

연구보고서

# 화학물질 유해성평가를 위한 실험동물의 자연발생 병변조사 연구

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## 요 약 문

### 1. 연구제목

화학물질 유해성평가를 위한 실험동물의 자연발생병변 조사연구

### 2. 연구 필요성 및 목적

본 연구는 향후 흡입독성평가센터에서 수행할 장기독성시험 평가를 위하여 실험동물에 대한 자연발생병변자료를 조사하고, 장기독성시험의 시험동물로 주로 사용되는 F344 랫드에 대한 요검사, 혈액검사, 자연발생병변 검사 등의 자체 병리검사 기초자료를 확보하고자하였다.

### 3. 연구내용 및 방법

본 연구에서는 미국 National Toxicology Program (NTP)에서 발암성시험 동물로 많이 사용하고 있는 F344 랫드 등 시험동물에 대한 자연발생병변을 조사하고 NTP 독성시험에 사용된 랫드, 마우스 등 설치류의 독성병변에 대한 표준 용어 및 표준 독성병변 아트라스를 제시하였다.

또한 본 연구에서는 향후 흡입독성평가센터에서 수행할 장기독성시험에 대한 자체 표준 독성병리자료를 확보하기 위하여 11주령의 F344 랫드를 도입하여 흡입챔버 내에서 물과 사료만 공급하면서 임상관찰을 하고 동물 도입 후 21주에 요검사와 혈액 및 혈액생화학검사를 실시하고, 시험동물을 부검한 후 각 시험동물의 장기무게를 측정하고 조직표본을 제작하여 조직병리검사를 하였다.

## 4. 연구결과

본 연구 결과, 하드리안선의 염증세포침윤은 수컷(50%)과 암컷(68%)에서 모두 많이 나타났다. 심장의 염증세포 침윤은 수컷(32%)이 암컷 (18%)보다 비교적 높게 나타났다. 수컷 신장에서는 유리질 축적(100%), 호염기성 세노관(84%), 유리질 원주(70%), 색소 축적(100%) 등이 빈도 높게 나타났으나, 암컷 신장에서는 무기질침착이 비교적 높게 나타났다(14%). 수컷 간에서는 골수외조혈(14%), 담도 증생(38%), 염증세포침윤(40%) 등이 많이 나타났으나, 암컷 간에서는 염증세포 침윤은 많이 나타났으나(44%) 국소적인 간세포 괴사는 7마리(14%)에서만 나타났다. 수컷 폐에서는 대식세포 축적(38%)과 혈관 주위 무기질침착(30%)이 비교적 많이 나타났으며, 세기관지와 폐포 부위에 샘종이 1마리(2%)에서 나타났으나, 암컷 폐에서는 무기질침착이 6마리(12%)에서만 나타났다. 수컷 이자에서는 샘파리세포 위축이 비교적 많이 나타났으나(24%), 암컷 이자에서는 샘파리세포 위축이 1마리(2%)에서만 나타났다. 비장의 골수외조혈은 수컷에서는 비교적 많이 나타났으나(24%), 암컷에서는 3마리(6%)에서만 나타났다. 흉선의 상피관 및 상피선 증생은 수컷(10%)과 암컷(12%)에서 비슷하게 나타났다. 갑상선의 ultimobranchial cyst는 수컷 1마리(2%)만 나타났다.

## 5. 활용방안 및 기대성과

본 연구를 통하여 생산된 시험동물의 자연발생병변에 대한 병리 기초자료는 화학물질 유해성평가를 위한 장기독성시험 평가를 위한 기초자료로 활용될 것이다.

## 6. 중심어

F344 Rat, background lesions, laboratory animals

## 7. 참고문헌 및 연락처

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# I. 서론

## 1. 연구목적

실험동물을 이용하여 화학물질에 대한 발암성을 평가하기 위하여 랫드, 마우스 등의 설치류가 사용된다. 랫드를 이용한 발암성시험은 2년(104주) 동안 시험물질에 노출시키고, 마우스를 이용한 발암성시험은 1년 6개월(78주) 동안 시험물질에 노출시킨다. 발암성시험은 시험기간이 길어 시험 도중에 다양한 질병도 나타나게 되고 시험 도중에 사망동물도 빈번하게 발생하게 된다. 발암성시험 등 장기독성 시험에서는 시험동물의 생존율과 자연발생 병변이 발암성시험의 평가에 중요한 고려 사항이다. 일반적으로 발암성 시험이 끝나는 시점에 고용량군의 시험동물의 생존율은 시험 시작할 때와 비교하여 최소한 50% 이상이 될 것을 권장하고 있다. 발암성시험 등 시험기간이 긴 독성시험 결과를 정확히 해석하기 위해서는 시험물질과 직접적인 관계없이 발생하는 자연발생질병에 대한 병리기초자료를 충분히 확보하고 있어야 한다(Haseman et al., 1984). 독성시험에 사용되는 시험동물은 시험동물 종에 따라 자연발생병변 발생 종류와 발생률이 다르며, 같은 종이라도 성별과 주령에 따라 자연발생질병의 종류가 다르고 발생빈도도 다르게 나타난다. 같은 종의 시험동물이라도 먹는 사료의 차이에 따라 체중증체율이 달라지고 평균 수명도 달라질 수 있다. 또한 발암성시험과 같이 시험기간이 긴 독성시험 결과를 제대로 해석하기 위해서는 동일한 환경에서 자란 시험동물에 대한 병리학적 기초자료를 충분히 확보하여야 한다.

발암성시험은 장기간 시험물질을 시험동물에 노출시키는 시험으로 시험물질에 의한 시험동물의 영향이 시험물질 농도에 비례하여 적절히 나타나야 한다. 너무 농도가 높아서 도중 사망 동물이 많아서도 안 되며, 너무 낮은 농도로 시험물질에

시험동물을 노출시켜 시험물질에 의한 영향을 평가하기가 어려워서도 안 된다. 발암성시험에서는 적절한 시험물질 농도를 결정하기 위하여 발암성시험을 수행하기 전에 13주 독성 농도결정시험을 한다. 13주 독성시험은 사전에 급성독성시험 및 2주 독성시험 등의 예비 시험을 통하여 시험물질이 시험동물에 미치는 영향을 평가한 후 적절한 농도로 13주 독성시험을 수행하게 된다. 이렇게 발암성시험을 하기 전에 급성독성시험, 2주 독성시험, 13주 독성시험 등 많은 사전 시험이 수행되며 사전 시험 과정에서도 다양한 자연발생병변이 발생한다.

발암성시험에서 생산된 시험물질 노출군의 병리검사는 동일한 시험의 대조군에서 발생한 병리검사와 비교를 한다. 하지만 대조군에서 발생하는 자연발생병변과 시험물질 노출군에서 발생하는 병변 발생률을 비교 분석하여 통계적으로 유의성을 평가하기에는 대조군의 암 수 각각 50마리는 너무 적다. 이러한 문제점을 보완하기 위하여 최근에는 2개의 대조군을 두어 노출군에서 발생하는 다양한 종류의 병변을 비교하여 평가하기도 한다. 장기독성시험의 시험동물에서 다양하게 나타나는 자연발생병변과 시험물질 노출군에서 나타나는 병변에 대한 분별 및 통계학적인 해석을 위하여 각 독성시험 시설에서는 동일한 품종으로 동일한 환경 조건에서 사육된 대조군 시험동물에 대한 병리검사 기초자료를 충분히 확보하여 해당 시험의 병리검사결과 자료와 비교하여 시험결과를 평가하게 된다. 각 독성시험 시설에서는 다른 독성시험 시설의 동일 시험 종에 대한 자연발생병변 발생율도 수집하여 해당 시험에 대한 병리검사 평가에 참고하기도 한다.

본 연구에서는 발암성시험 등 장기독성시험에 사용되는 F344 랫드 등의 실험동물에서 자연발생적으로 생길 수 있는 병변 자료를 문헌조사를 통하여 수집하였다. 또한 본 연구원에서 향후 수행될 장기흡입독성시험에 대한 독성평가를 위한 자체 병리기초자료를 축적하기 위하여 11주령의 F344 랫드를 도입하여 흡입 챔버 내에서 물과 사료만 공급하면서 임상관찰을 하고 시험동물 도입 후 21주(생후 32주령)에 요검사와 혈액 및 혈액생화학검사를 실시하고, 조직병리검사를 실시하였다.

## 2. 실험동물의 자연발생병변 발생률 조사

### 1) F344 랫드의 자연발생종양

1970년대와 1980년대에 미국 NCI(National Cancer Institute)와 NTP(National Toxicology Program)에서는 F344 랫드를 사용한 200종의 발암성시험이 수행되었다. 그 당시 40종의 발암성시험에서 무처치 대조군으로 사용된 F344 랫드와 39종의 발암성시험에서 옥수수유(corn oil) 위관 투여 대조군으로 사용된 F344 랫드에 대한 종양발생률 자료조사(Boorman et al. 1990)에 의하면, F344 랫드의 2년 생존률은 수컷(Male) 66%, 암컷(Female) 73%로 나타났다. F344 랫드의 무처치군과 옥수수유 위관 투여군의 종양발생률 차이는 표 1과 같이 종양에 따라 차이가 나타났다. 단핵세포 백혈병(Mononuclear cell leukemia)은 무처치군에서 33.6%가 나타났으나 옥수수유 위관 투여군에서는 17.1%로 낮게 나타났다. 이자샘과리세포선종(Pancreatic acinar cell adenoma)은 무처치군에서는 0.3% 나타났으나 옥수수유 위관 투여군에서는 5.4%로 높게 나타났다.

무처치군 F344 랫드의 성별 종양발생률은 표 2와 같이 수컷에서는 종양이 98%에서 나타났으며 그 중 53%가 악성으로 나타났다. 암컷에서는 종양이 87 %에서 나타났으며 그 중 39%가 악성으로 나타났다.

F344 랫드의 고빈도 자연발생 종양은 표 3과 같이 수컷에서는 고환 간질세포선종(Interstitial cell tumor of the testis)이 88%로 가장 빈도수가 높았으며, 단핵세포백혈병(Mononuclear cell leukemia)이 34%로 높게 나타났다. 암컷에서는 뇌하수체 선종(Pituitary adenoma)이 45%로 가장 높게 나타났고, 유선 섬유선종(Mammary gland fibroadenoma)이 29%로 높게 나타났다.

NTP 발암성시험에서 장기별 F344 랫드의 자연발생종양 발생률은 표 4와 같이 나타났다.

&lt;표 1&gt; F344 랫드 무처리군과 옥수수유 위관 투여군의 종양발생률

	Mononuclear cell leukemia	Pancreatic acinar cell adenoma
Untreated Group	33.6%	0.3%
Corn oil Group	17.1%	5.4%

&lt;표 2&gt; F344 랫드 성별 자연발생 종양발생률

	Male	Female
Tumor	98%	87%
Malignant neoplasms	53%	39%

&lt;표 3&gt; F344 랫드의 고빈도 자연발생 종양

Male	Female
Interstitial cell tumor of the testis 88%	Mammary gland fibroadenoma 29%
Adrenal pheochromocytoma 26%	Endometrial stromal polyp of the uterus 21%
Mononuclear cell leukemia 34%	Mononuclear cell leukemia 20%
Pituitary adenoma 23%	Pituitary adenoma 45%
Thyroid C-cell tumors 12%	Thyroid C-cell tumors 11%

&lt;표 4&gt; F344 랫드의 자연발생 종양발생률(NTP 발암성시험)

	F344 Rats					
	Male (untreated)			Female (untreated)		
	Animals with Tumors <sup>a</sup>	Rate <sup>b</sup> %	Range %	Animals with Tumors <sup>a</sup>	Rate <sup>b</sup> %	Range %
<b>CirculatorySystem</b>						
All Sites	(1936)			(1983)		
Hemangioma	2	0.1	0-2	3	0.2	0-2
Hemangiosarcoma	10	0.5	0-4	5	0.3	0-2
Heart	(1932)			(1972)		
Hemangiosarcoma	2	0.1	0-2	1	0.1	0-2
Atriocaval mesothelioma	0	0.0	-	1	0.1	0-2

	F344 Rats					
	Male (untreated)			Female (untreated)		
	Animals with Tumors <sup>a</sup>	Rate <sup>b</sup> %	Range %	Animals with Tumors <sup>a</sup>	Rate <sup>b</sup> %	Range %
Fibrosarcoma	0	0.0	-	0	0.0	-
Neurofibrosarcoma	0	0.0	-	1	0.1	0-2
Sarcoma	1	0.1	0-2	0	0.0	-
Malignant Schwannoma	1	0.1	0-2	4	0.2	0-4
Epididymis	(1936)					
Hemangioma	1	0.1	0-2			
Uterus				(1966)		
Hemangioma				2	0.1	0-2
Brain	(1928)			(1969)		
Hemangioma	0	0.0	-	1	0.1	0-2
Large Intestine	(1850)			(1920)		
Hemangioma	0	0.0	-	0	0.0	-
Pelvis	(1936)			(1983)		
Hemangiosarcoma	0	0.0	-	1	0.1	0-2
Skin/Subcutaneous Tissue	(1936)			(1983)		
Hemangioma	0	0.0	-	0	0.0	-
Hemangiosarcoma	1	0.1	0-2	1	0.1	0-2
Spleen	(1906)			(1961)		
Hemangioma	1	0.1	0-2	0	0.0	-
Hemangiosarcoma	6	0.3	0-4	2	0.1	0-2
Vertebra	(1936)			(1983)		
Hemangiosarcoma	1	0.1	0-2	0	0.0	-
Muscle	(1936)			(1983)		
Hemangiosarcoma	0	0.0	-	0	0.0	-
<b>Digestive System</b>						
Oral Mucosa (Anu Site)	(1936)			(1983)		
Squamous Cell Papilloma	1	0.1	0-2	1	0.1	0-2
Squamous Cell Carcinoma	1	0.1	0-2	1	0.1	0-2
Tooth	(1936)			(1983)		
Odontoma	2	0.1	0-2	0	0.0	-
Salivary Gland	(1985)			(1939)		
Adenoma	0	0.0	-	0	0.0	-
Adenocarcinoma	1	0.1	0-2	0	0.0	-
Fibrosarcoma	2	0.1	0-2	0	0.0	-
Sarcoma	2	0.1	0-2	0	0.0	-
Liver	(1928)			(1979)		
Neoplastic Nodule	80	4.1	0-12	45	2.3	0-10

	F344 Rats					
	Male (untreated)			Female (untreated)		
	Animals with Tumors <sup>a</sup>	Rate <sup>b</sup> %	Range %	Animals with Tumors <sup>a</sup>	Rate <sup>b</sup> %	Range %
Hepatocellular Carcinoma	20	1.0	0-6	3	0.2	0-2
Cholangiocarcinoma	0	0.0	-	0	0.0	-
Cholangioma	1	0.1	0-2	0	0.0	-
Lipoma	1	0.1	0-2	0	0.0	-
Esophagus	(1851)			(1909)		
Squamous Cell Carcinoma	0	0.0	-	0	0.0	-
Forestomach	(1912)			(1955)		
Squamous Cell Papilloma	3	0.2	0-2	5	0.3	0-4
Squamous Cell Carcinoma	2	0.1	0-2	1	0.1	0-2
Leiomyosarcoma	1	0.1	0-2	0	0.0	-
Glandular Stomach	(1912)			(1955)		
Adenocarcinoma	1	0.1	0-2	0	0.0	-
Fibrosarcoma	0	0.0	-	0	0.0	-
Neurofibrosarcoma	1	0.1	0-2	0	0.0	-
Sarcoma	0	0.0	-	1	0.1	0-2
Small Intestine	(1865)			(1939)		
Adenomatous Polyp	0	0.0	-	0	0.0	-
Adenocarcinoma	7	0.4	0-2	0	0.0	-
Fibrosarcoma	1	0.1	0-2	1	0.1	0-2
Sarcoma	1	0.1	0-2	1	0.1	0-2
Malignant Schwannoma	0	0.0	-	0	0.0	-
Leiomyoma	1	0.1	0-2	0	0.0	-
Leiomyosarcoma	3	0.2	0-2	2	0.1	0-2
Large Intestine/Rectum	(1936)			(1983)		
Adenomatous Polyp	0	0.0	-	0	0.0	-
adenocarcinoma	2	0.1	0-2	0	0.0	-
Fibroma	1	0.1	0-2	0	0.0	-
Fibrosarcoma	0	0.0	-	0	0.0	-
Lipoma	0	0.0	-	0	0.0	-
Malignant Schwannoma	1	0.1	0-2	0	0.0	-
Pancreas	(1868)			(1934)		
Acinar Cell Adenoma	5	0.3	0-4	3	0.2	0-2
Acinar Cell Carcinoma	0	0.0	-	0	0.0	-
Benign Mixed Tumor	0	0.0	-	0	0.0	-
Malignant Mixed Tumor	1	0.1	0-2	0	0.0	-
Pancreatic Duct	(1868)			(1934)		
Adenoma	1	0.1	0-2	0	0.0	-
<b>EndocrineSystem</b>						
Pancreatic Islets	(1868)			(1934)		
Islet Cell Adenoma	59	3.2	0-11	19	1.0	0-7
Islet Cell Carcinoma	39	2.1	0-8	5	0.3	0-4

	F344 Rats					
	Male (untreated)			Female (untreated)		
	Animals with Tumors <sup>a</sup>	Rate <sup>b</sup> %	Range %	Animals with Tumors <sup>a</sup>	Rate <sup>b</sup> %	Range %
Pituitary, Pars Distalis	(1868)			(1934)		
Adenoma	417	22.8	5-52	869	45.2	18-70
Carcinoma	42	2.3	0-11	72	3.7	0-16
Pituitary, Pars Intermedia	(1868)			(1934)		
Adenoma	3	0.2	0-4	2	0.1	0-2
Craniopharyngioma	0	0.0	-	0	0.0	-
Pituitary, Pars Nervosa	(1868)			(1934)		
Glioma	0	0.0	-	2	0.1	0-4
Adrenal Cortex	(1915)			(1968)		
Adenoma	23	1.2	0-8	56	2.8	0-12
Carcinoma	2	0.1	0-2	4	0.2	0-2
Adrenal Medulla	(1915)			(1968)		
Pheochromocytoma	489	25.5	6-65	99	5.0	0-16
Ganglioneuroma	5	0.3	0-2	3	0.2	0-2
Thyroid	(1904)			(1938)		
Follicular Cell Adenoma	13	0.7	0-5	12	0.6	0-2
Follicular Cell Carcinoma	10	0.5	0-2	7	0.4	0-2
C-Cell Adenoma	147	7.7	0-22	156	8.0	0-34
C-Cell Carcinoma	73	3.8	0-12	66	3.4	0-10
Parathyroid	(1303)			(1328)		
Adenoma	6	0.5	0-6	2	0.2	0-3
<b>Hematopoietic System</b>						
All Sites	(1936)			(1983)		
Mononuclear Cell Leukemia	651	33.6	10-72	401	20.2	6-31
Spleen	(1906)			(1961)		
Fibroma	0	0.0	-	0	0.0	-
Sarcoma	8	0.4	0-2	1	0.1	0-2
Leiomyoma	0	0.0	-	0	0.0	-
Leiomyosarcoma	0	0.0	-	1	0.1	0-2
Thymus	(1481)			(1597)		
Thymoma	4	0.2	0-2	2	0.1	0-2
<b>Integumentary System</b>						
	(1936)			(1983)		
Fibroma	101	5.2	0-12	25	1.3	0-6
Neurofibroma	2	0.1	0-4	0	0.0	-
Fibrosarcom	26	1.3	0-8	22	1.1	0-6
aNeurofibrosarcoma	7	0.4	0-6	6	0.3	0-4
Sarcoma	10	0.5	0-6	6	0.3	0-2
Squamous Cell Papilloma	28	1.4	0-5	5	0.3	0-2
Squamous Cell Carcinoma	17	0.9	0-6	6	0.3	0-4

F344 Rats						
	Male (untreated)			Female (untreated)		
	Animals with Tumors <sup>a</sup>	Rate <sup>b</sup> %	Range %	Animals with Tumors <sup>a</sup>	Rate <sup>b</sup> %	Range %
Basal Cell Tumor	13	0.7	0-6	0	0.0	-
Basal Cell Carcinoma	14	0.7	0-4	5	0.3	0-2
Trichoepithelioma	4	0.3	0-2	1	0.1	0-2
Keratoacanthoma	31	1.6	0-14	6	0.3	0-4
Malignant Fibrous Histiocytoma	4	0.2	0-2	2	0.1	0-2
Malignant Schwannoma	6	0.3	0-2	3	0.2	0-4
Lipoma	8	0.4	0-2	1	0.1	0-2
<b>MusculoskeletalSystem</b>	(1936)			(1983)		
Osteoma	0	0.0	-	0	0.0	-
Osteosarcoma	8	0.4	0-4	8	0.4	0-4
Fibrosarcoma	1	0.1	0-2	0	0.0	-
Neurofibrosarcoma	1	0.1	0-3	0	0.0	-
Sarcoma	0	0.0	-	0	0.0	-
Lipoma	0	0.0	-	0	0.0	-
Liposarcoma	1	0.1	0-2	1	0.1	0-2
Rhabdomyosarcoma	0	0.0	-	1	0.1	0-2
Chondrosarcoma	0	0.0	-	0	0.0	-
Synovial Sarcoma	1	0.1	0-2	0	0.0	-
<b>NervousSystem</b>						
Brain	(1928)			(1969)		
Granular Cell Tumor	4	0.2	0-2	0	0.0	-
Meningioma	2	0.1	0-2	2	0.1	0-2
Glioma	2	0.1	0-2	2	0.1	0-2
Ependymoma	0	0.0	-	0	0.0	-
Astrocytoma	9	0.5	0-4	18	0.9	0-6
Oligodendroglioma	2	0.1	0-2	3	0.2	0-2
Medulloblastoma	1	0.1	0-2	1	0.1	0-2
Spinal Cord	(1936)			(1983)		
Malignant Schwannoma	1	0.1	0-2	0	0.0	-
<b>ReproductiveSystem</b>						
(Male)						
Mammary Gland	(1936)					
Adenoma	2	0.1	0-2			
Fibroadenoma	51	2.6	0-12			
Carcinoma	3	0.2	0-2			
Preputial/Clitoral Gland	(1936)					
Adenoma	73	3.8	0-16			
Carcinoma	61	3.2	0-10			
Squamous Cell Papilloma	0	0.0	-			
Prostate	(1862)					
Adenoma	11	0.6	0-10			

	F344 Rats					
	Male (untreated)			Female (untreated)		
	Animals with Tumors <sup>a</sup>	Rate <sup>b</sup> %	Range %	Animals with Tumors <sup>a</sup>	Rate <sup>b</sup> %	Range %
Seminal Vesicle	(1936)					
Adenoma	0	0.0	–			
Carcinosarcoma	1	0.1	0–2			
Testis	(1910)					
Interstitial Cell Tumor	1677	87.8	64–98			
Epididymis	(1936)					
Sarcoma	0	0.0	–			
<b>Reproductive System</b>						
(Female)						
Mammary Gland	(1983)					
Adenoma	18	0.9	0–6			
Fibroadenoma	576	29.0	10–49			
Carcinoma	52	2.6	0–8			
Preputial/Clitoral Gland	(1983)					
Adenoma	56	2.8	0–20			
Carcinoma	59	3.0	0–12			
Squamous Cell Papilloma	0	0.0	–			
Vagina	(1983)					
Squamous Cell Papilloma	0	0.0	–			
Granular Cell Tumor	1	0.1	0–2			
Fibroma	0	0.0	–			
Sarcoma	1	0.1	0–2			
Leiomyosarcoma	0	0.0	–			
Uterus	(1966)					
Endometrial Stromal Polyp	420	21.4	8–37			
Endometrial Stromal Sarcoma	22	1.1	0–6			
Adenoma	4	0.2	0–2			
Adenocarcinoma	7	0.4	0–4			
Fibroma	0	0.0	–			
Sarcoma	3	0.2	0–2			
Leiomyoma	3	0.2	0–2			
Leiomyosarcoma	4	0.2	0–3			
Malignant Schwannoma	2	0.1	0–2			
Granular Cell Tumor	0	0.0	–			
Squamous Cell Carcinoma	2	0.1	0–2			
Ovary	(1958)					
Cystadenoma	0	0.0	–			
Tubular Adenoma	0	0.0	–			
Thecoma	0	0.0	–			
Sertoli Cell Tumor	1	0.1	0–2			
Luteoma	2	0.1	0–2			
Gonadal Stromal Tumor	0	0.0	–			
Granulosa Cell Tumor	14	0.7	0–4			
Granulosa Cell Tumor, Malignant	3	0.2	0–2			

	F344 Rats					
	Male (untreated)			Female (untreated)		
	Animals with Tumors <sup>a</sup>	Rate <sup>b</sup> %	Range %	Animals with Tumors <sup>a</sup>	Rate <sup>b</sup> %	Range %
Lipoma				0	0.0	-
Carcinoma				0	0.0	-
Fibroma				0	0.0	-
Sarcoma				1	0.1	0-2
<b>Respiratory System</b>						
Nasal Cavity	(1936)			(1983)		
Adenoma	0	0.0	-	0	0.0	-
Squamous Cell Papilloma	1	0.1	0-2	0	0.0	-
Squamous Cell carcinoma	1	0.1	0-2	0	0.0	-
Trachea	(1834)			(1896)		
Adenocarcinoma	1	0.1	0-2	0	0.0	-
Lung	(1933)			(1974)		
Alveolar/Bronchiolar Adenoma	25	1.3	0-6	16	0.5	0-4
Alveolar/Bronchiolar Carcinoma	20	1.0	0-6	6	0.3	0-3
Squamous Cell Carcinoma	3	0.2	0-2	0	0.0	-
<b>Special Sense Organs</b>						
Eye	(1936)			(1983)		
Glioma	0	0.0	-	0	0.0	-
Eye/conjunctiva	(1936)			(1983)		
Squamous Cell Carcinoma	1	0.1	0-2	0	0.0	-
Lacrimal Gland	(1936)			(1983)		
Adenoma	0	0.0	-	1	0.1	0-2
Nasolacrimal Duct	(1936)			(1983)		
Squamous Cell Carcinoma	2	0.1	0-2	0	0.0	-
Harderian Gland	(1936)			(1983)		
Adenoma	1	0.1	0-2	0	0.0	-
Ear	(1936)			(1983)		
Neural Crest Neoplasms	3	0.1	0-2	3	0.1	0-4
Zymbal Gland	(1936)			(1983)		
Squamous Cell Papilloma	2	0.1	0-2	0	0.0	-
Adenoma	0	0.0	-	0	0.0	-
Carcinoma	28	1.4	0-8	14	0.7	0-6
<b>Urinary System</b>						
Kidney	(1928)			(1977)		
Tubular Cell Adenoma	7	0.4	0-4	2	0.1	0-2

F344 Rats						
	Male (untreated)			Female (untreated)		
	Animals with Tumors <sup>a</sup>	Rate <sup>b</sup> %	Range %	Animals with Tumors <sup>a</sup>	Rate <sup>b</sup> %	Range %
Tubular Cell Adenocarcinoma	3	0.2	0-2	2	0.1	0-2
Transitional Cell Papilloma	3	0.2	0-2	0	0.0	-
Transitional Cell Carcinoma	2	0.1	0-2	0	0.0	-
Sarcoma	1	0.1	0-2	0	0.0	-
Nephroblastoma	1	0.1	0-2	0	0.0	-
Lipoma	2	0.1	0-2	0	0.0	-
Liposarcoma	0	0.0	-	0	0.0	-
Leiomyosarcoma	0	0.0	-	0	0.0	-
Urinary Bladder	(1858)			(1932)		
Transitional Cell Papilloma	3	0.2	0-2	3	0.2	0-3
Transitional Cell Carcinoma	0	0.0	-	1	0.1	0-2
Urethra	(1936)			(1983)		
Transitional Cell Carcinoma	1	0.1	0-2	0	0.0	-
<b>Body Cavities</b>	(1936)			(1983)		
Mesothelioma	53	2.7	0-10	2	0.1	0-2
Paraganglioma	1	0.1	0-2	1	0.1	0-2
Fibroma	1	0.1	0-2	2	0.1	0-3
Fibrosarcoma	1	0.1	0-2	0	0.0	-
Neurofibrosarcoma	1	0.1	0-2	1	0.1	0-2
Lipoma	1	0.1	0-2	2	0.1	0-2
Liposarcoma	0	0.0	-	0	0.0	-
Leiomyosarcoma	0	0.0	-	1	0.1	0-2
Sarcoma	4	0.2	0-2	3	0.2	0-2
<b>All Sites</b>	(1936)			(1983)		
Benign Tumors	1816	93.8	82-100	1457	73.5	58-86
Malignant Tumors	1024	52.9	38-82	767	38.7	18-56
Benign and/or Malignant Tumors	1895	97.9	90-100	1725	87.0	64-98

## 2) Harlan SD 랫드의 자연발생병변

미국 바텔(Battle Columbus Laboratories, Columbus, OH)에서 40일령의 암컷 SD 랫드를 도입하여 15일간 순화시킨 후 8주령에 이른 암컷 Harlan SD 랫드에 옥수수유와 아세톤을 99대 1의 비율로 섞은 vehicle을 대조군에 주입하며 자연발생병변을 조사하였다(Amy et., al., 2005).

## (1) 암컷 Harlan SD 랫드의 주령별 자연발생병변

대조군을 케이지 당 5마리씩 암컷 Harlan SD 랫드를 사육하여 시험개시 14주(70마리), 31주(70마리), 53주(56마리) 후에 암컷 Harlan SD 랫드의 자연발생병변을 조사한 결과는 표 5와 같다(Amy et., al., 2005). 부신 피질의 비대(Hypertrophy)는 14주차에서는 7.1%에서 발생하였으나 31주차에서는 27.1%, 53주차에서는 58.1%로 나타났다. 간장의 호염기성병소(Basophilic focus)는 14주차에서는 발생하지 않았으나 31주차에서는 1.4%, 53주차에서는 14.3%로 나타났다. 간장의 호산성병소(Eosinophilic focus)도 14주차에서는 발생하지 않았으나 31주차에서는 2.9%, 53주차에서는 5.4%로 나타났다. 간장의 복합 병소(Mixed focus)도 14주차에서는 발생하지 않았으나 31주차에서는 32.9%, 53주차에서는 62.5%로 높게 나타났다. 폐에서는 조직구 침투(Infiltration cellular, histiocyte)가 14주차에서는 1.4%에서 발생하였으나 31주차에서는 14.3%, 53주차에서는 53.6%로 높게 나타났다. 유선의 증생(Hyperplasia)은 14주차에서는 나타나지 않았으나 31주차에서는 4.3%, 53주차에서는 10.7%에서 나타났다. 뇌하수체의 증생(Par distalis, Hyperplasia)은 14주차에서는 나타나지 않았으나 31주차에서는 2.9%, 53주차에서는 5.4%에서 나타났다. 갑상선의 C 세포 증생(C-cell hyperplasia)과 C 세포 샘종(C-cell adenoma)은 14주차와 31주차에서는 나타나지 않았고 53주차에서 나타나기 시작하였다. 자궁에서는 편평상피 화생(Metaplasia, squamous)이 14주차에서는 4.3%에서 발생하였으나 31주차에서는 62.9%, 53주차에서는 87.5%로 높게 나타났다. 자궁내막 낭포 증생(Endometrium, Hperplasia, cystic)이 14주차와 31주차에서는 24.3%로 동일한 비율로 나타났으나 53주차에서는 58.9%로 높게 나타났다.

&lt;표 5&gt; 암컷 Harlan Sprague-Dawley 랫드의 주령별 자연발생병변 발생률

Organ, lesion	Incidence		
	14-week interim sacrifice	31-week interim sacrifice	53-week interim sacrifice
Adrenal Cortex			
Hypertrophy	7.1% (5/70)	27.1% (19/70)	58.1% (29/56)
Hyperplasia		1.4% (1/70)	7.1% (4/56)
Degeneration		1.4% (1/70)	7.1% (4/56)
Adrenal Medulla			
Hyperplasia		1.4% (1/70)	
Clitoral Gland			
Carcinoma			1.8% (1/56)
Liver			
Basophilic focus		1.4% (1/70)	14.3% (8/56)
Clear focus			7.1% (4/56)
Eosinophilic focus		2.9% (2/70)	5.4% (3/56)
Mixed focus		32.9% (23/70)	62.5% (35/56)
Lung			
Infiltration cellular, histiocyte	1.4% (1/70)	14.3% (10/70)	53.6% (30/56)
Mammary Gland			
Hyperplasia		4.3% (3/70)	10.7% (6/56)
Fibroadenoma		1.4% (1/70)	
Carcinoma	1.4% (1/70)		
Pancreas, Acinus			
Hyperplasia			1.8% (1/56)
Atrophy	1.4% (1/70)	7.1% (5/70)	
Pituitary Gland			
Pars distalis, Hyperplasia		2.9% (2/70)	5.4% (3/56)
Skin			
Sarcoma		1.4% (1/70)	
Thyroid Gland			
c-cell hyperplasia			14.3% (8/56)
c-cell adenoma			8.9% (5/56)
Uterus			
Metaplasia, squamous	4.3% (3/70)	62.9% (44/70)	87.5% (49/56)
Endometrium, Hyperplasia,	24.3% (17/70)	24.3% (17/70)	58.9% (33/56)
cystic			1.8% (1/56)
Polyp stromal			

## (2) 암컷 Harlan SD 랫드의 자연발생병변

7개의 발암성시험에 대조군으로 사용된 암컷 Harlan SD 랫드(총 371마리, 평균 생존률 41.5%)에서 발생한 자연발생병변을 조사한 결과는 표 6과 같다(Amy et., al., 2005). 부신에서는 피질의 증대(Hypertrophy)가 81%로 높게 나타났으며 부신 피질 증생(Hyperplasia)은 30%로 나타났다. 부신 속질의 증생(Hyperplasia)은 25.5%로 나타났다. 음핵선에서는 이중 낭포(Clitoral Gland Duet, cyst)가 72.9%로 높게 나타났다. 심장에서는 심근증(Cardiomypathy)이 28.5%로 비교적 높게 나타났다. 신장에서는 신증(Nephropathy) 61.1%로 높게 나타났으며 무기질 침착(Mineralization)도 75.1%로 높게 나타났다. 간에서는 담관증생(Bile duct hyperplasia)이 7.8%로 나타났으며, 호염기성병소(Basophilic focus)는 32.4%, 호산성병소(Eosinophilic focus)는 24%, 혼합세포병소(Mixed cell focus)는 52.3%로 나타났다. 폐에서는 폐포상피 증생(Alveolar epithelium, hyperplasia)이 28.1%로 나타났고, 조직구 침윤(Infiltration cellular, histiocyte)이 80.3%로 높게 나타났다. 유선(Mammary Gland)에서는 증생(Hyperplasia)이 50.9%로 나타났으며 섬유샘종(Fibroadenoma)이 70.9%로 높게 나타났다. 뇌하수체(Pituitary Gland)에서는 증생(Pars distalis, hyperplasia)이 34.1%로 나타났으며 샘종(Pars distalis, adenoma)도 41.2%에서 나타났다. 갑상선(Thyroid Gland)에서는 C세포 증생(C-cell hyperplasia)이 31.3%로 나타났으며, C세포 샘종(C-cell adenoma)은 26.2%가 나타났다. 자궁(Uterus)에서는 편평상피 화생(Metaplasia, squamous)이 44.2%로 비교적 높게 나타났으며 자궁내막 낭포 증생(Endometrium, hyperplasia, cystic)도 59.3%로 높게 나타났다.

