

Table 5-9

Blood chemistry in female cynomolgus monkeys

Study No. : SBL81-20

Group	Animal No.\Day	BUN (mg/dl)			Creat. (mg/dl)			IP (mg/dl)			Ca (mg/dl)		
		Pre	6	13	Pre	6	13	Pre	6	13	Pre	6	13
Control (i.n.)	3	25.9	27.7	27.5	0.83	0.88	0.92	5.41	3.97	3.43	10.4	10.1	10.1
Measles virus vaccine (i.n.)													
0.5 (mL/body)	6	27.1	27.8	27.7	0.84	0.72	0.82	3.54	2.49	3.08	10.7	10.7	10.2
	7	26.5	24.4	29.6	0.64	0.71	0.80	5.67	3.52	3.49	10.8	10.3	9.5
	Mean	26.80	26.10	28.65	0.740	0.715	0.810	4.605	3.005	3.285	10.75	10.50	9.85
Control (i.t.)	9	29.9	31.1	35.1	0.70	0.72	0.75	2.05	3.62	4.56	10.2	10.5	10.0
	10	27.2	29.8	28.0	0.84	0.84	0.77	4.72	3.61	3.48	10.5	10.8	9.8
	Mean	28.55	30.45	31.55	0.770	0.780	0.760	3.385	3.615	4.020	10.35	10.65	9.90
Measles virus vaccine (i.t.)													
0.3 (mL/body)	13	22.5	24.4	30.7	0.63	0.68	0.66	2.12	2.32	1.32	10.1	9.5	9.9
	14	21.2	29.7	28.1	0.70	0.79	0.68	3.02	2.30	1.67	10.2	10.1	10.4
	Mean	21.85	27.05	29.40	0.665	0.735	0.670	2.570	2.310	1.495	10.15	9.80	10.15

Notes) BUN : Blood urea nitrogen
Creat. : Creatinine
IP : Inorganic phosphorus
Ca : Calcium

i.n. : intranasal administration
i.t. : intratracheal administration

Table 5-10

Blood chemistry in female cynomolgus monkeys

Study No. : SBL81-20

Group	Animal No.\Day	Na (mEq/l)			K (mEq/l)			Cl (mEq/l)		
		Pre	6	13	Pre	6	13	Pre	6	13
Control (i.n.)	3	154	152	149	5.3	5.3	5.2	109	110	106
Measles virus vaccine (i.n.)										
0.5 (mL/body)	6	150	151	152	4.7	5.3	5.0	105	112	108
	7	149	153	148	5.0	5.6	5.3	107	116	113
	Mean	149.5	152.0	150.0	4.85	5.45	5.15	106.0	114.0	110.5
Control (i.t.)	9	146	154	148	5.5	5.5	5.4	106	108	110
	10	151	151	147	4.9	6.0	5.1	105	104	102
	Mean	148.5	152.5	147.5	5.20	5.75	5.25	105.5	106.0	106.0
Measles virus vaccine (i.t.)										
0.3 (mL/body)	13	150	150	147	5.2	5.0	5.0	112	109	108
	14	152	150	146	4.5	4.0	4.6	108	107	106
	Mean	151.0	150.0	146.5	4.85	4.50	4.80	110.0	108.0	107.0

Notes)

Na : Sodium
K : Potassium
Cl : Chloride

i.n. : intranasal administration
i.t. : intratracheal administration

Table 6-1 X ray examination in male cynomolgus monkeys

Group	Route	Animal No.	/Day	Pre	14
Control	i.t.	8		N	N
Measles virus vaccine 0.3 (mL/body)	i.t.	11 12		N N	N N

Notes) N: Normal

i.t.: intratracheal administration

Table 6-2 X ray examination in female cynomolgus monkeys

Group	Route	Animal No.	/Day	Pre	14
Control	i.t.	9		N	N
		10		N	N
Measles virus vaccine 0.3 (mL/body)	i.t.	13		N	N
		14		N	N

