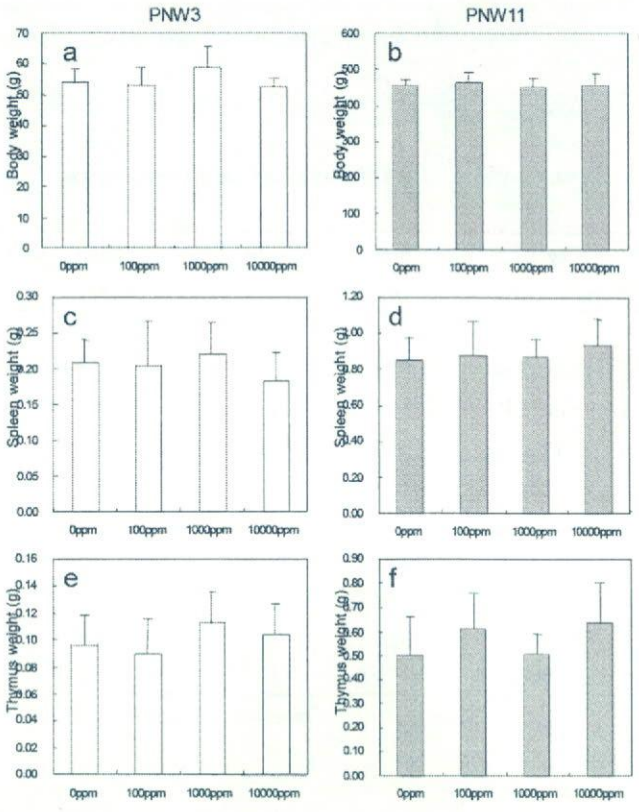


Fig. 77. TBBPA投与による体重・臓器重量変化

Table 66a

Hematological changes in 3-week old male rats exposed to TBBPA during the fetus and neonatal period

group	WBC x 10^2/ul	RBC x 10 4/ul	HGB g/dl	HCT %	MCV fL	MCH pg	MCHC g/dL	PLT x 10^4/ul	n
M-1 (control)	32.5±8.4	355.7±28.9	6.09±0.74	21.80±2.13	61.52±6.64	17.19±2.40	27.88±0.90	109.62±11.28	6
M-2 (TBBPA 100 ppm)	23.0±8.5	377.6±15.0	5.94±0.68	22.06±1.45	58.41±3.07	15.72±1.63	26.88±1.58	119.31±14.98	6
M-3 (TBBPA 1000 ppm)	33.4±9.6	357.9±20.9	6.47±0.56	22.87±1.66	63.88±2.69	18.07±0.89	28.28±0.58	114.12±8.68	9
M-4 (TBBPA 10000 ppm)	28.7±9.2	349.4±18.8	5.68±0.40	21.21±1.45	60.67±1.92	16.26±0.76	26.80±0.81*	16.12±10.12	10

Table 66b

Hematological changes in 11-week old male rats exposed to TBBPA during the fetus and neonatal period

group	WBC x 10^2/ul	RBC x 10 4/ul	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	PLT x 10^4/ul	n
M-1 (control)	105.5±23.9	699.5±29.0	13.96±0.39	42.72±1.42	61.09±1.08	19.97±0.45	32.70±0.44	106.00±9.88	10
M-2 (TBBPA 100 ppm)	105.2±34.1	712.0±31.7	14.10±0.56	43.06±1.68	60.52±1.78	19.82±0.71	32.75±0.69	98.35±7.44	10
M-3 (TBBPA 1000 ppm)	96.2±31.4	695.3±28.4	14.34±0.45	42.69±1.46	61.45±2.53	20.65±0.99	33.61±0.93*	09.51±8.13	10
M-4 (TBBPA 10000 ppm)	104.2±37.0	688.3±27.5	13.92±0.62	41.89±1.17	60.91±2.29	20.26±1.19	33.23±0.87	106.12±10.15	10

** <0.01, * <0.05 (t-test) Values are mean ± SD of 10 rats. 11-weeks old rats were used.

Table 67

White blood cell classification in male rats exposed to TBBPA during the fetus and neonatal period

group	n	Lymp %	Seg %	Eosi %	Mono %	Band %	Ebl n/100
3-week old rats							
M-1 (control)	6	79.83±2.64	17.48±1.8	0.6±0.51	2.08±1.1	0±0	0±0
M-2 (TBBPA 100ppm)	6	79.28±5.44	18.47±5.99	0.25±0.42	2±0.91	0±0	0±0
M-3 (TBBPA 1000ppm)	9	81.1±2.22	16.69±2.41	0.39±0.42	1.82±0.91	0±0	0.17±0.37
M-4 (TBBPA 10000ppm)	10	76.54±4.07	21.16±4.58	0.36±0.49	1.94±0.73	0±0	0.10±0.33
11-week old rats							
M-1 (control)	10	86.96±4.39	10.61±3.73	0.96±0.56	1.47±0.81	0±0	0±0
M-2 (TBBPA 100ppm)	10	86.36±4.59	11.24±4.35	0.95±0.93	1.45±0.9	0±0	0.05±0.16
M-3 (TBBPA 1000ppm)	10	87.75±2.56	10.29±2.59	0.9±0.77	1.06±0.75	0±0	0.10±0.21
M-4 (TBBPA 10000ppm)	10	82.13±8.02	15.72±8	1±1.11	1.15±0.67	0±0	0.05±0.16

**<0.01, *<0.05 (t-test) Values are mean ± SD.

Table 68.
Effects of HBCD on subpopulations of immune cells

T cell subpopulations

	Spleen 3w				Spleen 11w				Note
TBBPA (ppm)	0	100	1000	10000	0	100	1000	10000	
CD8a(+) CD4(+)	14.98 ± 2.43	12.25 ± 1.51*	12.59 ± 3.08	11.34 ± 2.41**	2.13 ± 0.32	3.26 ± 0.86	5.03 ± 1.11**	6.76 ± 2.66**	DP cell
CD3(+) CD4(+)	6.28 ± 1.57	4.68 ± 0.86**	6.27 ± 2.53	4.67 ± 1.53	20.26 ± 3.34	19.90 ± 4.67	9.28 ± 1.63**	11.54 ± 1.27**	CD4 T cell