&lt;표 6&gt; 암컷 Harlan Sprague-Dawley 랫드의 병변 발생률

Organ, lesion	Incidence
Adrenal cortex	
Hypertrophy	81% (229/369)
Hyperplasia	30% (114/369)
Degeneration, cystic	18.7% (69/369)
Adenoma	0.5% (2/369)
Carcinoma	0.5% (2/369)
Adrenal medulla	
Hyperplasia	25.5% (94/368)
Pheochromocytoma, benign	7.6% (28/368)
Pheochromocytoma, complex	0.3% (1/368)
Pheochromocytoma, malignant	0.3% (1/368)
Bone	
Osteosarcoma	0.3% (1/371)
Bone Marrow	
Lipoma	0.3% (1/371)
Brain	
Astrocytoma, malignant	0.5% (2/371)
Oligodendroglioma, malignant	0.3% (1/371)
Medulloblastoma, malignant	0.3% (1/371)
Clitoral Gland	
Duet, cyst	72.9% (269/363)
Adenoma	0.3% (1/363)
Ear	
Pinna, neural crest tumor	0.3% (1/371)
Forestomach	
Squamous cell papilloma	0
Squamous cell carcinoma	0.5% (2/371)
Heart	
Cardiomyopathy	28.5% (105/369)
Schwannoma, malignant	0.8% (3/369)
Hemangiosarcoma	0.3% (1/369)
Intestine Large, Cecum	
Leiomyoma	0.3% (1/371)
Intestine Large, Colon	
Carcinoma	0.3% (1/371)
Intestine Small, Jejunum	
Leiomyosarcoma	0.3% (1/371)
Fibrosarcoma	0.3% (1/371)
Islets, Pancreatic	
Adenoma	1.6% (6/367)
Carcinoma	0.5% (2/367)
Kidney	
Nephropathy	61.1% (226/370)
Transitional epithelium hyperplasia	5.7% (21/370)
Mineralization	75.1% (278/370)
Hemangiosarcoma	0.3% (1/370)
Nephroblastoma	0.5% (2/370)
Lipoma	0.3% (1/370)
Renal tubular adenoma	0.3% (1/370)

Tenal tubular carcinoma	0.3% (1/370)
Liver	
Bile duct hyperplasia	7.8% (29/371)
Basophilic focus	32.4% (120/371)
Clear cell focus	11.1% (41/371)
Eosinophilic focus	24% (89/371)
Mixed cell focus	52.3% (194/371)
Hepatocellular adenoma	1.3% (5/371)
Hemangioma	0.3% (1/371)
Lung	
Alveolar epithelium, hyperplasia	28.1% (104/370)
Infiltration cellular, histiocyte	80.3% (297/370)
Alveolar/bronchiolar adenoma	0.5% (2/370)
Lymph Node, Mesenteric	
Hemangiosarcoma	0.3% (1/371)
Mammary Gland	
Hyperplasia	50.9% (189/371)
Adenoma	3.0% (11/371)
Carcinoma	11.3% (42/371)
Fibroadenoma	70.9% (263/371)
Mesentery	
Schwannoma malignant	0.3% (1/371)
Multiple Organs	
Mononuclear cell leukemia	0.5% (2/371)
Malignant lymphoma	1.1% (4/371)
Oral Mucosa	
Gingival, squamous cell carcinoma	1.1% (4/371)
Ovary	
Luteoma	0.5% (2/367)
Granulosa cell tumor malignant	0.5% (2/367)
Cystadenoma	0.3% (1/367)
Pancreas, Acinus	
Atrophy	3.8% (14/366)
Hyperplasia	3.0% (11/367)
Adenoma	0.3% (1/366)
Parathyroid Gland	
Adenoma	0.3% (1/366)
Pituitary Gland	
Pars distalis, hyperplasia	34.1% (126/369)
Pars intermedia, hyperplasia	0.8% (3/369)
Pars distalis, adenoma	41.2% (152/369)
Pars distalis, carcinoma	0.3% (1/369)
Pars intermedia, adenoma	1.1% (4/369)
Skeletal Muscle	
Fibrous histiocyoma	0.3% (1/371)
Skin/Subcutaneous Tissue	
Basal cell carcinoma	0.3% (1/371)
Fibroma	1.4% (5/371)
Fibrosarcoma	0.3% (1/371)
Sarcoma	0.3% (1/371)
Schwannoma malignant	0.3% (1/371)
Keratoacanthoma	0.3% (1/371)
Squamous cell papilloma	0.3% (1/371)

Trichoepithelioma	0.3% (1/371)
Thymus	
Thymoma, benign	0.3% (1/371)
Thyroid Gland	
C-cell hyperplasia	31.3% (155/367)
C-cell adenoma	26.2% (96/367)
C-cell carcinoma	3.8% (14/367)
Follicular cell adenoma	0.5% (2/367)
Tooth	
Periodontal tissue, fibrosarcoma	0.3% (1/371)
Periodontal tissue, neurofibrosarcoma	0.3% (1/371)
Urinary Bladder	
Papilloma	0.3% (1/367)
Uterus	
Metaplasia, squamous	44.2% (164/371)
Endometrium, hyperplasia, cystic	59.3% (220/371)
Adenoma	0.5% (2/371)
Carcinoma	0.5% (2/371)
Fibroma	0.3% (1/371)
Leiomyoma	0.3% (1/371)
Leiomyosarcoma	0.3% (1/371)
Polyp stromal	15.6% (58/371)
Sarcoma stromal	0.3% (1/371)
Squamous cell papilloma	0.5% (2/371)
Squamous cell carcinoma	0.3% (1/371)
Schwannoma, malignant	0.3% (1/371)
Cervix, schwannoma malignant	0.5% (2/371)
Cervix, carcinoma	0.3% (1/371)
Vagina	
Sarcoma	0.3% (1/371)
Squamous cell papilloma	0.3% (1/371)
Squamous cell carcinoma	0.3% (1/371)
Malignant schwannoma	0.3% (1/371)
Zymbal's Gland	
Carcinoma	0.3% (1/371)

### (3) 섭취사료 종류별 랫드의 자연발생병변

시험동물에 사용되는 시험동물의 종에 따라 자연발생병변은 다르게 나타나지만, 같은 시험동물 종이라도 섭취하는 사료의 종류에 따라 자연발생병변은 다를 수 있다. NTP-2000 사료를 섭취한 SD 암컷 랫드의 평균 수명은 628.7일(평균생존률 41.3%), NTP-2000 사료를 섭취한 Fisher 암컷 랫드의 평균 수명은 707일(평균생존률 76%)로 알려져 있다(Haseman et al., 2003). NIH-07 사료를 섭취한 암컷 Fisher 랫드의 평균수명은 674일로 알려져 있다(Amy et., al., 2005). 동일한

Fischer 랫드지만 NTP-2000사료를 공여한 동물과 NTP-07 사료를 공여한 동물의 자연발생병변은 표 6과 같이 다르게 나타난다. 단핵세포백혈병, 음핵선 샘종과 암종, 뇌하수체(Pituitary gland, pars distalis) 샘종과 암종, 갑상선의 C세포 샘종 및 암종 유선의 섬유샘종 등은 NTP-2000사료를 섭취한 Fischer 랫드에 비하여 NTP-07 사료를 섭취한 동물에서 자연발생병변 발생률이 낮게 나타났다.

<표 7> 섭취 사료 종류별 랫드의 자연발생 종양발생률

Lesion	Incidence		
	Harlan Sprague-Dawley rats, gavage studies, NTP-2000 diet	Fischer rats, feed studies, NTP-2000 diet	Fischer rats, gavage studies, NIH-07 diet
Uterine polyp	16% (58/371)	17% (60/360)	20.2% (390/1934)
Mononuclear cell leukemia	< 1% (2/371)	24% (87/360)	19.3% (377/1950)
Clitoral gland adenoma/carcinoma	< 1% (1/363)	15% (52/353)	4.2% (83/1950)
Pituitary gland, pars distalis, adenoma or carcinoma	41% (153/367)	34% (121/359)	24.8% (813/1901)
Thyroid gland C-cell adenoma or carcinoma	30% (110/367)	16% (58/360)	11.4% (218/1913)
Mammary gland fibroadenoma	71% (263/371)	44% (160/360)	27.5% (536/1950)

## 2. 설치류의 독성병변 표준용어 및 아트라스 (NTP) 조사

OECD Test guideline 등 화학물질 유해성평가를 위한 독성시험법에서는 랫드, 마우스 등의 설치류를 시험동물로 사용한다. 시험동물로 사용되는 설치류는 특정한 화학물질에 노출되어 특정한 병변이 나타나기도 하지만, 나이가 들어감에 따라 특정한 원인 물질에 관계없이 자연적으로 병변이 발생하기도 한다.

최근 미국 NTP (National Toxicology Program, 2016)에서는 그동안의 독성시험에서 발생한 시험동물의 독성병변에 대한 자료를 제공하고 있다. NTP 독성시험에 사용된 랫드, 마우스 등 설치류의 독성병변에 대한 용어를 정리하고 해당

독성병변에 대한 표준 독성병변 아트라스를 제시함으로서 독성병변에 대한 판독 기준을 정립하고 있다.

본 연구에서는 NTP에서 제시하고 있는 설치류의 비증식성 독성병변 아트라스와 독성병변 용어를 정리하여 독성병리 판독기준을 제시함으로서 독성시험 결과 해석에 대한 신뢰성을 확보하고자 하였다(별첨).

## II. 연구 방법 및 내용

### 1. 시험동물 및 사육환경

시험동물은 SLC Japan에서 생산된 11주령의 특정병원체 부재 SPF(Specific pathogen free)의 F344 Rat 암수 각각 50마리를 도입하여 1주간 순화시킨 후 21주간 흡입챔버(내부용적 : 1 m<sup>3</sup>, Model No. SIS-20RG, SIBATA Co., LTD, Japan) 내의 철망케이지(W750 mm × L220 mm × H180 mm)에 개별 수용하였다.

사육환경은 온도  $22 \pm 3^{\circ}\text{C}$ , 상대습도  $50 \pm 20\%$ , 환기회수 12~15회/시간, 조명 (150~300 Lux)은 12시간 주기를 유지하였다. 사료는 실험동물용 멸균사료 Picolab Rodent Diet 5053(LabDiet, USA)을 자유롭게 섭식하도록 하였으며, 음용수는 미세 여과기와 자외선 살균기가 부착된 음용수 여과기(Model No. WFU-25, SIBATA Co., Japan)를 이용하여 정화된 상수도를 자유섭취 시켰다.

### 2. 시험항목

#### 1) 임상증상, 체중 변화

11주령의 시험동물을 도입하여 21주간의 시험기간 중 주 2회 모든 동물의 생사 유무, 외관, 운동성, 출혈, 호흡이상 등 일반증상의 변화를 관찰하였다.

체중측정은 군 분리 후 21주간의 시험기간 동안 매주 1회 측정하였다.

#### 2) 요검사

요검사는 11주령의 시험동물을 도입하여 21주간 사육한 후 32주령에 도달한

암 수 각각 30마리의 시험동물의 신선뇨를 취하여 요시험지(Multistix 10 SG, Siemens, Germany) 및 요분석장치(Clinitek Advantus, Siemens, Germany)를 이용하여 실시하였다.

### 3) 혈액학적 검사 및 혈액응고능 검사

혈액학적 검사는 32주령의 암 수 각각 30마리의 시험동물에서 채혈한 혈액을 EDTA 항응고제로 처리하여 자동혈액분석기(Advia 2120i, Siemens, Germany)로 측정하였다. 혈액응고능 검사는 혈액을 3.8% sodium citrate로 처리하여 3,000 rpm으로 10분간 원심분리하여 혈장을 수집하여 혈액응고검사기(ACL Elite, Instrumentation Laboratory, USA)로 측정하였다.

### 4) 혈액생화학학적 검사

혈액생화학검사는 32주령의 암 수 각각 30마리의 시험동물에서 채취한 혈액을 실온에서 일정시간 정치 후 3,000 rpm으로 10분간 원심분리를 하여 얻은 혈청을 자동혈액생화학분석기(TBA-120FR, Toshiba, Japan)를 사용하여 검사하였다.

### 5) 장기중량 측정 및 조직병리검사

11주령의 시험동물을 도입하여 21주간 사육한 후 32주령에 이른 암 수 각각 50마리의 시험동물을 부검하여 각 장기별로 육안소견을 관찰하고, 각 장기를 적출하여 장기무게를 측정하고 상대장기무게(장기/체중) %를 계산하였다. 적출한 장기는 10% 중성 포르말린 등으로 고정한 후 삭정하여 파라핀으로 포매하고 박절하여 제작한 조직표본 슬라이드를 Hematoxylin & Eosin (H&E)으로 염색하여 광학현미경으로 검경하였다.

### 3. 통계분석

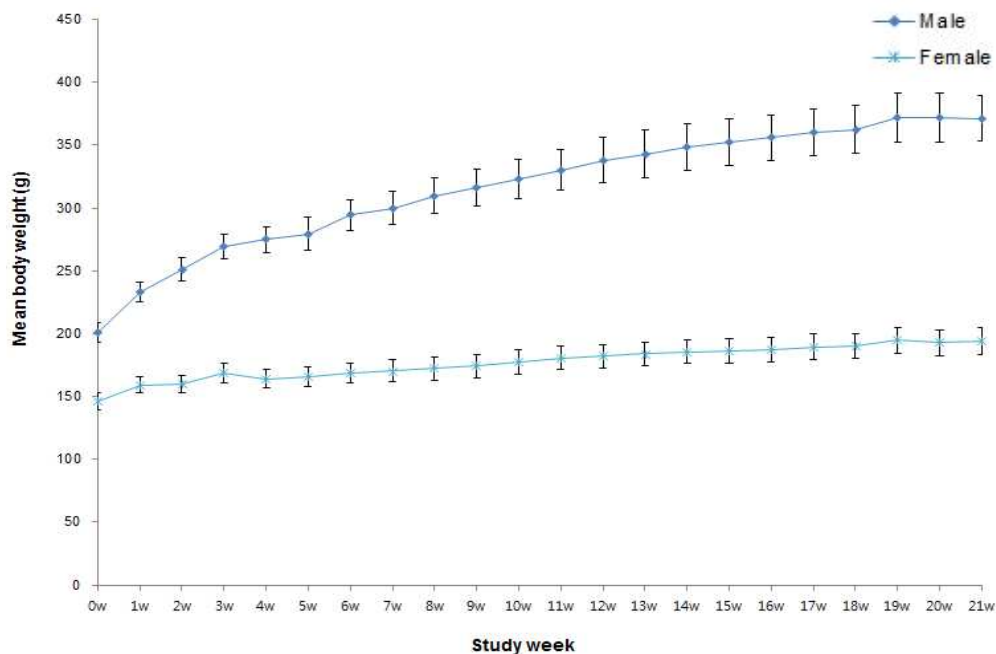
본 시험에 사용된 시험동물에 대한 시험검사 항목 중 체중 측정 결과, 뇨검사 결과, 혈액학적검사 결과, 혈액 생화학적 검사 결과 및 장기중량 측정 결과에 대하여는 평균과 표준편차로 표기하였다.

### III. 연구 결과

#### 1. 임상증상, 체중변화

11주령의 F344 랫드 시험동물을 도입하여 21주간 동안 주 2회 시험동물에 대하여 임상증상을 관찰한 결과, 특이한 임상증상은 관찰되지 않았다.

시험기간 동안 주 1회 체중변화를 관찰하였다(fig. 1, table 1) 시험동물의 평균 체중은 시험개시 때인 11주령에는 수컷 200 g, 암컷 146 g이었으나 시험 종료 시점인 32 주령에는 수컷 371 g, 암컷 194 g 으로 나타났다. 21주의 시험기간 동안 수컷은 171 g이 증가하였으나 암컷은 48 g이 증가하여 수컷에 비하여 상대적으로 완만한 증체율을 보였다.



[Fig 1] Changes of body weights during the experiment

&lt;Table 1&gt; Body weight of male and female rats for 21 weeks

Time (Week)	Male	Female
0	200.87 ± 8.04	146.16 ± 6.51
1	233.04 ± 7.95	159.00 ± 6.46
2	251.07 ± 9.21	159.76 ± 6.78
3	269.61 ± 9.76	168.39 ± 7.84
4	274.96 ± 10.44	164.21 ± 7.03
5	279.47 ± 12.88	165.69 ± 7.53
6	294.55 ± 12.26	168.57 ± 7.90
7	299.95 ± 12.85	170.15 ± 8.77
8	309.62 ± 14.43	172.15 ± 9.48
9	316.39 ± 14.82	174.23 ± 9.18
10	322.80 ± 15.90	177.42 ± 9.42
11	330.24 ± 16.42	180.81 ± 8.97
12	337.81 ± 18.06	182.04 ± 9.54
13	342.82 ± 19.10	183.81 ± 9.57
14	348.59 ± 18.30	185.68 ± 9.28
15	352.06 ± 18.43	186.36 ± 9.77
16	355.98 ± 18.27	187.50 ± 9.80
17	360.12 ± 18.95	189.33 ± 10.38
18	362.30 ± 18.92	190.38 ± 9.93
19	371.75 ± 19.53	194.76 ± 10.08
20	371.99 ± 19.51	192.78 ± 10.26
21	371.02 ± 18.16	194.33 ± 10.58

All values are expressed as mean ± SD

## 2. 뇨, 혈액 및 혈액생화학검사

## 1) 뇨검사

32주령의 시험동물의 요당(glucose), 빌리루빈(bilirubin), 케톤체(ketone body), 요비중(specific gravity), 적혈구(RBC), pH, 단백 질(protein), 유로빌리노젠(urobilinogen), 아질산염(nitrite), 백혈구(leukocyte) 등을 검사하였다(table 2, table 3).

&lt;Table 2&gt; Urinalysis of 32 weeks male rats

Tests	Results		Tests		Results			
Glucose	–	30	Ketone Body (mg/dℓ)		–	7		
	±	0			±	9		
	+	0			+	13		
	++	0			++	1		
	+++	0			+++	0		
	++++	0			++++	0		
Bilirubin	–	16	RBC	Negative	–	9		
	+	13		Non- Hemolyzed	±	11		
	++	1		Hemolyzed	++	0		
	+++	0			±	1		
Urobilinogen (EU/dℓ)	0.2	28			+	6		
	1	2			++	3		
	2	0		+++	0			
	4	0		1.000	0			
	≥8	0	Specific Gravity		1.005	0		
	–	2			1.010	3		
	±	4			1.015	2		
	+	11			1.020	4		
Leukocyte	++	13			1.025	8		
	+++	0			1.030	13		
	pH	5.0			0	Protein (mg/dℓ)	–	2
		5.5			1		±	1
6.0		18	+	7				
6.5		3	++	16				
7.0		5	+++	4				
7.5		3	++++	0				
8.0		0	Nitrite	–	29			
8.5		0		+	1			

Total no. of animal = 30

&lt;Table 3&gt; Urinalysis of 32 weeks female rats

Tests	Results		Tests		Results	
Glucose	–	30	Ketone Body (mg/dℓ)		–	19
	±	0			±	11
	+	0			+	0
	++	0			++	0
	+++	0			+++	0
	++++	0			++++	0
Bilirubin	–	21	RBC	Negative	–	22
	+	9		Non– Hemolyzed	±	0
	++	0		++	0	
	+++	0		±	3	
Urobilinogen (EU/dℓ)	0.2	28		Hemolyzed	+	5
	1	2			++	0
	2	0			+++	0
	4	0			1.000	0
	≥8	0	1.005		5	
Leukocyte	–	20	Specific Gravity		1.010	2
	±	10			1.015	0
	+	0			1.020	4
	++	0			1.025	5
	+++	0			1.030	14
pH	5.0	0	Protein (mg/dℓ)		–	10
	5.5	3			±	8
	6.0	4			+	10
	6.5	3			++	2
	7.0	5			+++	0
	7.5	8			++++	0
	8.0	5	Nitrite		–	27
	8.5	2			+	3

Total no. of animal = 30

## 2) 혈액학적 검사 및 혈액응고능 검사

32주령의 암 수 각각 50마리의 시험동물에 대하여 WBC(white blood cell count), NE(neutrophil), LYM(lymphocyte), MONO(monocyte), EOS(eosinophil), BASO(basophil), LUC(large unstained cells), LI(lobularity index), MPXI( mean peroxidase index), RBC(red blood cell count), HGB(hemoglobin), HCT(hematocrit), MCV(mean corpuscular volume), MCH(mean corpuscular hemoglobin), MCHC(mean corpuscular hemoglobin concentration), CHCM(corpuscular hemoglobin concentration mean), CH( corpuscular hemoglobin content), RDW(RBC distribution width), HDW( hemoglobin concentration distribution Width), PLT(platlet count), MPV( Mean platelet volume), RETI(reticulocyte count) PT(prothrombin time), APTT(activated partial thromboplastin time) 등의 혈액학적 검사 및 혈액응고능 검사 결과는 table 4와 같다.

&lt;Table 4&gt; Hematological values of 32 weeks male and female rats

Tests	Unit	Male	Female
WBC	$10^3/\mu\ell$	$4.91 \pm 0.88$	$2.77 \pm 0.73$
RBC	$10^6/\mu\ell$	$9.02 \pm 0.36$	$8.29 \pm 0.32$
HGB	g/dl	$14.88 \pm 1.90$	$15.25 \pm 0.53$
HCT	%	$42.77 \pm 1.63$	$42.64 \pm 1.85$
MCV	fL	$47.41 \pm 0.81$	$51.44 \pm 0.53$
MCH	pg	$16.86 \pm 0.33$	$18.39 \pm 0.25$
MCHC	g/dl	$35.56 \pm 0.67$	$35.77 \pm 0.64$
CHCM	g/dl	$33.70 \pm 0.37$	$34.13 \pm 0.38$
CH	pg	$15.98 \pm 0.26$	$17.57 \pm 0.13$
RDW	%	$13.31 \pm 0.37$	$11.64 \pm 0.20$
HDW	g/dl	$2.61 \pm 0.11$	$2.15 \pm 0.05$
PLT	$10^3/\mu\ell$	$675.53 \pm 99.33$	$648.77 \pm 85.09$

Tests	Unit	Male	Female
MPV	fL	8.72 ± 0.86	8.09 ± 0.52
NEUT %	%	40.19 ± 8.75	31.87 ± 8.17
NEUT #	10 <sup>3</sup> /μℓ	1.99 ± 0.63	0.87 ± 0.34
LYMPH %	%	54.61 ± 8.33	63.13 ± 8.03
LYMPH #	10 <sup>3</sup> /μℓ	2.67 ± 0.57	1.76 ± 0.54
MONO %	%	2.69 ± 0.72	2.46 ± 0.50
MONO #	10 <sup>3</sup> /μℓ	0.13 ± 0.04	0.07 ± 0.02
EOS %	%	1.53 ± 0.43	1.50 ± 0.77
EOS #	10 <sup>3</sup> /μℓ	0.07 ± 0.02	0.04 ± 0.02
BASO %	%	0.14 ± 0.07	0.13 ± 0.08
BASO #	10 <sup>3</sup> /μℓ	0.01 ± 0.00	0.00 ± 0.00
LUC %	%	0.77 ± 0.42	0.89 ± 0.41
LUC #	10 <sup>3</sup> /μℓ	0.04 ± 0.02	0.02 ± 0.01
RETIC %	%	2.30 ± 0.26	2.07 ± 0.25
RETIC #	10 <sup>3</sup> /μℓ	207.16 ± 24.56	170.96 ± 18.90
PT	sec	12.60 ± 1.43	10.03 ± 0.65
APTT	sec	16.65 ± 1.93	19.30 ± 4.10

Total no. of animal = 30. All values are expressed as mean ± SD.

WBC, white blood cell count; NE, neutrophil; LYM, lymphocyte; MONO, monocyte; EOS; eosinophil; BASO, basophil; LUC, large unstained cells; LI, lobularity index; MPXI, mean peroxidase index; RBC, red blood cell count; HGB, hemoglobin; HCT, hematocrit; MCV, mean corpuscular volume; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; CHCM, corpuscular hemoglobin concentration mean; CH, corpuscular hemoglobin content; RDW, RBC distribution width; HDW, hemoglobin concentration distribution Width; PLT, platelet count; MPV, Mean platelet volume, RETI, reticulocyte count; PT, prothrombin time; APTT, activated partial thromboplastin time

### 3) 혈액생화학적 검사

32주령의 암 수 각각 50마리의 시험동물에 대하여 sodium, potassium, chloride, total protein, albumin, creatinine, blood urea nitrogen, glucose, calcium, Inorganic phosphorus, total bilirubin, total cholesterol, triglyceride, aspartate aminotransferase, alanine aminotransferase, γ-glutamyl

transpeptidase, alkaline phosphatase, lactate dehydrogenase, creatine phosphokinase, albumin/globulin ratio 등의 혈액생화학검사를 수행한 결과는 table 5와 같다.

<Table 5> Serum biochemical values of 32 weeks male and female rats

Tests	Unit	Male	Female
Na	g/dℓ	143.77 ± 5.19	148.94 ± 1.82
K	g/dℓ	4.43 ± 0.28	4.64 ± 0.71
Cl	mg/dℓ	103.28 ± 3.78	107.76 ± 2.14
TP	mg/dℓ	6.76 ± 0.32	7.02 ± 0.37
ALB	mg/dℓ	4.33 ± 0.18	4.49 ± 0.21
CREA	IU/L	0.42 ± 0.03	0.43 ± 0.04
BUN	IU/L	19.88 ± 2.03	20.60 ± 2.17
GLU	IU/L	130.62 ± 9.88	120.34 ± 11.94
CA	IU/L	9.89 ± 0.41	10.81 ± 1.10
IP	mg/dℓ	6.19 ± 0.50	5.76 ± 1.19
TBIL	mg/dℓ	0.20 ± 0.03	0.14 ± 0.03
TCHO	mg/dℓ	76.15 ± 7.00	99.20 ± 12.78
TG	IU/L	100.39 ± 34.35	33.70 ± 15.98
GOT	IU/L	162.67 ± 42.17	136.76 ± 38.65
GPT	IU/L	111.52 ± 45.20	85.16 ± 40.49
GGT	mg/dℓ	0.68 ± 0.41	2.44 ± 0.88
ALP	mmol/L	317.16 ± 31.92	279.23 ± 37.24
LDH	mmol/L	894.92 ± 365.21	769.16 ± 293.86
CK	mmol/L	251.67 ± 95.39	172.70 ± 64.04
A/G	-	1.79 ± 0.08	1.78 ± 0.11

Total no. of animal = 30. All values are expressed as mean ± SD.

Na, sodium; K, potassium; Cl, chloride; TP, total protein; ALB, albumin; CREA, creatinine; BUN, blood urea nitrogen; GLU, glucose; CA, calcium; IP, Inorganic phosphorus; TBIL, total bilirubin; TCHO, total cholesterol; TG, triglyceride; AST, aspartate aminotransferase; ALT, alanine aminotransferase; GGT, γ-glutamyl transpeptidase; ALP, alkaline phosphatase; LDH, lactate dehydrogenase; CK, creatine phosphokinase; A/G, albumin/globulin ratio

### 3. 부검 및 장기중량

#### 1) 부검

11 주령의 암 수 각각 50마리의 실험동물을 도입하여 시험기간 21주 후인 32주령에 실험동물을 부검하여 관찰한 결과, 수컷에서는 갑상선과 지방조직, 신장, 폐, 간 등에서 육안 소견이 나타났다(table 6). 암컷에서는 간, 뇌하수체, 직장, 간 등에서 육안 소견이 나타났다(table 7).

<Table 6> Gross findings of male rats

Animal No.	Organ	Gross finding
1001	Thyroid gland	Cyst 1 (1 mm in diameter)
1001	Adipose Tissue	Mess 1, yellowish, around right epididymis (7x3x2 mm)
1003	Kidney	Cyst 1, (3 mm in diameter), right
1015	Lung	White focus 3, Lymph node congestion 1
1018	Liver	Diaphragmatic nodule 1
1040	Lung	Focus 1, white, left lobe
1048	Kidney	Recessed area 1, left

<Table 7> Gross findings of female rats

Animal No.	Organ	Gross finding
2012	Liver	Elevated area 1 (3x4 mm), Ventral
2013	Pituitary gland	Cyst 1 (1x1 mm), red
2019	Rectum	Diverticulum 1 (2x2 mm)
2027	Liver	Diaphragmatic nodule 1, Medial lobe
2039	Liver	Diaphragmatic nodule 1, Medial lobe
2046	Liver	Diaphragmatic nodule 1, Medial lobe

## 2) 장기중량

32주령의 암 수 각각 50마리의 시험동물을 부검 한 후 시험동물의 장기를 채취하여 장기중량을 측정하고, 체중에 대한 장기중량 백분율을 나타낸 상대장기무게는 table 8과 table 9와 같다.

&lt;Table 8&gt; Absolute and relative organ weights of 32 weeks male rats

	Absolute (g)	Relative (%)
TBW	354.408 ± 17.802	354.408 ± 17.802
Epididymides	1.1115 ± 0.0807	0.3142 ± 0.0260
Thyroid glands	0.0262 ± 0.0064	0.0074 ± 0.0018
Lung	1.234 ± 0.108	0.3486 ± 0.0310
Adrenal glands	0.0558 ± 0.0051	0.0158 ± 0.0016
Brain	1.979 ± 0.157	0.5592 ± 0.0448
Heart	0.957 ± 0.057	0.2701 ± 0.0134
Kidneys	2.1505 ± 0.1400	0.6072 ± 0.0337
Liver	9.737 ± 0.601	2.7480 ± 0.1107
Spleen	0.6959 ± 0.0456	0.1966 ± 0.0130
Testes	2.9637 ± 0.1412	0.8371 ± 0.0368
Thymus	0.1580 ± 0.0356	0.0447 ± 0.0104

Relative (%) = (organ weight / terminal body weights) x 100, TBW = terminal body weights.

All values are expressed as mean ± SD.

&lt;Table 9&gt; Absolute and relative organ weights of 32 weeks female rats

	Absolute (g)	Relative (%)
TBW	186.587 ± 10.530	186.587 ± 10.530
Thyroid glands	0.0179 ± 0.0043	0.0096 ± 0.0022
Uterus	0.6859 ± 0.2089	0.3670 ± 0.1058
Lung	0.859 ± 0.065	0.4614 ± 0.0362
Adrenal glands	0.0568 ± 0.0079	0.0305 ± 0.0042
Brain	1.784 ± 0.097	0.9589 ± 0.0758
Heart	0.592 ± 0.038	0.3180 ± 0.0201
Kidneys	1.3371 ± 0.0916	0.7174 ± 0.0447
Liver	4.852 ± 0.333	2.6011 ± 0.1132
Ovaries	0.0646 ± 0.0108	0.0347 ± 0.0058
Spleen	0.4279 ± 0.0328	0.2297 ± 0.0173
Thymus	0.1298 ± 0.0250	0.0695 ± 0.0121

Relative (%) = (organ weight / terminal body weights) x 100, TBW = terminal body weights,  
All values are expressed as mean ± SD.

#### 4. 조직병리 검사

##### 1) 수컷(Male)

32주령의 수컷 시험동물을 부검하여 시험동물의 간, 신장, 고환, 비장, 부신, 침샘, 근육, 척수, 좌골신경, 흉선, 갑상선, 부갑상선, 기관, 폐, 식도, 혀, 대뇌, 소뇌, 뇌하수체, 고환, 부고환, 전립선, 응고선, 정낭, 피부, 심장, 대동맥, 췌장, 위, 대퇴골, 방광, 비장, 림프절, 하드리안선, 안구 등의 장기를 광학현미경으로 관찰하였다.