Notes) N: Normal

i.t.: intratracheal administration

Table 7-1

Gross autopsy findings in male cynomolgus monkeys

Study No. : SBL81-20

Findings	Group	Control (i.n.)		Measles virus vaccine (i.n.) 0.5		Control (i.t.)	Measles virus vaccine (i.t.) 0.3	
	Dose (mL/body)							
	Animal No.	1	2	4	5	8	11	12
Spleen								
Accentuated follicle		-	-	-	-	P	-	-
Thyroid								
Cyst		-	-	-	-	P	-	-
Lymph node (Mesenteric)								
Enlargement		-	-	-	-	P	-	-
Lymph node (Inguinal)								
Enlargement		-	-	-	-	P	-	-
Lymph node (Axillary)								
Enlargement		-	-	-	-	P	-	-
Lymph node (Hilar)								
Enlargement		-	-	-	-	P	-	-

Notes) - : No abnormal changes P : Non-graded changes

i.n. : intranasal administration

i.t. : intratracheal administration

Table 7-2

Gross autopsy findings in female cynomolgus monkeys

Study No. : SBL81-20

	Group	Control (i.n.)	Measles virus vaccine (i.n.) 0.5	Control (i.t.)	Measles virus vaccine (i.t.) 0.3
Findings	Animal No.	3	6 7	9 10	13 14
Stomach					
Red focus, several, mucosa		-	- -	P -	- -

Notes) - : No abnormal changes P : Non-graded changes

i.n. : intranasal administration

i.t. : intratracheal administration

Table 8-1 Histopathological findings in cynomolgus monkeys (End of observation) - [H.E. staining]

Study No. : SBL81-20

Male								
Findings	Group	Control		Measles virus vaccine		Control	Measles virus vaccine	
	Dose (mL/body)	(i.n.)		(i.n.)		(i.t.)	(i.t.)	
	Animal No.	0.5		0.3				
		1	2	4	5	8	11	12
Axillar lymph node (left)								
Swelling, lymph follicle		-	-	-	-	2+	-	-
Brain stem(Included in Fourth ventricle)								
Mononuclear cell infiltration, choroid plexus		±	-	-	±	-	-	-
Mononuclear cell infiltration, leptomeninx		-	-	-	-	±	-	-
Brain stem(Included in Third ventricle)								
		-	-	-	-	-	-	-
Bronchus (left)								
Mononuclear cell infiltration, bronchial gland		±	±	±	±	±	±	±
Cerebellum								
		-	-	-	-	-	-	-
Cerebrum								
Mononuclear cell infiltration, leptomeninx		-	-	-	-	±	-	-
Esophageal mucosa								
		-	-	-	-	-	-	-

Notes) - :No abnormal changes, ± :Very slight, + :Slight, 2+ :Moderate, 3+ :Marked, P :Non-graded change, NE :Unexamined
i.n. :intranasal administration, i.t. :intratracheal administration

Table 8-2 Histopathological findings in cynomolgus monkeys (End of observation) - [H.E. staining]

Study No. : SBL81-20

Male									
Findings	Group	Control		Measles virus vaccine		Control		Measles virus vaccine	
	Dose (mL/body)	(i.n.)		(i.n.)		(i.t.)		(i.t.)	
	Animal No.	0.5		0.3					
		1	2	4	5	8	11	12	
Hilar lymph node (left)									
Inflammatory cell infiltration,									
sinus		-	±	-	±	-	-	-	
Swelling, lymph follicle		-	-	-	-	2+	-	-	
Inguinal lymph node (left)									
Swelling, lymph follicle		-	-	-	-	2+	-	-	
Lung (left)									
Inflammatory cell infiltration,									
alveolus		-	±	-	-	-	-	-	
Macrophage, alveolus		-	-	-	-	±	-	-	
Mesenteric lymph node									
Swelling, lymph follicle		-	-	-	-	2+	-	-	
Nasal mucosa (left)									
		-	-	-	-	-	-	-	
Olfactory bulb (left)									
		-	-	-	-	-	-	-	
Olfactory nerve									
		-	-	-	-	-	-	-	
Spinal code(Cervical)									
		-	-	-	-	-	-	-	