Activation of T/B cells

	Spleen 3w				Spleen 11w				Note
TBBPA (ppm)	0	100	1000	10000	0	100	1000	10000	
CD3(+) CD71(+)	0.20 ± 0.08	0.31 ± 0.16	0.23 ± 0.07	0.46 ± 0.22**	0.26 ± 0.07	0.34 ± 0.06	1.44 ± 0.71**	1.77 ± 0.51**	active T cell
CD3(+) CD71(-)	15.48 ± 3.08	16.91 ± 3.99	14.43 ± 3.57	17.30 ± 3.65	42.74 ± 3.91	42.41 ± 8.77	26.16 ± 6.13**	26.93 ± 2.40**	inactive T cell
CD71(+) CD45RA(+)	0.94 ± 0.56	1.23 ± 0.56	1.14 ± 0.54	1.77 ± 1.03	0.73 ± 31	0.88 ± 0.23	3.57 ± 1.39**	4.89 ± 0.79**	active B cell
CD3(+) CD45RA(-)	14.79 ± 3.06	16.27 ± 3.83	13.67 ± 3.43	16.20 ± 3.21	39.61 ± 3.97	37.94 ± 8.22	19.05 ± 5.64**	21.29 ± 1.97**	T cell
	Thymus 3w				Thymus 11w				Note
TBBPA (ppm)	0	100	1000	10000	0	100	1000	10000	
CD71(-) CD45RA(+)	0.07 ± 0.05	0.09 ± 0.04	0.11 ± 0.07	0.24 ± 0.30*	0.35 ± 0.14	0.38 ± 0.15	0.81 ± 0.26*	1.10 ± 0.72**	inactive B cell (?)
CD3(-) CD45RA(+)	0.07 ± 0.05	0.09 ± 0.03	0.09 ± 0.04	0.15 ± 0.13*	0.28 ± 0.13	0.29 ± 0.11	0.74 ± 0.31*	0.94 ± 0.62**	B cell(?)
	Peripheral Blood 3w				Peripheral Blood 11w				Note
TBBPA (ppm)	0	100	1000	10000	0	100	1000	10000	
CD3(+) CD71(+)	9.55 ± 3.71	12.18 ± 4.46	11.69 ± 3.63	15.37 ± 3.82*	0.66 ± 0.19	0.50 ± 0.36	1.37 ± 0.29**	1.40 ± 0.23**	active T cell
CD3(+) CD71(-)	26.28 ± 5.18	26.46 ± 5.65	26.62 ± 5.93	29.30 ± 4.75	44.02 ± 2.49	44.29 ± 10.86	50.28 ± 5.97	53.97 ± 5.11**	inactive T cell
CD71(+) CD45RA(+)	13.45 ± 3.58	14.81 ± 3.91	14.57 ± 4.22	15.88 ± 3.44	0.66 ± 0.18	0.76 ± 0.15	1.24 ± 0.34**	1.11 ± 0.13**	active B cell
CD3(+) CD45RA(-)	35.17 ± 7.77	37.94 ± 8.94	37.64 ± 8.04	44.21 ± 7.57	43.92 ± 2.59	44.11 ± 11.14	50.68 ± 6.16	54.56 ± 6.17**	T cell

Treg, NK, NKT(?) cells

	Spleen 3w				Spleen 11w				Note
TBBPA (ppm)	0	100	1000	10000	0	100	1000	10000	
CD4(+) CD25(+)	1.52 ± 0.23	1.56 ± 0.38	1.41 ± 0.30	1.48 ± 0.26	3.70 ± 0.47	3.89 ± 0.49	6.18 ± 0.89**	6.70 ± 0.94**	Treg
NKRP1A(+) CD4(+)	3.05 ± 0.73	3.18 ± 0.54	2.56 ± 0.82	2.75 ± 0.71	5.48 ± 1.77	5.46 ± 1.25	12.44 ± 2.77**	13.99 ± 2.94**	CD4NKT(?)
NKRP1A(+) CD4(-)	5.02 ± 0.62	5.34 ± 1.09	4.98 ± 0.90	5.03 ± 0.80	5.53 ± 0.81	4.91 ± 1.19	11.78 ± 2.46**	13.22 ± 2.50**	NK
	Thymus 3w				Thymus 11w				Note
TBBPA (ppm)	0	100	1000	10000	0	100	1000	10000	
NKRP1A(+) CD4(+)	0.18 ± 0.07	0.17 ± 0.07	0.15 ± 0.06	0.13 ± 0.06	1.91 ± 0.75	2.27 ± 0.46	0.48 ± 0.20**	0.65 ± 0.35**	CD4NKT(?)
	Peripehal Blood 3w				Peripheral Blood 11w				Note
TBBPA (ppm)	0	100	1000	10000	0	100	1000	10000	
CD4(+) CD25(+)	1.28 ± 30	1.72 ± 0.42	1.98 ± 0.64*	1.59 ± 0.46	1.83 ± 0.37	1.72 ± 0.28	2.47 ± 0.23**	2.43 ± 0.41**	Treg
NKRP1A(+) CD4(+)	7.07 ± 1.87	6.53 ± 3.17	8.95 ± 4.51	5.33 ± 4.06	13.55 ± 2.75	9.64 ± 1.92**	12.71 ± 2.26	12.99 ± 2.31	CD4NKT(?)

Dunnett test, n=10. ■ p<0.01, increase □ p<0.05, increase ▨ p<0.05, decrease ■ p<0.01, decrease

Table 69.
TBBPA暴露が仔ラットの血清学的パラメータに及ぼす影響

	TBBPA in diet (ppm)			
	0	100	1000	10000
PNW 3				
No. of offspring examined	10	10	10	10
T3 (ng/ml)	1.3 ± 0.12 [a]	1.1 ± 0.12 **	1.2 ± 0.1 **	1.20 ± 0.13
T4 (ug/dl)	4.9 ± 0.50	4.7 ± 0.64	4.9 ± 0.4	5.12 ± 0.5
TSH (ng/ml)	7.1 ± 1.32	6.7 ± 2.51	6.2 ± 1.8	5.45 ± 0.6
A/G ratio	2.6 ± 0.34	2.3 ± 0.56	2.2 ± 0.4	2.59 ± 0.4
albumin (g/dl)	3.5 ± 0.17	3.6 ± 0.25	3.6 ± 0.2	3.58 ± 0.1
PNW 11				
No. of offspring examined	10	10	10	10
T3 (ng/ml)	0.9 ± 0.08	0.9 ± 0.05	0.9 ± 0.08	0.9 ± 0.04
T4 (ug/dl)	4.8 ± 0.53	5.1 ± 0.93	5 ± 0.40	4.5 ± 0.80
TSH (ng/ml)	7.1 ± 2.06	7.2 ± 2.23	6.7 ± 1.90	6.2 ± 1.62
A/G ratio	2.1 ± 0.31	1.8 ± 0.23	1.9 ± 0.21	1.7 ± 0.35
albumin (g/dl)	4.18 ± 0.15	4.07 ± 0.14	4.10 ± 0.12	4.13 ± 0.29

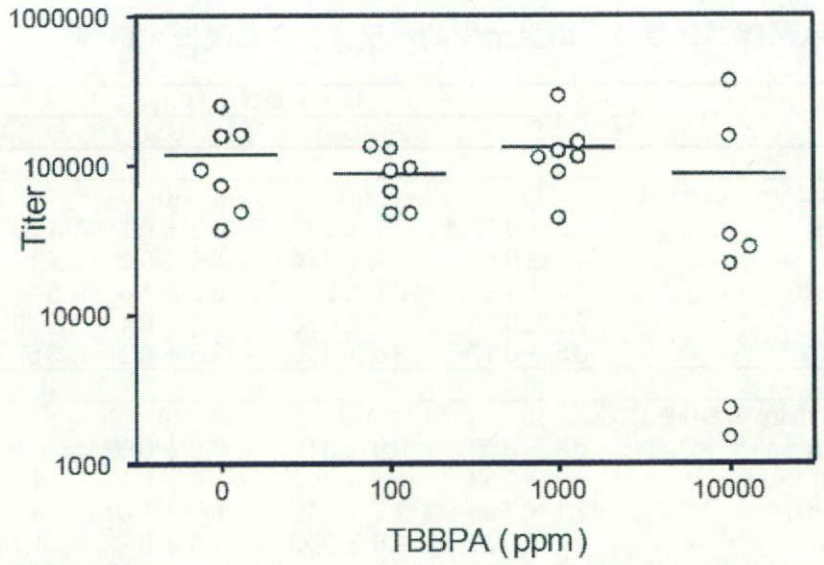
[a] Mean±SD.
** Significantly different from the controls by Dunnett's test or Dunnett-type rank-sum test (** p <0.01).

