TOXICOKINETICS OF POLYCHLORINATED DIBENZO-P-DIOXINS AND -FURANS (PCDD/Fs) IN SHEEP AND LAMBS.

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INTRODUCTION

Since 1989, PCDD/Fs have been monitored routinely in i.a. the milk of cows and fat of sheep in some parts of The Netherlands (1). In connection with this programme several toxicokinetic studies with PCDD/Fs in lactating and non-lactating cows were carried out to investigate the distribution and elimination of these compounds (2-5). From the results of the monitoring programme it appeared that in sheep higher concentrations of these compounds were found than in cows. To find an explanation for this difference, a toxicokinetic investigation in sheep was started. Additional objectives of this study were to clarify the role of fat metabolism in the distribution of these compounds in the organism and to study the transfer of PCDD/Fs from ewes to their lambs. A part of this study is presented here.

MATERIALS AND METHODS

Ten pregnant sheep were purchased from farms afflicted with dioxin contamination problems. All animals were in good health and weighed between 68 and 78 kg after lambing. After arrival at the Institute the animals were fed concentrate and hay obtained from a non-contaminated area in rations complying with Dutch Feeding Requirements. From the second week a mixture of PCDD/Fs (130 ng I-TEQ/animal/day) was added to the concentrate for eight consecutive days (see table 1). The last day this artificially contaminated feed was given to the animals was designated day nr. 0 of the experiment. Immediately after lambing the animals were divided in three groups depending on the date of partus. The first sheep to lamb was placed in group III, the next in group II and the third in group I etc. Any ewes with a single lamb which should have been allocated to group III were placed in either group I or II. The lambs of group I and II were slaughtered immediately after birth and fat samples were taken. The ewes in these groups were set dry. The sheep of group II received 5 mg/animal/day of the β-agonist Clenbuterol mixed with the concentrate for a period of eight weeks after lambing. The lambs in group III (two lambs per sheep) were allowed to suckle their mothers: one for four weeks and the other for eight weeks. Then the lambs were slaughtered and fat samples taken. Fat biopsies were taken

from the sheep under local anaesthesiac 1, 2, 4, 8, 16 and 32 weeks after lambing and milk samples were taken 1, 2, 4 and 8 weeks after lambing. All samples were analyzed by gas chromatography-mass spectrometry as described previously (6). Half-lives were derived from the last four data points of each sheep.

RESULTS AND DISCUSSION

During the experiment the animals were in good health. The weight of the animals in group I and II varied only slightly during the experiment. The sheep in groups III lost some weight. Because the sheep did not lamb simultaneously the PCDD/F-concentrations in fat were measured in different periods of the elimination phase. In figure 1 the concentrations (pg I-TEQ/g) in body fat of the sheep of each group are given. These figures suggest that after lambing a redistribution of the PCDD/Fs takes place. The higher concentrations in fat of two sheep in group III can be explained by a lower body fat content of these sheep in comparison with the other animals. From the figures it is also clear that the elimination rates are different for the groups, as expected. In table 1 the dose and the mean half-lives for the groups I and III are listed as far as they could be calculated.

Table 1. Dose and half-lives (mean ± s.d.) of PCDD/Fs in sheep of groups I (n=2) and III (n=3).

Congeners	Dose (ng/day for 8 days)	Half-lives (days) group I	Half-lives (days) group III
2378-TCDD	20	148 ± 2	74 ± 19
12378-PeCDD	20	168 ± 6	81 ± 20
123478-HxCDD	40	204 ± 15	96 ± 39
123678-HxCDD	112	210 ± 4	96 ± 35
123789-HxCDD	64	95 ± 11	51 ± 7
1234678-HpCDD	1470	176 ± 17	84 ± 48
23478-PeCDF	38	145 ± 0	77 ± 16
123478-HxCDF	60	226 ± 1	109 ± 42
123678-HxCDF	79	156 ± 22	68 ± 17
234678-HxCDF	101	124 ± 12	65 ± 15
1234678-HpCDF	606	166 ± 26	88 ± 47
I-TEQ	130	156 ± 1	79 ± 20

The half-lives found in non-lactating sheep are somewhat shorter than in non-lactating cows (5) and those in lactating sheep are twice as long as in lactating cows (4). This may be explained by assuming a relatively large fat compartment and a relatively low milk fat production rate in sheep as compared to cows. This lower elimination rate of PCDD/Fs