Notes) - :No abnormal changes, ± :Very slight, + :Slight, 2+ :Moderate, 3+ :Marked, P :Non-graded change, NE :Unexamined
i.n. :intranasal administration, i.t. :intratracheal administration

Study No. : SBL81-20

i.n. :intranasal administration, i.t. :intratracheal administration

Study No. : SBL81-20

Male

[illegible]

Table 8-5 Histopathological findings in cynomolgus monkeys (End of observation) - [H.E. staining]

Study No. : SBL81-20

Female								
Findings	Group	Control	Measles virus vaccine		Control	Measles virus vaccine		
		(i.n.)	(i.n.)		(i.t.)	(i.t.)		
	Dose (mL/body)		0.5			0.3		
	Animal No.	3	6	7	9	10	13	14
Axillar lymph node (left)								
Plasma cell infiltration		±	-	-	-	-	±	-
Brain stem(Included in Fourth ventricle)								
Mononuclear cell infiltration,								
choroid plexus		-	-	±	-	-	-	-
Brain stem(Included in Third ventricle)								
		-	-	-	-	-	-	-
Bronchus (left)								
Mononuclear cell infiltration,								
bronchial gland		±	-	-	±	±	±	±
Cerebellum								
		-	-	-	-	-	-	-
Cerebrum								
		-	-	-	-	-	-	-
Esophageal mucosa								
		-	-	-	-	-	-	-
Hilar lymph node (left)								
		-	-	-	-	-	-	-
Inguinal lymph node (left)								
Plasma cell infiltration		±	-	-	-	-	-	±

Notes) - :No abnormal changes, ± :Very slight, + :Slight, 2+ :Moderate, 3+ :Marked, P :Non-graded change, NE :Unexamined

i.n. :intranasal administration, i.t. :intratracheal administration

Table 8-6 Histopathological findings in cynomolgus monkeys (End of observation) - [H.E. staining]

Study No. : SBL81-20

		Female							
Group		Control	Measles virus vaccine		Control	Measles virus vaccine			
		(i.n.)	(i.n.)		(i.t.)	(i.t.)			
Dose (mL/body)			0.5			0.3			
Findings	Animal No.	3	6	7	9	10	13	14	
Lung (left)									
Macrophage, alveolus		—	—	±	—	—	—	—	
Mesenteric lymph node		—	—	—	—	—	—	—	
Nasal mucosa (left)		—	—	—	—	—	—	—	
Olfactory bulb (left)		—	—	—	—	—	—	—	
Olfactory nerve		—	—	—	—	—	—	—	
Spinal code(Cervical)		—	—	—	—	—	—	—	
Spinal code(Lumbar)		—	—	—	—	—	—	—	
Spleen									
Hyaline substance, germinal center		—	±	—	±	—	—	—	
Stomach(abnormal site)									
Hemorrhage, lamina propria					±				
Inflammatory cell infiltration, lamina propria					±				

Notes) — :No abnormal changes, ± :Very slight, + :Slight, 2+ :Moderate, 3+ :Marked, P :Non-graded change, NE :Unexamined

i.n. :intranasal administration, i.t. :intratracheal administration

Table 8-7 Histopathological findings in cynomolgus monkeys (End of observation) - [H.E. staining]