Table 70.
TBBPA暴露が仔ラットの胸腺及び脾臓に及ぼす組織病理学的影響

	TBBPA in diet (ppm)			
	0	100	1000	10000
PNW 3				
No. of animals examined (male/female)	10/10	10/10	10/10	10/10
Thymus				
No abnormalities detected	10/10	10/10	10/10	10/10
Spleen				
Atrophy of white pulp (±) [a]	0/0[c]	1/0	0/0	0/0
Increased extramedullary hematopoiesis (±)[b]	0/0	1/0	0/0	0/0
PNW 11				
No. of animals examined (male/female)	10/10	10/10	10/10	10/10
Thymus				
No abnormalities detected	10/10	10/10	10/10	10/10
Spleen				
No abnormalities detected	10/10	10/10	10/10	10/10

[a] Grade of change; ±, minimal.
[b] Increased myelocytes
[c] Total No. of animals with each finding.

(a) KLH-IgG 抗体価と TBBPA の濃度依存性



(b) 免疫方法

免疫原　50μg KLH　with alum,　免疫回数　3 回 (at　P N D 23, 33,43)

投与方法　　ip,　血清分取　at　P N D40, PND50

Fig. 78

Table 71－A　Effect of PTU treatment on RSV infection in adult mice

Treatment	Toxicological sign		
	Body weight change (g)	Food consumption (g/week)	Serum T4 level (ng/mL)
Control N=3	1.2 ± 1.5	46.9 ± 4.7	24.7 ± 4.3
PTU (1000 ppm) N=3	−1.7 ± 2.3	37.2 ± 5.6	11.8 ± 1.3

Table 71－B　Effect of PTU treatment on RSV infection in adult mice

Treatment	Pulmonary RSV titers			
	Infectivity (PFU/g lung)	Viral RNA (copies/μL)	Infectivity in BALF (PFU/mL)	IFN-γ level in BALF (pg/mL)
Control N=3	2,630 ± 1,368	16,181± 4,479	139 ± 19	1,144 ± 115
PTU (1000 ppm) N=3	6,973 ± 7,325	46,681 ± 15,560	433 ± 335	1,258 ± 528

Table 72－A Effect of PTU treatment on morbidity in RSV-infected mice (offspring)

Treatment	Serum T4 level (ng/mL)			
	Day 5		Day 6	
RSV infection				
Control	27.2 ± 9.3 *	(4)**	34.8 ± 9.3	(5)
PTU (10 ppm)	22.8 ± 12.9	(3)	47.4 ± 8.5	(4)
Mock infection				
Control	52.5 ± 8.9	(2)	80.1	(1)
PTU (10 ppm)	42.5	(1)	42.3	(1)

* Mean +/– SD, ** No. of mice

Table 72－B Effect of PTU treatment on morbidity in RSV-infected mice (offspring)

Treatment	Body weight (g)			
	Day 5		Day 6	
RSV infection				
Control	14.0 ± 0.8 *	(4)**	14.8 ± 1.4	(5)
PTU (10 ppm)	11.8 ± 0.6	(3)	10.8 ± 1.2	(4)
Mock infection				
Control	15.3 ± 1.0	(2)	13.3	(1)
PTU (10 ppm)	11.4	(1)	14.1	(1)

* Mean +/– SD, ** No. of mice

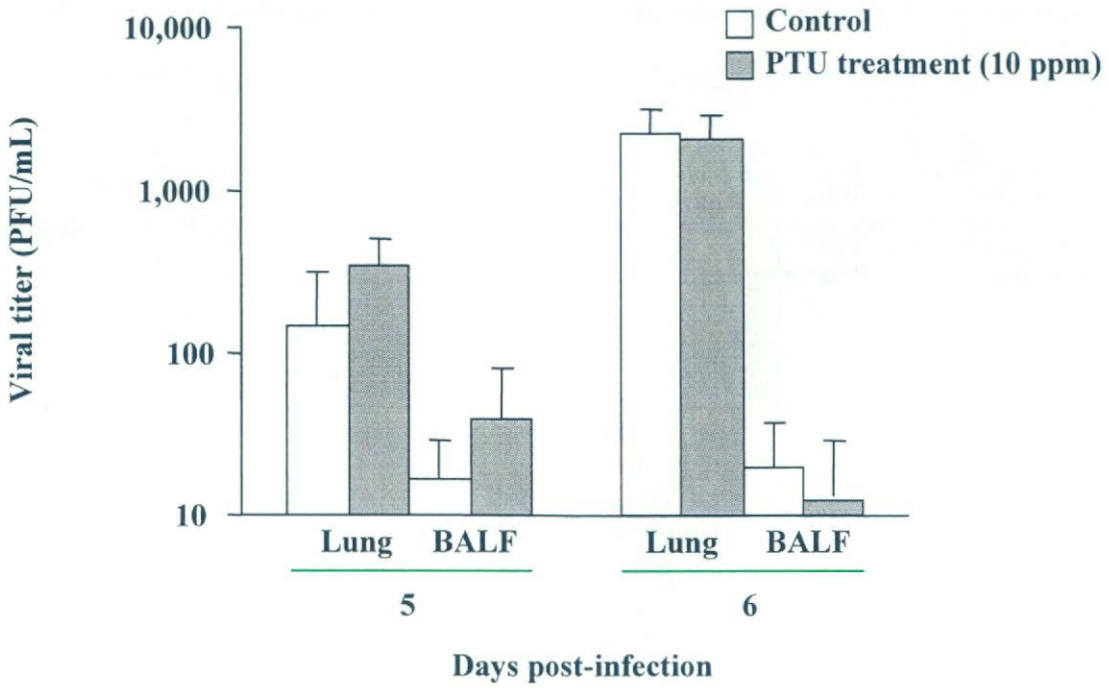


Fig. 79. Pulmonary viral titers in RSV-infected mice (offspring)

