

Table 7.

Serum levels of thyroid-related hormones of the offspring exposed to anti-thyroid agents during the period from mid-gestation to lactation

	Anti-thyroid agent in the drinking water			
	Untreated control	3 ppm PTU	12 ppm PTU	200 ppm MMI
PND 21				
No. of offspring examined	10	10	9 ^a	9
T3 (ng/ml)	1.22 ± 0.1 ^b	0.97 ± 0.31	0.25 ± 0.03 **	0.43 ± 0.19 **
T4 (ug/ml)	4.72 ± 0.84	1.86 ± 0.41	1.06 ± 0.32 **	1.06 ± 0.44 **
TSH (ng/ml)	6.80 ± 2.11	27.38 ± 13.66 **	27.69 ± 5.74 **	35.33 ± 12.69 **
PNW 11				
No. of offspring examined	10	10	6	10
T3 (ng/ml)	1.02 ± 0.08	0.93 ± 0.11	0.84 ± 0.10 **	0.88 ± 0.09 **
T4 (ug/ml)	5.11 ± 0.70	5.12 ± 0.73	4.05 ± 0.71	4.57 ± 1.04
TSH (ng/ml)	9.81 ± 3.16	9.10 ± 3.25	7.75 ± 2.23	9.41 ± 4.40

^a N=7 for measurement of T3 and T4 levels.

^b Mean±SD.

Abbreviations: PTU, propylthiouracil; MMI, methimazole; PND, postnatal day; PNW, postnatal week.

** Significantly different from the controls by Dunnett's test or Dunnett-type rank-sum test (** p < 0.01).

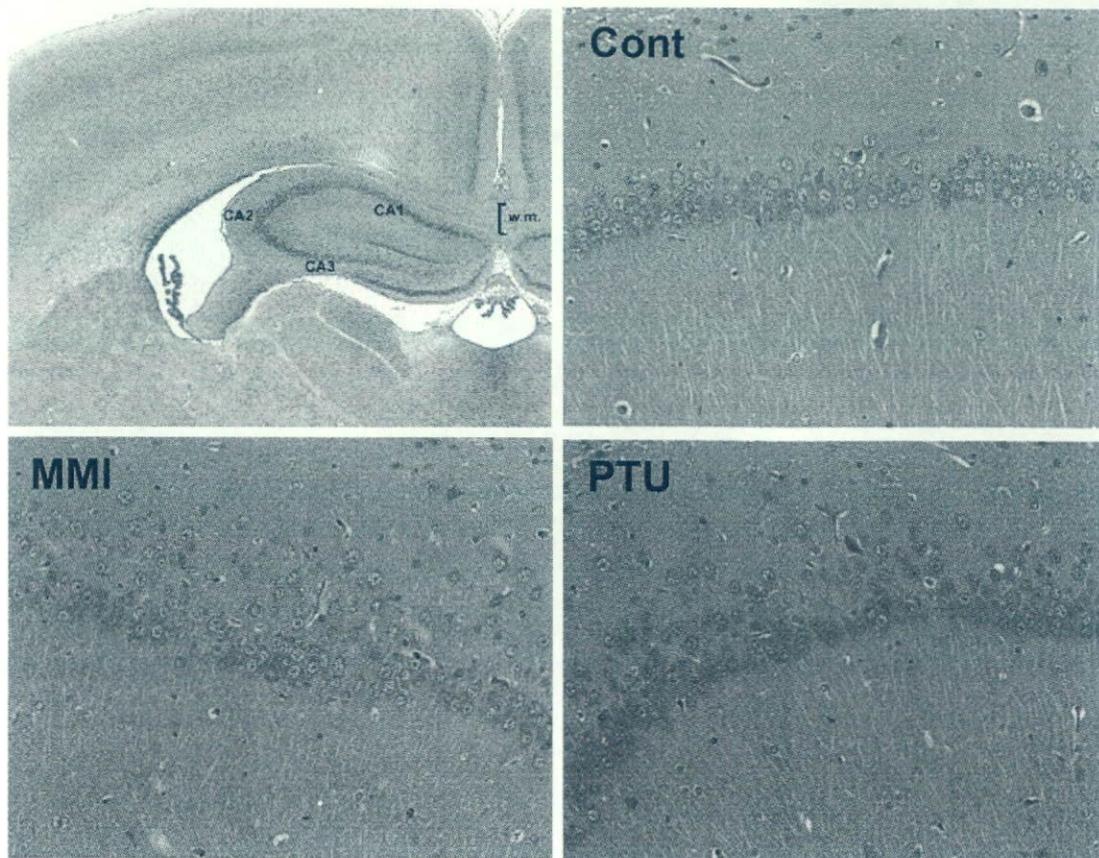


Fig. 18.

Changes in the hippocampal CA1 neurons of rats at PNW11 exposed perinatally to PTU or MMI

Table 8.**Measurement of the area of corpus callosum and density of CNPase-positive cells in the parietal cortex of male offspring at PNW11 exposed perinatally to PTU or MMI until weaning**

	Control	PTU (ppm)		MMI (ppm)
		3	12	200
No. of animals examined	10	10	6	10
Corpus callosum Area (mm ²)	0.137 ± 0.014 ^a	0.114 ± 0.022*	0.08 ± 0.029**	0.093 ± 0.023**
CNPase-positive cells Counts/mm ²	144.0 ± 22.1	115.3 ± 17.5	92.6 ± 9.5**	87.6 ± 6.8**

^aMean ± SD.*, **: Significantly different from the controls at $P < 0.05$ and $P < 0.01$, respectively

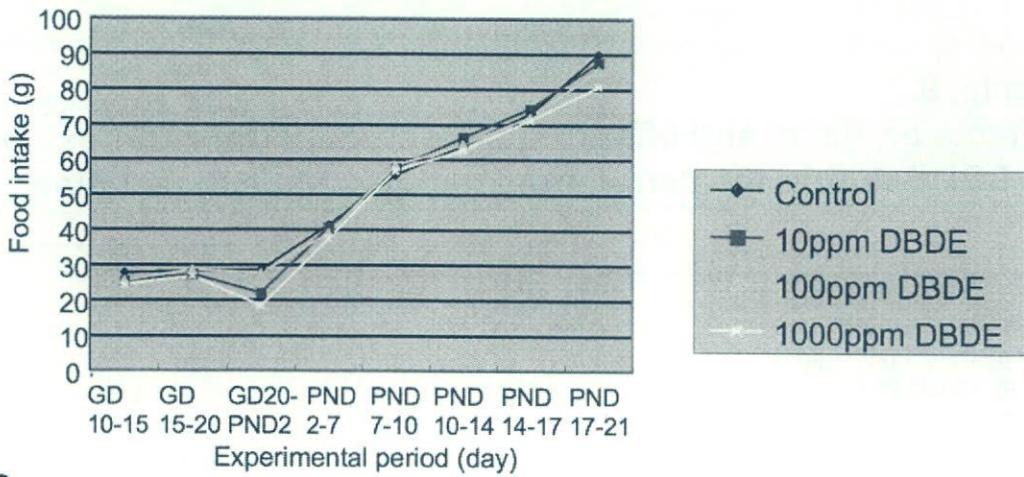


Fig. 19.
Food intake of dams exposed perinatally to DBDE during the period from mid-gestation to lactation

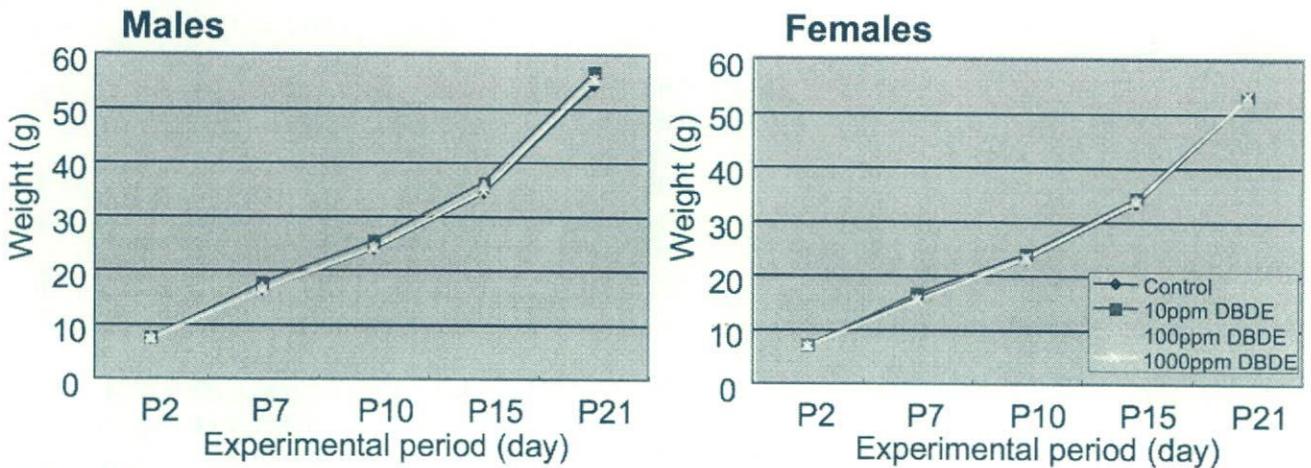


Fig. 20.
Growth curves during the lactation period of offspring exposed perinatally to DBDE during the period from mid-gestation