Study No. : SBL81-20

Female								
Findings	Group	Control	Measles virus vaccine		Control	Measles virus vaccine		
	Dose (mL/body)	(i.n.)	(i.n.)		(i.t.)	(i.t.)		
	Animal No.		0.5			0.3		
		3	6	7	9	10	13	14
Submandibular lymph node (left)								
Brown pigment deposition		±	-	-	-	-	-	-
Erythropoiesis		±	-	-	-	±	-	-
Inflammatory cell infiltration		±	-	-	-	±	-	-
Plasma cell infiltration		-	-	-	±	-	-	-
Thymus								
Cyst		-	-	-	±	-	-	-
Involution		-	-	-	+	-	+	+
Tonsil (left)								
Inflammatory cell infiltration, cavity		±	±	±	±	±	±	±
Trachea								
Dilatation, duct of tracheal gland		+	-	-	±	-	-	-
Inflammatory cell infiltration, lamina propria		-	-	-	±	-	-	-
Mononuclear cell infiltration, lamina propria		-	-	±	±	±	-	±
Mononuclear cell infiltration, tracheal gland		-	-	-	±	-	-	±

Notes) - :No abnormal changes, ± :Very slight, + :Slight, 2+ :Moderate, 3+ :Marked, P :Non-graded change, NE :Unexamined

i.n. :intranasal administration, i.t. :intratracheal administration

Table 9-1 Immunohistochemistry findings in cynomolgus monkeys (End of observation) - [Fluorecent antibody technique staining] Study No. : SBL81-20

		Male							
Group		Control		Measles virus vaccine		Control		Measles virus vaccine	
		(i.n.)		(i.n.)		(i.t.)		(i.t.)	
Dose (mL/body)				0.5				0.3	
Findings	Animal No.	1	2	4	5	8	11	12	
Axillar lymph node (right)		-	-	-	-	-	-	-	
Brain stem(Included in Fourth ventricle)		-	-	-	-	-	-	-	
Brain stem(Included in Third ventricle)		-	-	-	-	-	-	-	
Bronchus (right)									
Positive goblet cell, epithelium		P	P	P	P	P	P	P	
Cerebellum		-	-	-	-	-	-	-	
Cerebrum		-	-	-	-	-	-	-	
Esophageal mucosa		-	-	-	-	-	-	-	
Hilar lymph node (right)		-	-	-	-	-	-	-	
Inguinal lymph node (right)		-	-	-	-	-	-	-	
Lung (right)		-	-	-	-	-	-	-	

Notes) - :No abnormal changes, P :Non-graded change

i.n. :intranasal administration, i.t. :intratracheal administration

Table 9-2 Immunohistochemistry findings in cynomolgus monkeys (End of observation) - [Fluorecent antibody technique staining] Study No. : SBL81-20

Male								
Findings	Group	Control		Measles virus vaccine		Control	Measles virus vaccine	
		(i.n.)		(i.n.)		(i.t.)	(i.t.)	
	Dose (mL/body)			0.5			0.3	
Animal No.		1	2	4	5	8	11	12
Mesenteric lymph node		-	-	-	-	-	-	-
Nasal mucosa (right)		-	-	-	-	-	-	-
Olfactory bulb (right)		-	-	-	-	-	-	-
Spinal code(Cervical)		-	-	-	-	-	-	-
Spinal code(Lumbar)		-	-	-	-	-	-	-
Spleen		-	-	-	-	-	-	-
Submandibular lymph node (right)		-	-	-	-	-	-	-
Thymus		-	-	-	-	-	-	-
Tonsil (right)		-	-	-	-	-	-	-
Trachea								
Positive goblet cell, epithelium		-	-	P	P	P	-	P
Thyroid (right)						-		

Notes) - :No abnormal changes, P :Non-graded change

i.n. :intranasal administration, i.t. :intratracheal administration

Table 9-3 Immunohistochemistry findings in cynomolgus monkeys (End of observation) - [Fluorecent antibody technique staining] Study No. : SBL81-20