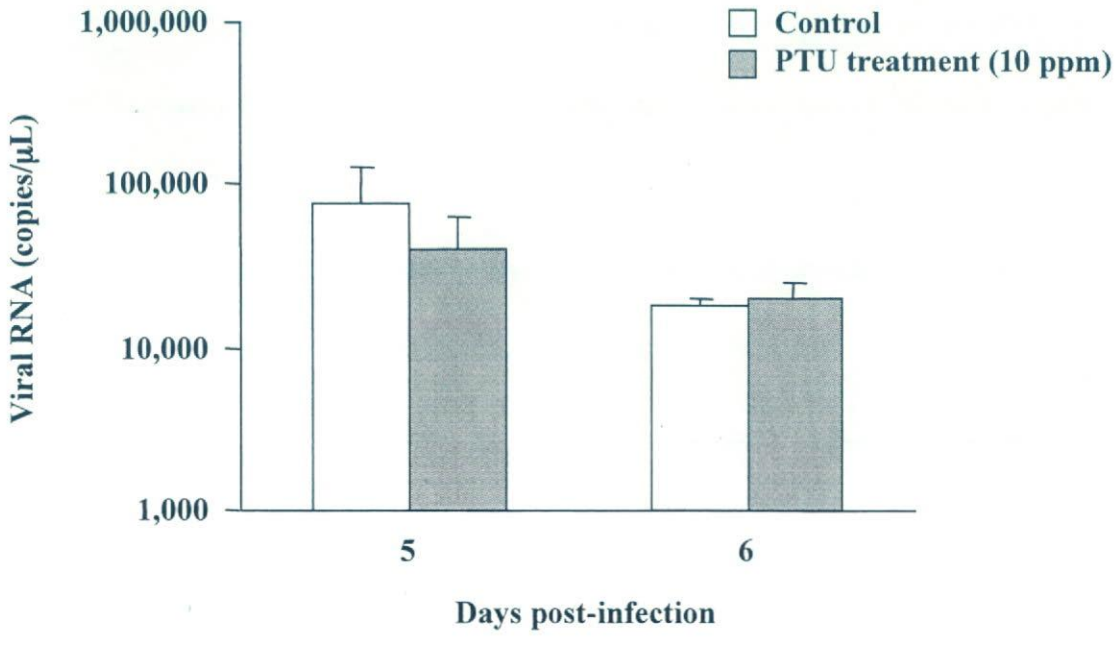


Fig. 80. Viral RNA (N-gene) levels in lung tissues from RSV-infected mice (offspring)

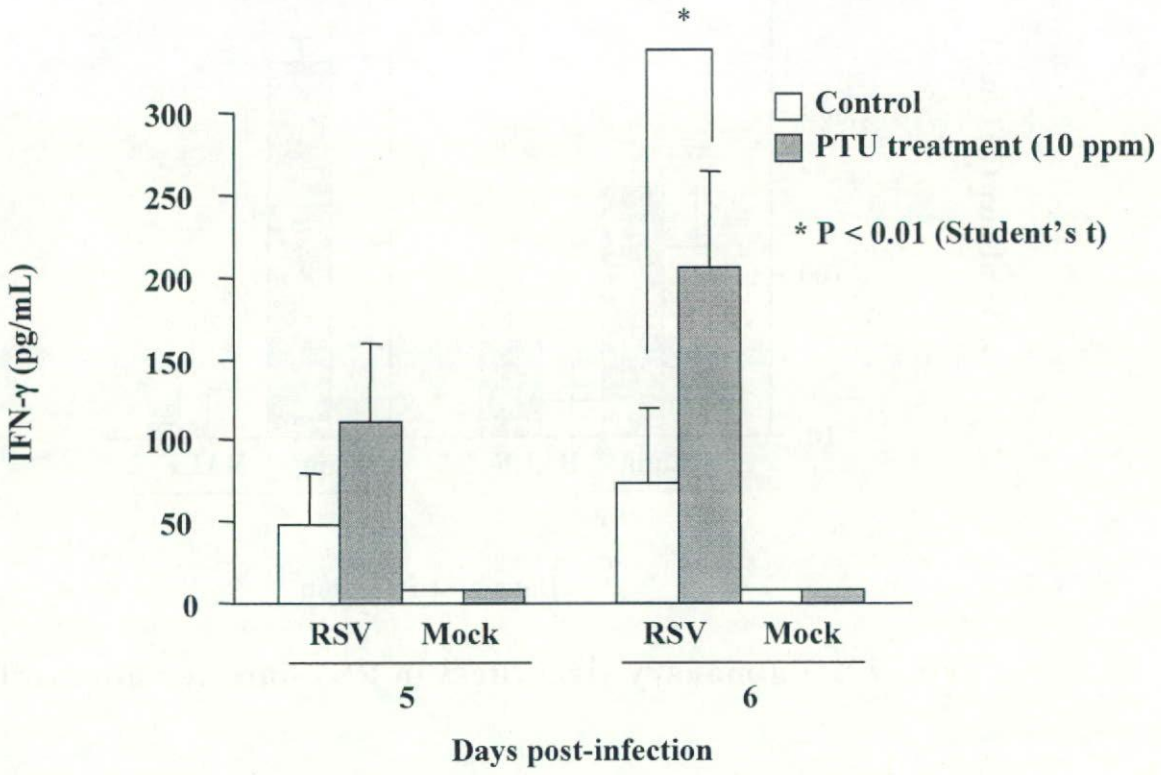


Fig. 81. IFN-γ levels in BALF from RSV- or mock-infected mice (offspring)

Table 73

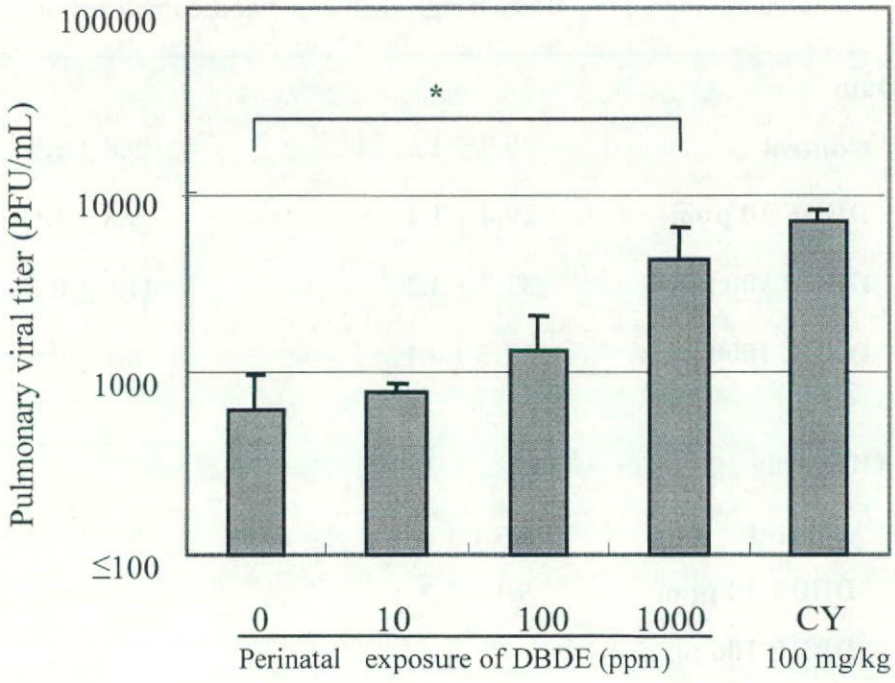
Body weights and food consumption of mice exposed to DBDE perinatally (GD10-PND21)