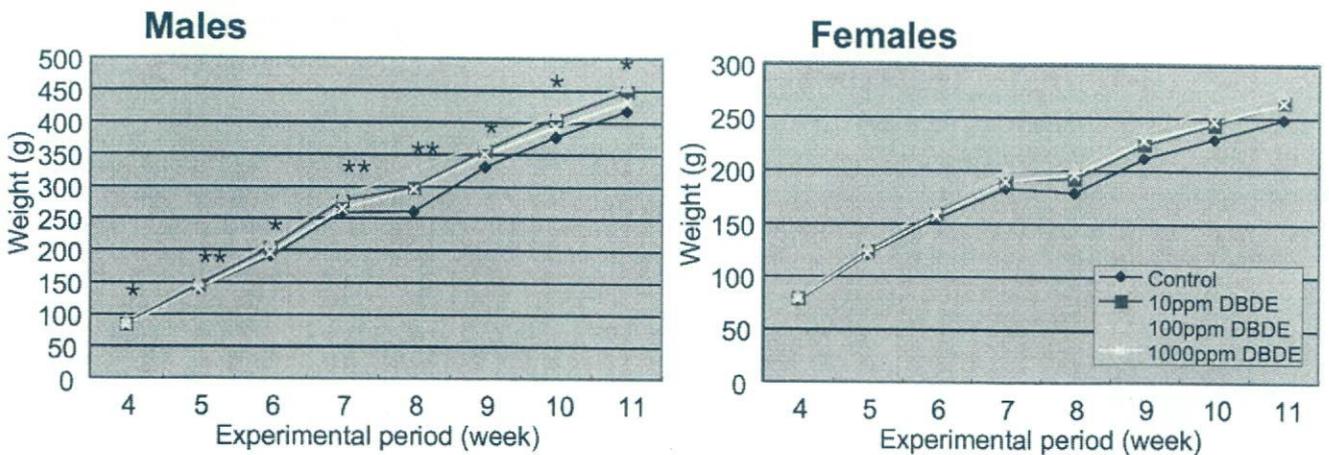


Fig. 21.
Growth curves after weaning for offspring exposed perinatally to DBDE during the period from mid-gestation

*P<0.05, **P<0.01 vs. control

Table 9.

Effects on dams and offspring until prepubertal necropsy of exposure to DBDE during the period from mid-gestation to lactation

	DBDE in diet (ppm)			
	0	10	100	1000
No. of dams examined	8	8	8	8
Maternal parameter				
Body weight gain (g/day)				
GD 10-GD 20	10.37 ± 1.55 ^a	10.47 ± 1.51	11.05 ± 1.67	10.99 ± 1.04
PND 2-PND 10	4.6 ± 1.17	5.59 ± 1.92	5.06 ± 1.54	5.54 ± 2.23
PND 10-PND 21	-0.23 ± 0.86	-0.37 ± 1.37	-0.7 ± 1.74	0.14 ± 1.48
PND 21				
BW (g)	302.0 ± 25.3	302.3 ± 21.8	311.4 ± 24.0	302.2 ± 23.5
Thyroid weight (mg/100 g BW)	5.95 ± 0.56	7.20 ± 0.93 [*]	6.48 ± 0.93	7.17 ± 1.08 [*]
Offspring parameter				
No. of implantation sites	13.0 ± 2.4	13.1 ± 1.5	12.4 ± 1.9	13.4 ± 1.3
No. of live offspring	12.4 ± 2.6	12.1 ± 1.7	11.5 ± 2.4	12.5 ± 2.0
Male ratio (%)	47.5 ± 16.2	53.7 ± 14.6	46.7 ± 17.3	38.4 ± 7.0
BW, PND 2 (g)				
Males	7.46 ± 0.58	7.45 ± 1.00	7.50 ± 1.06	7.07 ± 0.73
Females	7.05 ± 0.57	6.99 ± 0.87	6.92 ± 1.10	6.69 ± 0.82
AGD, PND 2 (mm)				
Males	3.89 ± 0.05	3.88 ± 0.29	4.07 ± 0.47	3.84 ± 0.12
Females	1.93 ± 0.14	1.87 ± 0.02	1.93 ± 0.01	1.78 ± 0.02
Relative organ weights, PND 21				
No. of offspring examined	10	10	10	10
Males				
BW (g)	51.6 ± 6.2	55.8 ± 4.0	52.7 ± 6.0	54.0 ± 3.0
Liver (g/100g BW)	3.62 ± 0.26	3.98 ± 0.12 [*]	3.90 ± 0.29 [*]	4.39 ± 0.27 ^{**}
Kidneys (g/100g BW)	1.08 ± 0.07	1.10 ± 0.04	1.09 ± 0.14	1.08 ± 0.08
Brain (g/100g BW)	2.94 ± 0.36	2.72 ± 0.15	2.83 ± 0.28	2.73 ± 0.17
Adrenals (mg/100g BW)	17.7 ± 6.9	21.9 ± 4.2	24.6 ± 8.6	19.3 ± 6.7
Testes (g/100g BW)	0.41 ± 0.04	0.40 ± 0.03	0.41 ± 0.04	0.41 ± 0.05
Epididymides (g/100g BW)	0.062 ± 0.009	0.074 ± 0.045	0.068 ± 0.047	0.056 ± 0.012
Females				
BW (g)	49.8 ± 4.2	48.4 ± 7.3	48.0 ± 4.5	51.3 ± 4.5
Liver (g/100g BW)	3.71 ± 0.23	3.77 ± 0.26	3.80 ± 0.26	4.31 ± 0.20 ^{**}
Kidneys (g/100g BW)	1.16 ± 0.06	1.17 ± 0.11	1.14 ± 0.10	1.15 ± 0.09
Brain (g/100g BW)	2.83 ± 0.16	2.98 ± 0.37	2.98 ± 0.29	2.74 ± 0.13
Adrenals (mg/100g BW)	22.7 ± 10.4	20.5 ± 6.3	18.4 ± 7.7	22.0 ± 4.9
Ovaries (mg/100g BW)	33.3 ± 17.9	29.0 ± 8.1	34.9 ± 15.4	31.5 ± 6.4
Uterus (g/100g BW)	0.072 ± 0.053	0.070 ± 0.015	0.069 ± 0.016	0.067 ± 0.013

^a Mean ± SD.

Abbreviations: DBDE, decabromodiphenyl ether; GD, gestational day; PND, postnatal day; BW, body weight; AGD

* ** Significantly different from the controls by Dunnett's test or Dunnett-type rank-sum test (* $p < 0.05$, ** $p < 0.01$).

Table 10.
Onset of puberty and estrous cyclicity of offspring exposed to DBDE during the period from mid-gestation to lactation

	DBDE in diet (ppm)			
	0	10	100	1000
Onset of puberty				
Males				
No. of animals examined	11	12	11	12
Age by day	41.1 ± 1.5 ^a	40.1 ± 1.5	41.5 ± 1.6	41.3 ± 2.1
BW	190 ± 14.4	192 ± 18.8	209 ± 28.6	193 ± 19.2
Females				
No. of animals examined	11	12	12	11
Age by day	35.1 ± 2.4	34.4 ± 2.0	34.7 ± 2.4	34.8 ± 2.4
BW	121.5 ± 8.99	126.0 ± 19.8	126.6 ± 15.2	121.9 ± 11.8
Estrous cyclicity during PNW 8-11				
No. of animals examined	10	10	10	10
Irregularity (Extended diestrus)	1	1	2	1

^a Mean ± SD.

Abbreviations: DBDE, decabromodiphenyl ether; BW, body weight; PNW, postnatal week.