수컷에서는 골수, 하드리안선, 심장, 신장, 간, 폐, 임파선, 이자, 뇌하수체, 전립선, 침샘, 비장, 위, 흉선, 갑상선, 기관, 지방조직 등에서 병변이 나타났다(table 10, Fig 2 ~ Fig 44).

## 2) 암컷(Female)

32주령의 시험동물을 부검하여 시험동물의 간, 신장, 비장, 부신, 침샘, 근육, 척수, 좌골신경, 흉선, 갑상선, 부갑상선, 기관, 폐, 식도, 혀, 대뇌, 소뇌, 뇌하수체, 난소, 질, 자궁, 피부, 심장, 대동맥, 췌장, 위, 대퇴골, 방광, 비장, 림프절, 하드리안선, 안구 등의 장기를 광학현미경으로 관찰하였다.

암컷에서는 부신, 골수, 하드리안선, 심장, 신장, 간, 폐, 이자, 뇌하수체, 침샘, 비장, 위, 흉선, 갑상선, 기관 등에서 병변이 나타났다(table 11, Fig 2 ~ Fig 44).

&lt;Table 10&gt; Histopathology of 32 weeks male rats

Organ	Lesions	No. of animals	Rate (%)
Bone marrow	Dilation, vascular	1	2
Harderian glands	Infiltration, adipocytes	1	2
	Infiltration, mononuclear cell	25	50
Heart	Fibrosis	1	2
	Necrosis/inflammatory cell infiltrate, cardiomyocyte	16	32
Kidneys	Accumulation, hyaline	50	100
	Basophilia, tubules	42	84
	Calculi	1	2
	Casts, hyaline	35	70
	Cyst(s)	3	6
	Infarct	1	2
	Infiltration, mononuclear cell, interstitial	3	6
	Mineralization, medulla	1	2
	Necrosis, tubular epithelial cell	1	2
	Pigment accumulation	50	100
	Vacuolation, tubular epithelial cell	1	2
Liver	Extramedullary hematopoiesis	7	14
	Fibrosis	1	2
	Focus of cellular alteration, basophilic	2	4
	Hyperplasia, bile duct	19	38
	Infiltration, mononuclear cell	20	40
	Necrosis, hepatocytes	5	25
Lung	Aggregates, macrophages, alveolar	2	4
	Aggregates, macrophages, foamy	19	38
	Adenoma, bronchiolo-alveolar	1	2
	Dilatation	1	2
	Fibrosis	1	2

Organ	Lesions	No of animals	Rate (%)
Lung	Hyperplasia, bronchiolo-alveolar, alveolar	1	2
	Inclusion	2	4
	Infiltration, mononuclear cell	8	16
	Metaplasia, osseous	5	10
	Mineralization, vascular	15	30
Lymph node, tracheobronchial	Hemorrhage with pigmentation	1	2
Pancreas	Atrophy, acinar cell	12	24
	Hyperplasia, ductal cell	1	2
Pituitary gland	Cyst(s), pars distalis	2	4
	Cyst(s), pars intermedia	4	8
Prostate gland	Inflammation	1	2
Salivary gland, sublingual	Ectopia, parotid gland	2	4
	Hyperplasia	1	2
	Metaplasia	6	12
Salivary gland, parotid	Basophilic hypertrophic foci	1	2
Spleen	Extramedullary hematopoiesis	12	24
Stomach	Degeneration	1	2
	Dilation, glands	7	14
Thymus	Hyperplasia, tubules and cords	5	10
Thyroid glands	Cyst(s), ultimobranchial duct	1	2
Trachea	Dilation, submucosal glands	1	2
Abdominal fat tissue	Granulomatous inflammation	1	2

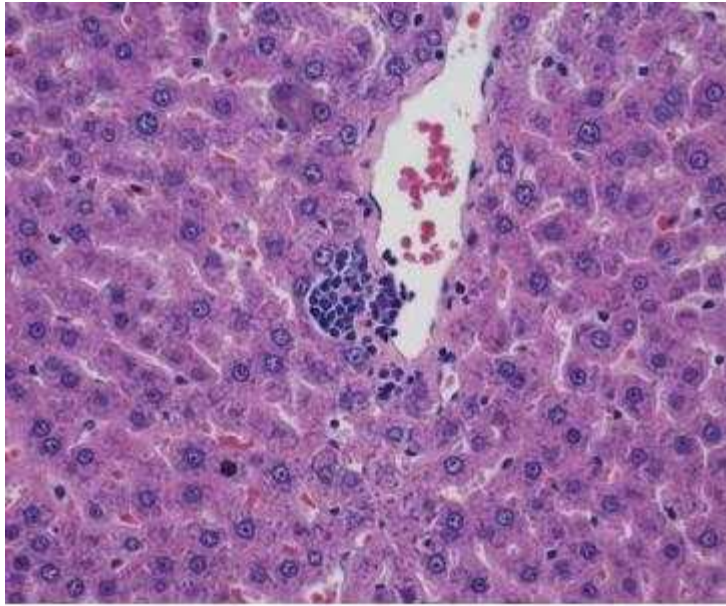
Total No. of animals = 50

&lt;Table 11&gt; Histopathology of 32 weeks female rats

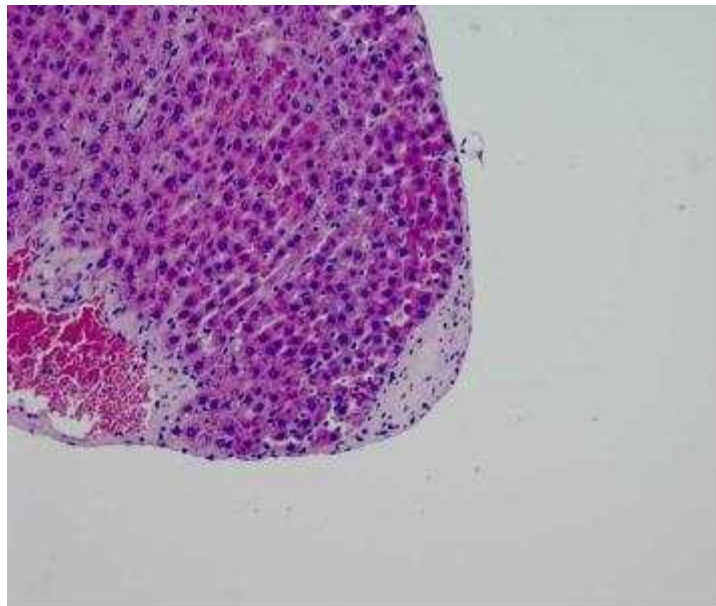
Organ	Lesions	No of animals	Rate (%)
Adrenal glands	Nodule, cortex, accessory	1	2
Bone marrow	Dilation, vascular	1	2
	Myelofibrosis	1	2
Harderian glands	Infiltration, mononuclear cell	34	68
Heart	Necrosis/inflammatory cell infiltrate, cardiomyocyte	9	18
Kidneys	Basophilia, tubules	3	6
	Calculi	1	2
	Casts, hyaline	1	2
	Infiltration, mononuclear cell, interstitial	1	2
	Mineralization, corticomedullary junction	1	2
	Mineralization, medulla	6	12
	Pigment accumulation	1	2
Liver	Hyperplasia, bile duct	1	2
	Infiltration, mononuclear cell	22	44
	Necrosis, focal, hepatocytes	7	14
	Necrosis, single cell	1	2
	Hepatodiaphragmatic nodule	3	6
Lung	Aggregates, macrophages, foamy	3	6
	Hyperplasia, bronchiolo-alveolar	4	8
	Inclusion, eosinophilic, terminal bronchiole	1	2
	Infiltration, mononuclear cell	4	8
	Mineralization, vascular	6	12
	Pigmentation, macrophages	4	8

Organ	Lesions	No of animals	Rate (%)
Pancreas	Atrophy, acinar cell	1	2
	Hyperplasia, ductal cell	2	4
Pituitary gland	Cyst(s), intermedia	4	8
	Cyst(s), pars distalis	1	2
Salivary gland, parotid	Basophilic hypertrophic foci	3	6
	Infiltration, mononuclear cell	1	2
Salivary gland, sublingual	Ectopia, parotid gland	1	2
Spleen	Extramedullary hematopoiesis	3	6
Stomach	Dilation, glands	1	2
Thymus	Extramedullary hematopoiesis	1	2
	Hyperplasia, epithelial tubules and cords	6	12
Thyroid glands	Inflammation	1	2
Trachea	Dilation, submucosal glands	1	2

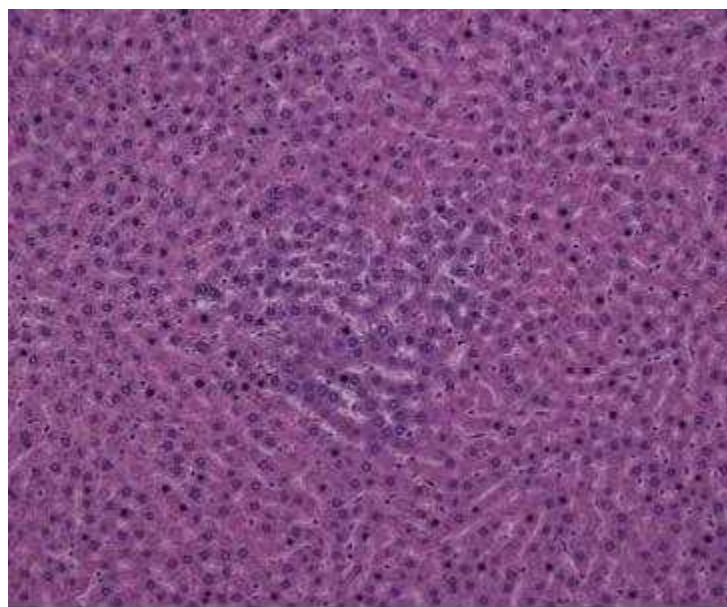
Total No. of animals = 50



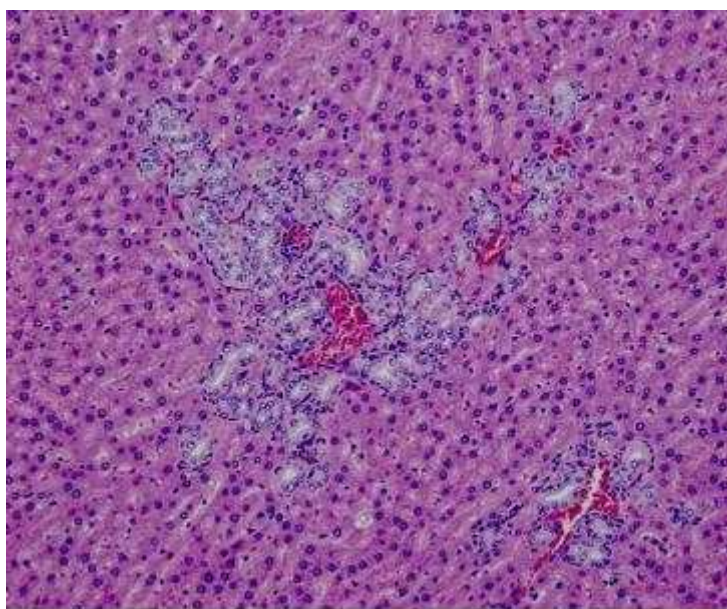
[Fig. 2] Liver, Extramedullary hematopoiesis, x400



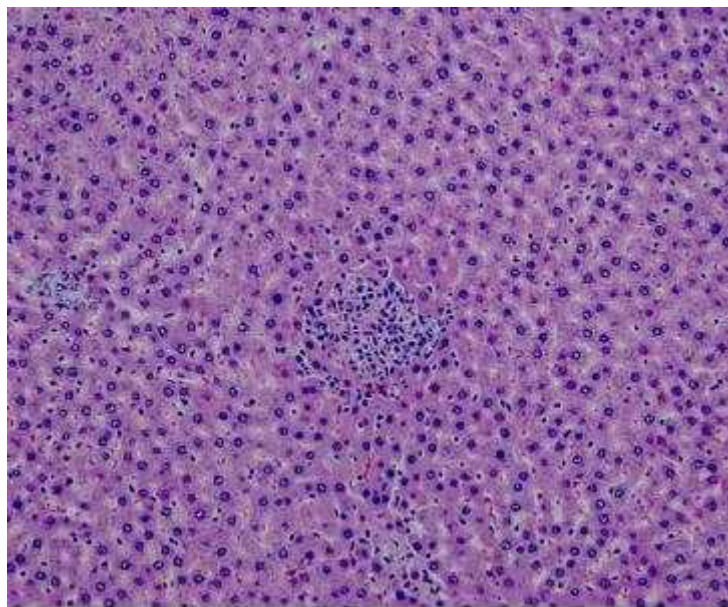
[Fig. 3] Liver, Fibrosis, capsular, x200



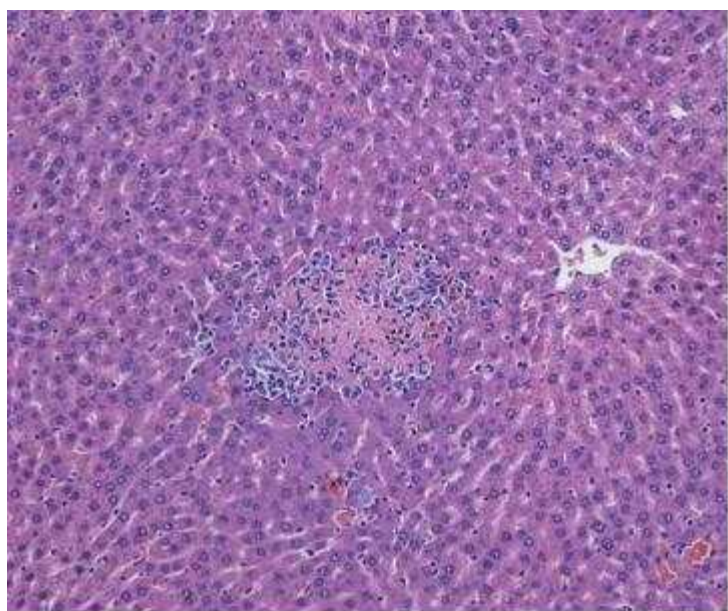
[Fig. 4] Liver, Focus of cellular alteration, basophilic, x200



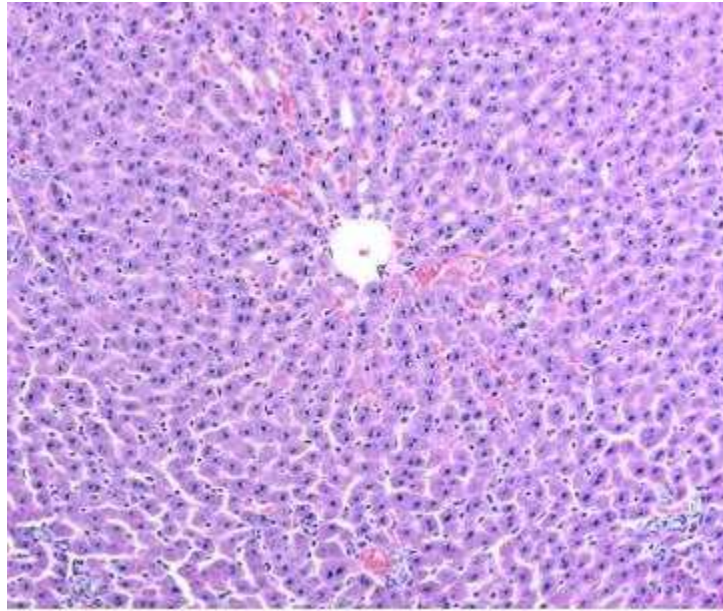
[Fig. 5] Liver, Hyperplasia, bile duct, x200



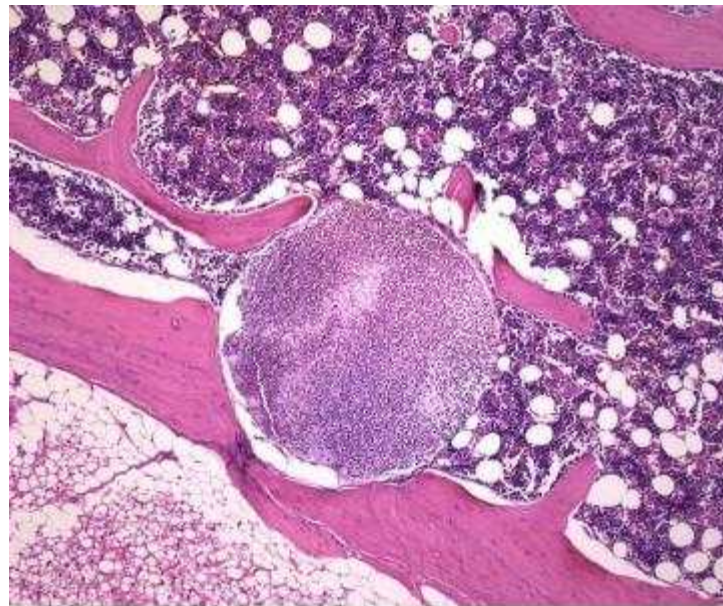
[Fig. 6] Liver, Infiltration, mononuclear cell, x200



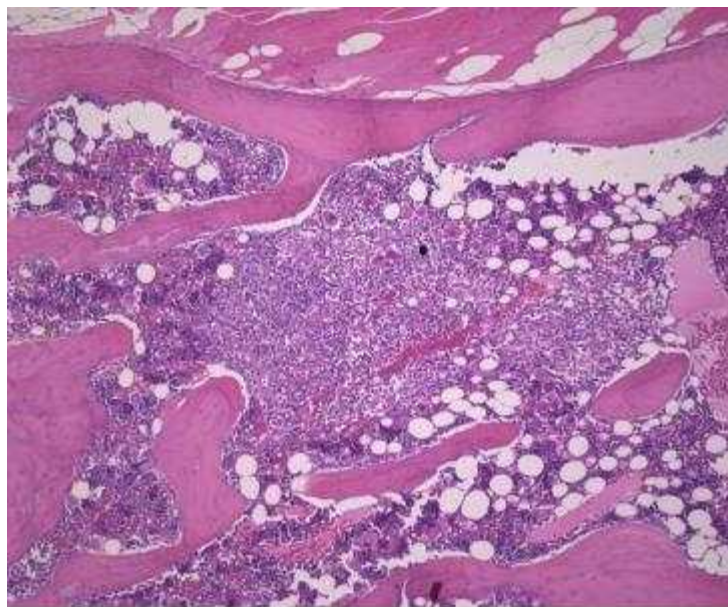
[Fig. 7] Liver, necrosis, hepatocytes, x200



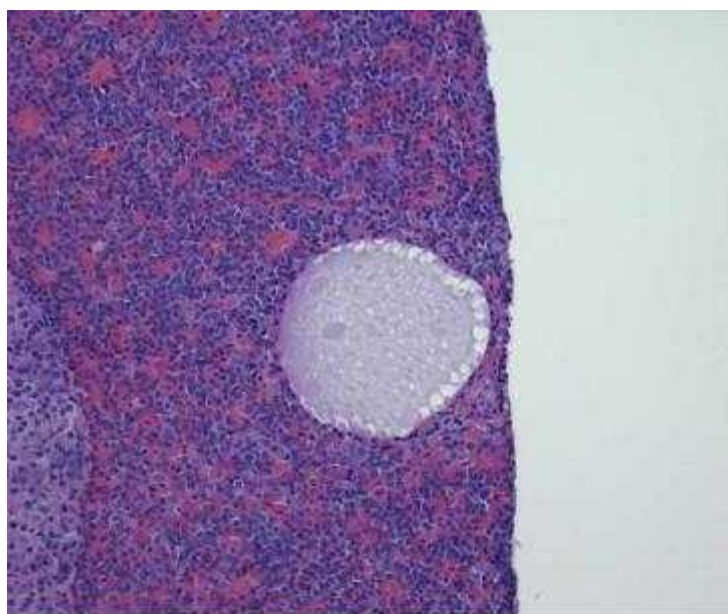
[Fig. 8] Liver, Hepatodiaphragmatic nodule, x100



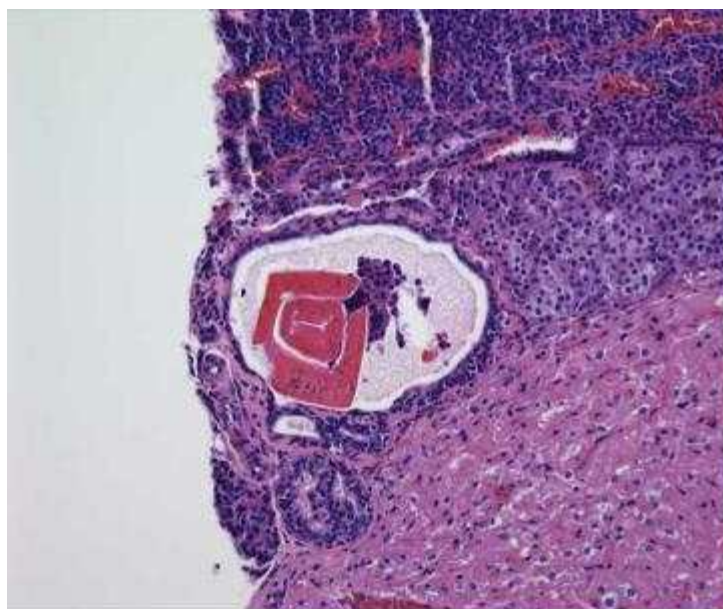
[Fig. 9] Bone marrow, Dilation, vascular, x100



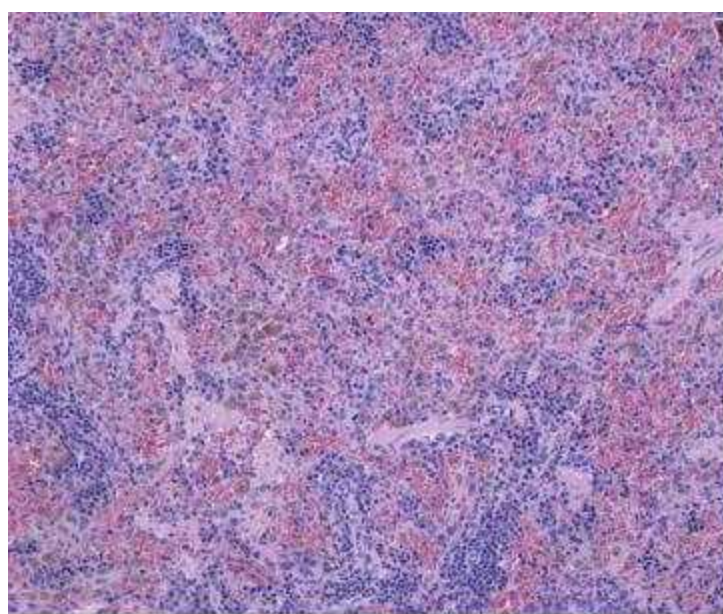
[Fig. 10] Bone marrow, Myelofibrosis, x100



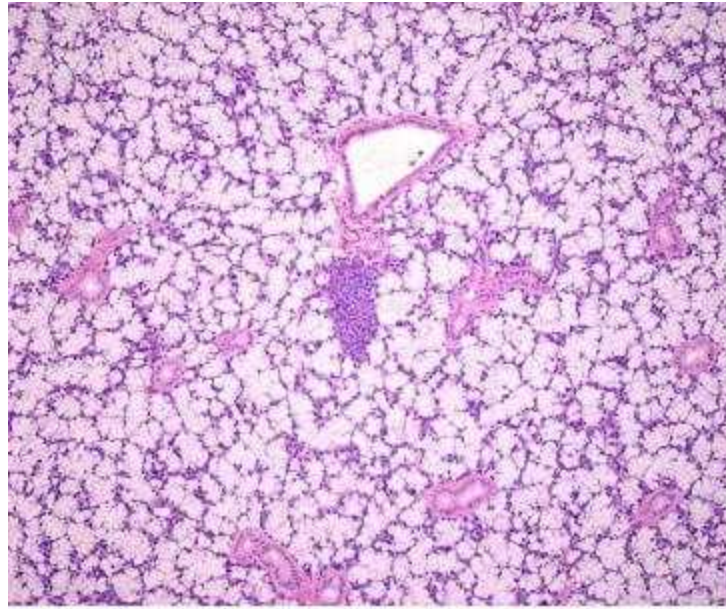
[Fig. 11] Pituitary, Cyst, pars distalis, x200



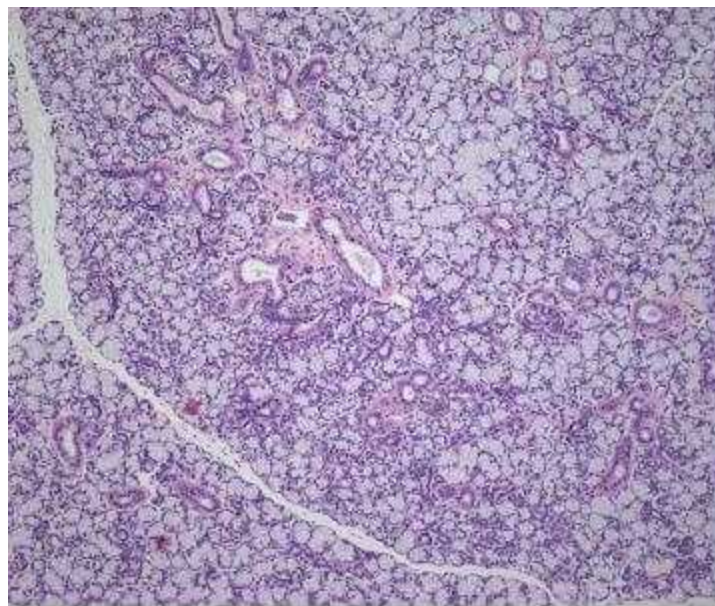
[Fig. 12] Pituitary, Cyst, pars intermedia, x200



[Fig. 13] Spleen, Extramedullary hematopoiesis, x200



[Fig. 14] Salivary gland, sublingual, Ectopia, parotid, x100



[Fig. 15] Salivary gland, sublingual, Hyperplasia, duct, x100

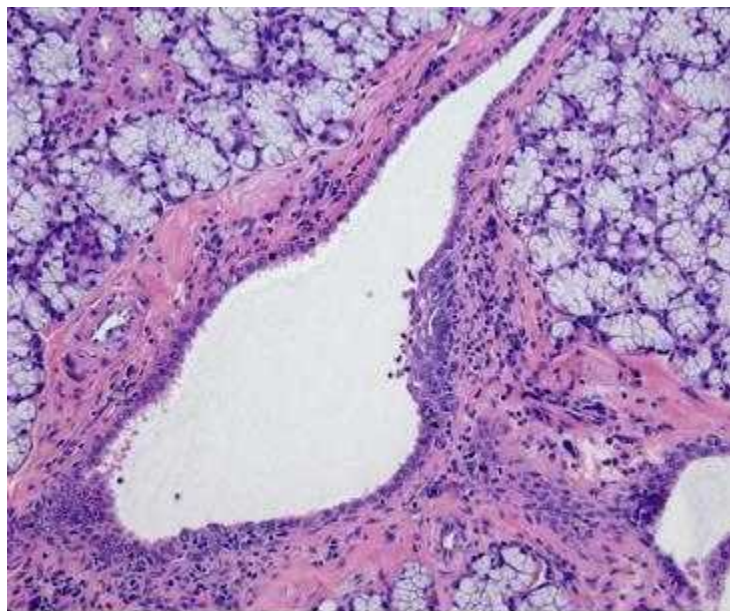


Fig. 16. Salivary gland, sublingual, Metaplasia, squamous, x200

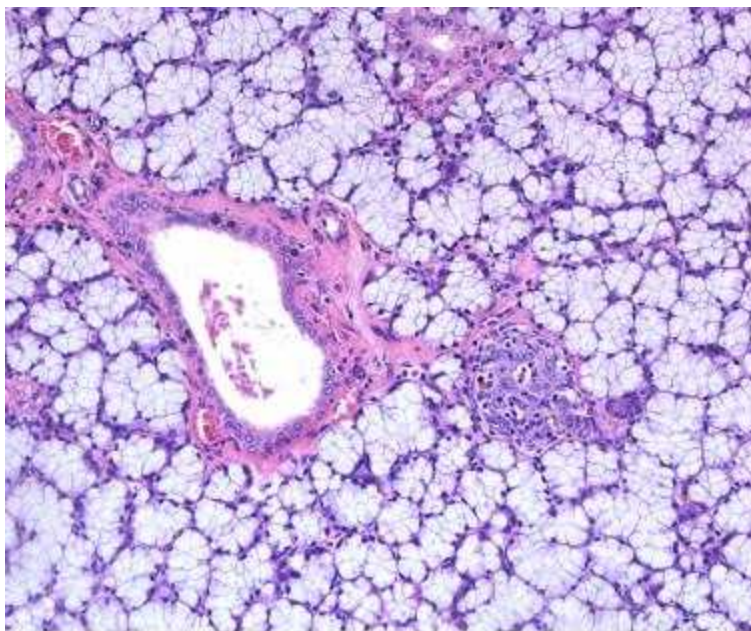
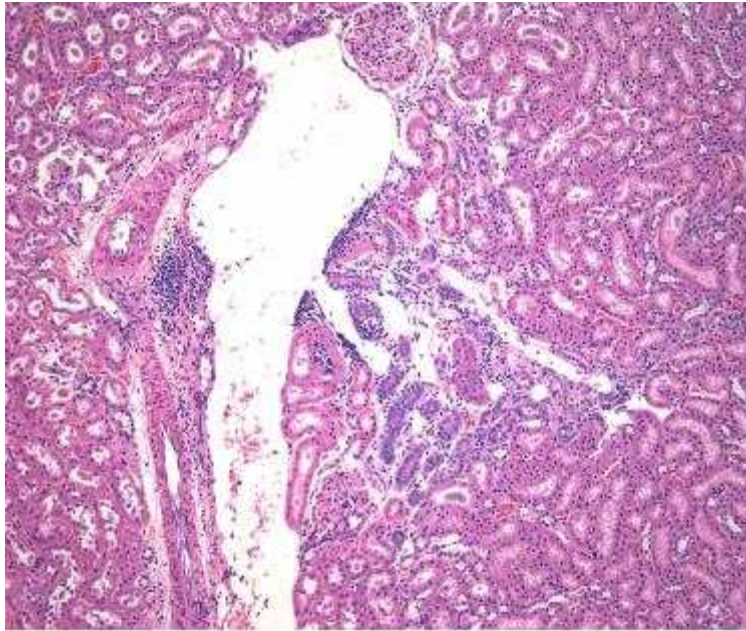
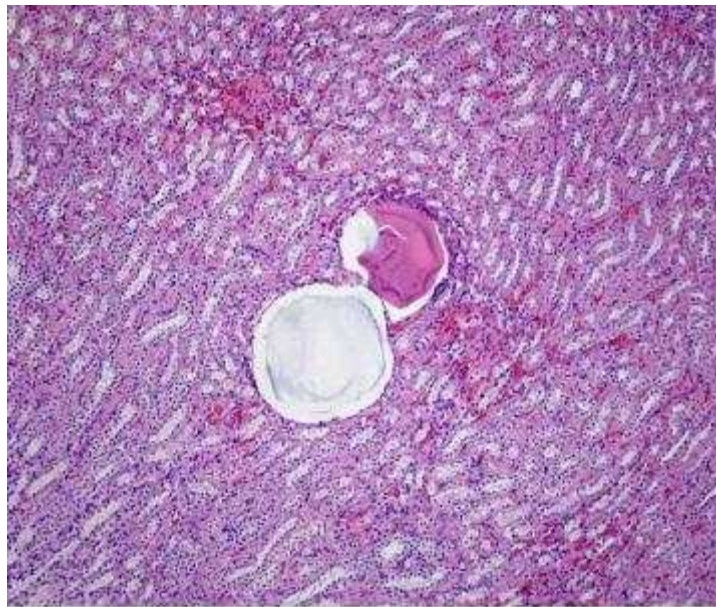


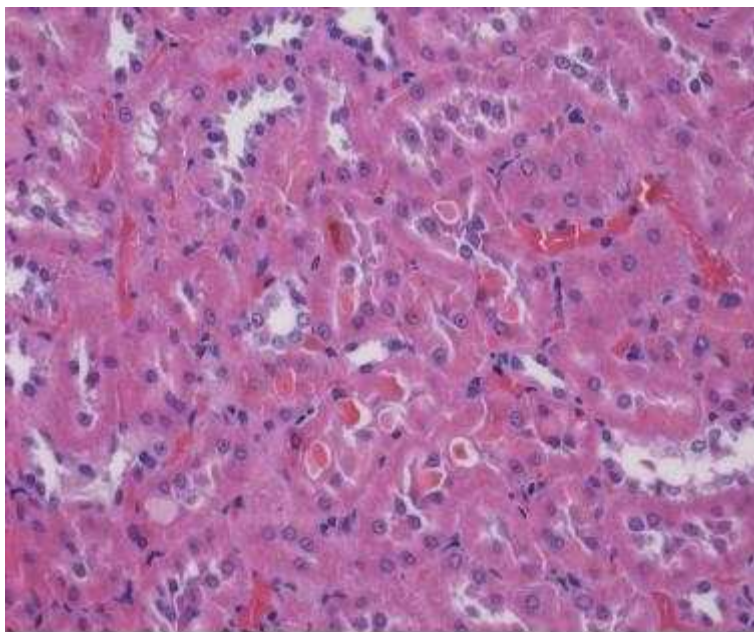
Fig. 17. Sublingual gland, Granulomatous Inflammation, x400