Mice	Body weight (g)	Food consumption (g/day)
Dam		
Control	30.9 ± 1.6	9.8 ± 1.9
DBDE 10 ppm	29.4 ± 1.4	9.8 ± 1.5
DBDE 100 ppm	32.7 ± 3.2	11.0 ± 0.6
DBDE 1000 ppm	31.5 ± 4.1	8.1 ± 0.5
Offspring		
Control	9.5 ± 1.4	-
DBDE 10 ppm	9.1 ± 2.3	-
DBDE 100 ppm	9.9 ± 1.0	-
DBDE 1000 ppm	8.1 ± 1.1*	-

*P < 0.01 by Student's t-test (vs Control)

Fig. 82

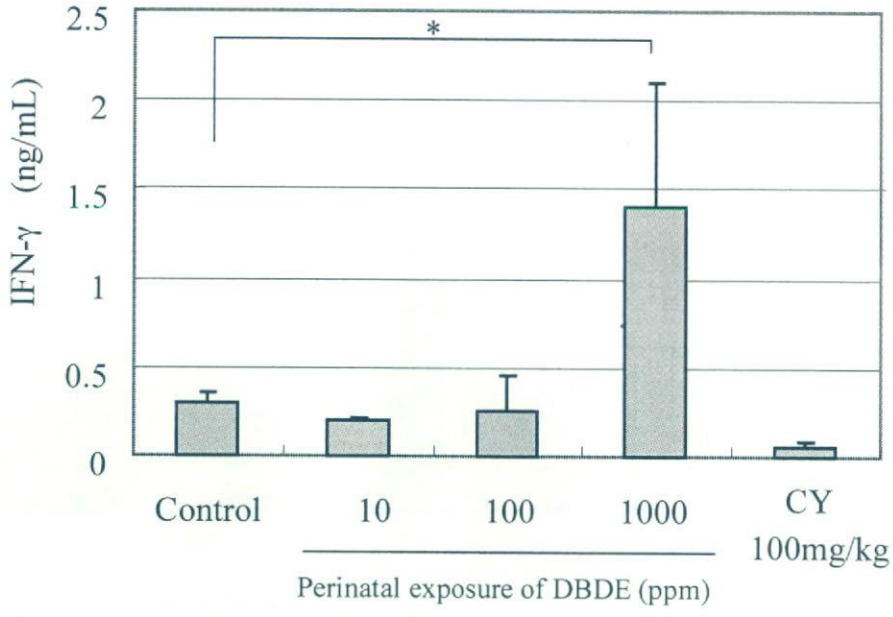
Effect of perinatal exposure to DBDE on pulmonary viral titers in RSV-infected offspring mice



*P<0.01 (Student's t-test)

Fig. 83

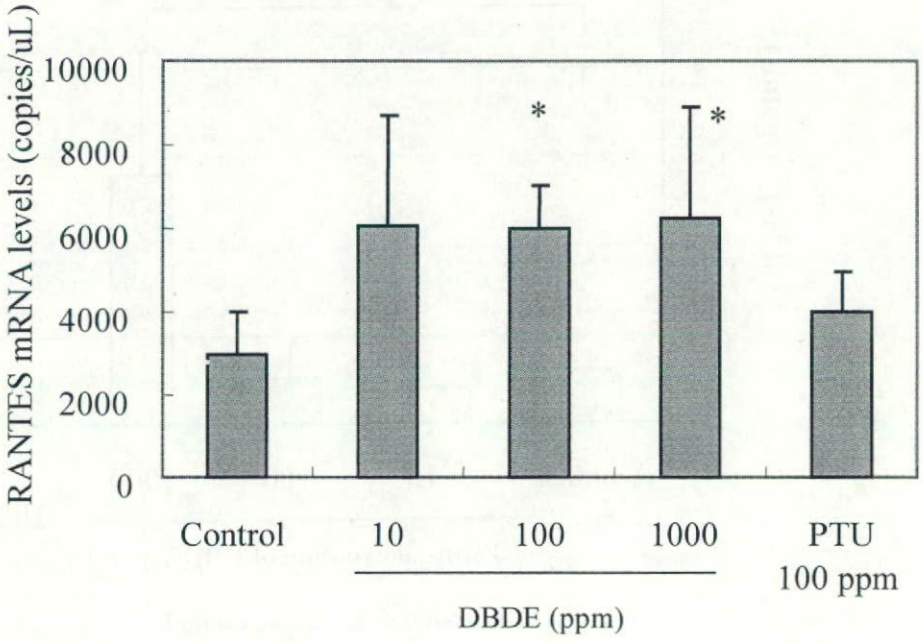
Effect of perinatal exposure to DBDE on IFN-γ level in BALF in RSV-infected offspring mice



*P<0.05 (Mann-Whitney U-test, vs Control)

Fig. 84

Effect of perinatal exposure to DBDE or PTU on the levels of RANTES mRNA in lung tissues in RSV- infected offspring mice



*P<0.01 (Mann-Whitney U-test, vs Control)

Fig. 85

Effect of perinatal exposure to HBCD on pulmonary viral titers or IFN-γ level in BALF in RSV-infected offspring mice