Table 11.
Serum levels of thyroid-related hormones of the offspring exposed to DBDE during the period from mid-gestation to lactation

	DBDE in diet (ppm)			
	0	10	100	1000
PND 21				
No. of offspring examined	10	10	10	10
T3 (ng/ml)	1.39 ± 0.11 ^a	1.35 ± 0.15	1.33 ± 0.18	1.17 ± 0.10 ^{**}
T4 (ug/ml)	5.19 ± 0.74	4.89 ± 0.84	5.66 ± 0.71	4.89 ± 0.54
TSH (ng/ml)	5.38 ± 0.89	5.12 ± 0.71	5.85 ± 1.22	4.74 ± 0.69
PNW 11				
No. of offspring examined	10	10	10	10
T3 (ng/ml)	0.99 ± 0.09	1.01 ± 0.08	1.01 ± 0.11	1.02 ± 0.11
T4 (ug/ml)	6.02 ± 0.70	6.00 ± 0.66	5.98 ± 0.94	5.17 ± 0.57 [*]
TSH (ng/ml)	8.30 ± 3.40	8.81 ± 1.63	9.71 ± 3.45	10.47 ± 2.35

^a Mean±SD.

Abbreviations: DBDE, decabromodiphenyl ether; PND, postnatal day; PNW, postnatal week
^{*}, ^{**} Significantly different from the controls by Dunnett's test or Dunnett-type rank-sum test (* p<0.05, ** p<0.01).

Table 12.**Body and organ weights of offspring exposed to DBDE during the period from mid-gestation to lactation. PNW 11.**

	DBDE in diet (ppm)			
	0	10	100	1000
Males				
No. of animals examined	10	10	10	10
BW (g)	414.4 ± 22.3 ^a	447.8 ± 24.1 *	455.1 ± 22.9 **	423.2 ± 34.5
Liver (g/100g BW)	3.66 ± 0.18	3.65 ± 0.20	3.62 ± 0.10	3.42 ± 0.29
Kidneys (g/100g BW)	0.69 ± 0.03	0.67 ± 0.05	0.70 ± 0.03	0.66 ± 0.06
Brain (g/100g BW)	0.50 ± 0.03	0.47 ± 0.03 *	0.46 ± 0.02 *	0.50 ± 0.04
Adrenals (mg/100g BW)	10.9 ± 1.8	9.8 ± 1.8	11.0 ± 1.8	10.9 ± 2.5
Testes (g/100 g BW)	0.74 ± 0.14	0.73 ± 0.05	0.72 ± 0.05	0.77 ± 0.04
Epididymides (g/100g BW)	0.24 ± 0.02	0.22 ± 0.01	0.22 ± 0.02	0.24 ± 0.03
Females				
No. of animals examined	10	11	10	11
BW (g)	254.0 ± 20.8	260.4 ± 17.8	278.2 ± 26.7	267.7 ± 30.3
Liver (g/100g BW)	3.34 ± 0.2	3.36 ± 0.28	3.44 ± 0.22	3.45 ± 0.35
Kidneys (g/100g BW)	0.68 ± 0	0.65 ± 0.04	0.67 ± 0.04	0.63 ± 0.06
Brain (g/100g BW)	0.78 ± 0.1	0.75 ± 0.06	0.70 ± 0.06 *	0.73 ± 0.06
Adrenals (mg/100g BW)	21.1 ± 2.2	20.4 ± 3.1	19.7 ± 3.4	20.7 ± 3.0
Ovaries (mg/100g BW)	32.0 ± 5.1	32.1 ± 3.8	32.4 ± 5.5	34.4 ± 6.6
Uterus (g/100g BW)	0.19 ± 0.02	0.20 ± 0.06	0.16 ± 0.02	0.20 ± 0.05

^a Mean ± SD.

Abbreviations: DBDE, decabromodiphenyl ether; PNW, postnatal week.

*, ** Significantly different from the controls (* p<0.05, ** p<0.01).

Table 13.**Measurement of the area of corpus callosum and density of CNPase-positive cells in the parietal cortex of male offspring at PNW11 exposed perinatally to DBDE until weaning**

	DBDE (ppm)			
	0	10	100	1000
No. of animals examined				
Corpus callosum				
Area (mm ²)	0.18 ± 0.03 ^a	0.15 ± 0.02	0.12 ± 0.02 **	0.13 ± 0.03 **
CNPase-positive cells				
Counts/mm ²	150.9 ± 23.0	137.7 ± 10.8	122.4 ± 13.9 **	124.9 ± 13.0 **

** Significantly different from the controls (**p<0.01).

Table 14.
Body and organ weights of dams at weaning in the preliminary dose-finding studies of HBCD and TBBPA

	Control	HBCD (ppm)		TBBPA (ppm)	
		1000	10,000	1000	10,000
No of animals	3	3	3	3	3
Body weight (g)	337.7±43.0	342.7±21.8	334.5±5.3	344.9±39.2	340.6±20.2
Thyroid (mg)	17.6±2.5	19.4±3.3	21.0±4.9	15.5±4.3	23.2±3.6
Thyroid (mg/100g BW)	5.23±0.76	5.64±0.61	6.28±1.53	4.44±0.74	6.81±0.79
Liver (g)	16.9±1.7	16.4±0.8	18.5±0.4	16.5±2.4	16.2±1.1
Liver (g/100g BW)	5.0±0.3	4.8±0.3	5.5±0.2	4.8±0.1	4.8±0.1

Table 15.
Pregnancy and delivery-related parameters in the preliminary dose-finding studies of HBCD and TBBPA

	Control	HBCD (ppm)		TBBPA (ppm)	
		1000	10,000	1,000	10,000
No of animals	3	3	3	3	3
Duration of pregnancy (d)	21.7±0.6	21.3±0.6	22.0±0.0	21.0±0.0	21.7±0.6
No. of implantation sites	14.7±1.2	13.7±1.2	14.0±2.0	13.3±1.5	13.3±2.5
No. of pups delivered	14.3±0.6	12.7±0.6	13.7±2.1	13.0±1.0	12.0±2.6
No. of dead offspring	0.33±0.58	0	0	0	0.33±0.58
Male ratio	44.1±21.6	60.2±9.7	42.5±10.0	28.1±11.1	55.5±1.7

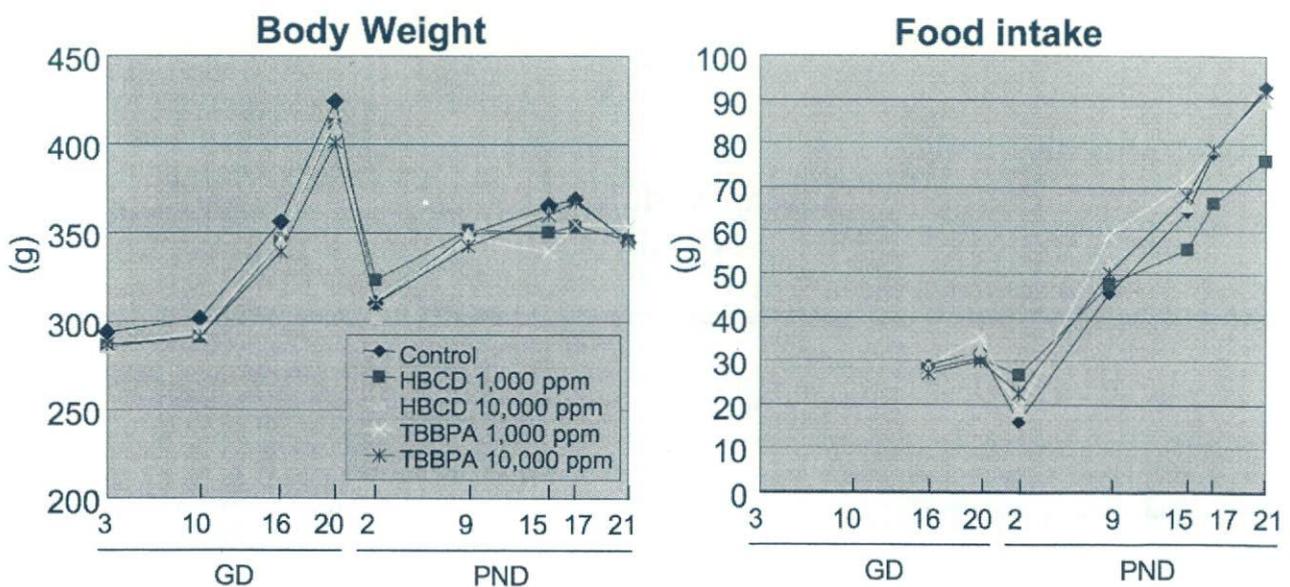


Fig. 22.
Growth curves and food intake of dams during exposure in the preliminary dose-finding studies of HBCD and TBBPA