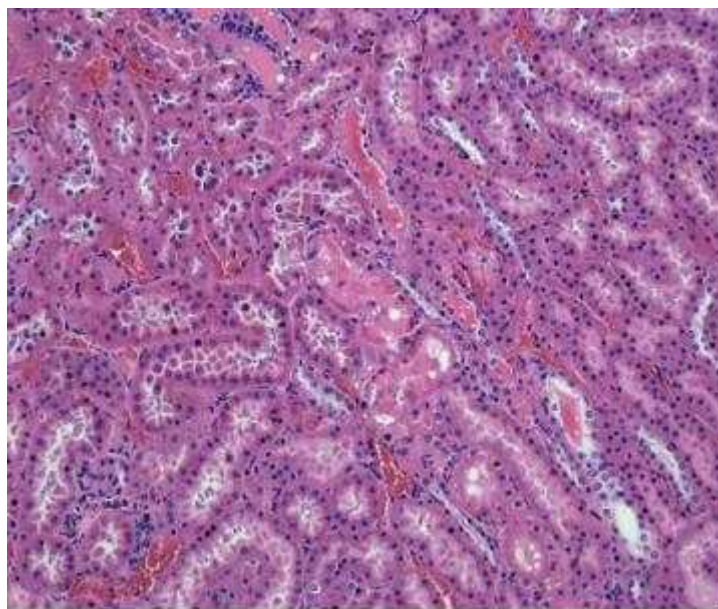
[Fig. 18] Kidney, Basophilia, tubules and Infiltration, mononuclear cells, interstitial, x100



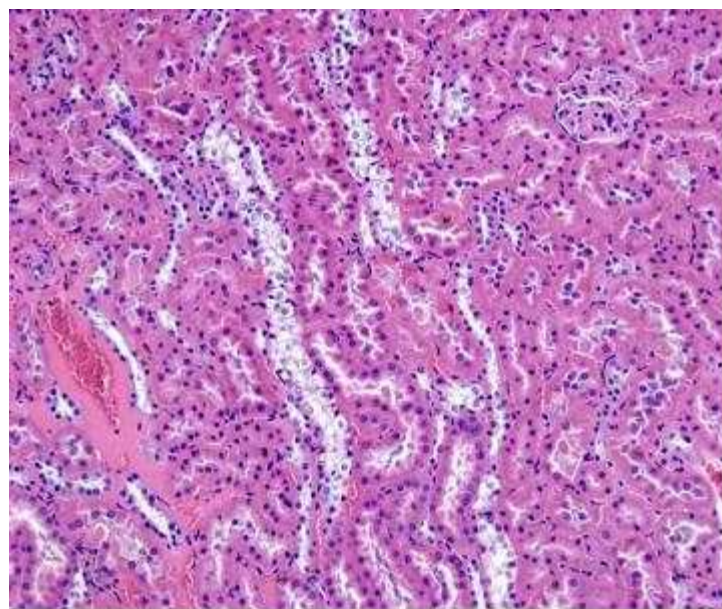
[Fig. 19] Kidney, Cysts, x200



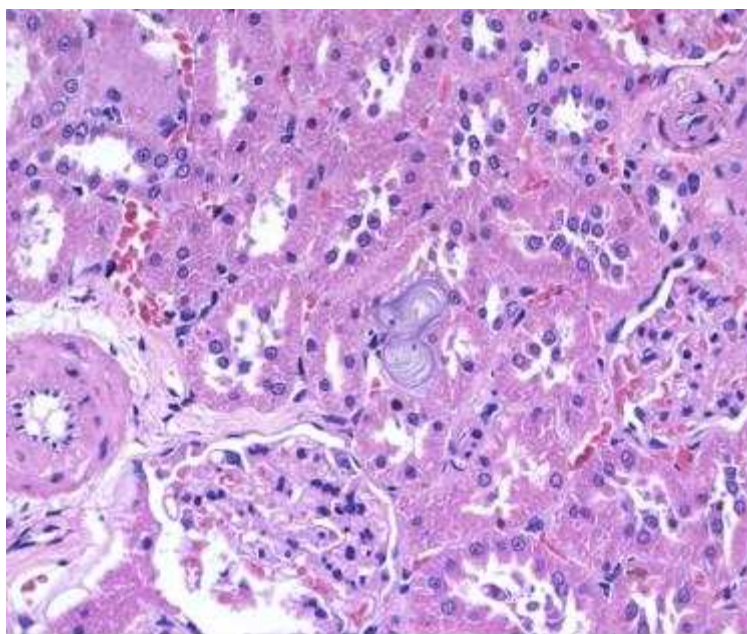
[Fig. 20] Kidney, Deposition, pigments and Accumulation, hyaline globule, x400



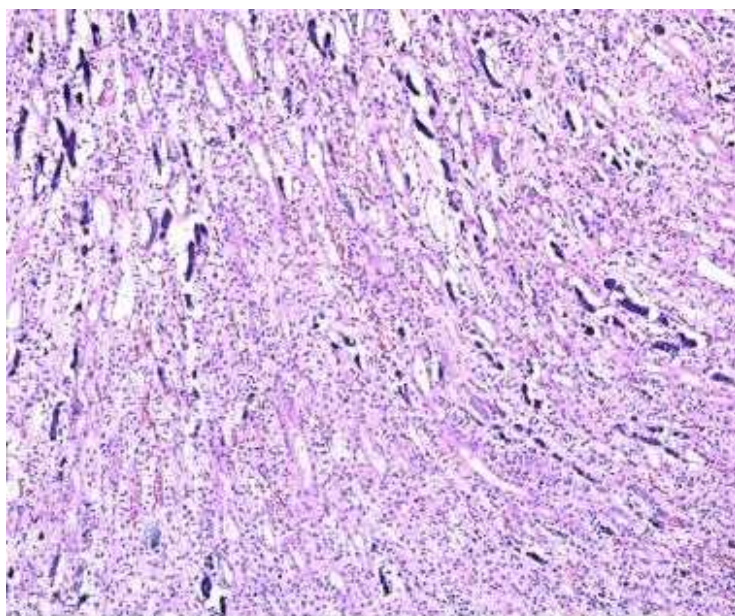
[Fig. 21] Kidney, Necrosis, tubular epithelium, x200



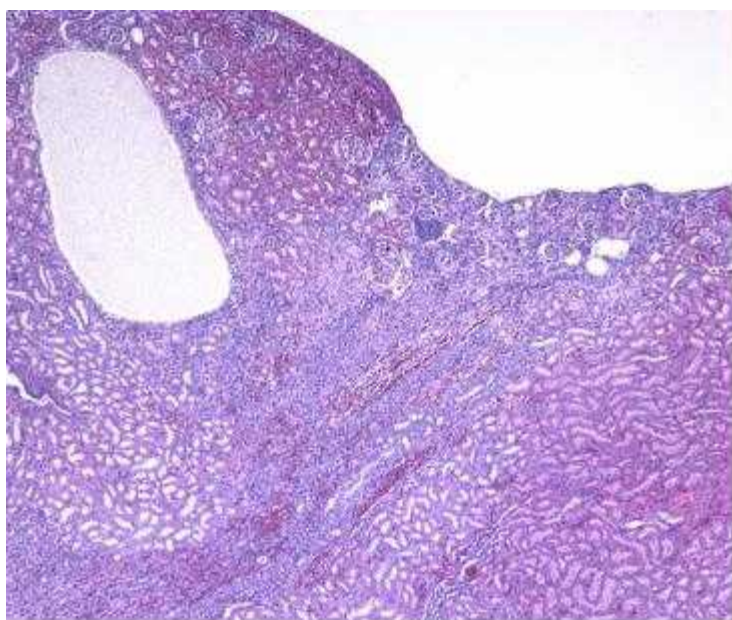
[Fig. 22] Kidney, Vacuolation, tubular epithelium, x200



[Fig. 23] Kidney, Calculi, x400



[Fig. 24] Kidney, Mineralization, medulla, x100



[Fig. 25] Kidney, Infarct, cortical, x50

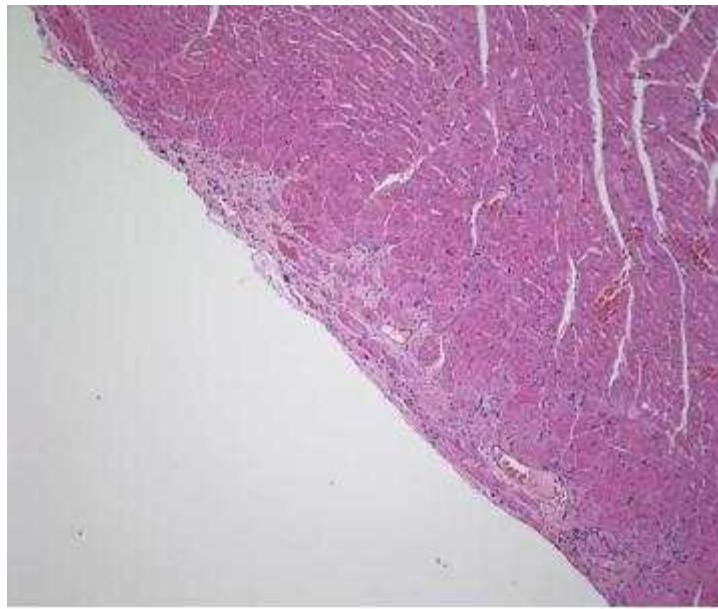
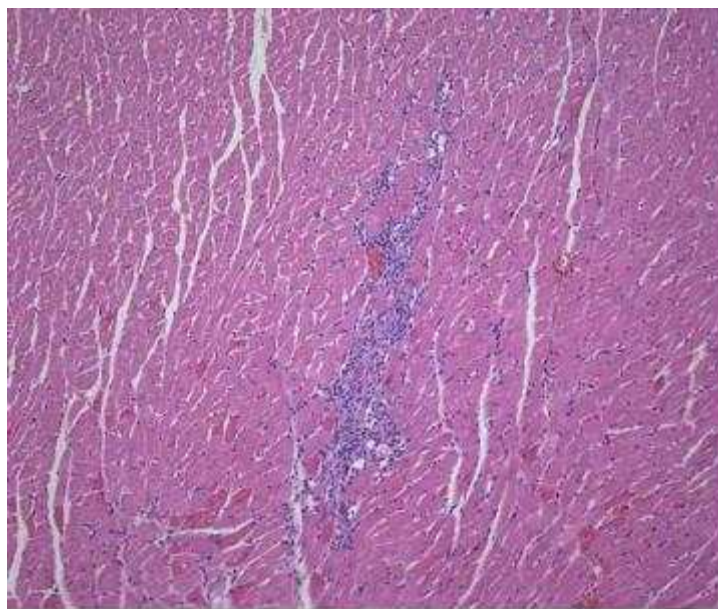
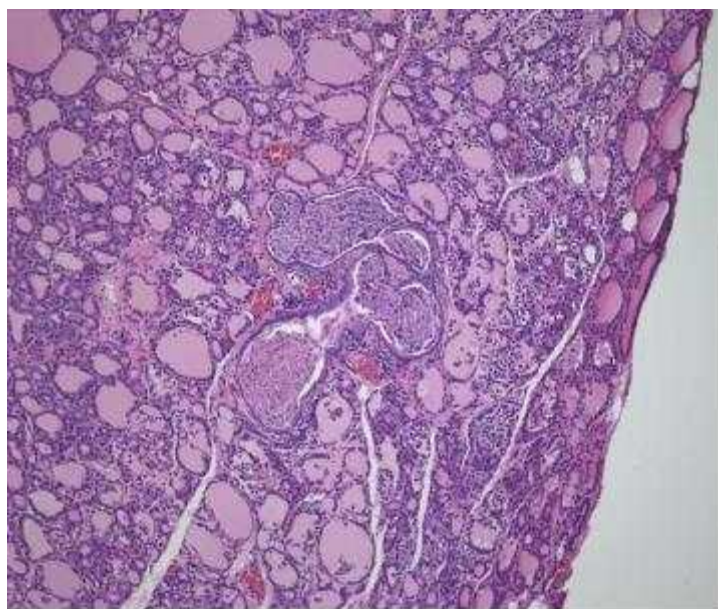


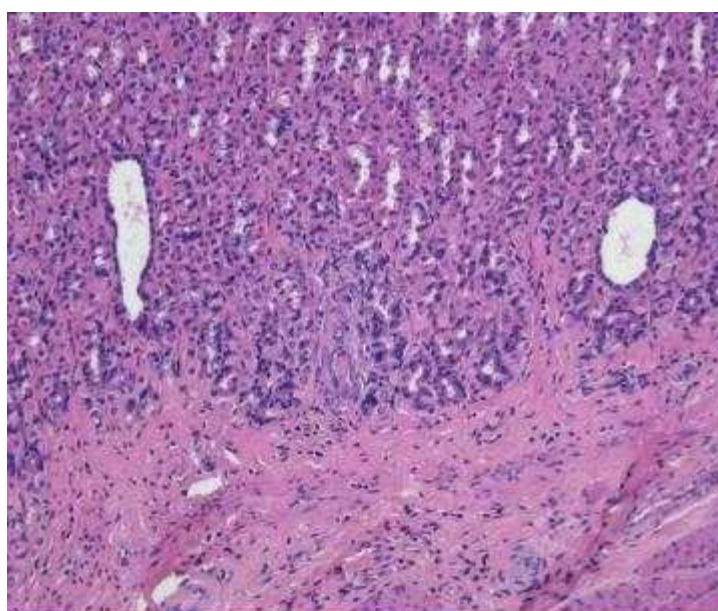
Fig. 26. Heart, Fibrosis, x100



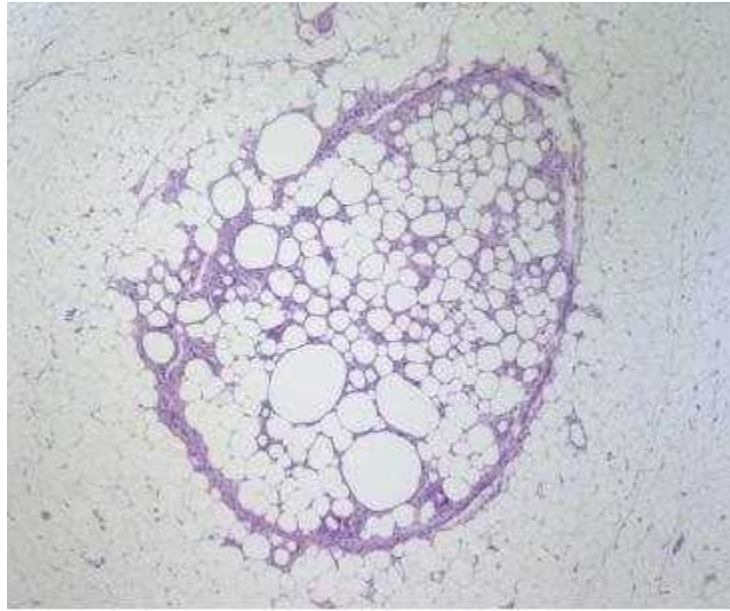
**Fig.27.**Heart, Necrosis/Inflammatory cell infiltration, x100



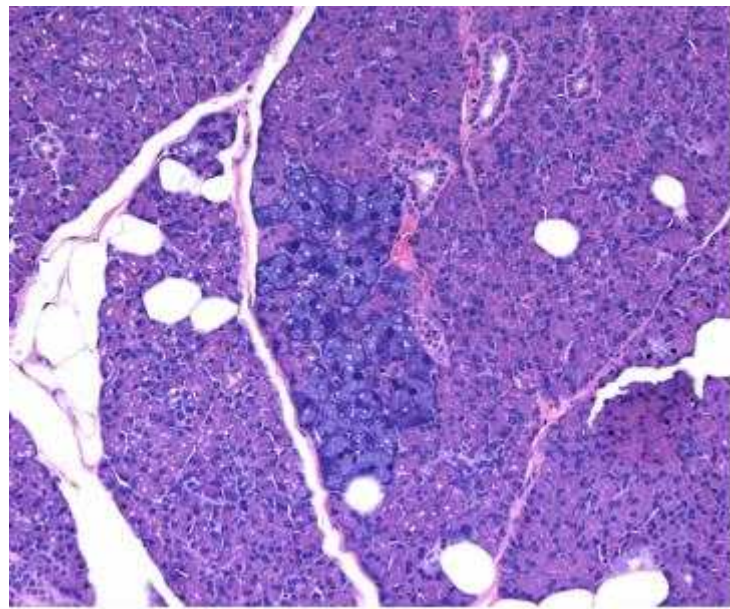
[Fig. 28] Thyroid, Ultimobranchial cyst, x100



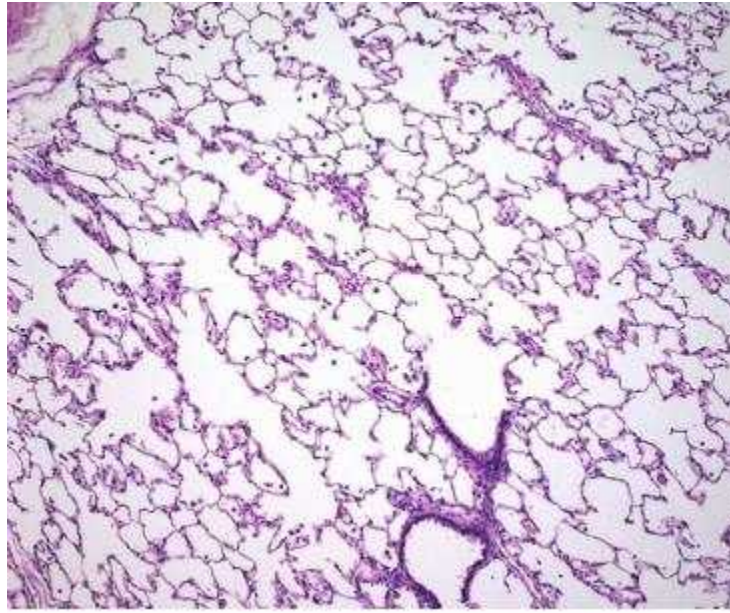
[Fig. 29] Stomach, Degeneration and dilation, gland, x200



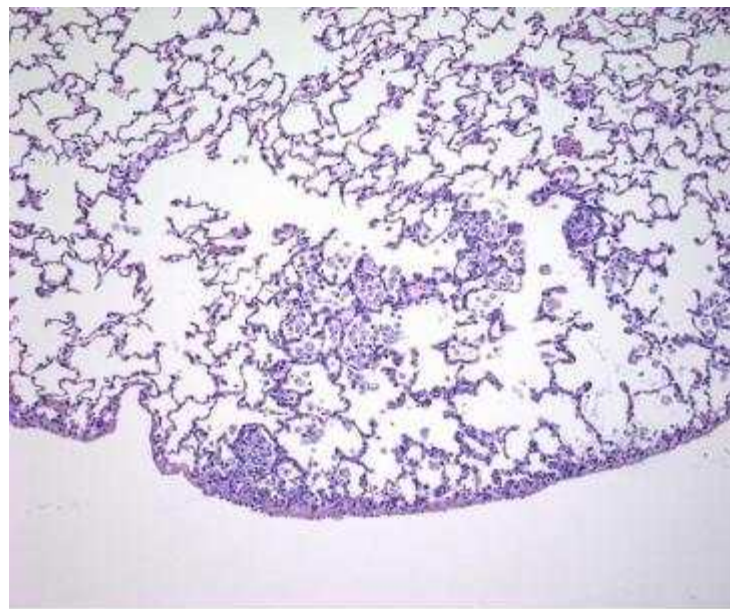
[Fig. 30] Abdominal fat tissue, Granulomatous inflammation, x100



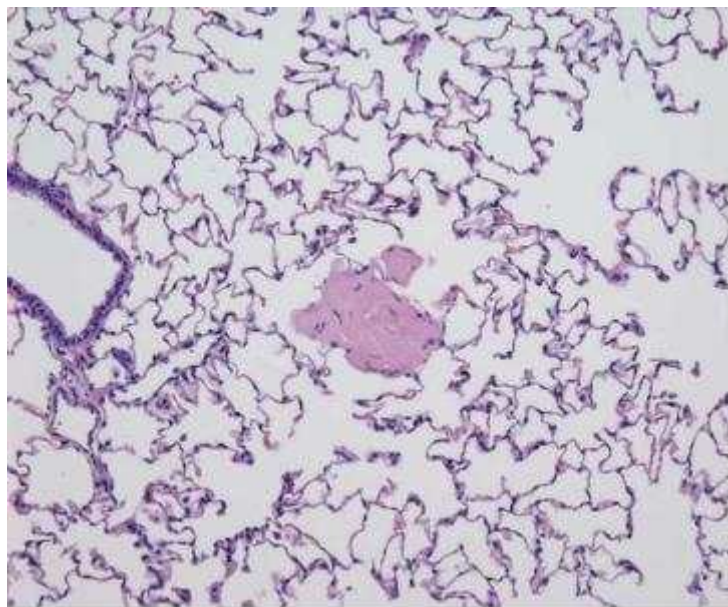
[Fig. 31] Parotid gland, Basophilic hypertrophic foci, x200



[Fig. 32] Lung, Aggregates, macrophage, alveolar, x100



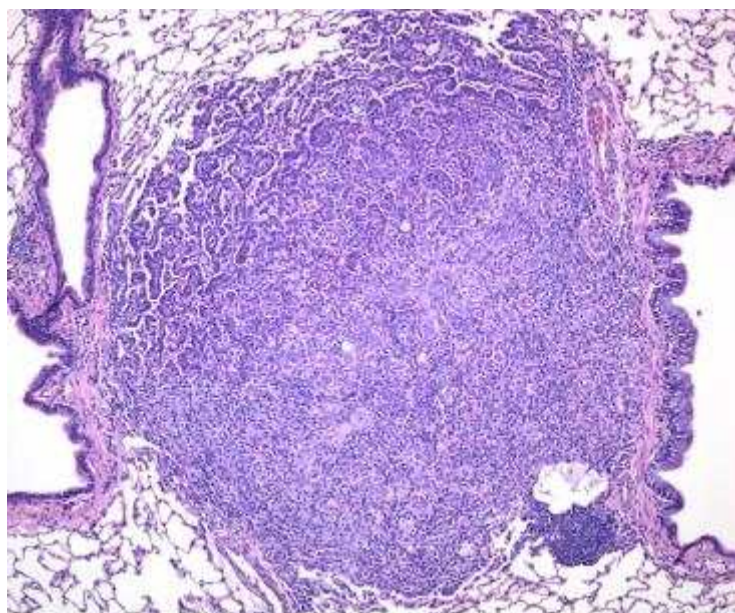
[Fig. 33] Lung, Aggregates, macrophage, foamy, x100



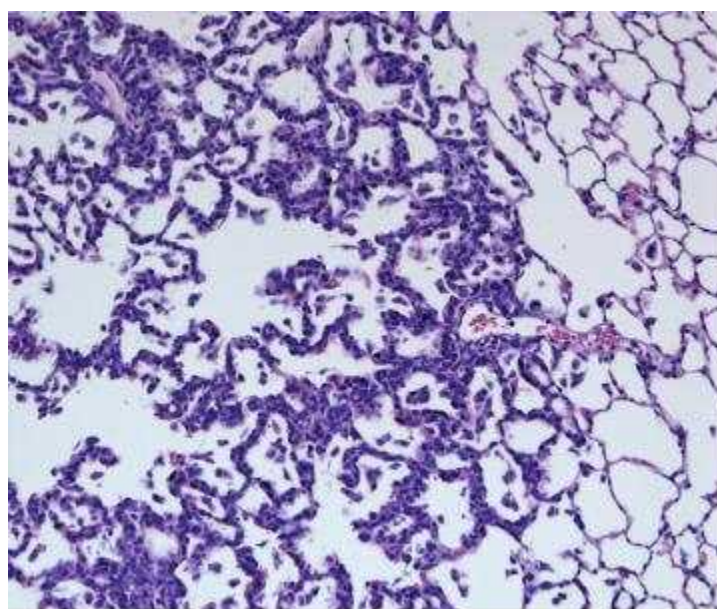
[Fig. 34] Lung, Metaplasia, osseous, x200



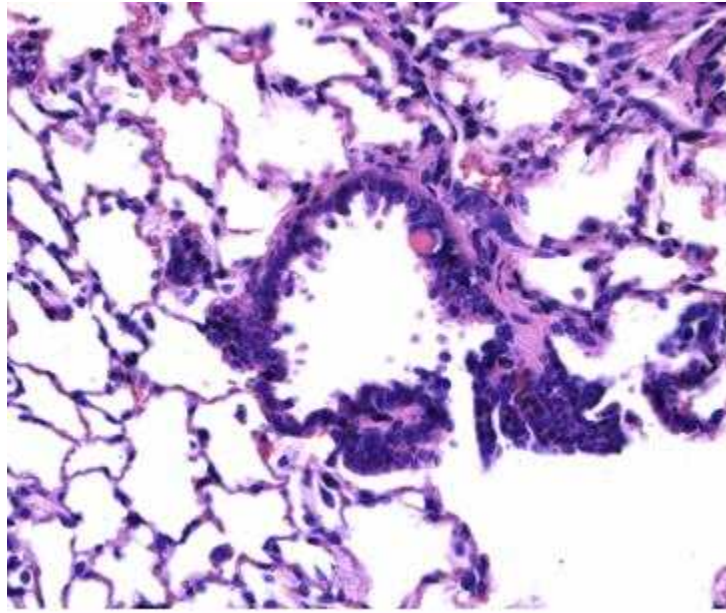
[Fig. 35] Lung, Mineralization, vascular, x100



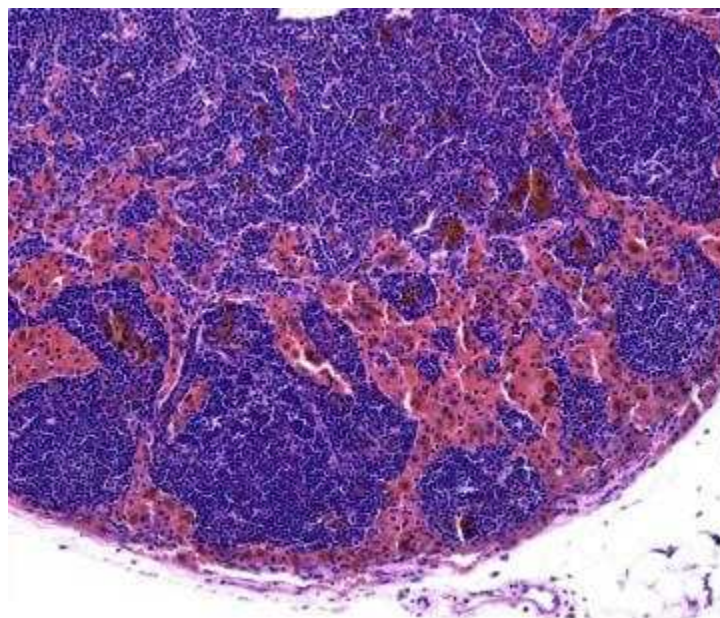
[Fig. 36] Lung, Bronchiolar-Alveolar adenoma, x100



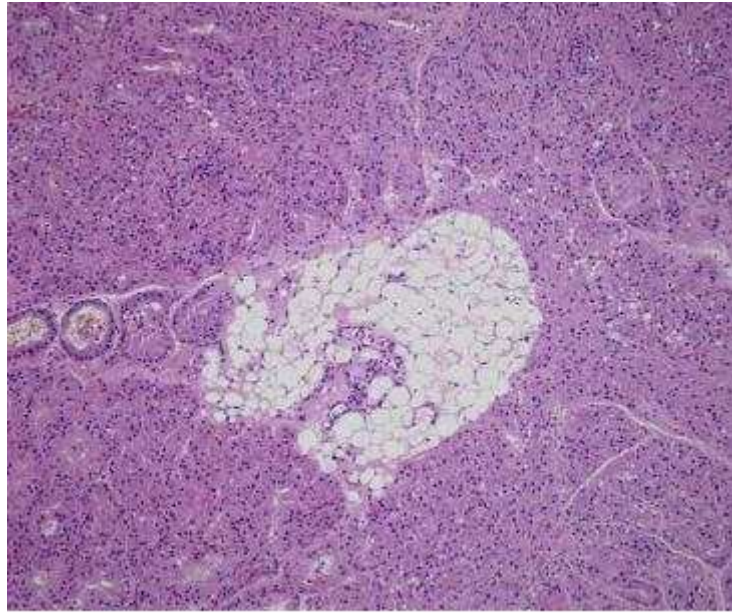
[Fig. 37] Lung, Hyperplasia, bronchiolo-alveolar, alveolar, x200



[Fig. 38] Lung, Eosinophilic inclusion, epithelium, terminal bronchiole x 400



[Fig. 39] Lymph node, tracheobronchial, hemorrhage with pigmentation, x200



[Fig. 40] Harderian gland, Infiltration, adipocytes, x100

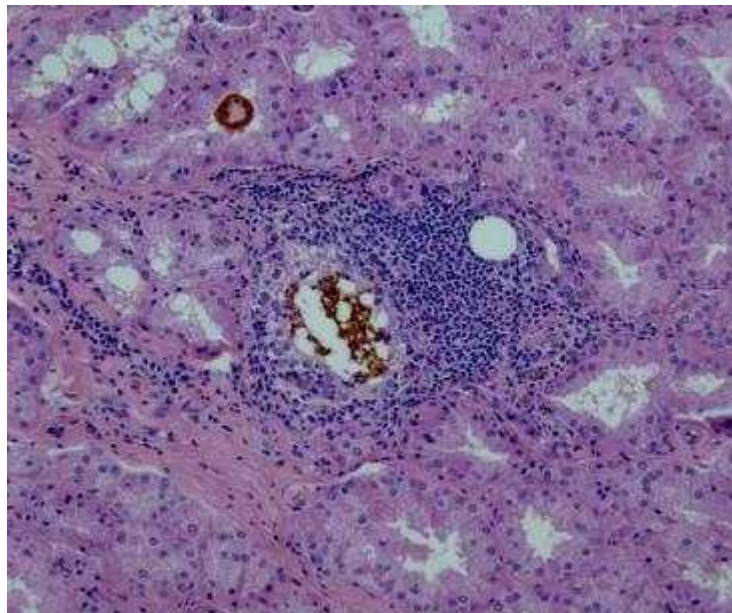
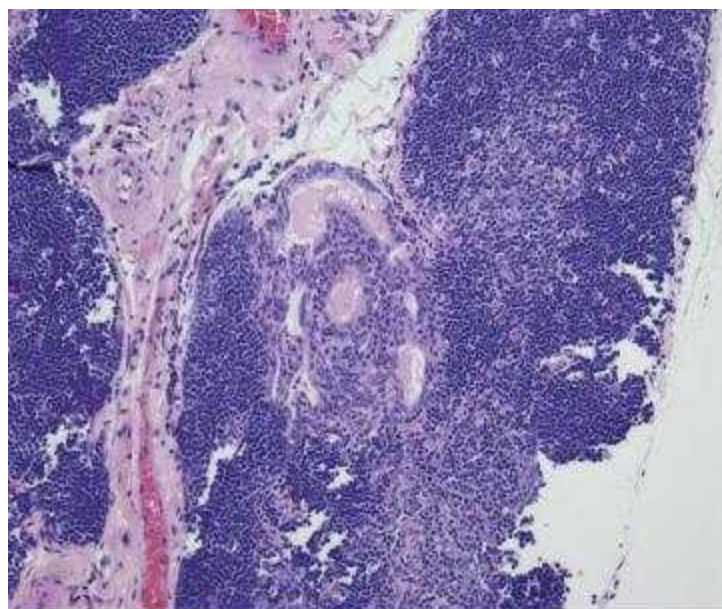


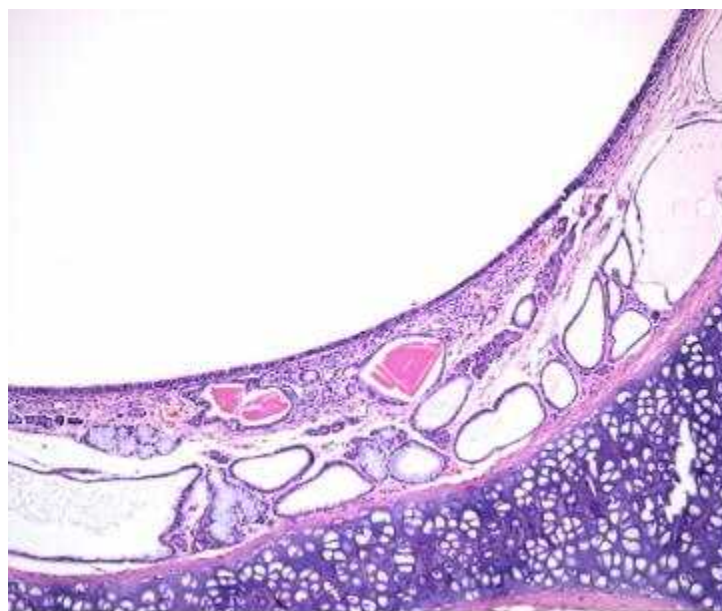
Fig. 41. Harderian gland, Infiltration, mononuclear cells, x200



[Fig. 42] Thymus, hyperplasia, tubules and cords, x200



[Fig. 43] Prostate gland, Inflammation, x 200



[Fig. 44] Larynx, Dilatation with eosinophilic material, submucoal gland, x 200

## IV. 고찰

본 연구는 향후 산업안전보건연구원에서 수행될 발암성시험 등 장기 흡입독성 시험 수행에 사용되는 시험동물에 대한 신뢰성 있는 평가를 위하여 필요한 자체 실험동물 병리기초 자료를 생산하기 위하여 수행하였다.