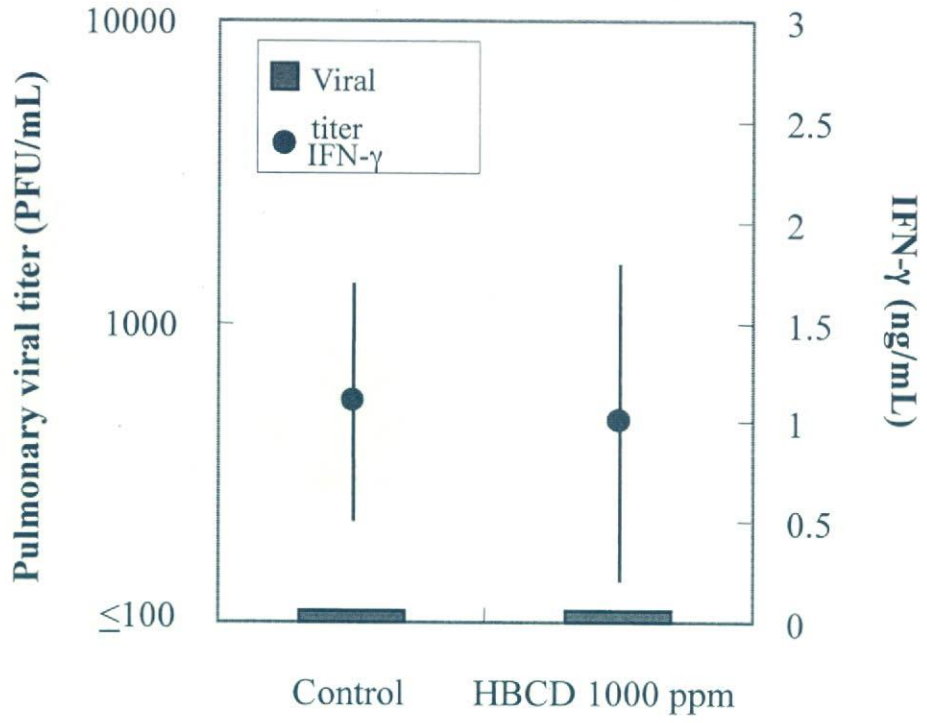


Table 74

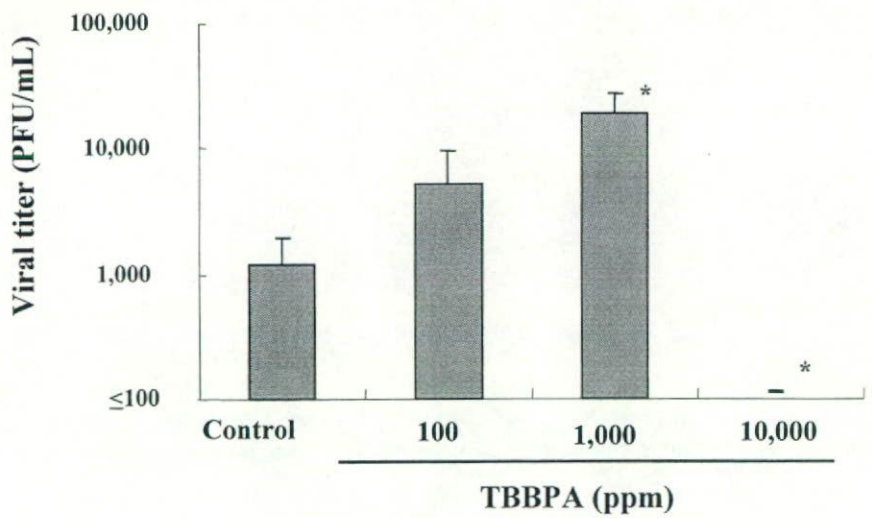
Serum T4 levels of dam and offspring mice exposed to TBBPA perinatally

Mice	T4 (ng/mL)	
	Dam	Offspring
Control	34.5 ± 25.5	92.5 ± 17.0
TBBPA		
100 ppm	31.5 ± 10.5	73.5 ± 18.5
1000 ppm	1195.5 ± 254.0*	64.0 ± 16.5*
10,000 ppm	708.0 ± 320.0*	55.8 ± 10.0*

*P < 0.05 by Mann-Whitney *U*-test (vs Control)

Fig. 86

Effect of perinatal exposure to TBBPA on pulmonary viral titers in RSV-infected offspring mice



*P<0.01 (vs Control, Mann-Whitney *U*-test)

Fig. 87

Effect of TBBPA on RSV growth *in vitro*

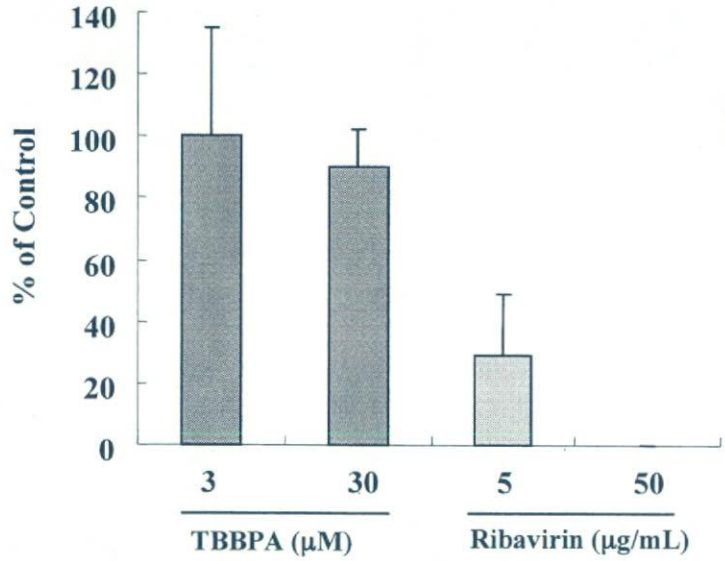
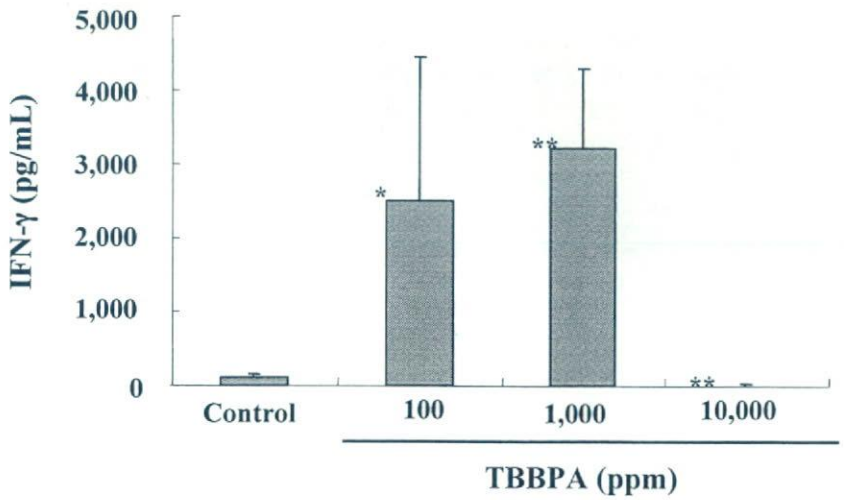


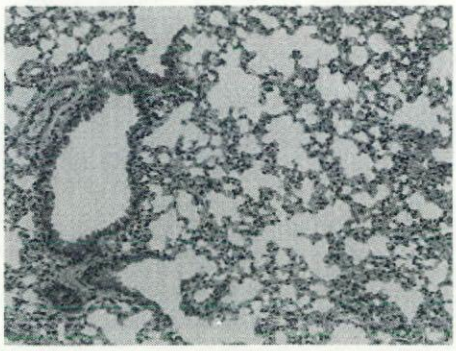
Fig. 88

Effect of perinatal exposure to TBBPA on IFN-γ level in BALF in RSV-infected offspring mice

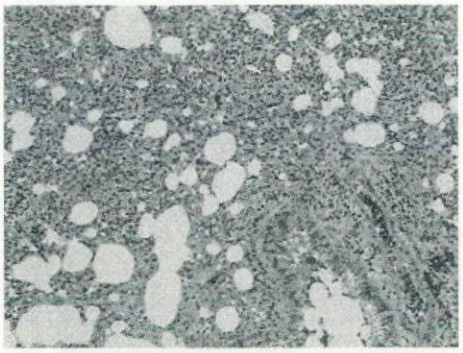


*P<0.05 (vs Control, Mann-Whitney U-test)
**P<0.001 (vs Control, Mann-Whitney U-test)