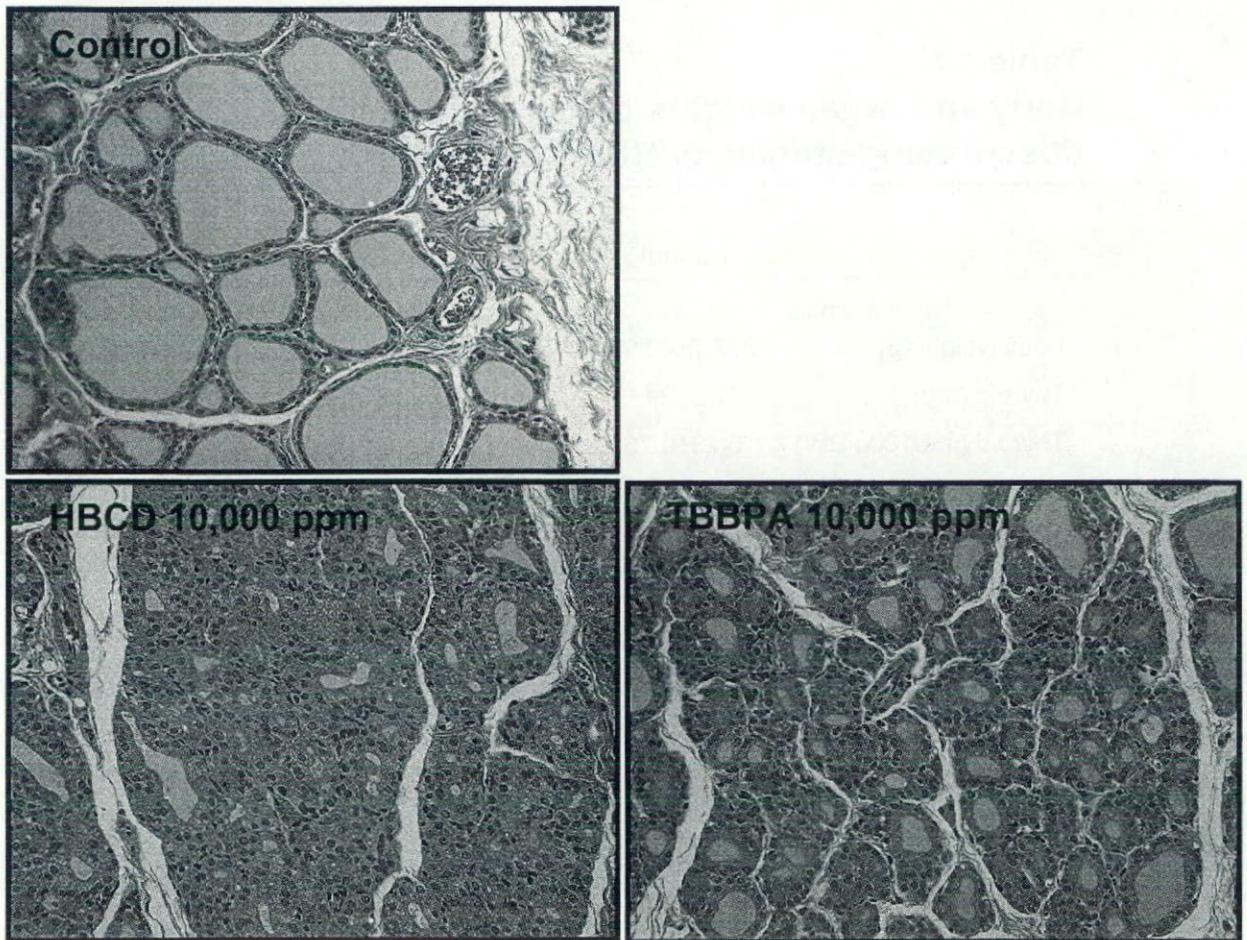


Fig. 23.
Histopathology of the thyroid lesions of dams exposed to HBCD or TBBPA during the period from mid-pregnancy and lactation

Table 16.
Histopathological grading of diffuse follicular cell hypertrophy of dams exposed to HBCD or TBBPA during the period from mid-pregnancy and lactation

	Control	HBCD (ppm)		TBBPA (ppm)	
		1000	10,000	1,000	10,000
Diffuse follicular cell Hypertrophy (-/±/+/++)	(2, 1, 0, 0)	(0, 2, 1, 0)	(0, 0, 2, 1)	(1, 2, 0, 0)	(0, 2, 1, 0)

Table 17.

Anogenital distance of offspring at PND2 exposed to HBCD or TBBPA during the period from mid-pregnancy and lactation

AGD (mm)	Control	HBCD (ppm)		TBBPA (ppm)	
		1000	10,000	1000	10,000
Males	3.90±0.20	3.93±0.23	3.93±0.06	3.70±0.20	4.07±0.15
Females	1.93±0.06	1.93±0.06	1.93±0.06	1.87±0.12	1.93±0.06

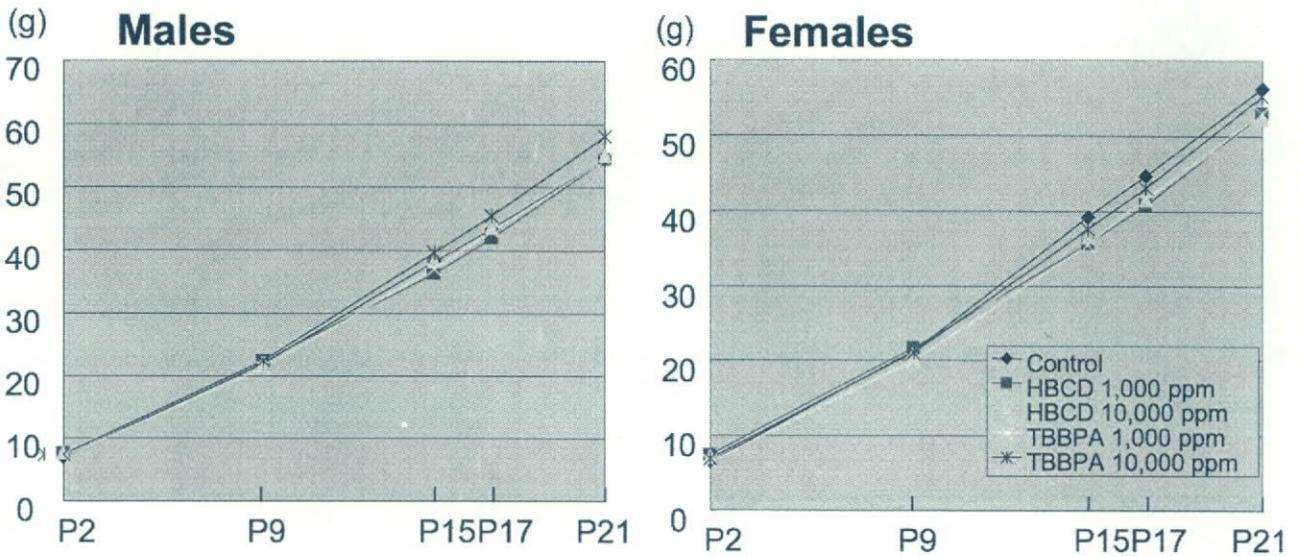


Fig. 24.

Body weight of offspring exposed to HBCD or TBBPA during the period from mid-pregnancy and lactation

Table 18.
Morphometry of the hippocampal CA1 region of the offspring exposed to antithyroid agents during the period from the mid-gestation to the end of lactation examined at PNW11.

	0	MMI (ppm)		PTU (ppm)	
		200	3	12	
No. of offspring examined	10	10	10	6	
Hippocampal CA1 neurons					
Mean distance from the baseline of the pyramidal cell layer (μm)	29.2 \pm 2.6 ^a	49.7 \pm 11.1*	65.2 \pm 13**	61.0 \pm 13.2**	
No. of neurons located outside of the pyramidal cell layer (/mm baseline)	11.0 \pm 3.9	86.8 \pm 32.8**	110.8 \pm 25.7**	82.7 \pm 19.5**	
Ratio of abnormally migrated neurons/ total neurons (%)	4.6 \pm 1.4	31.1 \pm 11.1**	29.9 \pm 7.6**	37.0 \pm 11.1**	

^a Mean \pm SD.

Abbreviations: MMI, methimazole; PTU, proptlthiouracil; PNW, postnatal week

* ** Significantly different from the controls by Dunnett's test or Dunnett-type rank-sum test (* $p < 0.05$, ** $p < 0.01$).

Table 19.
Morphometry of the hippocampal CA1 region of the offspring exposed to decabromodiphenyl ether during the period from the mid-gestation to the end of lactation examined at PNW11.

	DBDE in diet (ppm)			
	0	10	100	1000
No. of offspring examined	10	10	10	10
Hippocampal CA1 neurons				
Mean distance from the baseline of the pyramidal cell layer (μm)	33.8 \pm 4.4 ^a	32.5 \pm 3.4	32.3 \pm 3.5	32.2 \pm 5.3
No. of neurons located outside of the pyramidal cell layer (/mm baseline)	5.3 \pm 2.4	7.2 \pm 3.2	5.8 \pm 2.6	5.2 \pm 2.4
Ratio of abnormally migrated neurons/ total neurons (%)	2.7 \pm 0.9	3.2 \pm 1.3	2.9 \pm 1.1	2.6 \pm 1.0

^a Mean \pm SD.