Female									
Findings	Group	Control	Measles virus vaccine		Control	Measles virus vaccine			
		(i.n.)	(i.n.)		(i.t.)	(i.t.)			
	Dose (mL/body)		0.5			0.3			
	Animal No.	3	6	7	9	10	13	14	
Axillar lymph node (right)		—	—	—	—	—	—	—	
Brain stem(Included in Fourth ventricle)		—	—	—	—	—	—	—	
Brain stem(Included in Third ventricle)		—	—	—	—	—	—	—	
Bronchus (right)									
Positive goblet cell, epithelium		P	P	P	P	P	P	P	
Cerebellum		—	—	—	—	—	—	—	
Cerebrum		—	—	—	—	—	—	—	
Esophageal mucosa		—	—	—	—	—	—	—	
Hilar lymph node (right)		—	—	—	—	—	—	—	
Inguinal lymph node (right)		—	—	—	—	—	—	—	
Lung (right)		—	—	—	—	—	—	—	

Notes) — :No abnormal changes, P :Non-graded change
 i.n. :intranasal administration, i.t. :intratracheal administration

Table 9-4 Immunohistochemistry findings in cynomolgus monkeys (End of observation) - [Fluorecent antibody technique staining] Study No. : SBL81-20

Female								
Findings	Group	Control	Measles virus vaccine		Control	Measles virus vaccine		
		(i.n.)	(i.n.)		(i.t.)	(i.t.)		
	Dose (mL/body)		0.5			0.3		
Animal No.		3	6	7	9	10	13	14
Mesenteric lymph node		—	—	—	—	—	—	—
Nasal mucosa (right)		—	—	—	—	—	—	—
Olfactory bulb (right)		—	—	—	—	—	—	—
Spinal code(Cervical)		—	—	—	—	—	—	—
Spinal code(Lumbar)		—	—	—	—	—	—	—
Spleen		—	—	—	—	—	—	—
Submandibular lymph node (right)		—	—	—	—	—	—	—
Thymus		—	—	—	—	—	—	—
Tonsil (right)		—	—	—	—	—	—	—
Trachea								
Positive goblet cell, epithelium		P	P	—	P	P	P	—

Notes) — :No abnormal changes, P :Non-graded change

i.n. :intranasal administration, i.t. :intratracheal administration

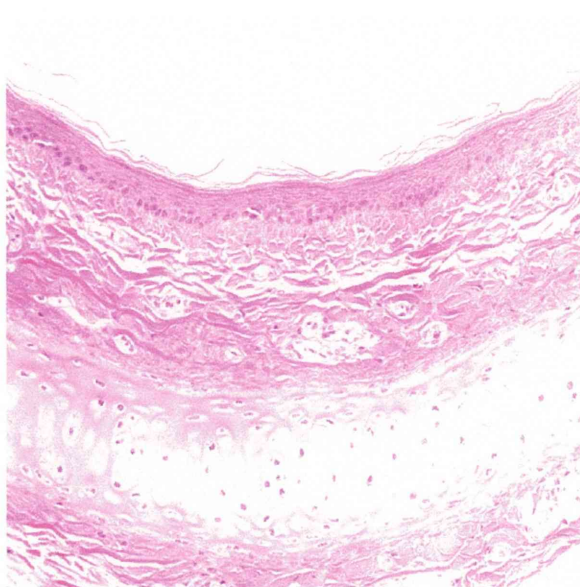


Photo 1 Animal No. 1, Male, Control
End of observation
Nasal mucosa, left
No abnormal changes
(H.E. 2.5×20)

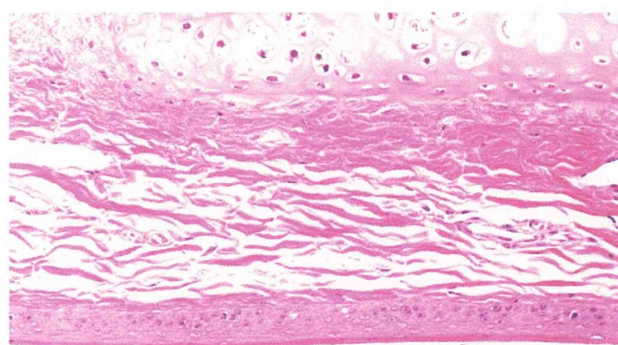


Photo 2 Animal No. 4, Male, Measles virus vaccine, 0.5 mL/body
End of observation
Nasal mucosa, left
No abnormal changes
(H.E. 2.5×20)