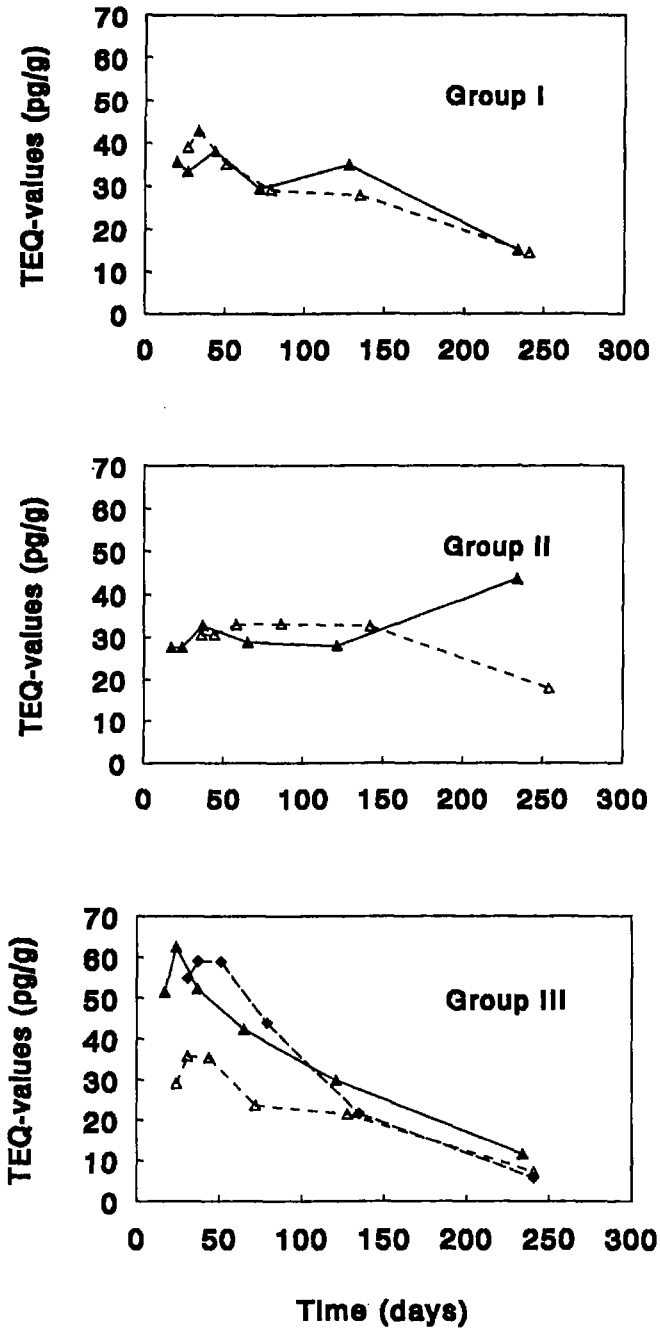

Figure 1. I-TEQ-values (pg/g) in fat of sheep after lambing. Group I: Non-lactating; Group II: Non-lactating and 5 mg/animal/day Clenbuterol during 8 weeks; Group III: Lactating for 8 weeks.

could explain why higher concentrations were found in sheep than in cows from the same area. Alternatively, the lactation period of sheep is much shorter than that of cows, so that accumulation of PCDD/Fs can take place over a longer period. In table 2 the concentration ratios of PCDD/Fs in body fat of lambs and their mothers are listed. At birth all ratios were low except for the tetra-substituted congeners. However, after the beginning of lactation the concentration ratios of all con-geners increased rapidly until the fourth week. Between week four and week eight no further increase was seen.

Table 2. Mean ratios (n=2) of PCDD/F-concentrations in fat of lambs after feeding with contaminated milk and their mothers on different days after lambing.

Congeners	Day 0[1]	Day 28	Day 56
2378-TCDD	0.65	1.20	1.24
12378-PeCDD	0.20	0.94	1.02
123478-HxCDD	0.05	0.53	0.49
123678--HxCDD	0.05	0.54	0.55
123789-HxCDD	0.01	0.46	0.35
2378-TCDF	0.29	0.14	0.21
12378-PeCDF	0.07	0.11	-
23478-PeCDF	0.20	0.92	0.83
123478-HxCDF	0.06	0.66	0.58
123678-HxCDF	0.08	0.51	0.38
234678-HxCDF	0.03	0.49	0.35
I-TEQ	0.27	0.88	0.80

[1] Concentration ratio of lamb fat at birth and mother fat one week after lambing.

CONCLUSIONS

The half-life of PCDD/Fs (expressed as I-TEQ) in non-lactating sheep is about 160 days. In lactating sheep the half-life is about half of that in non-lactating sheep. The main exposure route for lambs is the milk from their mothers. Total exposure by milk is at least a factor of four larger than via the placenta. Placenta transfer was higher for the lower substituted congeners, particularly for 2378-TCDD.

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