Abbreviations: DBDE, decabromodiphenyl ether; PNW, postnatal week

** Significantly different from the controls by Dunnett's test or Dunnett-type rank-sum test (** $p < 0.01$).

Table 20.
Histopathologic findings for male and female rats exposed to decabromodiphenyl ether during the period from the mid-gestation to the end of lactation.

	DBDE in diet (ppm)			
	0	10	100	1000
PNW 3				
Males				
No. of animals examined	10	10	10	10
Liver				
Diffuse liver cell hypertrophy (\pm /+/++) ^a	0	10 ^b (8/2/0) ^c *** ^{##}	10 (4/6/0)** ^{##}	10 (0/2/8)** ^{##}
Kidneys				
Increased eosinophilia, cytoplasm, cortical proximal tubules (\pm /+)	1 (1/0)	4 (4/0)	7 (5/2)** [#]	10 (1/9)** ^{##}
Thyroid				
Diffuse follicular cell hypertrophy (\pm /+)	0	1 (1/0)	3 (2/1)	9 (3/6)** ^{##}
Females				
No. of animals examined	10	10	10	10
Liver				
Diffuse liver cell hypertrophy (\pm /+)	0	0	3 (2/1)	7 (1/6)** ^{##}
Kidneys				
Increased eosinophilia, cytoplasm, cortical proximal tubules (\pm /+)	0	7 (5/2)** ^{##}	6 (5/1)* [#]	7 (4/3)** ^{##}
Thyroid				
Diffuse follicular cell hypertrophy (\pm /+)	0	2 (2/0)	0	3 (3/0)
Ovaries				
Increase of interstitial glands (+)	0	0	0	2
PNW 11				
Males				
No. of animals examined	10	10	10	10
Thyroid				
Diffuse follicular cell hypertrophy (\pm /+/++)	0	3 (1/2/0)	2 (2/0/0)	4 (2/1/1)
Mammary gland				
Diffuse lobular atrophy (\pm /+/++)	2 (0/1/1)	3 (1/2/0)	6 (2/2/2)	3 (2/0/1)
Females				
No. of animals examined	10	11	10	11
Thyroid				
Diffuse follicular cell hypertrophy (\pm /+)	0	0	1 (1/0)	1 (0/1)
Uterus				
Hydrometra (+)	0	1	0	3

^a Grade of change: (\pm /+), slight; (++) , moderate, marked.

^b Total No. of animals with each finding.

^c No. of animals with each grade.

*** Significantly different from the controls by Fisher's exact probability test (* $p < 0.05$, ** $p < 0.01$).

^{##} Significantly different from the controls by Mann-Whitney's *U*-test ([#] $p < 0.05$, ^{##} $p < 0.01$).

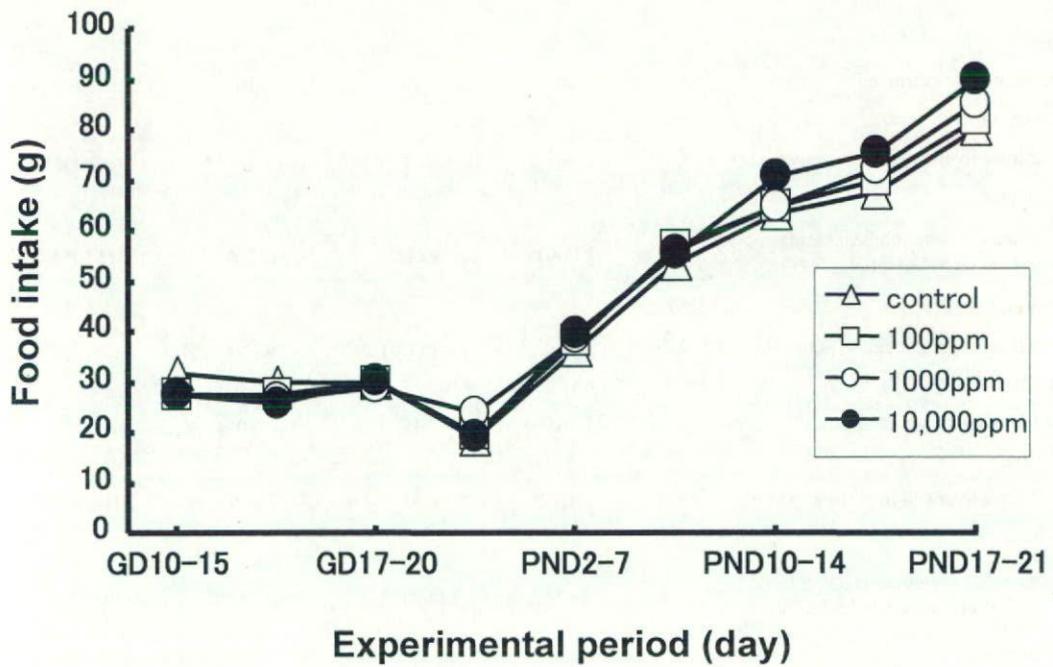


Fig. 25.
Food intake of dams exposed to hexabromocyclododecane (HBCD) during the period from the mid-gestation to the end of lactation.

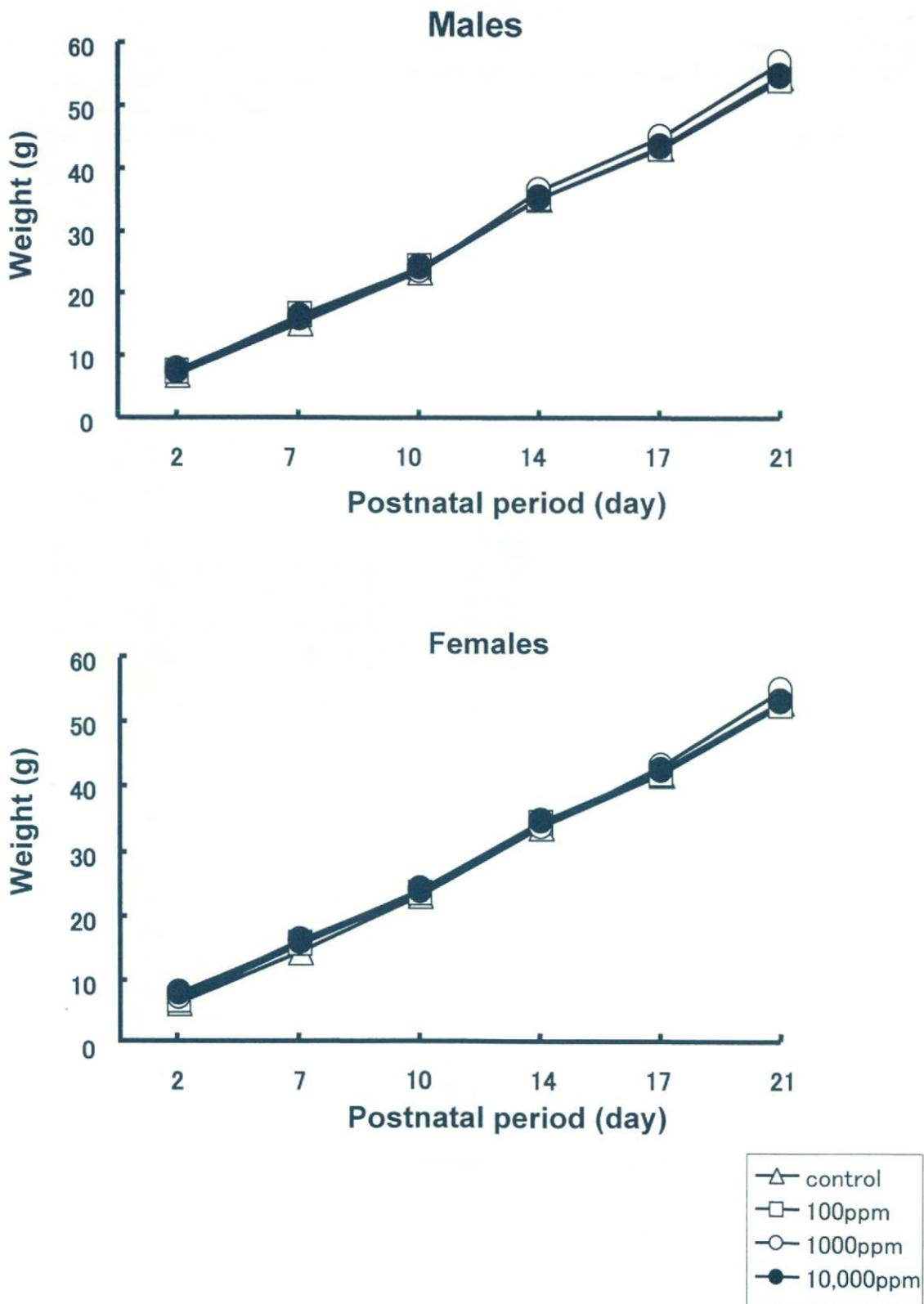


Fig. 26. Growth curves during the lactation period of offspring exposed to hexabromocyclododecane (HBCD) during the period from the mid-gestation to the end of lactation.