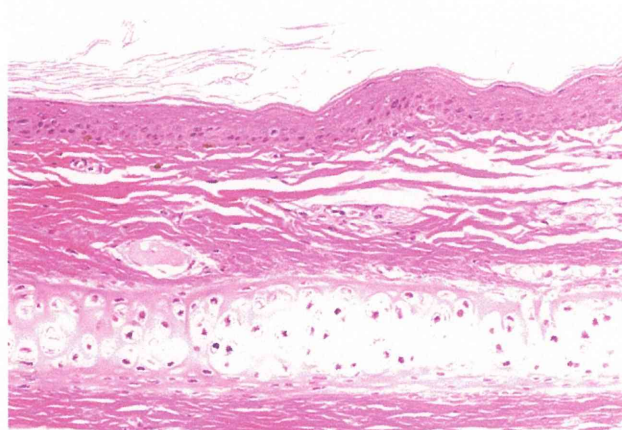


Photo 3 Animal No. 11, Male, Measles virus vaccine, 0.3 mL/body
End of observation
Nasal mucosa, left
No abnormal changes
(H.E. 2.5×20)

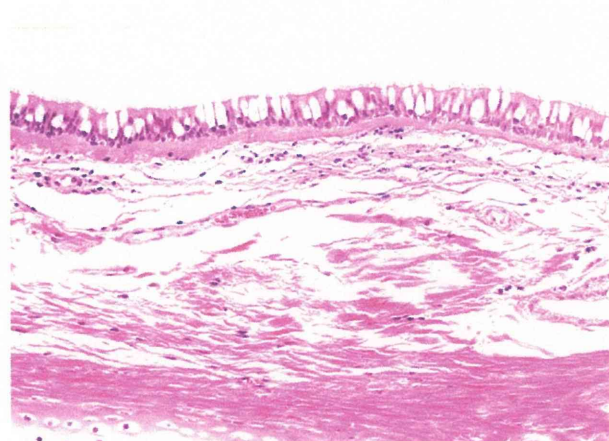


Photo 4 Animal No. 1, Male, Control
End of observation
Trachea
No abnormal changes
(H.E. 2.5×20)



Photo 5 Animal No. 4, Male, Measles virus vaccine, 0.5 mL/body
End of observation
Trachea
No abnormal changes in this photo

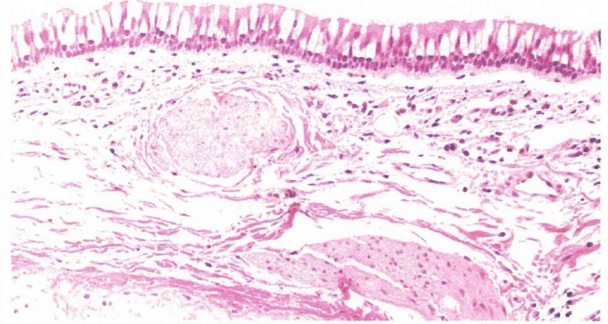


Photo 6 Animal No. 11, Male, Measles virus vaccine, 0.3 mL/body
End of observation
Trachea
No abnormal changes in this photo