독성시험에 사용되는 랫드와 마우스의 종은 다양하다. 시험동물의 종이 다른 종양의 발생양상, 실험동물의 수명, 질병 감수성, 동물의 성장속도 등도 다르다. 발암성 시험에는 두 종의 설치류가 사용된다. 마우스는 CD-1 마우스와 C57BL/6 마우스가 주로 사용된다. 랫드는 유럽에서는 Wistar 랫드가 주로 사용되고, 미국에서는 SD(Sprague-Dawley) 랫드 혹은 F344 랫드가 주로 사용된다.

미국 National Toxicology Program (NTP))에서는 발암성 시험용으로 주로 사용하는 F344 랫드는 SD 랫드보다 몸집이 작고, 비교적 사망률도 낮은 점 등의 장점이 있어서 오랫동안 발암성평가를 위한 시험동물로 사용하였다. 이러한 이유로 발암성시험에 많이 사용된 F344 랫드의 자연발생병변에 대한 충분한 자료를 확보하고 있지만, 시험목적에 따라서 다른 종의 랫드가 선택되기도 한다. F344 랫드는 고환의 간질세포 선종(Interstitial cell adenoma)과 단핵세포 백혈병(Mononuclear cell leukemia)이 많이 발생하는 반면, SD 랫드는 뇌하수체 선종(Pituitary adenoma)이 많이 발생한다(Amy et al., 2005). 시험동물로 사용된 동물에서 빈발 종양이 많으면 시험물질에 의해 발생하는 동일한 종양을 예민하게 검색하기가 쉽지 않다. NTP는 다이옥신(Dioxin-like compounds, DLCs)에 대한 만성독성과 발암성을 평가하는 시험에서는 주로 사용하던 F344 랫드를 사용하지 않고 단핵세포 백혈병(Mononuclear cell leukemia)의 발생률이 낮은 Harlan SD 랫드를 시험동물로 선택한 바 있다(Amy et al., 2005).

발암성 시험도 일반 독성시험과 마찬가지로 시험물질에 노출된 시험군과 대조

군을 비교하는 방법으로 결과를 평가한다. 독성시험 결과를 해석할 때 비교 근거가 되는 대조군에 대한 자료에 매우 민감할 수밖에 없다. 그러나 발암성 시험의 병리검사 결과는 매우 변이가 심하고, 발암의 양상도 다르게 나타나서 대조군 사이에서도 자연발생 종양이 각각 다르게 나타날 수 있으며, 시험동물의 사육관리 및 사육실 환경도 종양발생률에 많은 영향을 미친다(Amy et al., 2005).

본 연구에서 32주령의 시험동물을 부검하여 시험동물의 병변을 관찰한 결과, 나이가 들어감에 따라 많이 나타나는 것으로 알려진 하드리안선의 염증세포침윤은 본 연구에서도 수컷(50%)과 암컷(68%) 모두 많이 나타났다(Katsuhiko & Gary, 1990). 자연 발생적으로 나타날 수 있는 심장의 염증세포 침윤은 수컷(32%)에서 암컷(18%)보다 비교적 높게 나타났다(William & Roger, 1990). 본 연구에서 수컷 신장에서는 유리질 축적(100%), 호염기성 세뇨관(84%), 유리질 원주(70%), 색소 축적(100%) 등이 빈도 높게 나타났으나, 암컷 신장에서는 수컷에서는 잘 나타나지 않는 무기질침착(14%)이 비교적 높게 나타났다(Haseman et al., 1990). 본 연구에서 수컷 간에서는 골수외조혈(14%), 담도 증생(38%), 염증세포 침윤(40%) 등이 많이 나타났다. 암컷 간에서는 염증세포침윤(44%)은 많이 나타났으나 국소적인 간세포 괴사는 7마리(14%)에서만 나타났다. 수컷 폐에서는 대식세포 축적(38%)과 혈관 주위 무기질침착(30%)이 비교적 많이 나타났으나 암컷 폐에서는 무기질침착이 가장 많이 나타났다(12%). 본 연구에서 증식성 병변은 폐에서 유일하게 나타났다. 폐는 NTP가 화학물질 평가를 위하여 마우스를 이용한 발암성독성시험에서 2번째로 많이 나타나는 종양 장기이다(Darlene et al., 2008). 랫드를 이용한 발암성시험에서는 암컷에서는 3번째로 종양이 많이 나타나는 장기이나 수컷에서는 종양이 잘 나타나지 않는 장기로 알려져 있다(Darlene et al., 2008). 폐에서 가장 많이 나타나는 종양 부위는 세기관지 폐포(brochiolo-alveolar) 부위이다(Darlene et al., 2008). NTP가 2006년에 최근 5년간 발암성시험에 사용된 F344 랫드 1500마리와 B6C3F1 마우스 1500마리에 대한 자연발생병변을 정리한 자료에 의하며 F344 랫드의 세기관지 폐포 종양(neoplasm) 발병은

암 수 모두 4%이하로 나타났으나(NTP Historical Control Database, 2006), B6C3F1 마우스의 세기관지 폐포 샘종(adenoma)은 암수 각각 평균 17.4%와 4.6%로 나타났다(NTP Historical Control Database, 2006). 본 연구에서는 수컷 1마리에서 세기관지와 폐포 부위에 샘종(Adenoma, brochiolo-alveolar)이 나타났다. 수컷 이자에서는 샘파리세포 위축(24%)이 비교적 많이 나타났으나, 암컷 이자에서는 샘파리세포 위축이 1마리(2%)에서만 나타났다. 비장의 골수외조혈은 수컷(24%)에서는 비교적 많이 나타났으나, 암컷에서는 3마리(6%)에서만 나타났다. 흉선의 상피관 및 상피선 증생은 수컷(10%)과 암컷(12%)에서 비슷하게 나타났다. 수컷 갑상선에서 나타난 ultimobranchial cyst는 F344 랫드에서 선천적으로 나타날 수 있는 것으로(Jerry & Gary, 1990) 본 연구에서는 수컷 1마리(2%)에서만 나타났다.

## V. 결 론

본 연구를 통하여 항 후 흡입독성평가센터에서 수행될 장기독성시험 평가를 위한 병리검사 기초로서 F344 랫드 등 장기독성시험에 주로 사용되는 설치류에 대한 자연발생병변자료와 자연발생병변 표준 아틀라스를 확보하였으며, 32주령의 F344에 대한 요검사와 혈액 및 혈액생화학검사 자료 그리고 자연발생병변 조직병리검사 자료를 확보하였다.

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## Abstract

### A Study on Spontaneous lesions on 33 weeks Fischer 344 rats

Yong Hyun Chung · Yong Hoon Lee · Mi Ju Lee · Eun Sang Cho · Jeong Hee Han

· Seo Ho Shin

**Objectives:** This study was carried out to investigate the spontaneous lesions data on experimental animals in order to secure the reliability of the evaluation of the long-term toxicity test to be performed on Chronic Inhalation Toxicity Test Center.

**Methods:** Each of the 50 male and female animals of 11-week-old F344 rats were observed for 21 weeks. During the test period the body weight of the animals were measured once a week. After the end of the test the urinalysis, hematologic examination, biochemical examination of blood and blood coagulation time of the animals were performed. The test animals that autopsied were performed histopathological examination.

**Results:** Inflammatory cell infiltration of the Adrenal gland was a lot of both males(50%) and females(68%). Inflammatory cell infiltration of the heart appeared relatively higher males(32%) than female(18%). In the kidney of males hyaline accumulation(100%), basophilic tubules (84%), hyaline casts(70%), pigment accumulation(100%) appeared very frequently. In females

kidney mineralization(14%) was relatively frequent. In males liver, there were many case of extramedullary hematopoiesis(14%), bile duct hyperplasia(38%), inflammatory cell infiltration(40%). In females liver, inflammatory cell infiltration(44%) appeared frequently but focal necrosis of hepatocytes occurred in only 7 animals(14%). Macrophage accumulation(38%) and perivascular mineral deposition(30%) were relatively frequent in male lung, and 1 male was found adenoma in bronchioles and alveoli. In female lung, only 6 animals (12%) showed mineral deposition. In males, follicular atrophy(24%) occurred, whereas in females only follicular atrophy was observed in 1 (2%). Bone marrow extracellular hematopoiesis of the spleen was relatively high in male(24%) but only in 3 animals(6%) in female. Hyperplasia of tubules and cords in the thymus was similar in males(10%) and females(12%). The ultimobranchial cyst of the thyroid gland appeared only in 1 male(2%).

**Conclusions:** In this study, spontaneous lesion data of SD rats and F344 rats and spontaneous lesion standard atlas of the rodents were obtained, and the Data of urinalysis, blood and blood biochemical data, and histopathological data on 32-week-old F344 could be used as the basis for the pathological examination for the long-term toxicity test.

Keywords : Fischer 344 rat, Spontaneous lesions

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## <<연 구 기 간>>

2016. 1. 1 ~ 2016. 11. 30



본 연구보고서에 기재된 내용은 연구책임자의 개인적 견해이며, 우리 연구원의 공식견해와 다를 수도 있음을 알려드립니다.

**산업안전보건연구원장**

**화학물질유해성평가를 위한  
실험동물 자업발생병변조사연구**

(2016-연구원-1250)

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발 행 일 : 2016년 11월  
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연구보고서(별첨)

# 화학물질 유해성평가를 위한 실험동물의 자연발생 병변조사 연구

정용현, 이용훈, 이미주, 조은상, 한정희, 신서호

산업재해예방

**안전보건공단**

산업안전보건연구원





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# 별첨자료

Nonneoplastic Lesion Atlas

A guide for standardizing terminology in toxicologic pathology for  
rodents

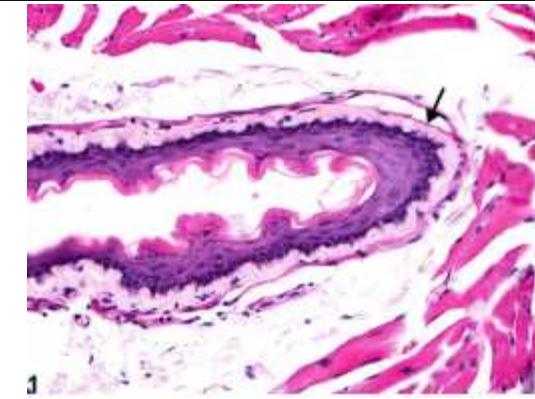
National Toxicology Program



## 1. 소화기계

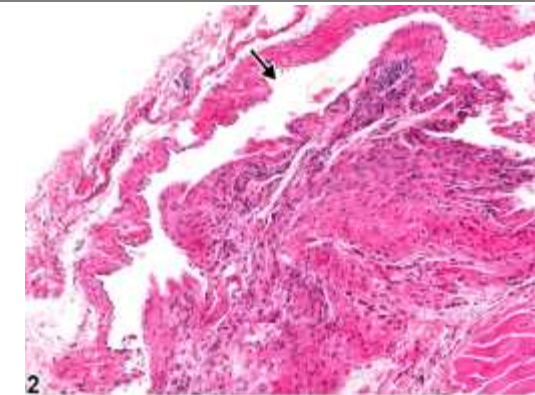
## 1) 식도

## Esophagus - Amyloid (아밀로이드)



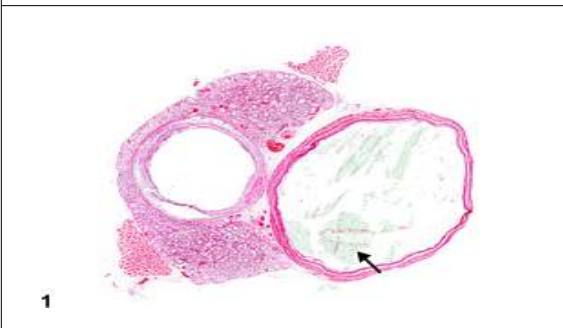
Esophagus - Amyloid in a male Swiss Webster mouse from a chronic study. There is a cellular, eosinophilic material (amyloid) in the submucosa of the esophagus (arrow).

## Esophagus - Angiectasis (혈관확장)



Esophagus - Angiectasis in a female F344/N rat from a chronic study. Dilated vascular spaces (arrow) are visible in the wall of the esophagus.

### Esophagus - Dilation (확장)



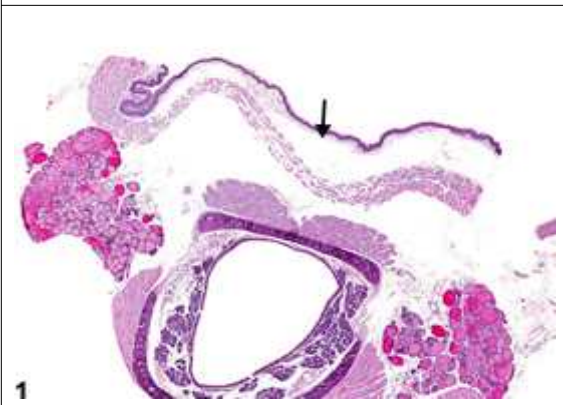
Esophagus - Dilation in a male Wistar Han rat from a chronic study. The dilated esophagus contains feed material (arrow).

### Esophagus - Diverticulum (계실)



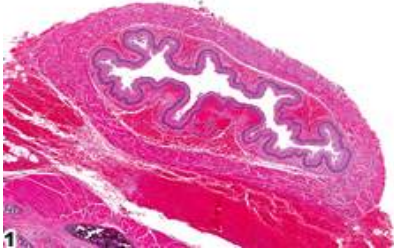
Esophagus - Diverticulum in a female F344/N rat from a chronic study. The diverticulum (arrow) adjacent to the esophagus (arrowhead) is filled with feed material (asterisk = trachea).

### Esophagus - Edema (부종)



Esophagus - Edema in a male B6C3F1 mouse from a chronic study. Separation of tissues by clear space is visible (arrow).

## Esophagus - Hemorrhage (출혈)



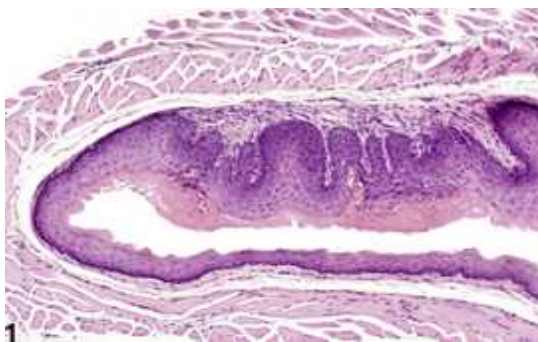
Esophagus - Hemorrhage in a male F344/N rat from a chronic study. There is free blood around the esophagus and in the lamina propria.

## Esophagus - Hyperkeratosis (각막비후증)



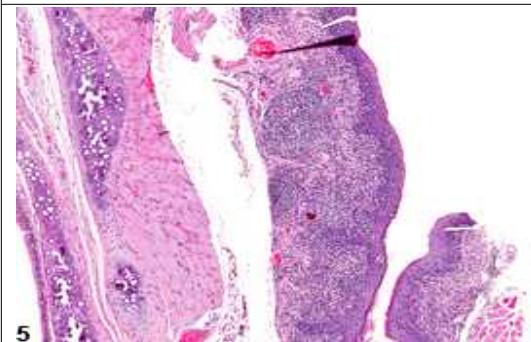
Esophagus - Hyperkeratosis in a female F344/N rat from a chronic study. There are excess, anuclear keratin layers on the surface of the epithelium.

## Esophagus - Hyperplasia (증생)



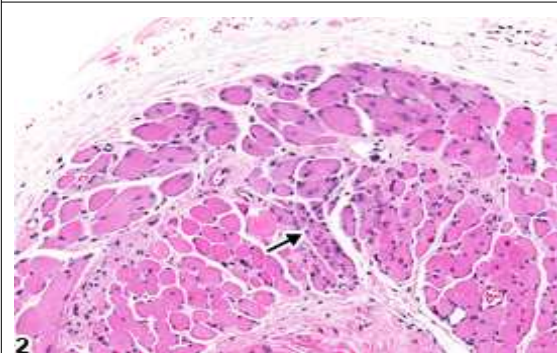
Esophagus, Epithelium - Hyperplasia in a female B6C3F1 mouse from a chronic study. There are rete peg-like structures and accompanying hyperkeratosis.

### Esophagus - Inflammation (염증)



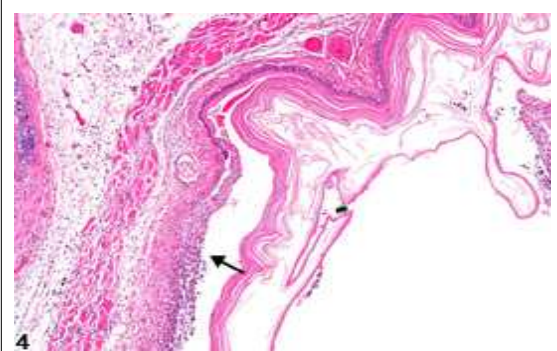
Esophagus - Inflammation, Chronic in a female F344/N rat from a chronic study. The inflammation is composed primarily of lymphocytes and plasma cells.

### Esophagus, Muscularis - Degeneration (변성)



Esophagus, Muscularis - Degeneration in a male F344/N rat from a chronic study. Note the decreased muscle fiber size (arrow).

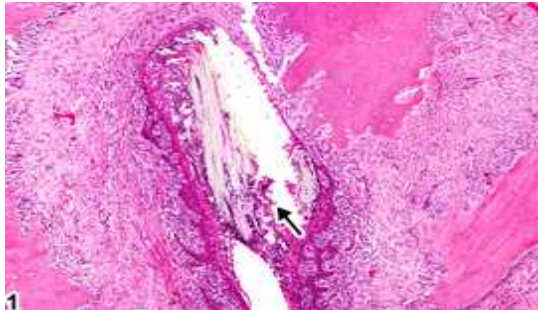
### Esophagus - Ulcer (궤양)



Esophagus - Ulcer in a female F344/N rat from a chronic study. The denuded epithelium is replaced by necrotic debris and inflammatory cells (arrow).

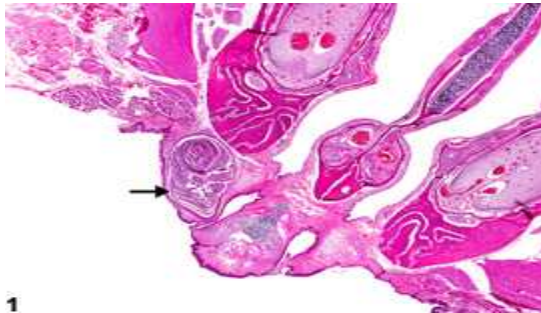
## 2) 구강 점막

## Oral Mucosa - Foreign Body (이물질)



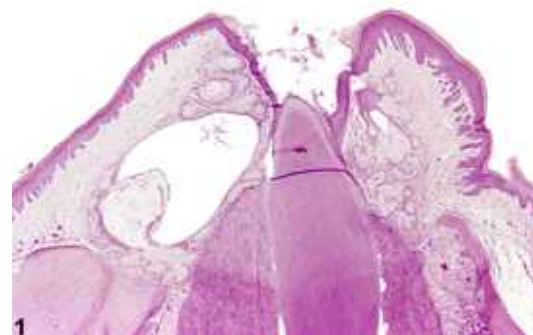
Oral mucosa - Foreign body in a male F344/N rat from a chronic study. The foreign body (arrow) is surrounded by suppurative inflammation.

## Oral Mucosa - Cyst, Squamous (편평상피 낭포)



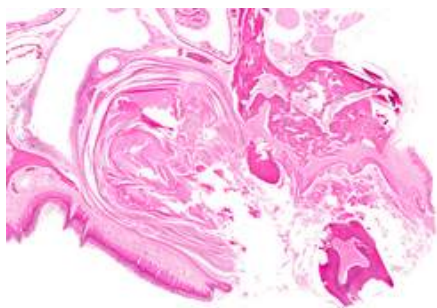
Oral mucosa - Cyst, Squamous in a female F344/N rat from a chronic study. There is a keratin-filled squamous cyst (arrow) beneath the mucosa in the hard palate.

## Oral Mucosa, Gingiva - Ectopic Tissue (이소성 조직)



Oral mucosa, Gingiva - Ectopic tissue, Sebaceous gland in male F344/N rat from a chronic study. There are clusters of sebaceous glands in the gingiva.

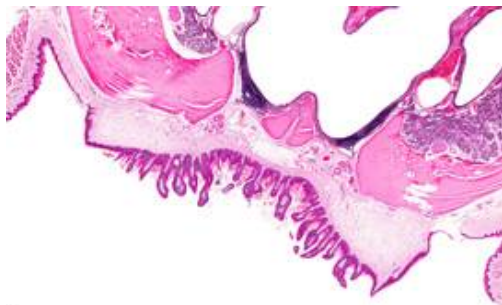
### Oral Mucosa - Hyperplasia, Cystic, Keratinizing (낭포성 각질 증생)



1

Oral mucosa - Hyperplasia, Cystic, Keratinizing in a male Harlan Sprague-Dawley rat from a chronic study. The keratin-filled cyst is distorting normal architecture, including that of the nasal cavity. The keratin-filled cyst with destruction of maxillary bone is shown.

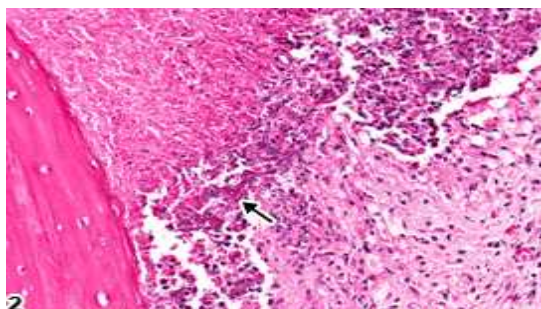
### Oral Mucosa - Hyperplasia, Squamous (편평상피 증생)



1

Oral mucosa - Hyperplasia, Squamous in a female F344/N rat from chronic study. There is hyperplasia of the squamous epithelium of the hard palate.

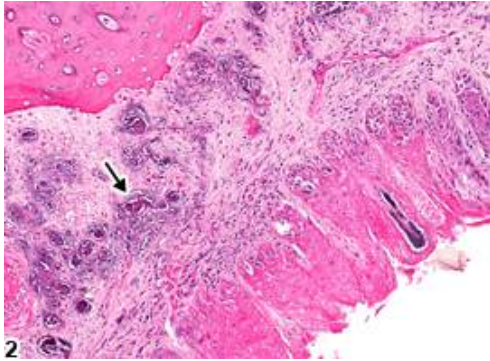
### Oral Mucosa - Inflammation (염증)



2

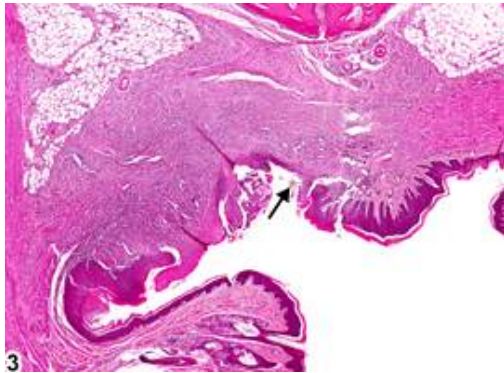
Oral mucosa - Inflammation, Suppurative in a male F344/N rat from a chronic study. There is an area of suppurative inflammation with necrosis and fungal organisms (arrow).

## Oral Mucosa - Necrosis (괴사)



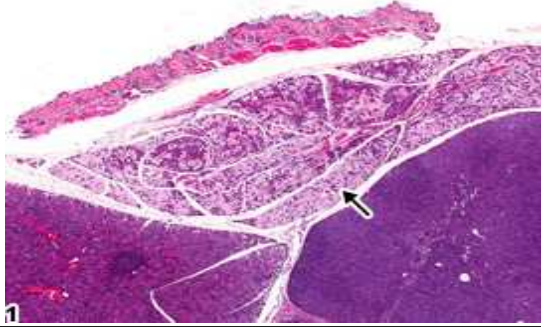
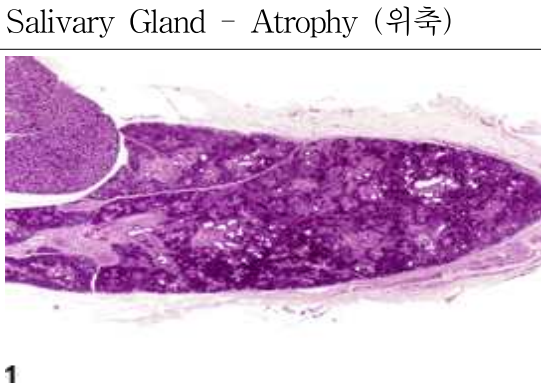
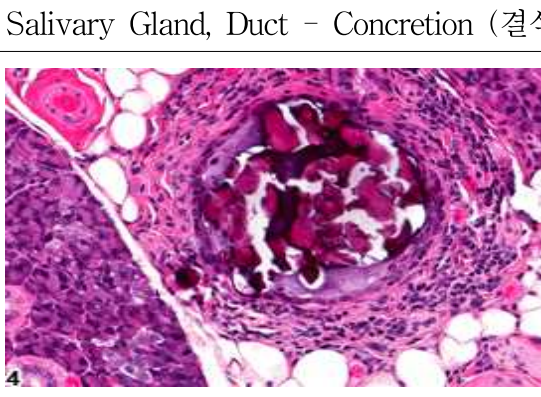
Oral mucosa - Necrosis in a male F344/N rat from a subchronic study. There is necrosis of the epithelium on the hard palate mucosa, with bacterial colonies in the submucosa (arrow).

## Oral Mucosa - Ulcer

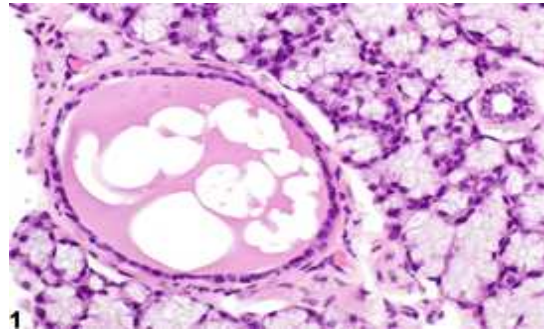


Oral mucosa - Ulcer in a female F344/N rat from a chronic study. A portion of the hard palate mucosa is absent (arrow), exposing the inflamed underlying connective tissue.

### 3) 침샘

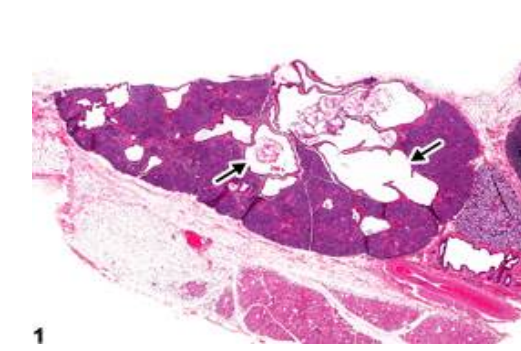
Salivary Gland - Amyloid (아밀로이드)	
	<p>Salivary gland - Amyloid in a female Swiss Webster mouse from a chronic study. The deposition of amyloid is affecting an entire lobe of the salivary gland (arrow).</p>
Salivary Gland - Atrophy (위축)	
	<p>Salivary gland - Atrophy in a male F344/N rat from a chronic study. There is a decrease in the number and size of the glands and an increase in the connective tissue.</p>
Salivary Gland, Duct - Concretion (결석)	
	<p>Salivary gland, Duct - Concretion in a male B6C3F1 mouse from a subchronic study (higher magnification of Figure 3). The concretion is eliciting a chronic inflammatory response around the duct with fibrosis.</p>

## Salivary Gland, Duct - Cyst (낭포)



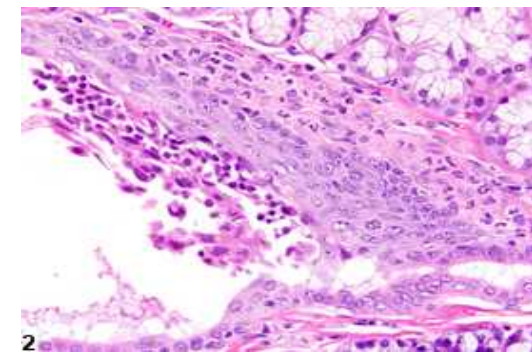
Salivary gland, Duct - Cyst in a female B6C3F1 mouse from a chronic study. The cyst is roughly circular, and the epithelium is somewhat flattened.

## Salivary Gland, Duct - Dilation (팽창)



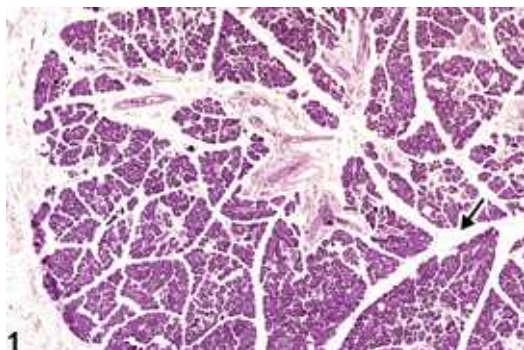
Salivary gland, Duct - Dilation in a female F344/N rat from a chronic study. Multiple ducts in this gland are dilated (arrows).

## Salivary Gland, Duct - Metaplasia, Squamous (편평상피 화생)



Salivary gland, Duct - Metaplasia, Squamous in a male F344/N rat from a chronic study (higher magnification of Figure 1). The normally cuboidal ductal epithelial cells have been replaced by stratified squamous epithelium.

### Salivary Gland - Edema (부종)



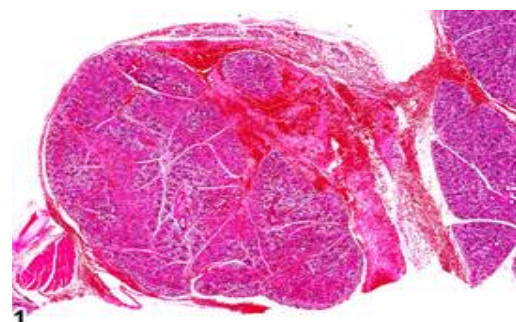
Salivary gland - Edema in a male F344/N rat from a chronic study. The clear space between the lobules (arrow) is evidence of edema.

### Salivary Gland - Fibrosis (섬유화)



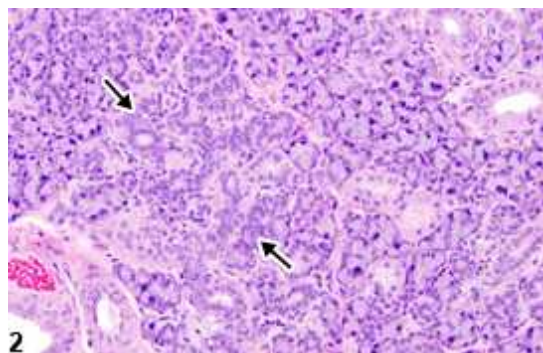
Salivary gland - Fibrosis in a male F344/N rat from a subchronic study. Fibrillar eosinophilic material (fibrosis) surrounds the salivary gland and separates the lobules.

### Salivary Gland - Hemorrhage (출혈)



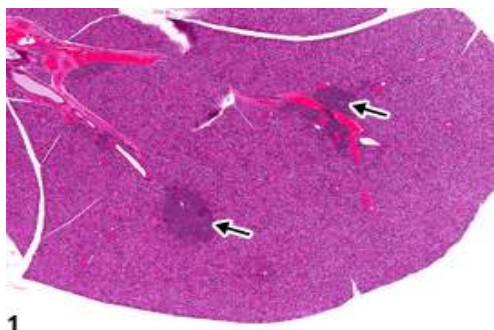
Salivary gland - Hemorrhage in a female B6C3F1 mouse from a chronic study.

## Salivary Gland - Hyperplasia (증생)



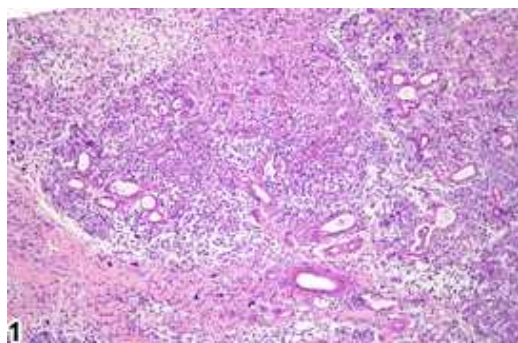
Salivary gland, Sublingual, Duct - Hyperplasia in a male F344/N rat from a subchronic study. There is an increase in the number of ductular epithelial cells within the gland (arrows).

## Salivary Gland - Infiltration, Cellular (세포 침윤)

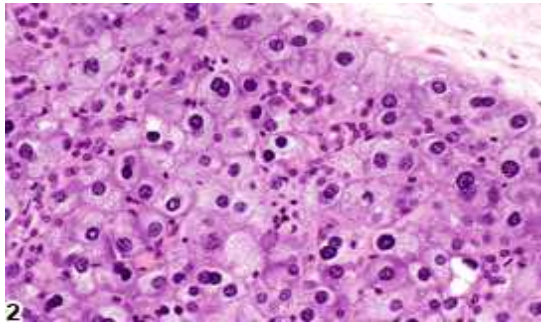
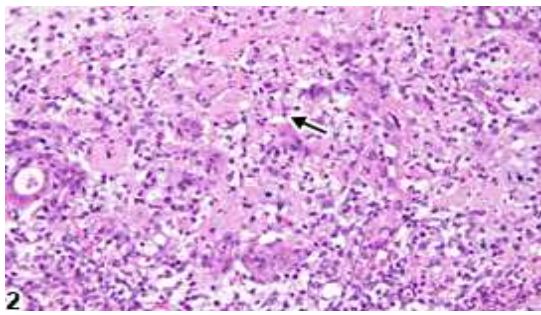
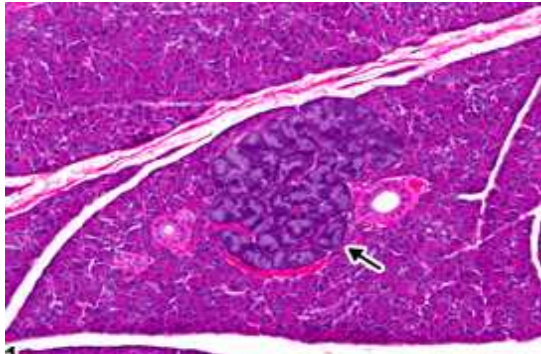


Salivary gland - Infiltration, Cellular, Lymphocyte in a female B6C3F1 mouse from a chronic study. The cellular infiltrates (arrows) are more deeply basophilic than the glandular tissue.