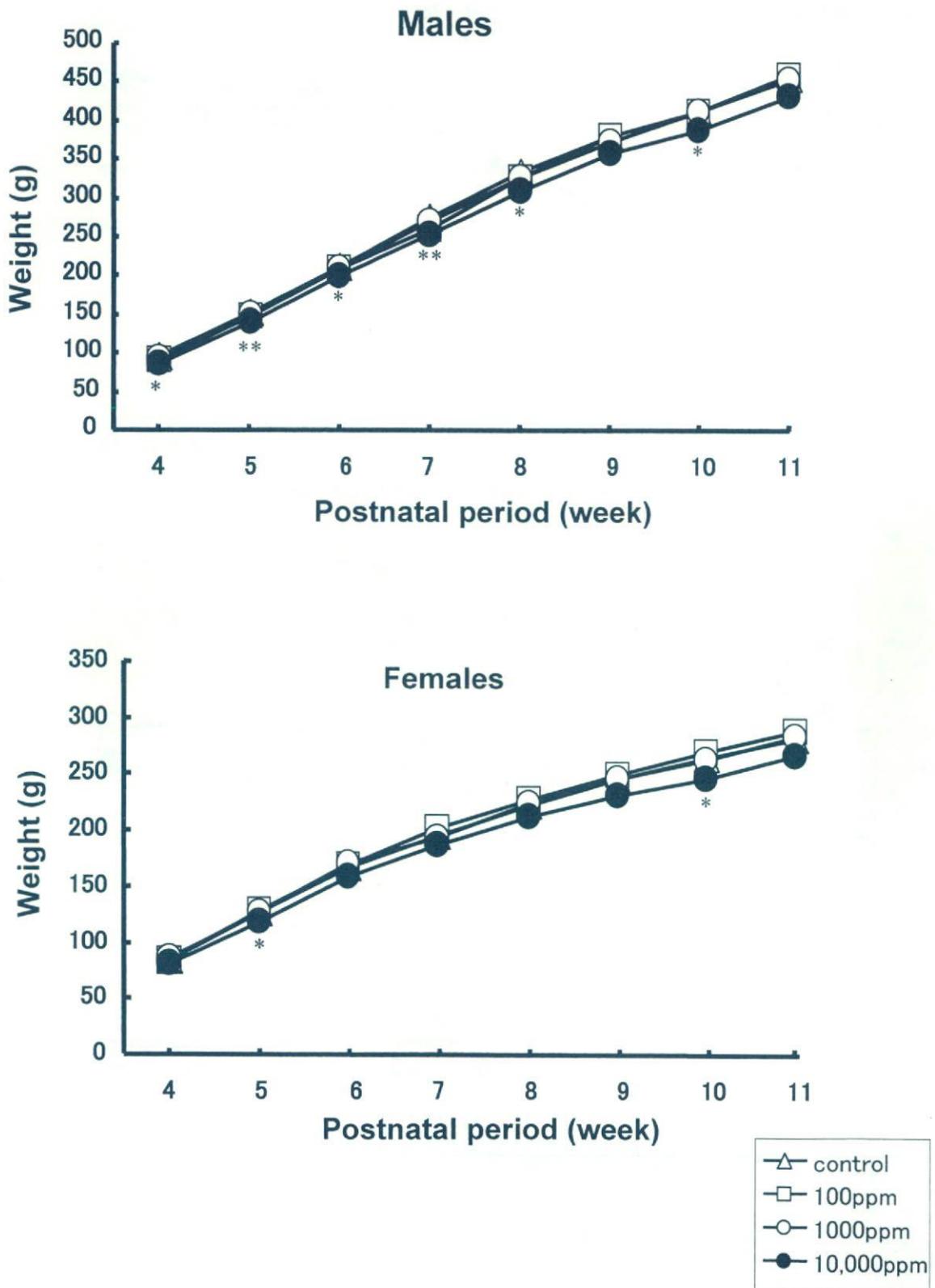
Table 21.
Effects on dams and offspring until prepubertal necropsy in the exposure study of hexabromocyclododecane during the period from the mid-gestation to the end of lactation

	HBCD in diet (ppm)			
	0	100	1000	10,000
No. of dams examined	10	10	10	10
Maternal parameter				
Body weight gain (g/day)				
GD 10-GD 20	11.22 ± 1.85 ^a	11.08 ± 1.34	10.72 ± 1.18	11.34 ± 1.12
PND 2-PND 10	4.70 ± 1.82	4.20 ± 2.70	4.00 ± 1.49	5.02 ± 1.74
PND 10-PND 21	1.58 ± 1.11	0.64 ± 0.96	1.16 ± 1.15	1.13 ± 1.17
PND 21				
BW (g)	339.3 ± 27.3	323.3 ± 26.6	334.0 ± 25.7	336.5 ± 26.4
Thyroid weight (mg/100 g BW)	5.73 ± 0.90	6.75 ± 0.99	6.30 ± 0.80	7.47 ± 1.05*
Offspring parameter				
No. of implantation sites	13.7 ± 1.9	14.2 ± 1.6	12.4 ± 1.4	14.0 ± 1.6
No. of live offspring	13.0 ± 1.8	13.0 ± 1.6	11.6 ± 1.6	12.9 ± 1.4
Male ratio (%)	48.5 ± 16.2	59.3 ± 14.2	48.7 ± 20.2	45.7 ± 9.5
BW, PND 2 (g)				
Males	7.11 ± 0.66	7.22 ± 0.56	7.65 ± 0.95	7.15 ± 0.80
Females	6.53 ± 0.59	6.84 ± 0.50	7.28 ± 0.75	6.84 ± 0.81
AGD, PND 2 (mm)				
Males	3.88 ± 0.23	3.96 ± 0.20	4.08 ± 0.30	4.01 ± 0.23
Females	2.13 ± 0.60	1.94 ± 0.08	2.00 ± 0.17	2.03 ± 0.12
Relative organ weights, PND 21				
No. of offspring examined				
Males				
BW (g)	54.3 ± 3.5	51.2 ± 7.3	56.7 ± 4.1	54.0 ± 3.3
Liver (g/100g BW)	3.68 ± 0.11	3.82 ± 0.31	3.98 ± 0.15	4.66 ± 0.35*
Kidneys (g/100g BW)	1.12 ± 0.05	1.12 ± 0.05	1.12 ± 0.05	1.09 ± 0.05
Brain (g/100g BW)	2.76 ± 0.20	3.00 ± 0.46	2.67 ± 0.18	2.78 ± 0.34
Spleen (g/100g BW)	0.39 ± 0.05	0.35 ± 0.09	0.41 ± 0.06	0.37 ± 0.06
Thymus (g/100g BW)	0.36 ± 0.06	0.40 ± 0.06	0.42 ± 0.04	0.39 ± 0.05
Adrenals (mg/100g BW)	26.6 ± 2.5	29.7 ± 2.6	31.9 ± 5.2*	31.0 ± 5.5
Testes (g/100g BW)	0.43 ± 0.04	0.43 ± 0.03	0.43 ± 0.05	0.40 ± 0.03
Epididymides (g/100g BW)	0.063 ± 0.016	0.068 ± 0.008	0.071 ± 0.012	0.068 ± 0.013
Females				
BW (g)	50.3 ± 3.4	50.0 ± 6.0	53.7 ± 5.5	51.3 ± 2.9
Liver (g/100g BW)	3.77 ± 0.17	3.83 ± 0.23	4.01 ± 0.25	4.83 ± 0.26*
Kidneys (g/100g BW)	1.21 ± 0.07	1.12 ± 0.08*	1.17 ± 0.08	1.17 ± 0.05
Brain (g/100g BW)	2.88 ± 0.23	2.89 ± 0.29	2.72 ± 0.23	2.73 ± 0.12
Spleen (g/100g BW)	0.38 ± 0.05	0.36 ± 0.06	0.41 ± 0.05	0.37 ± 0.04
Thymus (g/100g BW)	0.39 ± 0.08	0.41 ± 0.09	0.46 ± 0.07	0.42 ± 0.07
Adrenals (mg/100g BW)	31.4 ± 6.3	30.3 ± 3.6	30.3 ± 2.1	27.8 ± 4.9
Ovaries (mg/100g BW)	32.3 ± 3.9	30.9 ± 4.9	28.1 ± 6.3	28.7 ± 3.4
Uterus (g/100g BW)	0.078 ± 0.013	0.078 ± 0.010	0.075 ± 0.010	0.071 ± 0.011

^a Mean ± SD.