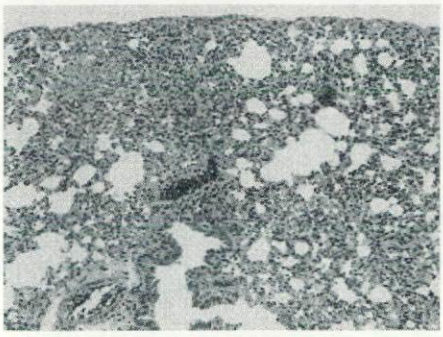
Fig. 89



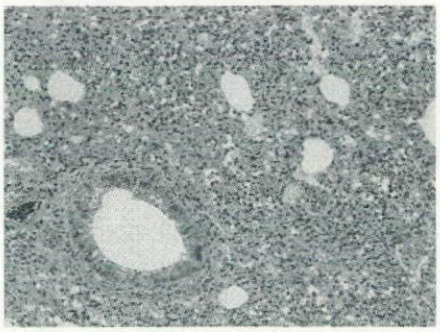
Mock



RSV/Control



RSV/TBBPA 1,000 ppm



RSV/TBBPA 10,000 ppm

Table 75
Final body and organ weights of dams fed diet containing DBDE

Dose (%)	0 (Control)	0.001	0.01	0.25	2.5
No. of animals	4	5	5	5	5
Final body weight (g)	199±8	213±11	201±13	206±5	201±8
Absolute organ weights					
Liver (g)	8.5±0.9	9.2±0.8	8.6±0.6	9.2±0.5	9.6±0.8
Kidneys (g)	1.4±0.1	1.5±0.0	1.5±0.0	1.5±0.1	1.5±0.1
Thyroids (mg)	14±2	14±2	12±1	14±2	14±2
Relative organ weights					
Liver (g%)	4.3±0.3	4.3±0.2	4.3±0.2	4.5±0.2	4.8±0.3
Kidneys (g%)	0.7±0.0	0.7±0.0	0.7±0.0	0.7±0.0	0.7±0.0
Thyroids (mg%)	7±1	6±1	6±1	7±1	7±1

Each value represents the mean±S.D.

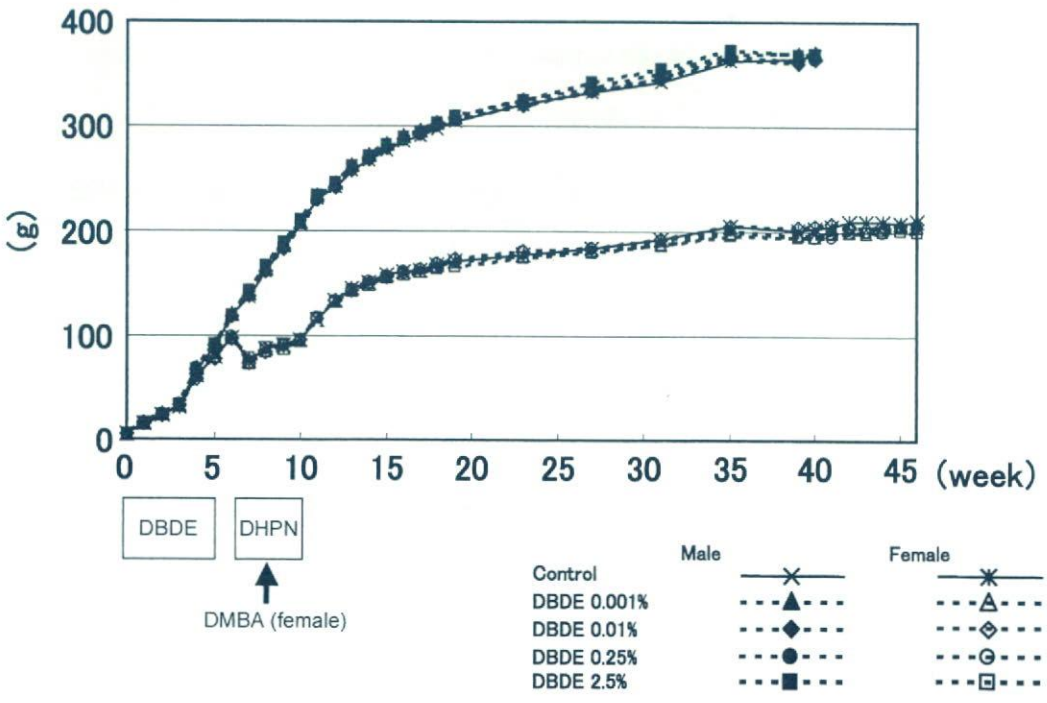


Fig. 90. Body weight curves of rats exposed to DHPN and DMBA following prepubertal DBDE treatment

Table 76 Final body and organ weights of rats exposed to DHPN and DMBA following prepubertal DBDE treatment

	Dose (%)	0 (Control)	0.001	0.01	0.25	2.5
Male	No. of animals	16	20	20	20	20
	Final body weight (g)	361±26	367±22	359±26	364±19	370±17
	Absolute organ weights					
	Liver (g)	9.6±1.0	10.0±0.7	9.5±0.9	9.5±0.8	9.9±0.7
	Kidneys (g)	7.5±13.0	6.0±16.8	9.7±19.6	3.6±5.2	2.4±0.8
	Thyroids (mg)	58±49	49±34	60±90	88±180	33±26
	Relative organ weights					
	Liver (g%)	2.7±0.2	2.7±0.1	2.7±0.2	2.6±0.2	2.7±0.1
	Kidneys (g%)	2.3±4.3	1.9±5.7	3.0±6.4	1.0±1.6	0.7±0.2
	Thyroids (mg%)	16±14	13±9	17±26	25±53	9±7
Female	No. of animals	15	18	17	20	19
	Final body weight (g)	203±17	195±33	202±17	193±34	197±17
	Absolute organ weights					
	Liver (g)	5.4±0.6	5.3±1.3	5.5±0.5	5.0±1.3	4.9±0.8
	Kidneys (g)	4.7±9.6	5.9±13.6	8.7±16.3	6.2±10.9	1.9±1.9
	Thyroids (mg)	27±18	20±10	23±16	38±80	19±11
	Relative organ weights					
	Liver (g%)	2.7±0.4	2.7±0.4	2.7±0.2	2.5±0.4	2.5±0.5
	Kidneys (g%)	2.4±5.0	2.6±4.8	4.5±8.7	3.2±5.2	1.0±1.0
	Thyroids (mg%)	14±10	10±5	11±7	20±44	10±5

Each value represents the mean±S.D.

Table 77-1

Incidence and multiplicity of renal mesenchymal tumor and nephroblastoma in kidneys of rats exposed to DHPN and DMBA following prepubertal DBDE treatment

	Dose	No. of rats	Renal mesenchymal tumor (RMT)		Nephroblastoma (NB)	
			Incidence	Multiplicity	Incidence	Multiplicity
Male	Control	15	10 (67)	1.07±1.03	3 (20)	0.27±0.59
	0.001%	19	7 (37)	0.53±0.77	0 (0)	0
	0.01%	20	8 (40)	0.55±0.83	7 (35)	0.35±0.49
	0.25%	20	15 (75)	0.90±0.64	1 (5)	0.05±0.22
	2.5%	20	4 (20)**	0.20±0.41 *	0 (0)	0
Female	Control	15	10 (67)	1.07±1.28	4 (27)	0.33±0.62
	0.001%	18	10 (56)	1.11±1.28	7 (39)	0.39±0.50
	0.01%	15	8 (53)	0.73±0.88	5 (33)	0.40±0.63
	0.25%	20	8 (40)	0.60±0.82	6 (30)	0.30±0.47
	2.5%	19	4 (21)**	0.32±0.67	2 (11)	0.16±0.50

Each multiplicity value represents the mean±S.D.