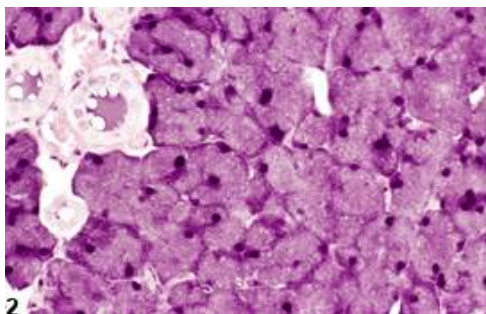
## Salivary Gland - Inflammation (염증)



Salivary gland - Inflammation, Acute in a male F344/N rat from a subchronic study. There is widespread destruction of the salivary tissue with abundant inflammatory cells.

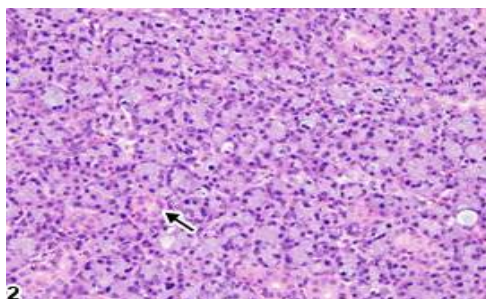
Salivary Gland - Karyomegaly (거핵)	
	<p>Salivary gland - Karyomegaly in a male B6C3F1 mouse from a chronic study. The nuclei in the acinar cells are enlarged.</p>
Salivary Gland - Necrosis (괴사)	
	<p>Salivary gland - Necrosis in a male F344/N rat from a subchronic study. There is necrosis of the acinar cells (arrow) with chronic active inflammation.</p>
Salivary Gland, Parotid - Basophilic Hypertrophic Focus (호염성 비대 병소)	
	<p>Salivary gland, Parotid - Basophilic hypertrophic focus in a female F344/N rat from a chronic study. A focus of hypertrophied cells with increased basophilia is present (arrow).</p>

## Salivary Gland, Parotid, Acinus - Hypertrophy (선방세포 비대)



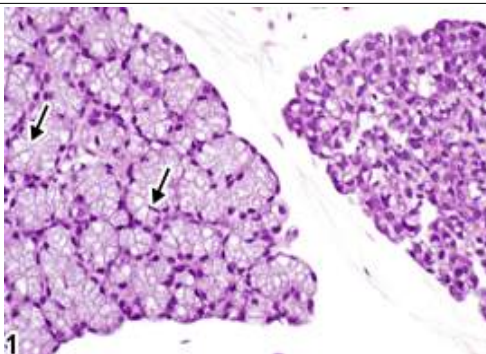
Salivary gland, Parotid, Acinus - Hypertrophy in a male F344/N rat from a subchronic study. The acinar cells are diffusely enlarged.

## Salivary Gland, Submandibular - Secretory Depletion (분비 소실)

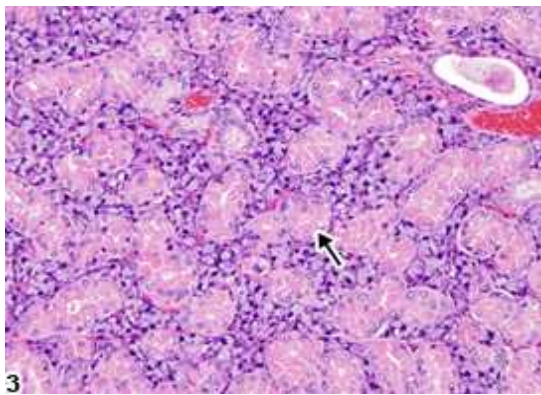


Salivary gland, Submandibular - Secretory depletion in a female F344/N rat from a subchronic study. The acinar and ductular (arrow) cells are smaller.

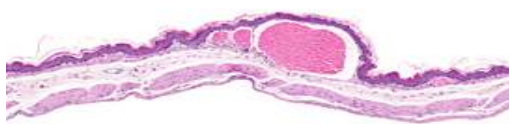
## Salivary Gland - Vacuolation, Cytoplasmic (세포질 공포화)

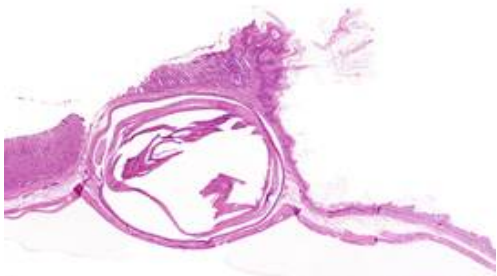


Salivary gland - Vacuolation, Cytoplasmic in a female B6C3F1 mouse from a chronic study. There are small, clear spaces (vacuoles) in the cytoplasm of the acinar cells (arrows).

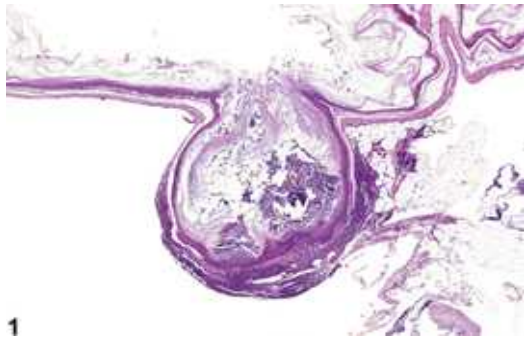
Salivary Gland, Submandibular, Duct - Cytoplasmic Alteration (세포질 변성)	
 <p>3</p>	<p>Salivary gland, Duct - Cytoplasmic alteration in a female B6C3F1 mouse from a chronic study. In this submandibular salivary gland, there are increased numbers of eosinophilic, cytoplasmic granules in the ducts (arrow), reminiscent of the male ducts.</p>

#### 4) 전위

Stomach, Forestomach - Angiectasis (혈관확장)	
 <p>1</p>	<p>Stomach, Forestomach - Angiectasis in a male B6C3F1 mouse from a chronic study. There are several cross sections of dilated blood vessels in the lamina propria.</p>

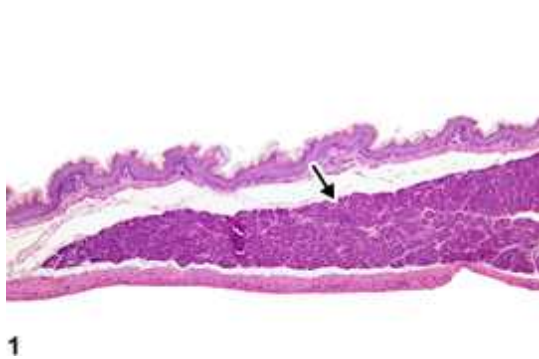
Stomach, Forestomach - Cyst (낭포)	
 <p>2</p>	<p>Stomach, Forestomach - Cyst in a female F344/N rat from a chronic study. A keratin-filled cyst is present in the submucosa at the junction of the forestomach and glandular stomach.</p>

## Stomach, Forestomach - Diverticulum (계실)



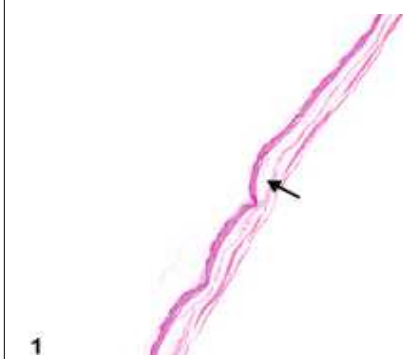
Stomach, Forestomach - Diverticulum in a female B6C3F1 mouse from a chronic study. An out-pouching of the wall of the forestomach filled with keratin, inflammatory cells, and ingesta is present.

## Stomach, Forestomach - Ectopic Tissue (이소성 조직)



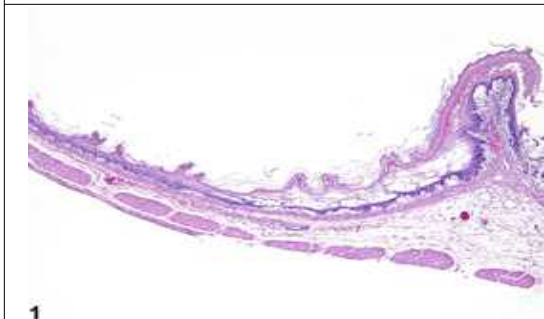
Stomach, Forestomach - Ectopic pancreas in a female B6C3F1 mouse from a chronic study. Ectopic pancreatic acinar cells are present in the submucosa of the forestomach (arrow).

## Stomach, Forestomach - Edema (부종)



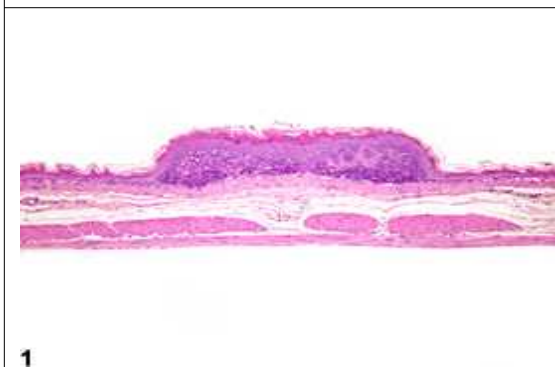
Stomach, Forestomach - Edema in a male F344/N rat from a chronic study. Edema fluid of low protein content results in clear spaces in the tissues (arrow).

Stomach, Forestomach, Epithelium - Degeneration (변성)



Stomach, Forestomach, Epithelium  
- Degeneration in a female F344/N rat from a subchronic study. There is vacuolation along the basement membrane and below the keratin layer.

Stomach, Forestomach, Epithelium - Hyperplasia, Atypical (이형상피 증생)



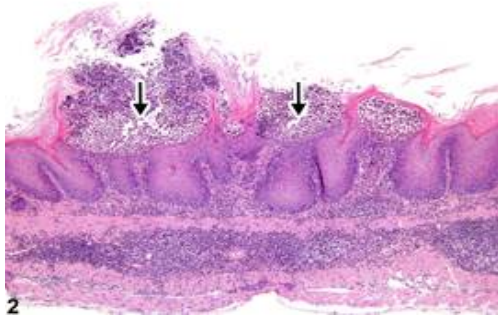
Stomach, Forestomach, Epithelium  
- Hyperplasia, Atypical in a female F344/N rat from a subchronic study. Focal epithelial hyperplasia with large, atypical cells is present.

Stomach, Forestomach, Epithelium - Hyperplasia, [Focal, Diffuse] (상피세포 증생)



Stomach, Forestomach, Epithelium  
- Hyperplasia in a male F344/N rat from a subchronic study. The epithelial hyperplasia is diffuse.

## Stomach, Forestomach - Erosion (미란)



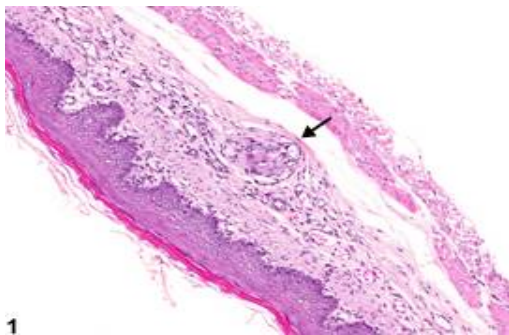
Stomach, Forestomach - Erosion in a female B6C3F1 mouse from a chronic study. The superficial layers of the hyperplastic squamous epithelium have been lost (arrows).

## Stomach, Forestomach - Fibrosis (섬유증)



Stomach, Forestomach - Fibrosis in female F344/N rat from a chronic study. The submucosa is expanded by fibrotic tissue.

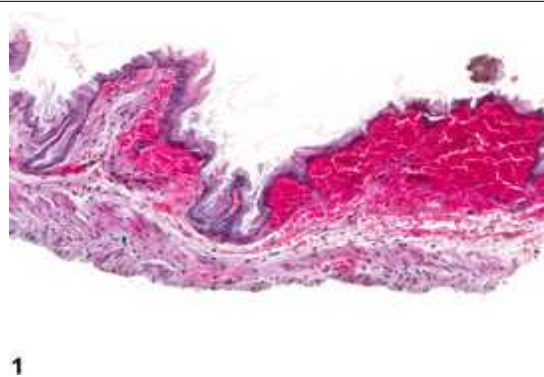
## Stomach, Forestomach - Foreign Body (이물질)



Stomach, Forestomach - Foreign body in a male F344/N rat from a chronic study. A foreign body (hair) (arrow) has penetrated the epithelium and submucosa.

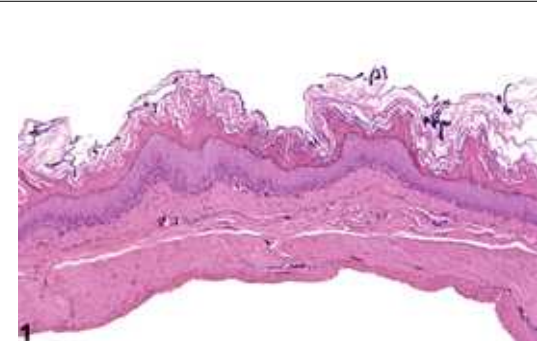
A foreign body (hair) (arrow) with associated granulomatous inflammation is present in the submucosa.

### Stomach, Forestomach - Hemorrhage (출혈)



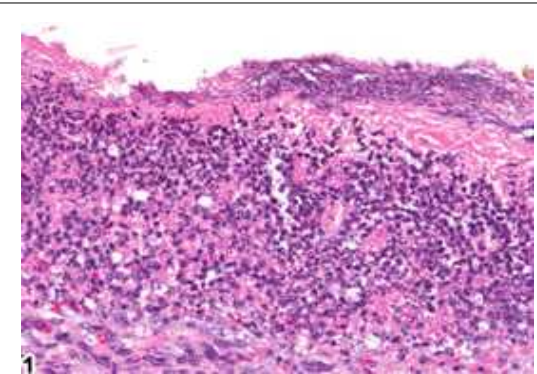
Stomach, Forestomach - Hemorrhage in a female B6C3F1 mouse from a chronic study. Hemorrhage is present in the submucosa of the forestomach.

### Stomach, Forestomach - Hyperkeratosis (각화과다증)



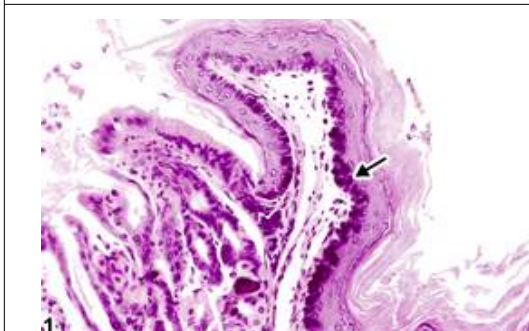
Stomach, Forestomach - Hyperkeratosis in a male F344/N rat from a subchronic study. A thickened keratin layer in the forestomach associated with epithelial hyperplasia.

### Stomach, Forestomach - Inflammation (염증)



Stomach, Forestomach - Inflammation, Suppurative in a male F344/N rat from a chronic study. This suppurative inflammation is associated with an ulcer.

## Stomach, Forestomach - Mineralization (무기질침착)



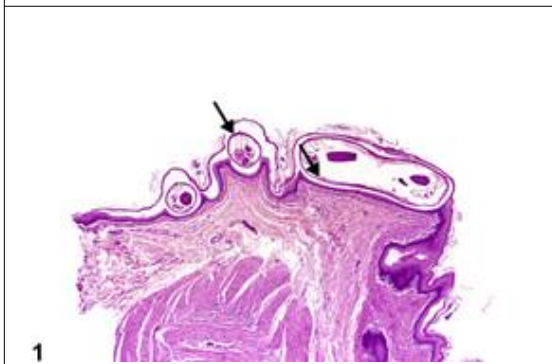
Stomach, Forestomach - Mineralization in a male B6C3F1 mouse from a chronic study. Mineralization (arrow) is present along the basement membrane of the forestomach.

## Stomach, Forestomach - Necrosis (괴사)

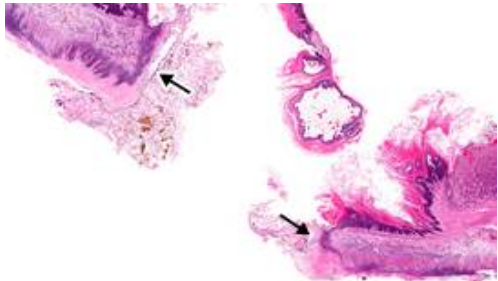



Stomach, Forestomach - Necrosis in a female B6C3F1 mouse from a chronic study. There is loss of cellular detail indicative of necrosis (arrow).

## Stomach, Forestomach - Parasite, Metazoan (기생충)

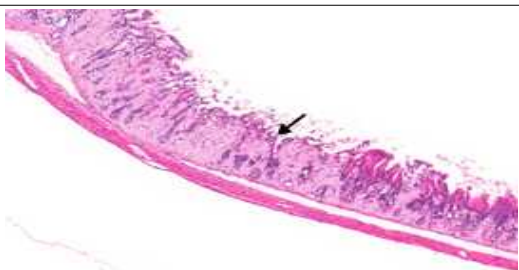


Stomach, Forestomach - Parasite, Metazoan in a male F344/N rat from a chronic study. Nematodes (arrows) are present within the mucosa of the forestomach.

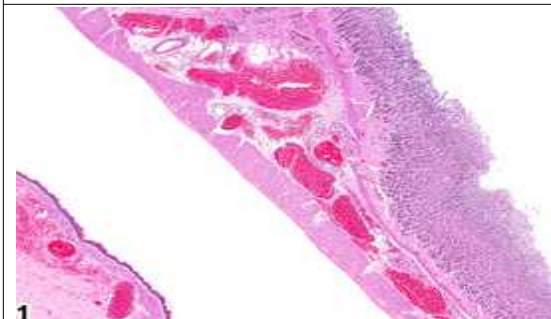
Stomach, Forestomach - Perforation (천공)	
 <p>1</p>	<p>Stomach, Forestomach - Perforation in a male F344/N rat from a chronic study. The arrows indicate the edges of the perforation.</p>

Stomach, Forestomach - Ulcer (궤양)	
 <p>1</p>	<p>Stomach, Forestomach - Ulcer in a male F344/N rat from a chronic study. A portion of the epithelium is absent, exposing the underlying submucosa.</p>

## 5) 선위

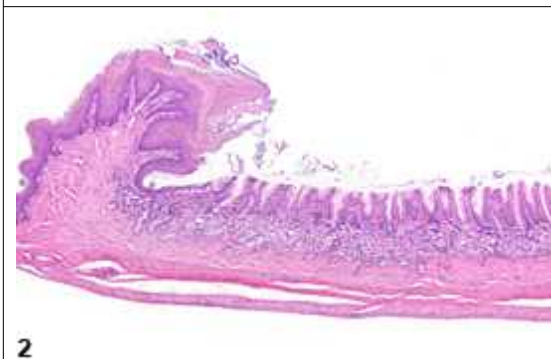
Stomach, Glandular Stomach - Amyloid (아밀로이드)	
 <p>1</p>	<p>Stomach, Glandular stomach - Amyloid in a female Swiss Webster mouse from a chronic study. Amyloid (arrow) is deposited in the lamina propria.</p>

## Stomach, Glandular Stomach - Angiectasis (혈관확장)



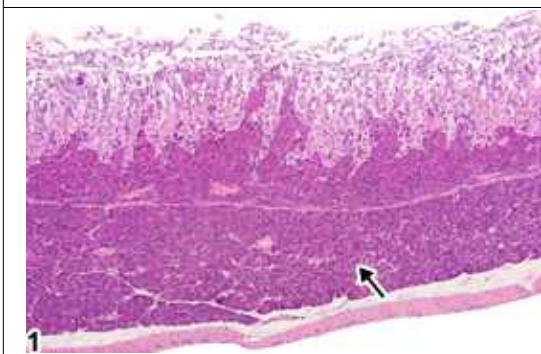
Stomach, Glandular stomach - Angiectasis in a male F344/N rat from a chronic study. Dilated blood vessels are present in the submucosa of the glandular stomach.

## Stomach, Glandular Stomach - Atrophy (위축)



Stomach, Glandular stomach - Atrophy in a female F344/N rat from a chronic study. There is thinning of the glandular mucosa near the limiting ridge.

## Stomach, Glandular Stomach - Ectopic Tissue (이소성 조직)



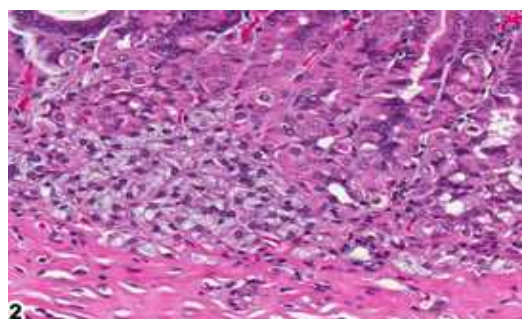
Stomach, Glandular stomach - Ectopic tissue, Pancreas in a female B6C3F1 mouse from a chronic study. There are pancreatic acinar cells in submucosa of the glandular stomach (arrow).

Stomach, Glandular Stomach - Edema (부종)



Stomach, Glandular stomach - Edema in a female B6C3F1 mouse from a chronic study. The submucosa is expanded by fluid.

Stomach, Glandular Stomach, Epithelium - Hyperplasia (상피세포 증생)



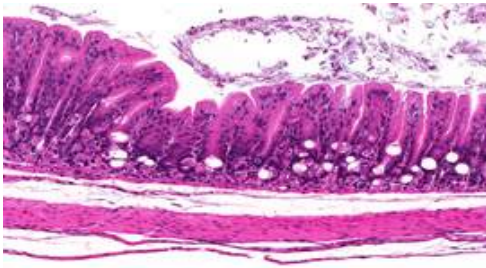
Stomach, Glandular stomach, Epithelium - Hyperplasia in a female F344/N rat from a chronic study. The basophilic cells are smaller and more crowded, and there slight compression of the adjacent mucosa.

Stomach, Glandular Stomach, Epithelium - Hyperplasia, Atypical (이형상피 증생)



Stomach, Glandular stomach, Epithelium - Hyperplasia, Atypical in a female B6C3F1 mouse from a chronic study. There is an expansile focus of hyperplasia within the mucosa (arrow).

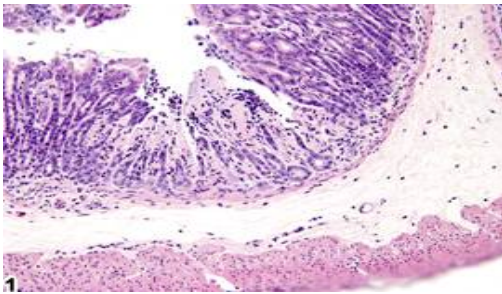
## Stomach, Glandular Stomach, Epithelium - Vacuolation, Cytoplasmic (세포질 공포)



1

Stomach, Glandular stomach, Epithelium - Vacuolation, Cytoplasmic in a male F344/N rat from a subchronic study. There is vacuolation of epithelial cells in the mucosal glands.

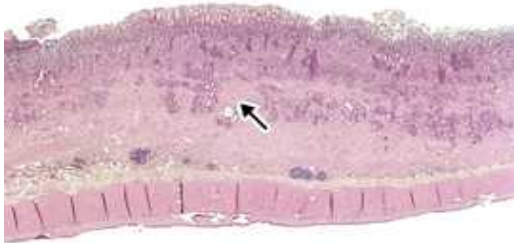
## Stomach, Glandular Stomach - Erosion (미란)



1

Stomach, Glandular stomach - Erosion in male B6C3F1 mouse from a subchronic study. The lesion does not extend through the entire mucosa.

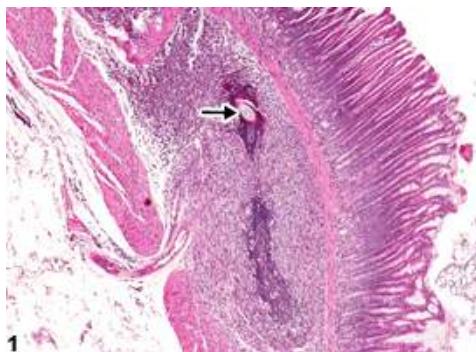
## Stomach, Glandular Stomach - Fibrosis (섬유증)



1

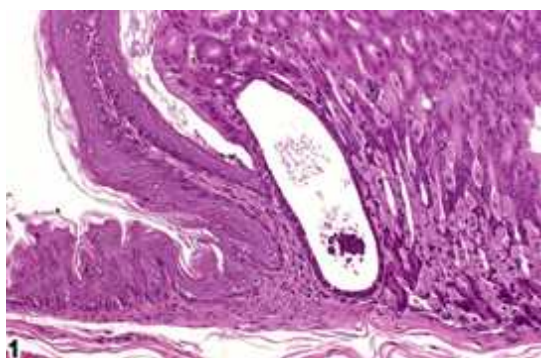
Stomach, Glandular stomach - Fibrosis in a male F344/N rat from a chronic study. Dense collagen (arrow) separates and replaces glands in the mucosa.

### Stomach, Glandular Stomach - Foreign body (이물질)



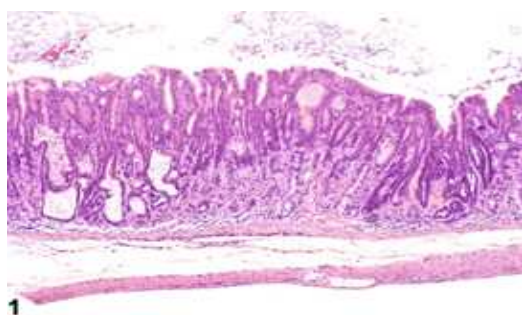
Stomach, Glandular stomach - Foreign body in a male B6C3F1 mouse from a chronic study. There is a foreign body (arrow) in the submucosa with secondary inflammation.

### Stomach, Glandular Stomach, Glands - Cyst (선 낭포)



Stomach, Glandular stomach, Glands - Cyst in a male B6C3F1 mouse from a subchronic study. This cystic gland is lined by slightly flattened epithelium.

### Stomach, Glandular Stomach, Glands - Dilation (확장)



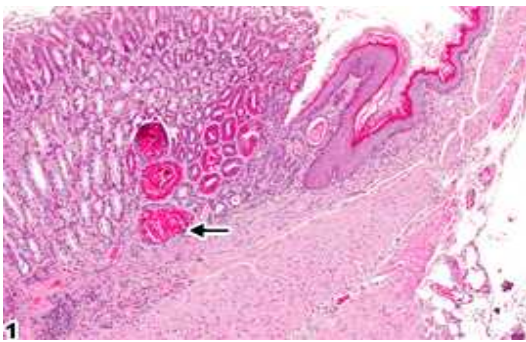
Stomach, Glandular stomach, Glands - Dilation in a male B6C3F1 mouse from a chronic study. Glandular dilation predominantly at the base of the glands.

## Stomach, Glandular Stomach - Hemorrhage (출혈)



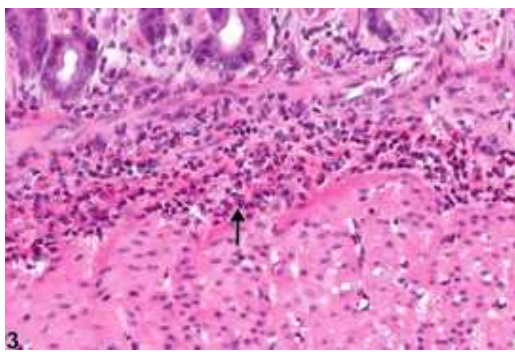
Stomach, Glandular stomach - Hemorrhage in a male F344/N rat from a chronic study. There is hemorrhage in the mucosa and a vascular thrombus in the submucosa (arrow).

## Stomach, Glandular Stomach - Hyaline Droplet (초자)



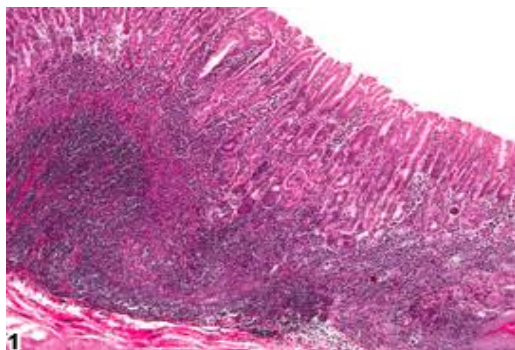
Stomach, Glandular stomach - Accumulation, Hyaline droplet in a female B6C3F1 mouse from a chronic study. The epithelial cells of several gastric glands contain hyaline droplets (arrow) with some crystals in the lumens.

## Stomach, Glandular Stomach - Infiltration, Cellular (세포 침윤)



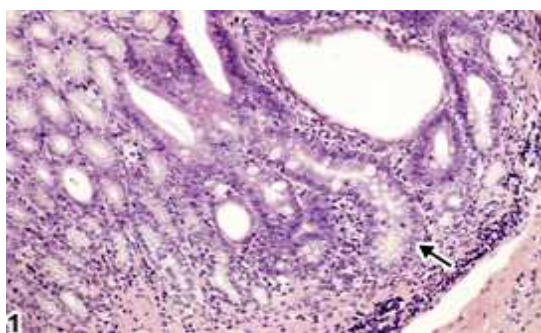
Stomach, Glandular stomach - Infiltration, Cellular, Eosinophil in a female B6C3F1 mouse from a subchronic study (higher magnification of Figure 3). Eosinophilic cellular infiltrate is present in the submucosa of the glandular stomach (arrow).

### Stomach, Glandular Stomach - Inflammation (염증)



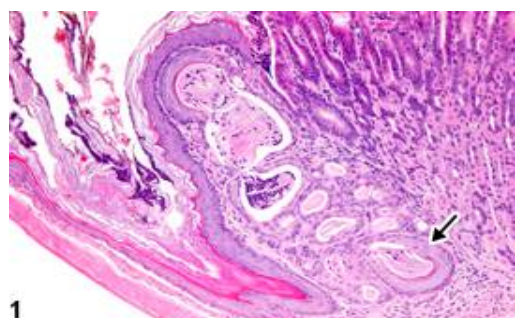
Stomach, Glandular stomach - Inflammation, Chronic in a male B6C3F1 mouse from a chronic study. Lymphocytes (primarily) are present within the submucosa and lamina propria.

### Stomach, Glandular Stomach - Metaplasia, Intestinal (장 화생)



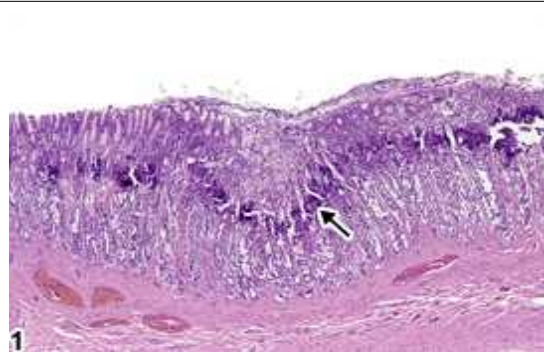
Stomach, Glandular stomach - Metaplasia, Intestinal in a male F344/N rat from a chronic study. Metaplasia of fundic glands to intestinal glands (arrow).

### Stomach, Glandular Stomach - Metaplasia, Squamous (편평상피 화생)



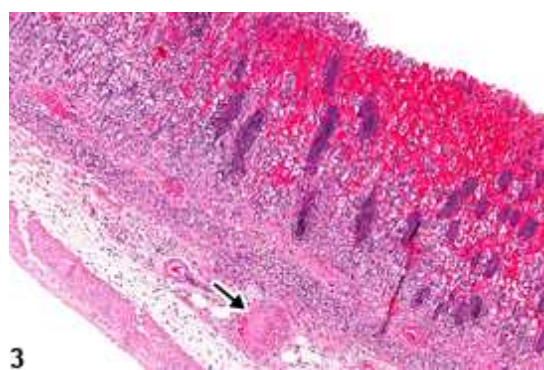
Stomach, Glandular stomach - Metaplasia, Squamous in a male B6C3F1 mouse from a chronic study. The normal epithelium of the gastric glands is replaced by squamous epithelium (arrow).

## Stomach, Glandular Stomach - Mineralization (무기질침착)



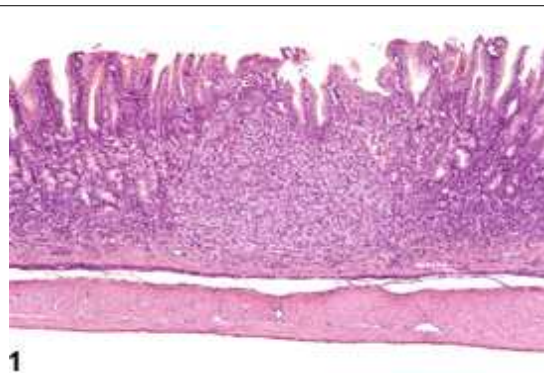
Stomach, Glandular stomach - Mineralization in a male F344/N rat from a chronic study. There is a linear band of mineralization paralleling the parietal rich region in gastric fundus (arrow).