Abbreviations: DBDE, decabromodiphenyl ether; GD, gestational day; PND, postnatal day; BW, body weight; AGD, anogenital distance.

* Significantly different from the controls by Dunnett's test or Dunnett-type rank-sum test (* $p < 0.01$).



* $P < 0.05$, ** $P < 0.01$ vs. control

Fig. 27.
 Growth curves after weaning for offspring exposed to hexabromocyclododecane (HBCD) during the period from the mid-gestation to the end of the lactation.

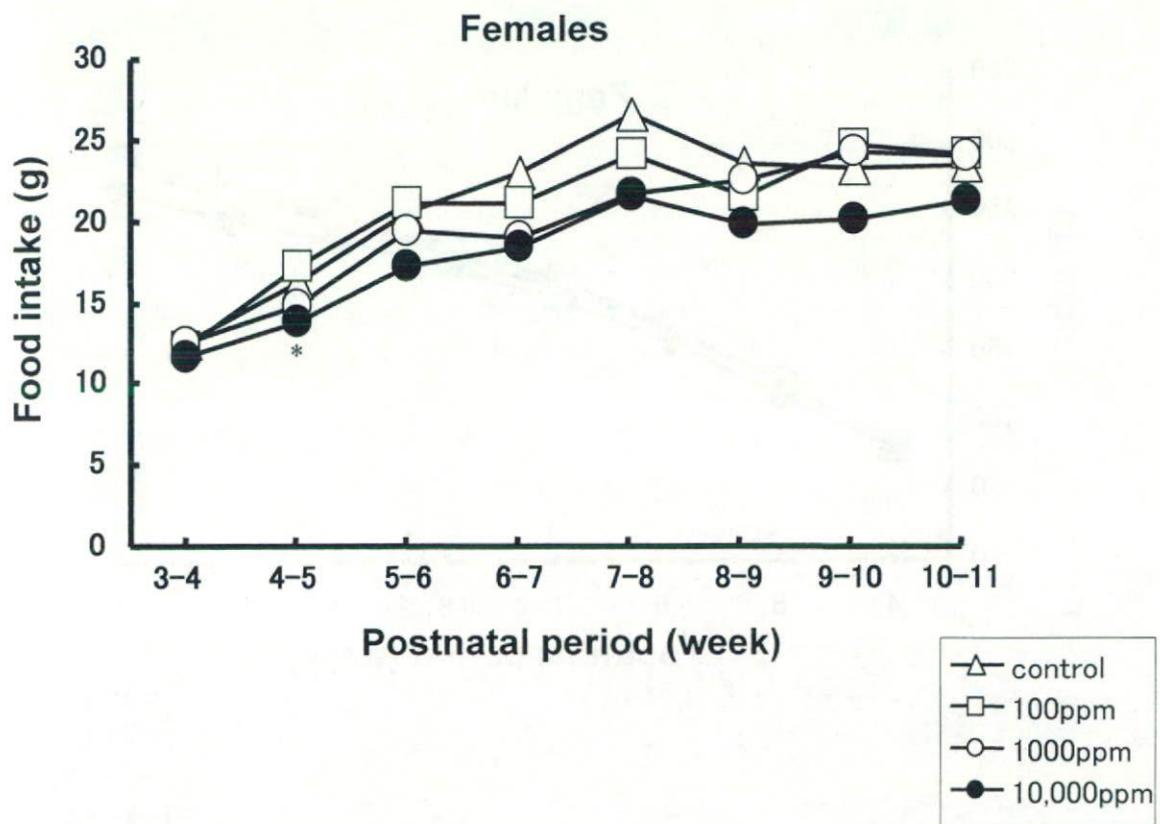
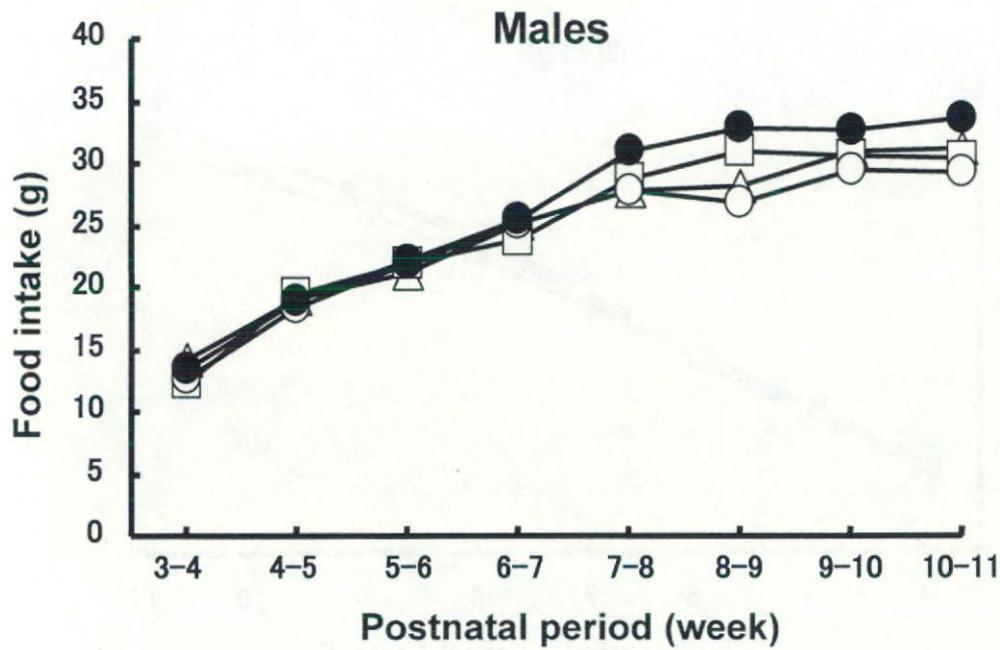


Fig. 28. Food intake of offspring exposed to hexabromocyclododecane (HBCD) during the period from the mid-gestation to the end of lactation.

Table 22.**Onset of puberty and estrous cyclicity of the offspring exposed to hexabromocyclododecane during the period from the mid-gestation to the end of lactation**

	HBCD in diet (ppm)			
	0	100	1000	10,000
Onset of puberty				
Males				
No. of animals examined	13	14	12	14
Age by day	40.7 ± 1.9 ^a	40.6 ± 1.3	40.8 ± 2.0	41.1 ± 1.6
BW	204.3 ± 15.7	198.3 ± 20.4	203.2 ± 15.0	195.8 ± 10.1
Females				
No. of animals examined	14	12	14	13
Age by day	35.4 ± 1.9	35.6 ± 1.8	34.9 ± 1.7	34.4 ± 2.1
BW	130.8 ± 11.7	133.8 ± 10.8	129.2 ± 13.5	118.6 ± 11.7*
Estrous cyclicity during PNW 8–11				
No. of animals examined	10	10	10	10
Irregularity (Extended diestrus)	1	2	0	0

^a Mean ± SD.

Abbreviations: HBCD, hexabromocyclododecane; BW, body weight; PNW, postnatal week.

* Significantly different from the controls by Dunnett's test or Dunnett-type rank-sum test (* p<0.05).

Table 23.**Serum levels of thyroid-related hormones of the offspring exposed to hexabromocyclododecane during the period from the mid-gestation to the end of lactation**

	HBCD in diet (ppm)			
	0	100	1000	10,000
PND 21				
No. of offspring examined	10	10	10	10
T3 (ng/ml)	1.09 ± 0.11 ^a	1.13 ± 0.12	1.06 ± 0.08	0.93 ± 0.10**
T4 (µg/dl)	4.39 ± 0.93	4.20 ± 0.77	4.78 ± 0.49	4.20 ± 0.52
TSH (ng/ml)	5.40 ± 0.62	6.66 ± 1.24	6.07 ± 1.41	7.00 ± 1.31*
PNW 11				
No. of offspring examined	10	10	10	10
T3 (ng/ml)	0.96 ± 0.06	0.93 ± 0.07	0.88 ± 0.05*	0.89 ± 0.06**
T4 (µg/dl)	4.77 ± 0.70	4.84 ± 0.59	5.21 ± 0.65	5.20 ± 0.98
TSH (ng/ml)	4.74 ± 0.62	5.81 ± 1.72	5.36 ± 1.11	4.96 ± 0.80

^aMean±SD.

