in that regimen, these results suggest that further investigation of each component is indeed warranted. The proportional contribution of the four agents comprising this regimen should be evaluated singly and in combination under controlled conditions.

Acknowledgements

The authors would like to thank Dr. James Locke, DVM, of the Redmond, Oregon, Veterinary Clinic for his contribution of professional service, time and advice which were vital to the success of solving this problem. We also wish to thank Dr. J. Berger, DVM, and Mr. R. Cooley, of the Oregon State Veterinarians Office and Drs. R. R. Claeys, J. M. Witt, and Mr. J. Capizzi of the Oregon Agricultural Experiment Station for their capable and extensive assistance. In addition, the Burns Pharmaceutical Company, the Shell Chemical Company, the Oregon Beef Industry, and the Agricultural Research Service of the USDA provided financial assistance and technical support. Cooperation of Drs. R. D. Radecliff and H. F. Crookshank and Mr. D. E. Clark of the USDA was excellent.

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