## Stomach, Glandular Stomach - Necrosis (괴사)



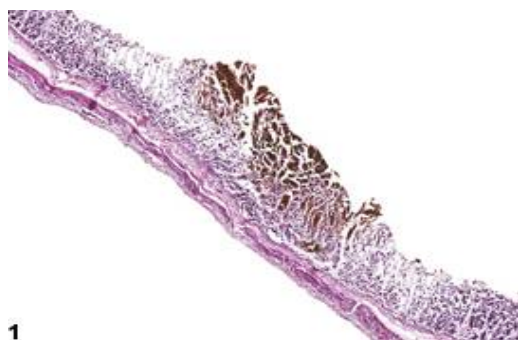
Stomach, Glandular stomach - Necrosis in a male F344/N rat from a chronic study. There is a thrombosed vessel in the submucosa (arrow), resulting in an area of necrosis (infarct) with hemorrhage.

## Stomach, Glandular Stomach, Neuroendocrine Cell - Hyperplasia (신경내분비세포 증생)



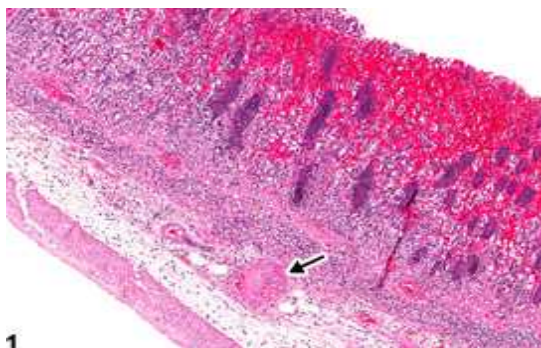
Stomach, Glandular stomach, Neuroendocrine cell - Hyperplasia in a female F344/N rat from a chronic study. The mucosa is expanded by a pale focus of cells. The hyperplastic cells have small cytoplasmic vacuoles and are grouped into small clusters separated by a fine vascular stroma.

### Stomach, Glandular Stomach - Pigment (색소)



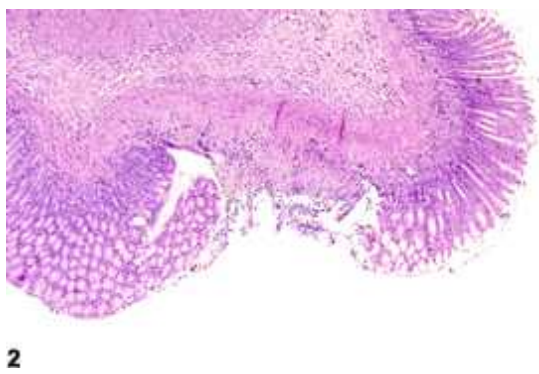
Stomach, Glandular stomach - Pigment in female B6C3F1 mouse from a chronic study. Pigment (likely hemosiderin) is present within a necrotic area of the mucosa.

### Stomach, Glandular Stomach - Thrombus (혈전)



Stomach, Glandular stomach - Thrombus in a male F344/N rat from a chronic study. The thrombus in the submucosa (arrow) resulted in mucosal necrosis.

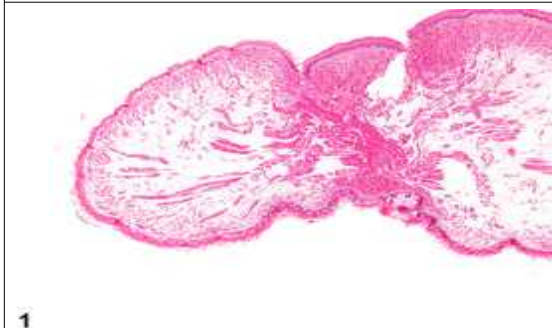
### Stomach, Glandular Stomach - Ulcer (궤양)



Stomach, Glandular stomach - Ulcer in a male F344/N rat from a chronic study. The lesion extends through the entire mucosa.

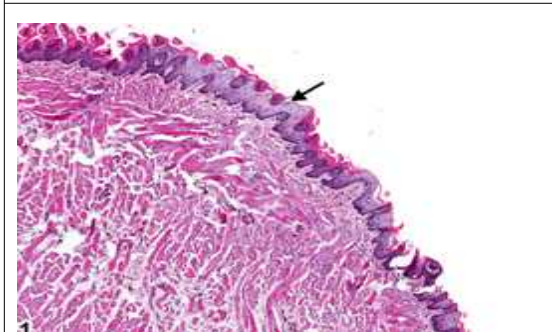
## 6) 혀

## Tongue - Edema (부종)



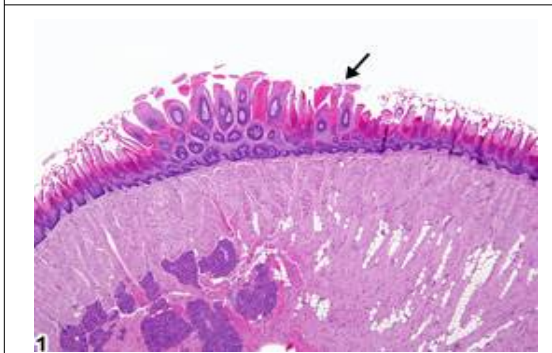
Tongue - Edema in a male F344/N rat from a chronic study. Edema in the tongue is evidenced by the clear spaces in the tissue.

## Tongue, Epithelium - Degeneration (변성)



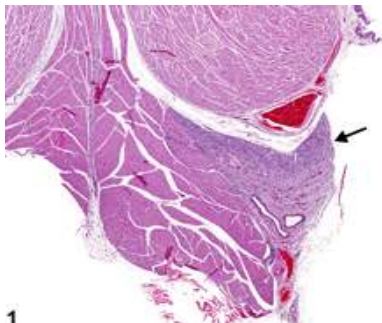
Tongue, Epithelium - Degeneration in a male F344/N rat from a chronic study. An area on the tongue has epithelial cells that are pale and swollen (arrow).

## Tongue, Epithelium - Hyperplasia (증생)

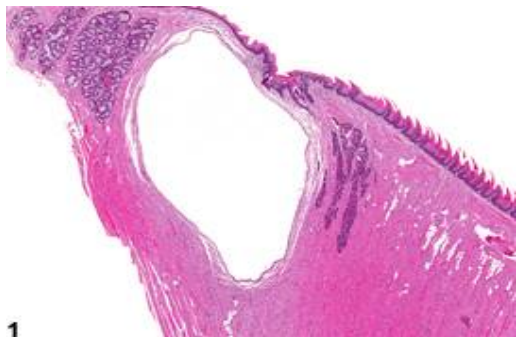


Tongue, Epithelium - Hyperplasia in a female F344/N rat from a chronic study. A focus of epithelial hyperplasia is present on the tongue (arrow).

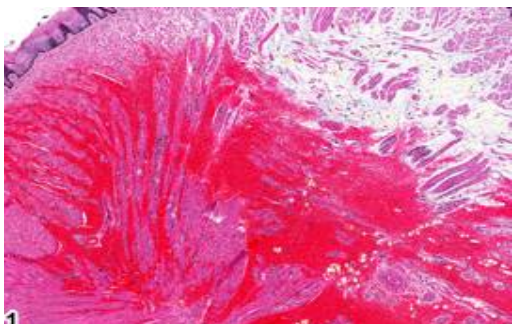
### Tongue - Fibrosis (섬유증)

 <p>1</p>	<p>Tongue - Fibrosis in a male F344/N rat from a subchronic study. There is an area of fibrosis with associated inflammation in the tongue (arrow).</p>
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### Tongue, Glands - Cyst (낭포)

 <p>1</p>	<p>Tongue, Gland - Cyst in a female B6C3F1 mouse from a chronic study. There is a large cyst amid the salivary tissue in the tongue.</p>
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### Tongue - Hemorrhage (출혈)

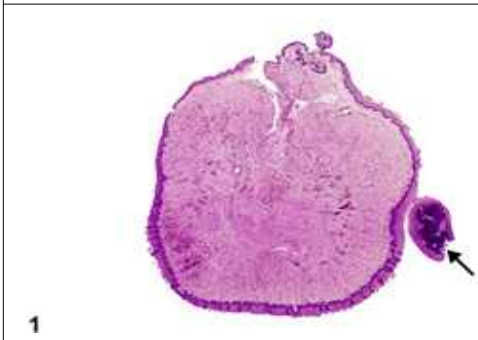
 <p>1</p>	<p>Tongue - Hemorrhage in a female Harlan Sprague-Dawley rat from a chronic study.</p>
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## Tongue - Hyperkeratosis (각화과다증)



Tongue - Hyperkeratosis in a female F344/N rat from a chronic study. The keratin layer on the surface of the tongue is thickened (arrow).

## Tongue, Mucosa - Fibroepithelial Polyp (섬유상피 용종)



Tongue, Mucosa - Fibroepithelial polyp in a male B6C3F1 mouse from a chronic study. There is a small polypoid mass at the lateral margin of the tongue (arrow).

## Tongue - Necrosis (괴사)



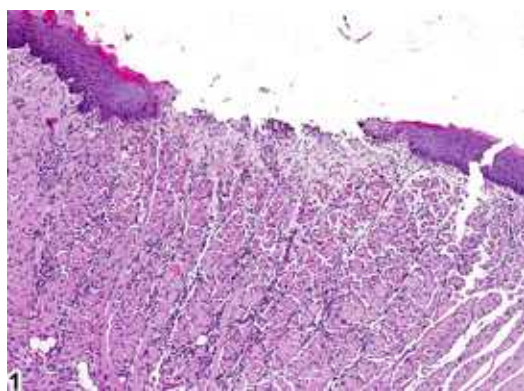
Tongue - Necrosis in a male Swiss CD-1 mouse from a chronic study. There is widespread necrosis of the tip of the tongue.

### Tongue - Squamous Cyst (편평상피 낭포)



Tongue - Squamous cyst in a male F344/N rat from a subchronic study. A cyst filled with keratin (arrow) is present in the tongue.

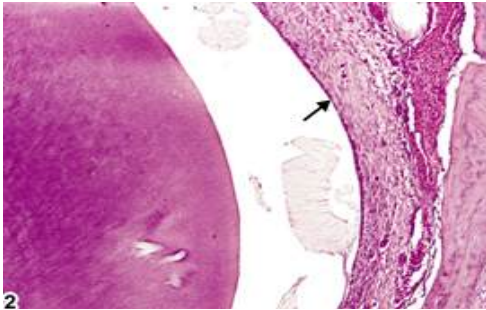
### Tongue - Ulcer (궤양)



Tongue - Ulcer in a female F344/N rat from a chronic study. A portion of the keratinized squamous epithelium of the tongue has been lost, exposing the underlying lamina propria.

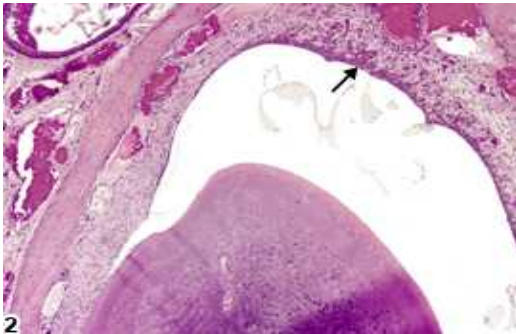
## 7) 이

## Tooth, Ameloblast - Atrophy (위축)



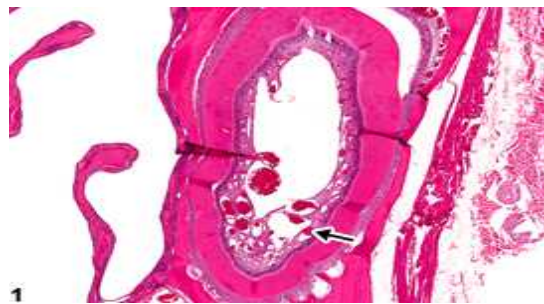
Tooth, Ameloblast - Atrophy in a male F344/N rat from a chronic study. The ameloblast layer is thin (compare with Figure 1), due to the decreased size of the ameloblasts (arrow).

## Tooth, Ameloblast - Metaplasia, Squamous (편평상피 화생)



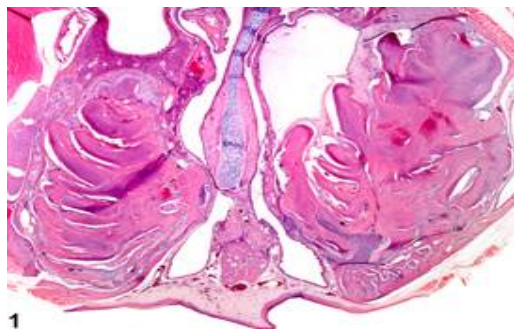
Tooth, Ameloblast - Metaplasia, Squamous in a male F344/N rat from a chronic study. The ameloblasts (compare with Figure 1) have been replaced by squamous epithelium (arrow).

## Tooth - Angiectasis (혈관확장)



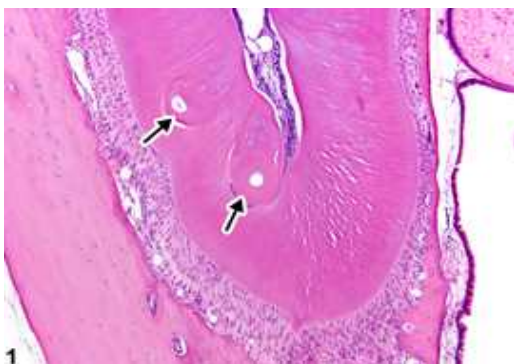
Tooth - Angiectasis in a male F344/N rat from a chronic study. There are numerous dilated blood vessels in the tooth pulp (arrow), consistent with angiectasis.

### Tooth - Dental Dysplasia (형성 장애)



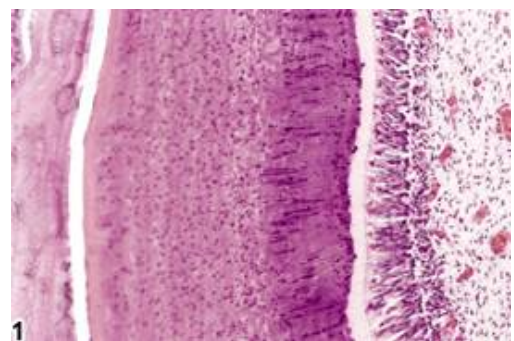
Tooth - Dental dysplasia, Bilateral in a male B6C3F1 mouse from a subchronic study. There is abnormal growth of dental tissues characteristic of dental dysplasia.

### Tooth - Denticle (상아립)



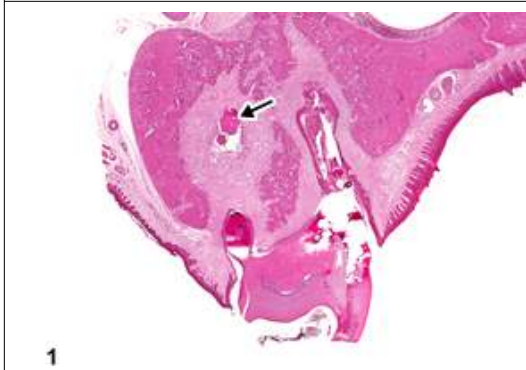
Tooth - Denticle in a male B6C3F1 mouse from a chronic study. There are 2 denticles within the dentin layer (arrows).

### Tooth, Dentin - Basophilic Granules (상아질 호염기성과립)



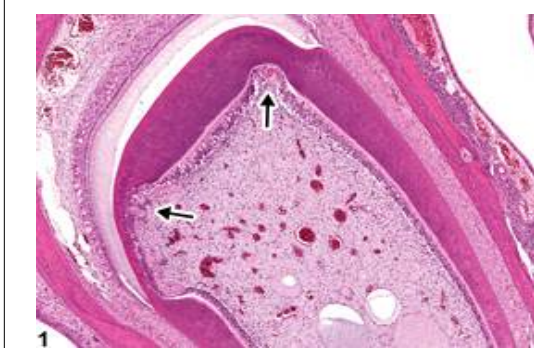
Tooth, Dentin - Basophilic granules in a male F344/N rat from a chronic study. There are numerous, small basophilic granules within the dentin.

## Tooth - Fibrosis (섬유증)



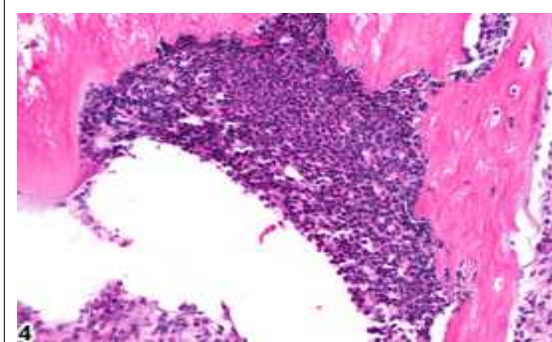
Tooth - Fibrosis in a female Harlan Sprague-Dawley rat from a chronic study. There is fibrosis within the alveolar bone and a possible sequestrum of bone or osteodentin (arrow).

## Tooth, Incisor - Degeneration (전치 변성)



Tooth, Incisor - Degeneration in a female Harlan Sprague-Dawley rat from a subchronic study. Odontoblast degeneration and dentin niche formation (arrows) are present.

## Tooth - Inflammation (염증)



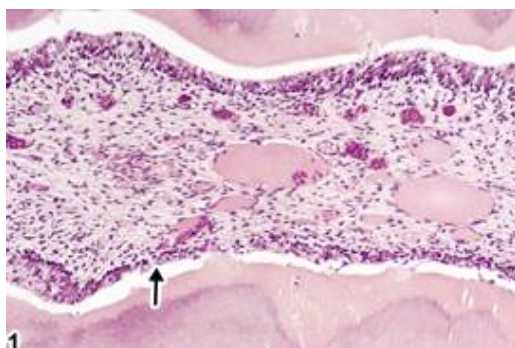
Tooth - Inflammation in a male B6C3F1 mouse from a chronic study (higher magnification of Figure 3). Chronic active inflammation of the tooth is present.

### Tooth - Necrosis (괴사)



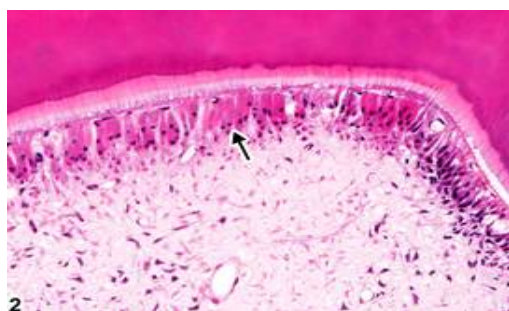
Tooth - Necrosis in a male B6C3F1 mouse from a chronic study. There is necrosis of most components of the tooth, including the 2 denticles in the pulp (arrow), and suppurative inflammation of the tooth pulp (arrowhead).

### Tooth, Odontoblast - Degeneration (치아모세포 변성)



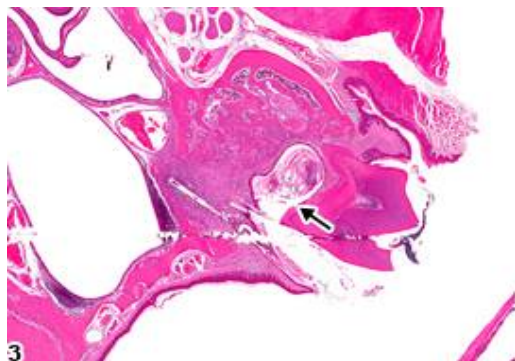
Tooth, Odontoblast - Degeneration in a male F344/N rat from a chronic study. The odontoblasts are small and disorganized (arrow).

### Tooth, Odontoblast - Necrosis (치아모세포 괴사)



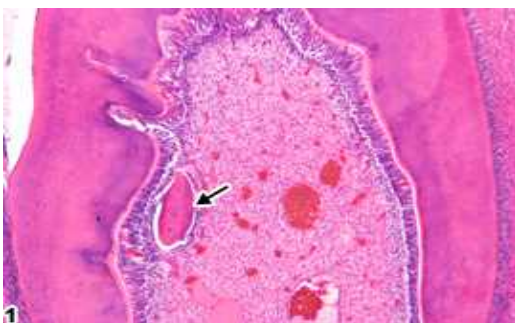
Tooth, Odontoblast - Necrosis in a female F344/N rat from a subchronic study. The odontoblasts lining the dorsal tooth pulp have eosinophilic cytoplasm and pyknotic nuclei (arrow) indicative of necrosis.

## Tooth - Periodontal Pocket (치주낭)



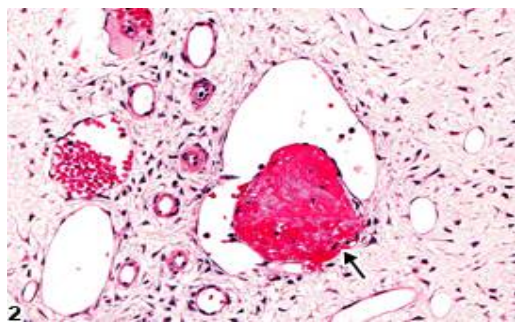
Tooth - Periodontal pocket in a male F344/N rat from a chronic study. The opening of the pocket (arrow) to the oral cavity is adjacent to the tooth.

## Tooth, Pulp - Osteodentin (치수 상아질)



Tooth, Pulp - Osteodentin in a male F344/N rat from a chronic study. There is a small deposit of osteodentin (arrow) in the pulp cavity.

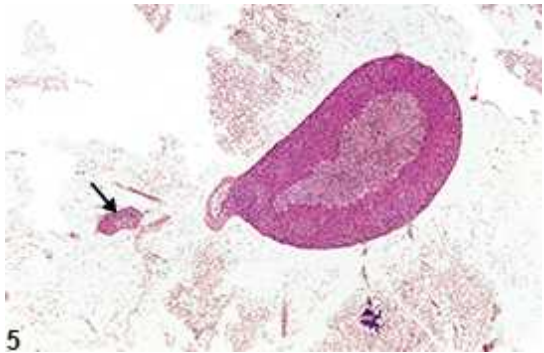
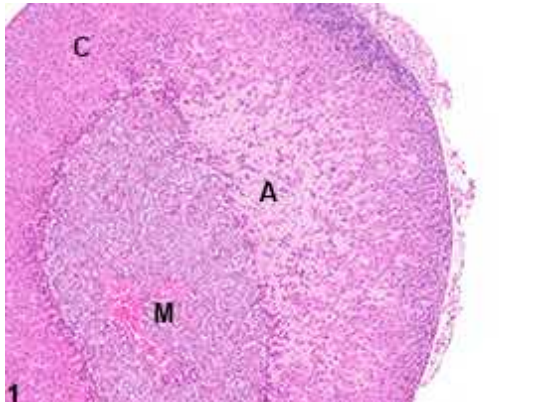
## Tooth, Pulp - Thrombus (치수 혈전)



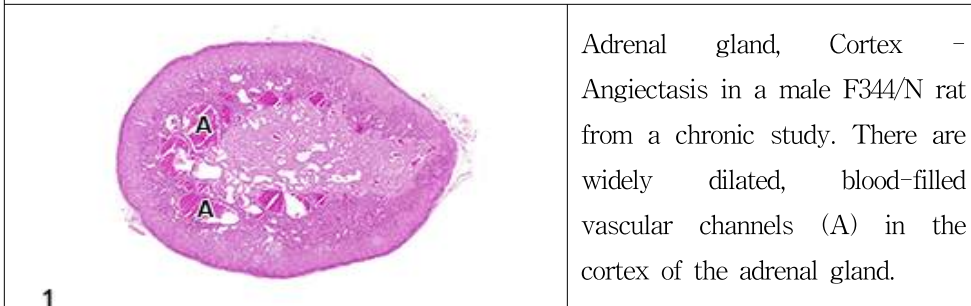
Tooth, Pulp - Thrombus in a female F344/N rat from a subchronic study. A small thrombus is present in the tooth pulp (arrow).

## 2. 내분비계

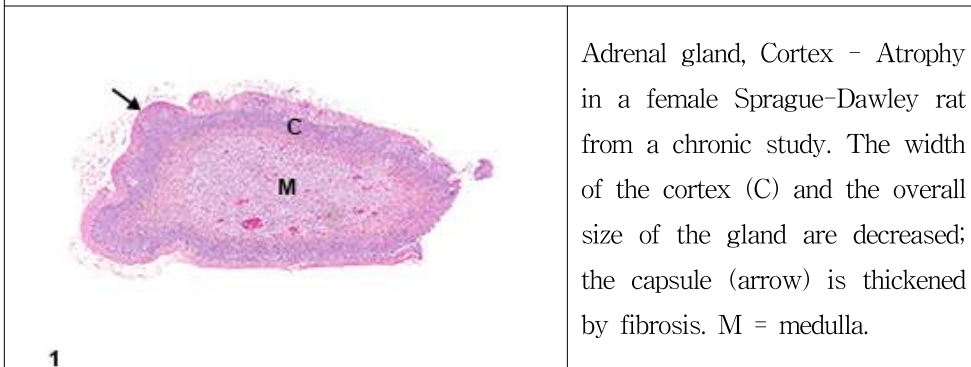
### 1) 부신

Adrenal Gland - Accessory Adrenocortical Nodule (부부신피질 결절)	
	<p>Periadrenal fat - Accessory adrenocortical nodule in a male B6C3F1/N mouse from a chronic study. An accessory cortical nodule (arrow) is present in the periadrenal (retroperitoneal) fat.</p>
Adrenal Gland - Amyloid (아밀로이드)	
	<p>Adrenal gland, Cortex - Amyloid in a male B6C3F1/N mouse from a chronic study. There is homogeneous, amorphous, pale eosinophilic material (amyloid, A) expanding the zona fasciculata and zona reticularis; C = cortex, M = medulla.</p>

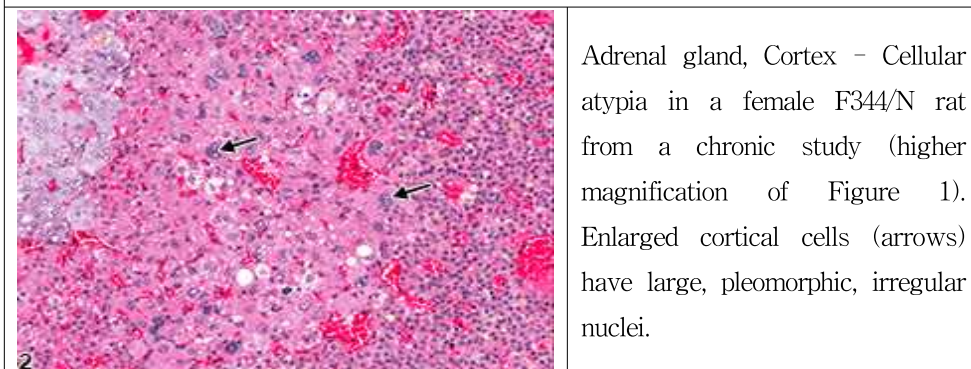
## Adrenal Gland - Angiectasis (혈관확장)



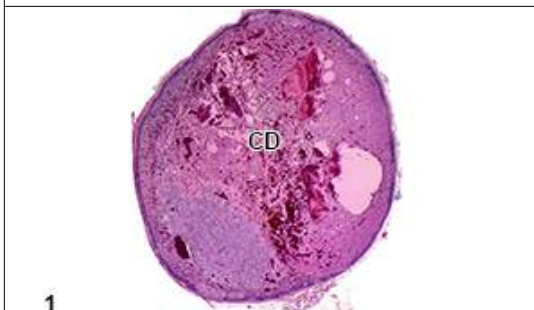
## Adrenal Gland, Cortex - Atrophy (피질, 위축)



## Adrenal Gland, Cortex - Cellular Atypia (피질, 세포 이형성)

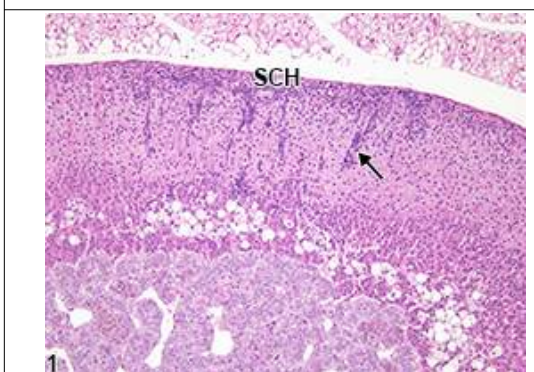


Adrenal Gland, Cortex - Degeneration, Cystic (피질, 낭성 변성)



Adrenal gland, Cortex - Degeneration, Cystic in a female Sprague-Dawley rat from a chronic study. The cortex is distended by dilated spaces filled with proteinaceous fluid and/or blood (CD).

Adrenal Gland, Cortex - Hyperplasia, Subcapsular (피질, 피막 증생)



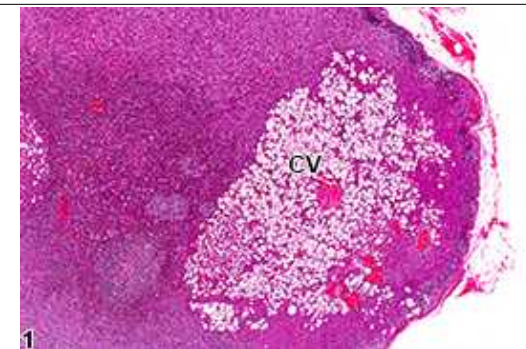
Adrenal gland, Cortex - Hyperplasia, Subcapsular in a female Tg.AC (FVB/N) hemizygous mouse from a subchronic study. Early-stage subcapsular cell hyperplasia (SCH) is characterized by subcapsular foci of small, basophilic cells that extend into the zona fasciculata (arrow).

Adrenal Gland, Cortex - Hypertrophy (피질, 비대)



Adrenal gland, Cortex - Hypertrophy in a female Sprague-Dawley rat from a chronic study. There is a well-demarcated, noncompressive focal area in which the cells are enlarged (FH). C = cortex, M = medulla.

## Adrenal Gland, Cortex - Vacuolization, Cytoplasmic (피질, 세포질 공포)



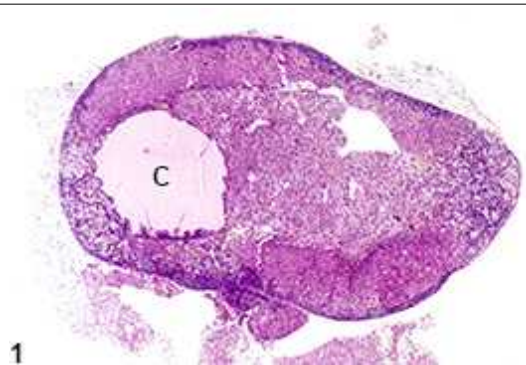
Adrenal gland, Cortex - Vacuolization, Cytoplasmic in a female F344/N rat from a chronic study. A large focus of vacuolated cells (CV) in the zona fasciculata causes little if any compression of the adjacent cortex.

## Adrenal Gland, Cortex, X-Zone - Atrophy (피질, X 위축)



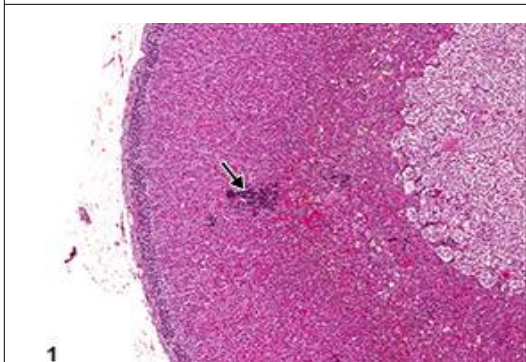
Adrenal gland, Cortex, X-zone - Normal in a female B6C3F1/N mouse from a subchronic study. Adrenal gland with moderate numbers of vacuolated cells in an age-matched control virgin female is shown for comparison with Figure 3. M = medulla, XZ = X-zone, ZF = zona fasciculata.

## Adrenal Gland - Cyst(낭포)



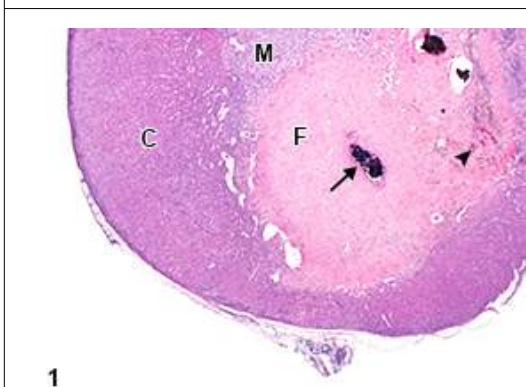
Adrenal gland, Cortex - Cyst in a female B6C3F1/N mouse from a chronic study. An adrenal cortical cyst (C), filled with amorphous pale eosinophilic material, compresses adjacent cortex and medulla.

### Adrenal Gland - Extramedullary Hematopoiesis (수질의 조혈)



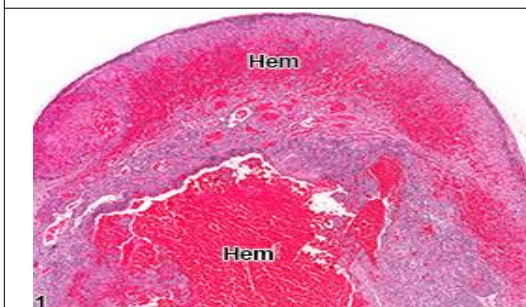
Adrenal gland, Cortex - Extramedullary hematopoiesis in a female F344/N rat from a chronic study. There is a focus of hematopoietic cells (arrow) in the cortex (zona fasciculata).