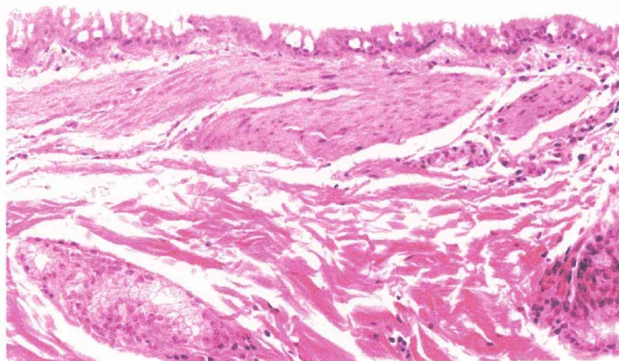


Photo 7 Animal No. 1, Male, Control
End of observation
Bronchus, left
No abnormal changes

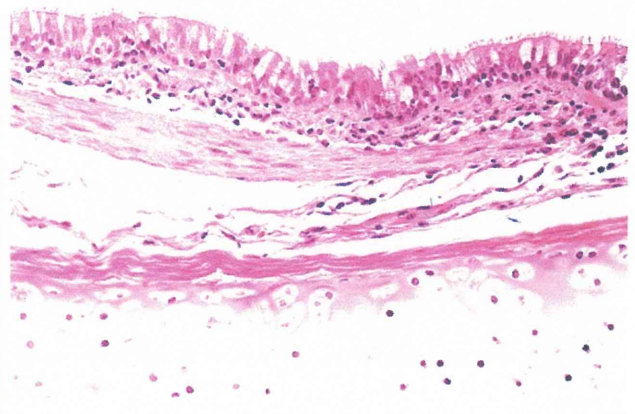


Photo 8 Animal No. 4, Male, Measles virus vaccine, 0.5 mL/body
End of observation
Bronchus, left
No abnormal changes

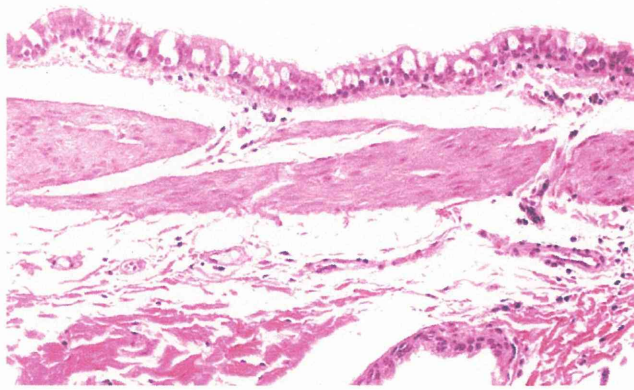


Photo 9 Animal No. 11, Male, Measles virus vaccine, 0.3 mL/body
End of observation
Bronchus, left
No abnormal changes

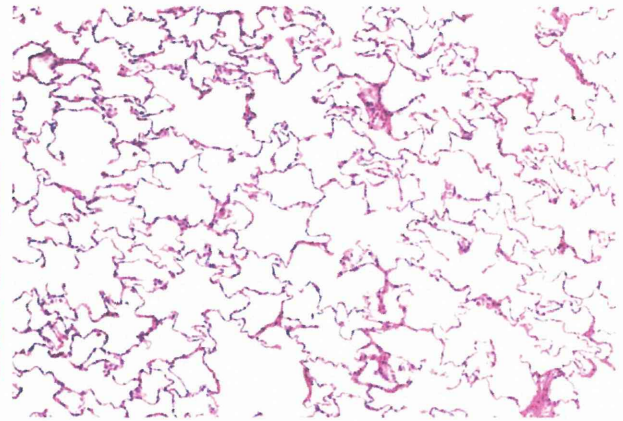


Photo 10 Animal No. 1, Male, Control
End of observation
Lung, left
No abnormal changes