Abbreviations: HBCD, hexabromocyclododecane; PND, postnatal day; PNW, postnatal week.

*, ** Significantly different from the controls by Dunnett's test or Dunnett-type rank-sum test (* p<0.05, ** p<0.01).

Table 24.

Body and organ weights of the offspring exposed to hexabromocyclododecane during the period from the mid-gestation to the end of lactation examined at PNW 11.

	HBCD in diet (ppm)			
	0	100	1000	10,000
Relative organ weights, PNW 11				
Males				
No. of animals examined	10	10	10	10
BW (g)	454.3 ± 25.4 ^a	456.9 ± 24.8	450.8 ± 33.4	435.1 ± 24.6
Brain (g/100g BW)	0.46 ± 0.03	0.46 ± 0.02	0.47 ± 0.04	0.47 ± 0.02
Pituitary (mg/100g BW)	3.35 ± 0.19	3.43 ± 0.35	3.30 ± 0.21	3.24 ± 0.30
Spleen (g/100g BW)	0.18 ± 0.02	0.21 ± 0.03	0.19 ± 0.02	0.19 ± 0.02
Thymus (g/100g BW)	0.13 ± 0.03	0.14 ± 0.03	0.12 ± 0.04	0.12 ± 0.03
Liver (g/100g BW)	3.45 ± 0.27	3.81 ± 0.23**	3.58 ± 0.24	3.53 ± 0.22
Kidneys (g/100g BW)	0.66 ± 0.05	0.67 ± 0.05	0.67 ± 0.04	0.66 ± 0.05
Adrenals (mg/100g BW)	13.0 ± 1.5	12.4 ± 1.2	11.6 ± 1.8	12.3 ± 2.5
Testes (g/100 g BW)	0.77 ± 0.07	0.73 ± 0.04	0.78 ± 0.09	0.74 ± 0.05
Epididymides (g/100g BW)	0.23 ± 0.02	0.21 ± 0.01*	0.22 ± 0.02	0.21 ± 0.01
Prostate, ventral (mg/100g BW)	0.13 ± 0.02	0.13 ± 0.04	0.12 ± 0.03	0.12 ± 0.01
Prostate, dorso-lateral (mg/100g BW)	0.13 ± 0.03	0.13 ± 0.01	0.14 ± 0.03	0.13 ± 0.02
Seminal vesicles (mg/100g BW)	0.27 ± 0.05	0.26 ± 0.03	0.26 ± 0.05	0.26 ± 0.05
Thyroid (mg/100g BW)	4.85 ± 0.69	5.66 ± 0.67	5.78 ± 0.82*	6.20 ± 1.03**
Females				
No. of animals examined	10	10	10	10
BW (g)	286.2 ± 25.2	293.4 ± 21.5	289.2 ± 24.4	270.7 ± 19.6
Brain (g/100g BW)	0.68 ± 0.07	0.65 ± 0.05	0.68 ± 0.06	0.71 ± 0.04
Pituitary (mg/100g BW)	5.94 ± 1.00	5.63 ± 0.64	5.72 ± 1.31	5.71 ± 0.63
Spleen (g/100g BW)	0.19 ± 0.02	0.20 ± 0.03	0.21 ± 0.02	0.20 ± 0.03
Thymus (g/100g BW)	0.18 ± 0.03	0.19 ± 0.06	0.17 ± 0.04	0.16 ± 0.05
Liver (g/100g BW)	3.35 ± 0.20	3.59 ± 0.19	3.44 ± 0.25	3.30 ± 0.22
Kidneys (g/100g BW)	0.69 ± 0.03	0.65 ± 0.03	0.69 ± 0.06	0.65 ± 0.05
Adrenals (mg/100g BW)	21.1 ± 3.4	22.6 ± 2.0	23.7 ± 2.3	24.2 ± 4.7
Ovaries (mg/100 g BW)	31.8 ± 6.1	32.8 ± 2.6	32.2 ± 5.7	34.0 ± 4.8
Uterus (g/100g BW)	0.16 ± 0.04	0.15 ± 0.02	0.16 ± 0.02	0.17 ± 0.03
Thyroid (mg/100g BW)	8.20 ± 2.94	6.84 ± 0.81	7.35 ± 0.87	7.72 ± 0.83

^a Mean ± SD.

Abbreviations: HBCD, hexabromocyclododecane; PNW, postnatal week.

*, ** Significantly different from the controls by Dunnett's test or Dunnett-type rank-sum test (* p<0.05, ** p <0.01).

Table 25.

Brain morphometry of the white matter components of the offspring exposed to hexabromocyclododecane during the period from the mid-gestation to the end of lactation examined at PNW11.

	HBCD in diet (ppm)			
	0	100	1000	10,000
No. of offspring examined	10	10	10	10
CC region area (mm ²)	0.15 ± 0.02 ^a	0.15 ± 0.02	0.14 ± 0.01	0.14 ± 0.01
CNPase-positive cell count (count/mm ²)	181.6 ± 28.2	167.6 ± 23.2	160.3 ± 28.1	138.7 ± 23.7*

^aMean±SD.

Abbreviations: HBCD, hexabromocyclododecane; CC, corpus callosum; PNW, postnatal week

* Significantly different from the controls by Dunnett's test or Dunnett-type rank-sum test (* p < 0.01).

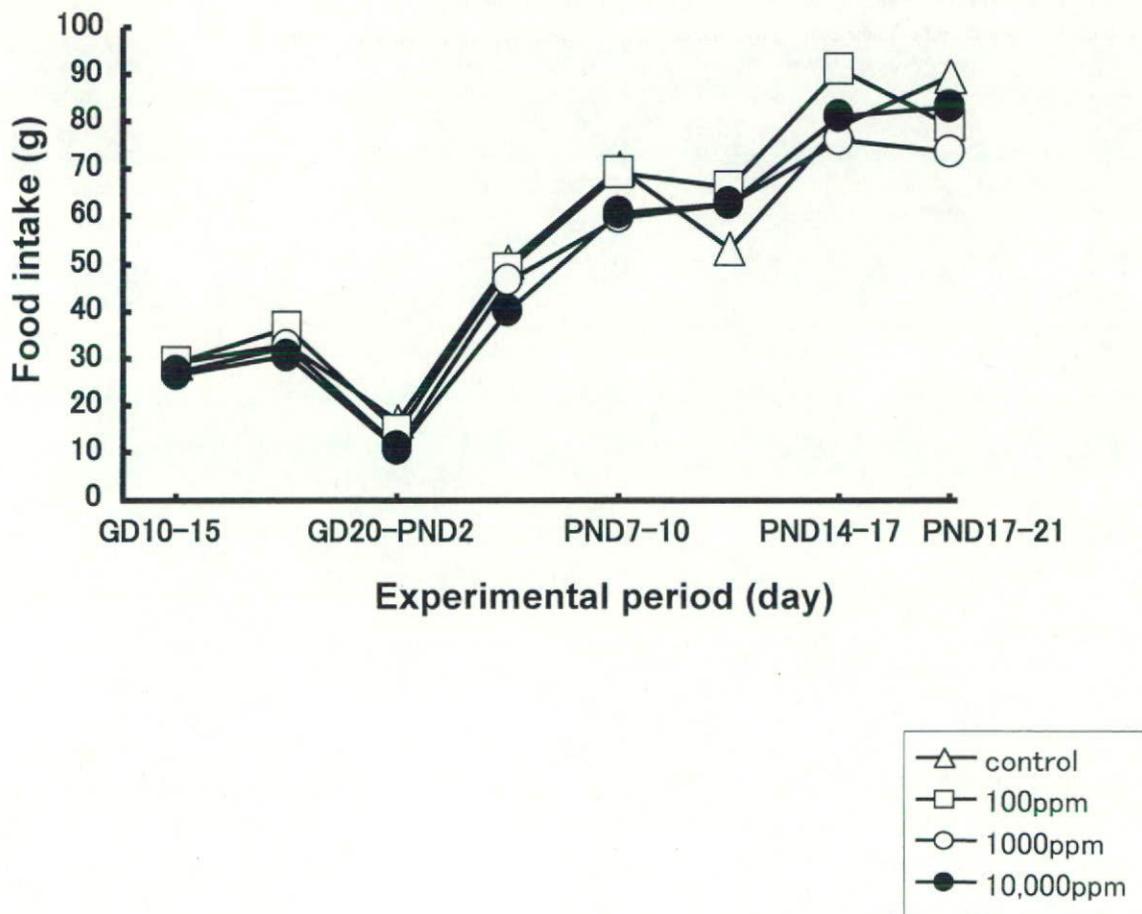


Fig. 29.
Food intake of dams exposed perinatally to tetrabromobisphenol A (TBBPA) during the period from the mid-gestation to the end of lactation.