Table 77-2

Incidence and multiplicity of proliferative/neoplastic lesions of tubule epithelial cell in kidneys of rats exposed to DHPN and DMBA following prepubertal DBDE treatment

	Dose	No. of rats	Renal cell							
			Hyperplasia		Adenoma		Carcinoma		Ad+Ca	
			Incidence	Multiplicity	Incidence	Multiplicity	Incidence	Multiplicity	Incidence	Multiplicity
Male	0%	15	9 (60)	1.20±1.21	5 (33)	0.40±0.63	3 (20)	0.20±0.41	7 (47)	0.60±0.74
	0.001%	19	14 (74)	1.26±1.19	4 (21)	0.21±0.42	4 (21)	0.26±0.56	7 (37)	0.47±0.70
	0.01%	20	8 (40)	0.50±0.69	3 (15)	0.30±0.80	4 (20)	0.35±0.81	7 (35)	0.65±1.04
	0.25%	20	13 (65)	1.15±0.99	9 (45)	0.60±0.75	0 (0)	0	9 (45)	0.60±0.75
	2.5%	20	9 (45)	0.45±0.51	1 (5)*	0.05±0.22	1 (5)	0.05±0.232	2 (10)*	0.10±0.31
Female	0%	15	8 (53)	0.67±0.72	2 (13)	0.13±0.35	0 (0)	0	2 (13)	0.13±0.35
	0.001%	18	10 (56)	0.83±0.99	7 (39)	0.56±0.78	2 (11)	0.11±0.32	9 (50)*	0.67±0.77
	0.01%	15	8 (53)	0.67±0.72	2 (13)	0.20±0.56	0 (0)	0	2 (13)	0.20±0.56
	0.25%	20	6 (30)	0.45±0.76	6 (30)	0.30±0.47	1 (5)	0.05±0.22	7 (35)	0.35±0.49
	2.5%	19	12 (63)	1.16±1.34	6 (32)	0.42±0.69	0 (0)	0	6 (32)	0.42±0.69

Each multiplicity value represents the mean±S.D.

Table 77-3

Incidence and multiplicity of proliferative/neoplastic lesions of transitional cell in kidneys of rats exposed to DHPN and DMBA following prepubertal DBDE treatment

	Dose	No. of rats	Transitional cell							
			Hyperplasia		Papilloma		Carcinoma		Pa+Ca	
			Incidence	Multiplicity	Incidence	Multiplicity	Incidence	Multiplicity	Incidence	Multiplicity
Male	0%	15	9 (60)	0.87±0.92	1 (7)	0.07±0.26	3 (20)	0.20±0.41	4 (27)	0.27±0.46
	0.001%	19	5 (26)	0.37±0.68	2 (11)	0.11±0.32	2 (11)	0.11±0.32	4 (21)	0.21±0.42
	0.01%	20	6 (30)	0.40±0.75	7 (35)	0.45±0.69	6 (30)	0.30±0.47	12 (60)	0.75±0.72*
	0.25%	20	5 (25)*	0.35±0.67	2 (10)	0.10±0.31	5 (25)	0.25±0.44	7 (35)	0.35±0.49
	2.5%	20	7 (35)	0.55±1.00	3 (15)	0.15±0.37	4 (20)	0.20±0.41	6 (30)	0.35±0.59
Female	0%	15	6 (40)	0.87±1.30	1 (7)	0.13±0.52	1 (7)	0.07±0.26	2 (13)	0.20±0.56
	0.001%	18	8 (44)	0.83±1.34	1 (6)	0.06±0.24	2 (11)	0.11±0.32	3 (17)	0.17±0.38
	0.01%	15	6 (40)	0.53±0.74	3 (20)	0.20±0.41	1 (7)	0.07±0.26	4 (27)	0.27±0.46
	0.25%	20	5 (25)	0.35±0.67	0 (0)	0	0 (0)	0	0 (0)	0
	2.5%	19	3 (16)	0.21±0.54	0 (0)	0	2 (11)	0.11±0.32	2 (11)	0.11±0.32

Each multiplicity value represents the mean±S.D.

Table 77-4

Incidence and multiplicity of follicular cell proliferative/neoplastic lesions in thyroids of rats exposed to DHPN and DMBA following prepubertal DBDE treatment

	Dose	No. of rats	Focal hyperplasia		Adenoma		Adenocarcinoma		Ad/Ca	
			Incidence	Multiplicity	Incidence	Multiplicity	Incidence	Multiplicity	Incidence	Multiplicity
Male	Control	16	15 (94)	2.94±1.88	11 (69)	1.00±0.97	12 (75)	1.38±1.09	14 (88)	2.38±1.31
	0.001%	20	20 (100)	4.25±1.71	17 (85)	1.85±1.31	13 (65)	2.00±2.29	19 (95)	3.85±2.68
	0.01%	20	18 (90)	3.65±1.93	14 (70)	1.50±1.28	13 (65)	1.05±1.19	18 (90)	2.55±1.99
	0.25%	20	19 (95)	3.40±2.46	13 (65)	1.00±0.92	13 (65)	1.10±1.12	18 (90)	2.10±1.52
	2.5%	20	20 (100)	3.30±1.17	13 (65)	1.05±1.00	12 (60)	0.90±0.97	18 (90)	1.95±1.54
Female	Control	15	14 (93)	2.47±1.41	8 (53)	0.80±0.94	12 (80)	1.00±0.65	13 (87)	1.80±1.15
	0.001%	18	16 (89)	2.39±1.75	10 (56)	0.67±0.69	10 (56)	0.89±1.23	15 (83)	1.56±1.62
	0.01%	17	14 (82)	1.88±1.41	10 (59)	0.88±0.86	5 (29) **	0.47±0.87 *	12 (71)	1.35±1.27
	0.25%	19	16 (84)	2.26±1.56	10 (53)	0.89±0.99	8 (42) *	0.74±1.15	14 (74)	1.63±1.46
	2.5%	19	14 (74)	1.63±1.42	8 (42)	0.53±0.70	5 (26) **	0.32±0.58 *	9 (47) *	0.84±1.07

*, **: Significantly different from corresponding 0% group at $p<0.05$, 0.01, respectively

Each multiplicity value represents the mean±S.D.

Table 77-5

Incidence and multiplicity of liver tumors of rats exposed to DHPN and DMBA following prepubertal DBDE treatment

	Dose	No. of rats	Adenoma		Carcinoma	
			Incidence	Multiplicity	Incidence	Multiplicity
Male	Control	16	3 (19)	0.19±0.40	0 (0)	0
	0.001%	20	1 (5)	0.05±0.22	0 (0)	0
	0.01%	20	1 (5)	0.05±0.22	0 (0)	0
	0.25%	20	2 (10)	0.15±0.49	1 (5)	0.05±0.22
	2.5%	20	1 (5)	0.05±0.22	0 (0)	0
Female	Control	15	9 (60)	1.33±1.59	0 (0)	0
	0.001%	18	13 (72)	1.22±1.22	0 (0)	0
	0.01%	17	11 (65)	1.65±1.77	2 (12)	0.12±0.33
	0.25%	20	14 (70)	1.60±1.47	0 (0)	0
	2.5%	19	10 (53)	1.21±1.40	1 (5)	0.05±0.23

Each multiplicity value represents the mean±S.D.