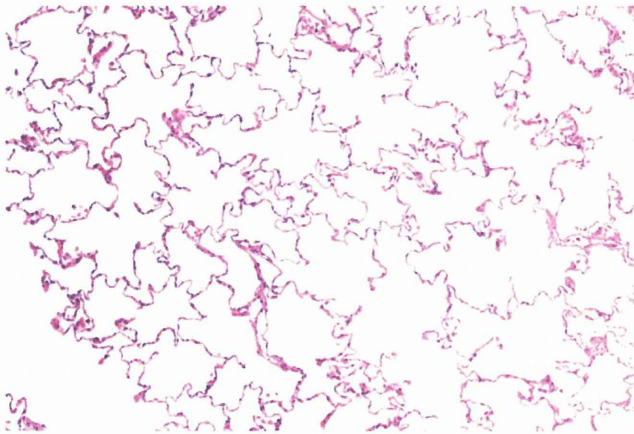


Photo 11 Animal No. 4, Male, Measles virus vaccine, 0.5 mL/body
End of observation
Lung, left
No abnormal changes

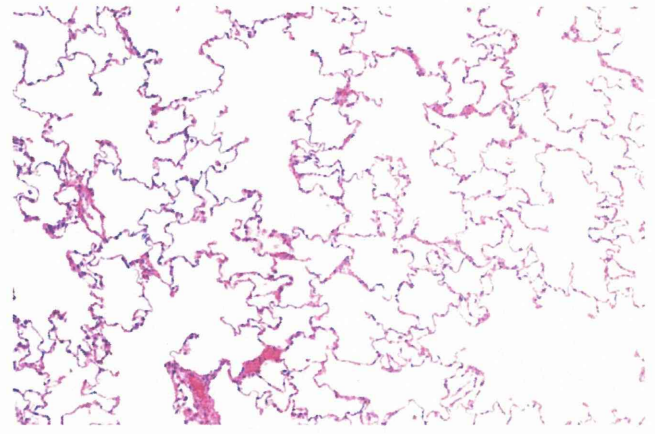


Photo 12 Animal No. 11, Male, Measles virus vaccine, 0.3 mL/body
End of observation
Lung, left
No abnormal changes

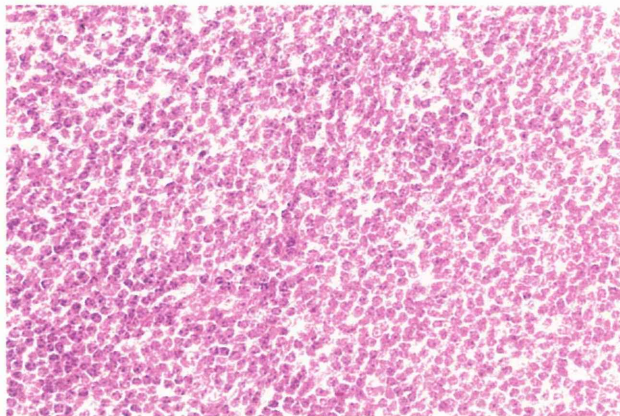


Photo 13 Animal No. 1, Male, Control
End of observation
Hilar lymph node, left
No abnormal changes

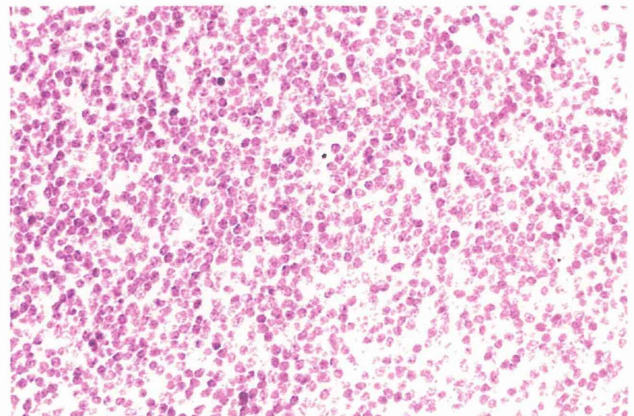


Photo 14 Animal No. 4, Male, Measles virus vaccine, 0.5 mL/body
End of observation
Hilar lymph node, left
No abnormal changes