### Adrenal Gland - Fibrosis (섬유증)



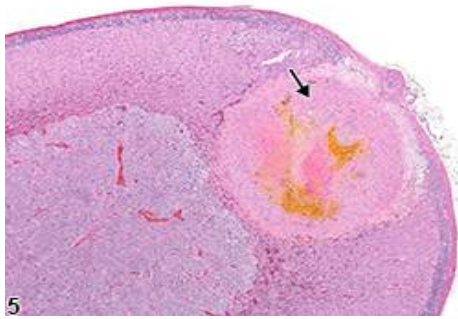
Adrenal gland - Fibrosis in a female F344/N rat from a chronic study. A large focal area of mature fibrous connective tissue (F) replaces parts of the normal cortex (C) and medulla (M); there is also focal mineralization (arrow) and a cluster of pigment-laden macrophages (arrowhead).

### Adrenal Gland - Hemorrhage (출혈)



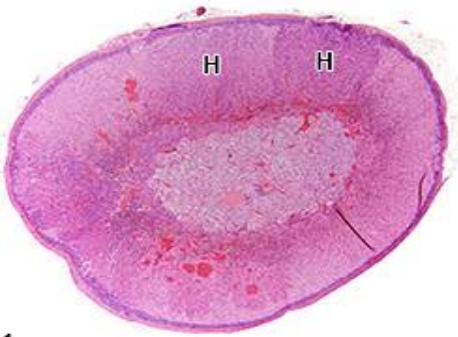
Adrenal gland - Hemorrhage in a female F344/N rat from a chronic study. Extensive, diffuse hemorrhage (Hem) is present in the cortex and medulla.

## Adrenal Gland - Fibrosis (섬유증)



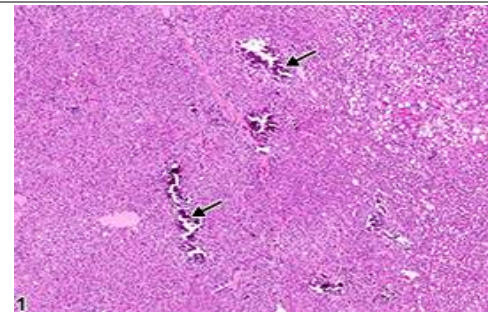
Adrenal gland, Cortex - Fibrosis in a female Sprague-Dawley rat from a chronic study. Focal fibrosis in the cortex is associated with an organized thrombus (arrow).

## Adrenal Gland - Hyperplasia (증생)



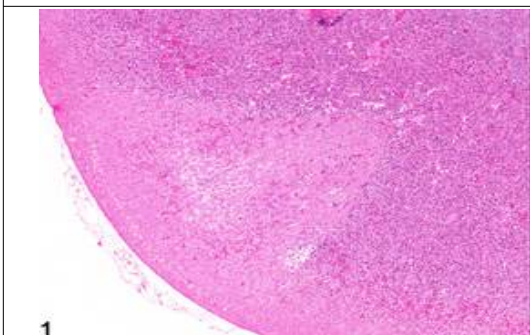
Adrenal gland, Cortex - Hyperplasia in a male Sprague-Dawley rat from a chronic study. There are two adjacent foci of hyperplasia (H) in the zona fasciculata.

## Adrenal Gland - Mineralization (무기질침착)



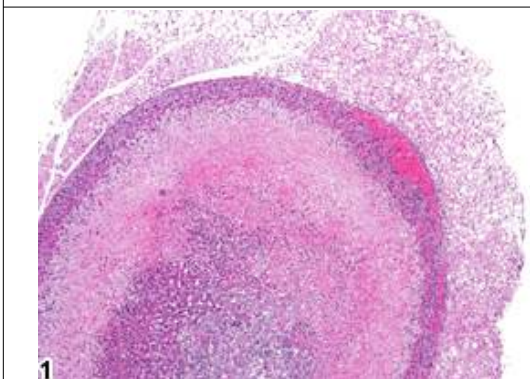
Adrenal gland, Cortex - Mineralization in a male F344/N rat from a chronic study. There are multiple foci of coarsely granular, dark basophilic material in the cortex (arrows).

### Adrenal Gland - Infarct (경색)



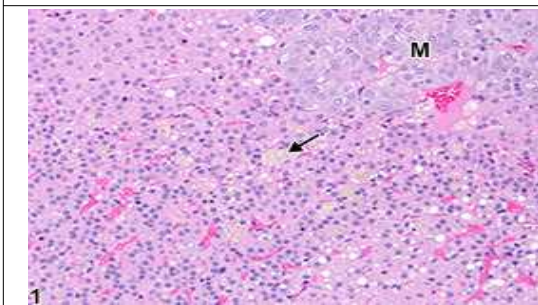
Adrenal gland, Cortex - Infarct in a female F344/N Rat from a chronic study. There is a focal, acute infarct in the adrenal cortex characterized by a wedge-shaped zone of necrosis.

### Adrenal-Gland - Necrosis (괴사)



Adrenal gland, Cortex - Necrosis in a female B6C3F1 mouse from a subchronic study. Diffuse cortical necrosis involves primarily the zona fasciculata.

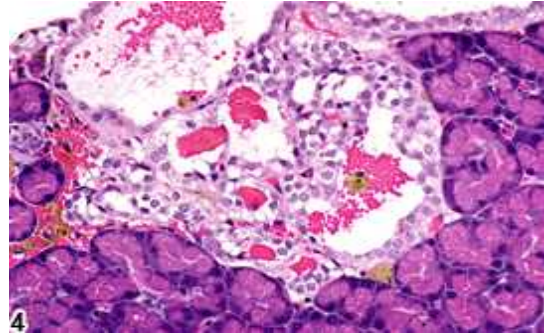
### Adrenal Gland - Pigment (색소)



Adrenal gland, Cortex - Pigment in a male F344/N rat from a chronic study. There are scattered individual cells in the inner cortex (arrow) containing yellow-brown pigment. M = medulla.

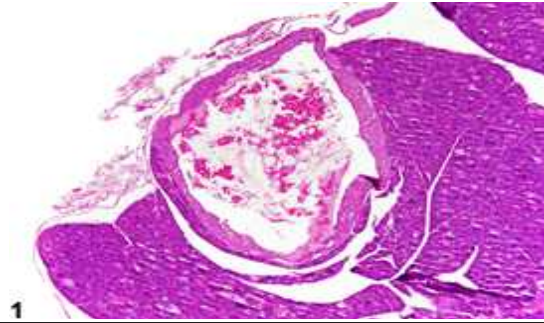
## 2) 이자

## Pancreatic Islets - Angiectasis (혈장확장)



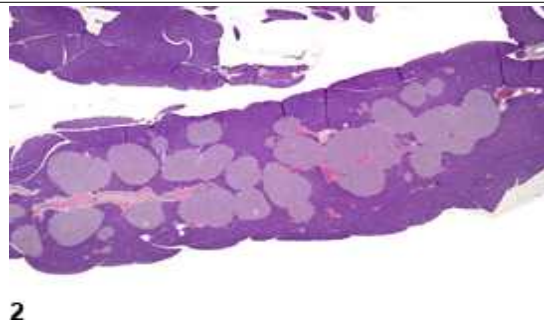
Pancreatic islet - angiectasis. Dilated vascular channels in this islet contain erythrocytes and some hemosiderin pigment in a male F344/N rat from a chronic study.

## Pancreatic Islets - Cyst (낭포)



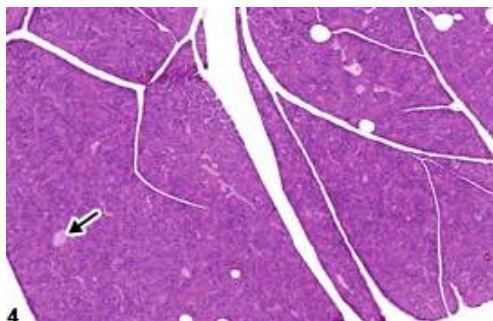
Pancreatic islet - cyst. The central portion of this islet is markedly dilated and is considered a cyst that contains some erythrocytes in a male B6C3F1 mouse from a chronic study.

## Pancreatic Islets - Hyperplasia (증생)



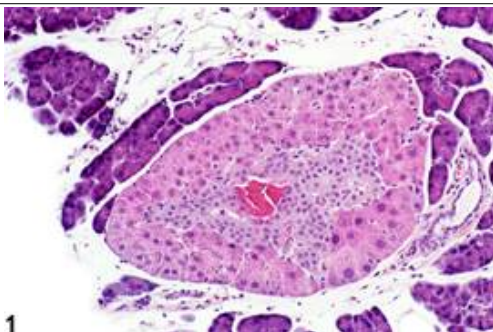
Pancreatic islet - hyperplasia. Section of pancreas represents mild islet hyperplasia in a control male B6C3F1 mouse from the same chronic study as in Figure 1.

### Pancreatic Islets - Hypoplasia (저형성)



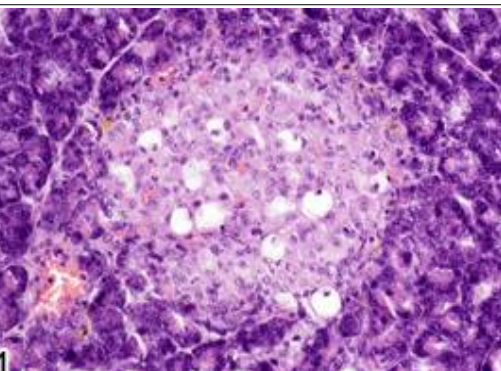
Pancreatic islet - hypoplasia. Islet hypoplasia diagnosed in a treated female F344/N rat from a chronic study: only a single hypoplastic islet (arrow) is present within a large sampling of pancreas.

### Pancreatic Islets - Metaplasia, Hepatocyte (간세포 화생)



Pancreatic islet - metaplasia, hepatocyte. A band of metaplastic hepatocytes has encircled this islet in a female F344/N rat from a subchronic study.

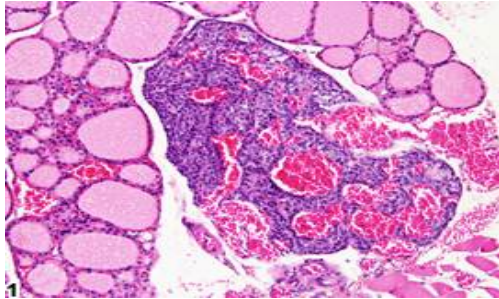
### Pancreatic Islets - Necrosis (괴사)



Pancreatic islet - necrosis. Dropout of individual islet beta cells appears as clear vacuoles in a female F344/N rat from a chronic study.

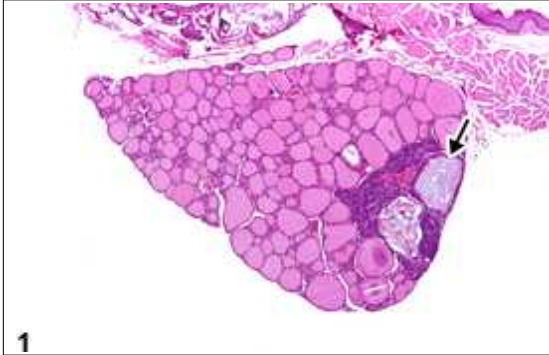
## 3) 부갑상선

## Parathyroid Gland - Angiectasis (혈관확장)



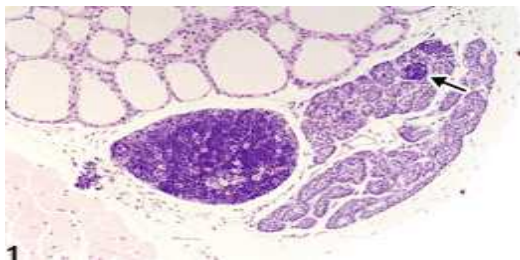
Parathyroid Gland - Angiectasis in a male BALB/c mouse from a subchronic study. Multiple dilated vascular structures filled with erythrocytes are present in the parathyroid.

## Parathyroid Gland - Cyst, Congenital (선천적 낭포)



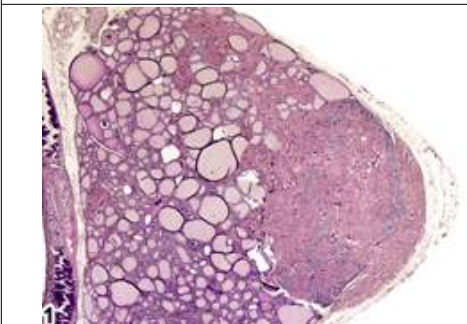
Parathyroid Gland - Cyst, Congenital in a male B6C3F1 mouse from a chronic study. Two cysts are present in the parathyroid. One cyst contains vacuolated proteinaceous material (arrow), and the second cyst contains proteinaceous material, cellular debris, and eosinophilic crystals.

## Parathyroid Gland - Ectopic Tissue (이소성 조직)



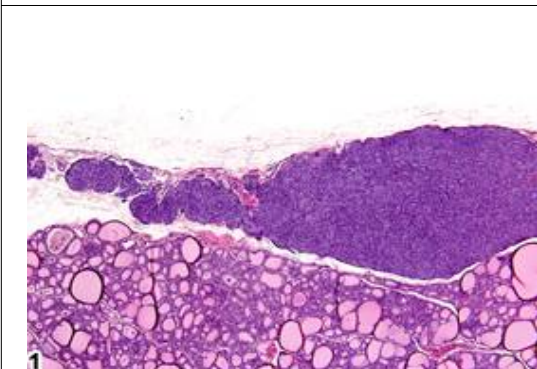
Parathyroid Gland - Ectopic Tissue, Thymus in a female B6C3F1 mouse from a subchronic study. A large piece of ectopic thymus with pronounced basophilic staining is adjacent to the parathyroid and thyroid, and a small focus of ectopic thymus is present within the parathyroid parenchyma (arrow).

### Parathyroid Gland - Fibrosis (섬유증)



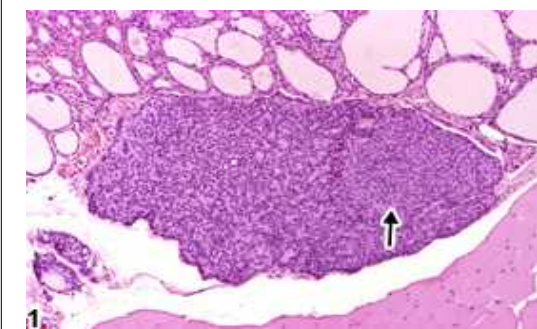
Parathyroid Gland - Fibrosis in a female F344/N rat from a chronic study. Extensive fibrosis has replaced the parathyroid parenchyma and extended into the thyroid.

### Parathyroid Gland - Hyperplasia, Diffuse (증생)



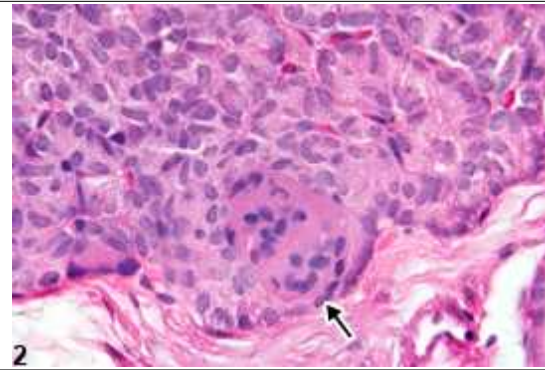
Parathyroid gland - Hyperplasia, Diffuse in a male F344/N rat from a chronic study. The parathyroid gland is increased in volume.

### Parathyroid Gland - Hyperplasia, Focal (국소 증생)



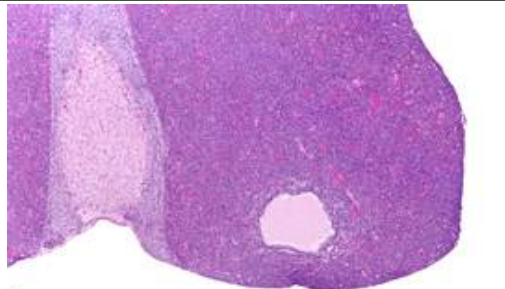
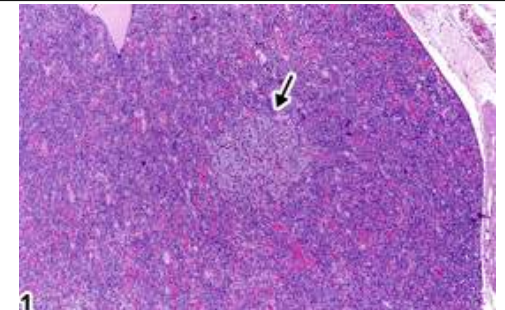
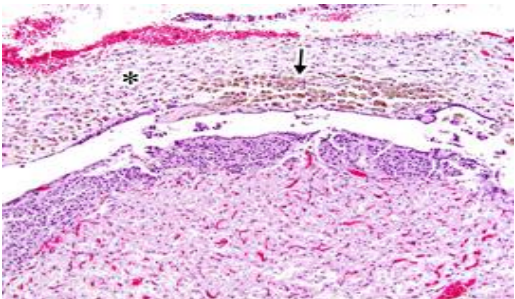
Parathyroid Gland - Hyperplasia, Focal in a male F344/N rat from a chronic study. This low-magnification photomicrograph contains a focus of hyperplasia (arrow) with a growth pattern distinct from the adjacent parathyroid parenchyma.

## Parathyroid Gland - Syncytial Giant Cell (거대 합포체 세포)

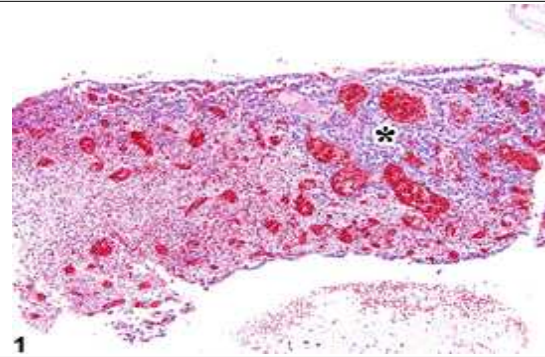


Parathyroid Gland - Syncytial giant cell in a male F344/N rat from a subchronic study. Figure 2 showing the multinucleated syncytial cell with eosinophilic cytoplasm formed by fusion of adjacent chief cells (arrow).

#### 4) 뇌하수체

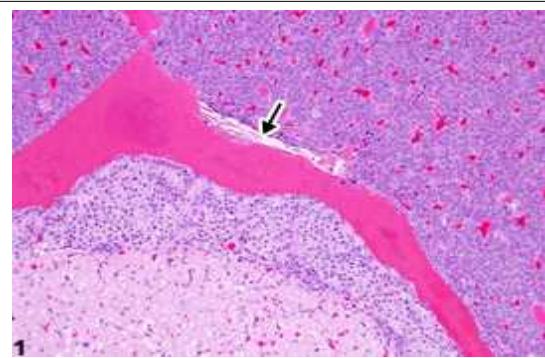
<p>Pituitary Gland - Cyst (낭포)</p>  <p>1</p>	<p>Pituitary Gland - Cyst in a female Harlan Sprague-Dawley rat from a chronic study. A cyst filled with pale eosinophilic proteinaceous fluid is present in the pars distalis.</p>
<p>Pituitary Gland - Hyperplasia (증생)</p>  <p>1</p>	<p>Pituitary Gland, Pars distalis - Hyperplasia in a female Harlan Sprague-Dawley rat from a chronic study. A small focus of hyperplasia (arrow) in the pars distalis is recognized by the paler staining cells.</p>
<p>Pituitary Gland, Pars Distalis - Atrophy (위축)</p> 	<p>Pituitary Gland, Pars distalis - Atrophy in a female F344/N rat from a chronic study. Higher magnification of Figure 1 shows the reduction in the size of the pars distalis (asterisk) and the focal aggregate of macrophages (arrow) containing yellow-brown pigment (likely hemosiderin).</p>

## Pituitary Gland, Pars Distalis - Necrosis (괴사)



Pituitary Gland, Pars distalis - Necrosis in a female R344/N rat from a subchronic study. Loss of cellular detail is present in the area of necrosis with normal pituitary present in the upper right (asterisk); vascular congestion is present in both areas.

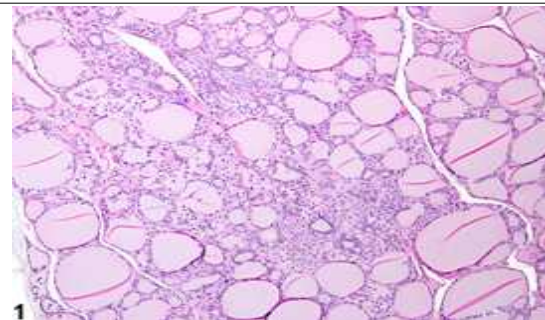
## Pituitary Gland, Rathke's Cleft - Dilation (확장)



Pituitary, Rathke's cleft - Dilation in a female F344/N rat from a chronic study. The dilated Rathke's cleft is filled with intensely eosinophilic proteinaceous material with cholesterol clefts (arrow) present at the edge of the dilated cleft.

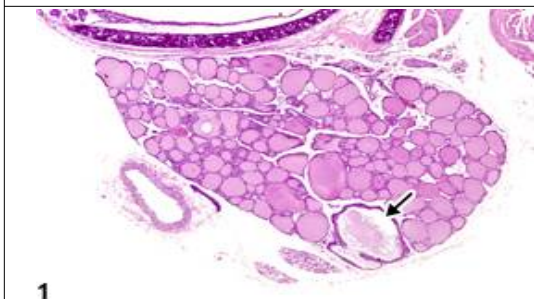
## 5) 갑상선

## Thyroid Gland - C Cell Hyperplasia (증생)



Thyroid gland, C cell - Hyperplasia in a treated female F344 rat from a chronic study. Aggregates and small nests of C cells have replaced follicles in this thyroid gland.

### Thyroid Gland - Cyst, Congenital (선천성 낭포)



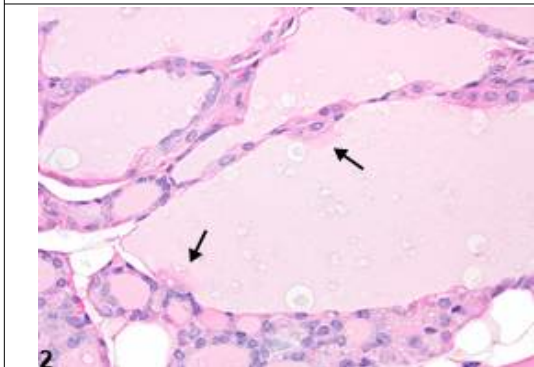
Thyroid gland - Cyst, Congenital in a female F344 rat from a chronic study. An enlarged follicle is present (arrow).

### Thyroid Gland - Ectopic Tissue (이소성 조직)



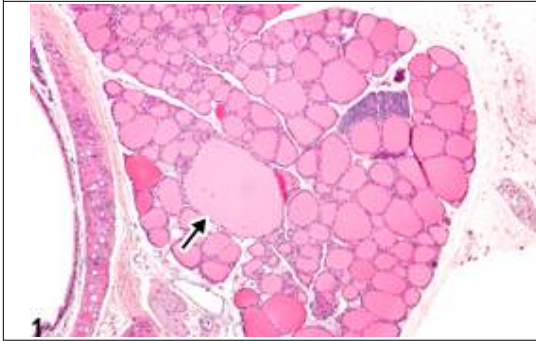
Thyroid Gland - Ectopic tissue, Thymus in a female F344/N rat from a subchronic study. Well-formed thymic tissue is present adjacent to the thyroid gland.

### Thyroid Gland, Follicle - Degeneration (변성)



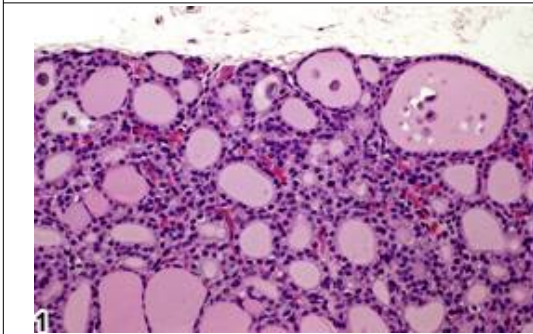
Thyroid Gland, Follicle - Degeneration in a female B6C3F1 mouse from a chronic study. Degenerating follicles are partially lined by ciliated cells (arrows).

## Thyroid Gland, Follicle - Dilation (팽창)



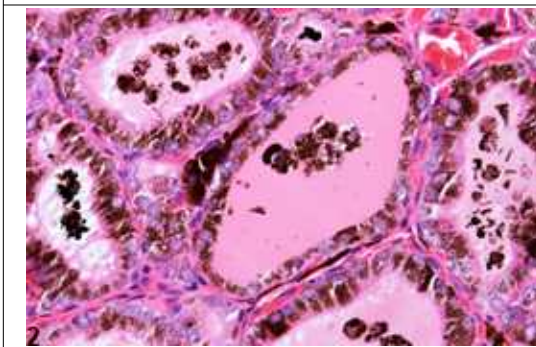
Thyroid gland, Follicle - Dilation in a male B6C3F1 mouse from a chronic study. There is a single dilated follicle (arrow).

## Thyroid Gland, Follicle - Mineralization (무기질침착)



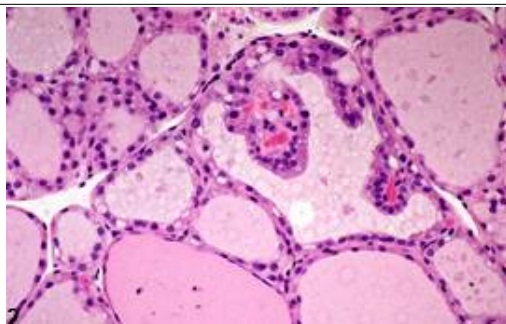
Thyroid gland, Follicle - Mineralization in a male F344/N rat from a chronic study. There is focal mineralization within the colloid of two follicles.

## Thyroid Gland, Follicle - Pigment (색소)



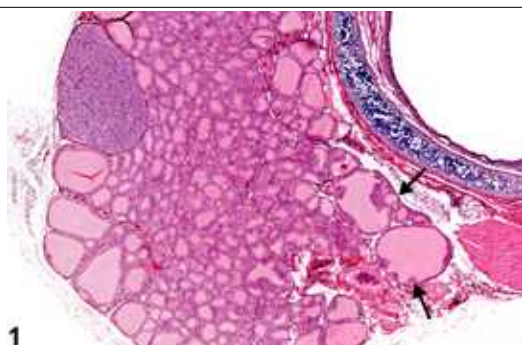
Thyroid gland, Follicle - Pigment in a male F344/N rat from a subchronic study. the pigment deposits in the follicular epithelium colloid in Figure 2.

### Thyroid Gland, Follicle, Epithelium - Hyperplasia (증생)



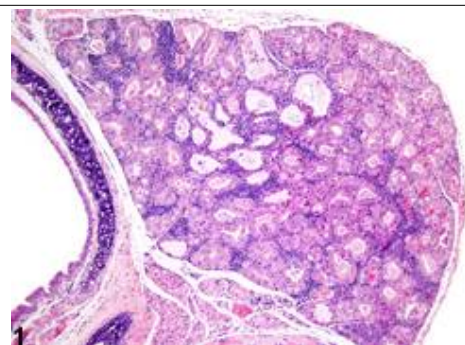
Thyroid gland, Follicle, Epithelium  
- Hyperplasia in a male B6C3F1 mouse from a chronic study. Figure 2 shows the proliferative projections of hyperplastic epithelium in more detail.

### Thyroid Gland, Follicular Cell - Hypertrophy (비대)



Thyroid Gland, Follicular Cell - Hypertrophy in a male F344/N rat from a subchronic study. Focal hyperplasia is present in two adjacent follicles (arrows).

### Thyroid Gland - Inflammation (염증)

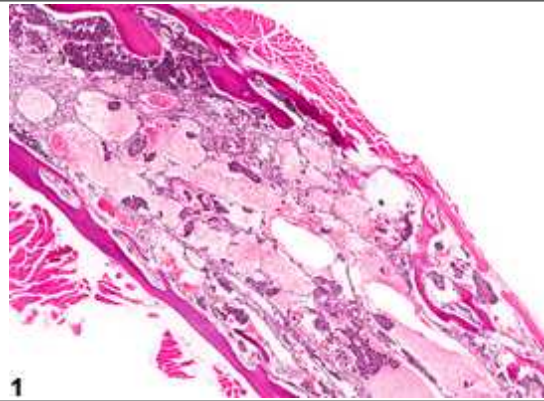


Thyroid Gland - Inflammation, chronic in a female Tg.AC (FVB/N) mouse from a subchronic study. Small aggregates of lymphoid cells are present at multiple sites between follicles

### 3. 조혈기계

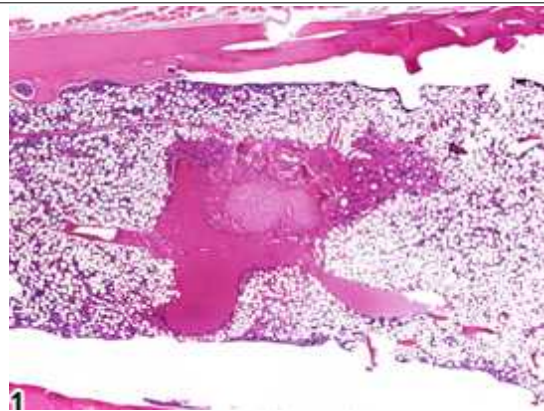
#### 1) 골수

##### Bone Marrow - Angiectasis (혈관확장)



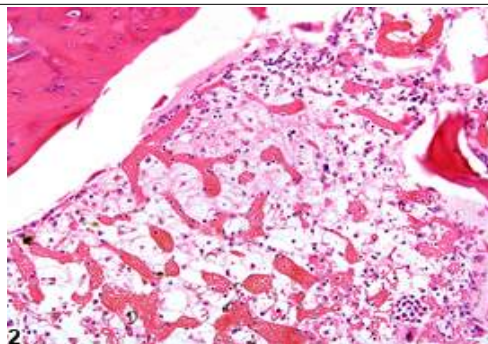
Angiectasis in the bone marrow sinuses in a female B6C3F1 mouse from a chronic study

##### Bone Marrow - Fibrosis (섬유증)



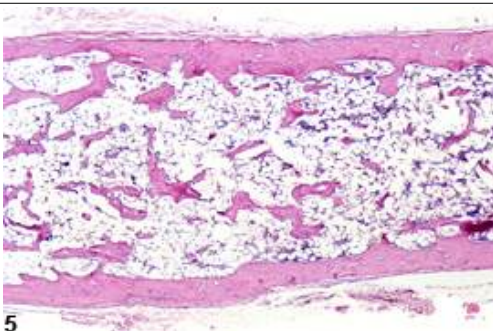
Dense fibrous tissue surrounded by areas of angiectasis is present in bone marrow in a male F344/N rat from a chronic study.

### Bone Marrow - Gelatinous Transformation (제라틴 변형)



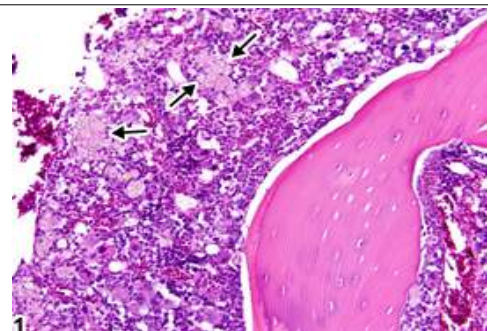
Gelatinous transformation of bone marrow in a female F344/N rat from a subchronic study. The marrow is characterized by severe hypocellularity, atrophied fat cells, and the presence of eosinophilic granular ground substance.

### Bone Marrow - Hypocellularity (세포 저형성)



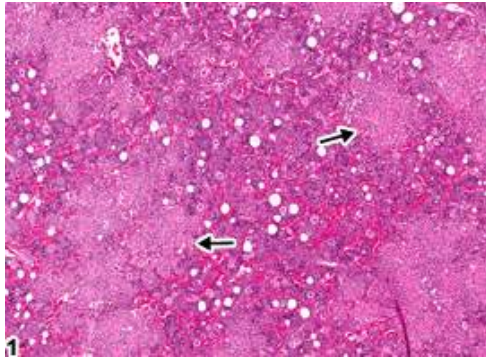
Severely hypocellular bone marrow in a male B6C3F1 mouse from a subchronic study. The marrow space is largely devoid of hematopoietic cells and consists primarily of adipose tissue and vascular sinuses due to treatment-induced aplastic anemia.

### Bone Marrow - Infiltration Cellular, Histiocyte (조직구 침윤)



Bone marrow in a female F344/N rat from a 2-year study. Increased numbers of pale-staining vacuolated histiocytes (arrows) can be seen among the hematopoietic cells.

## Bone Marrow - Inflammation (염증)



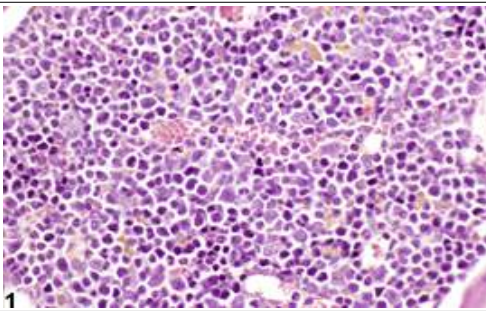
Bone marrow in a male F344/N rat from a chronic study. This low-power view shows relatively pale eosinophilic areas of granulomatous inflammation consisting of aggregates of macrophages (arrows).

## Bone Marrow - Necrosis (괴사)



Bone marrow in male B6C3F1 mouse from a chronic study (low magnification), showing a large well-demarcated eosinophilic area representing necrosis (asterisk). Arrows represent the line of demarcation between viable cells and the area of necrosis.


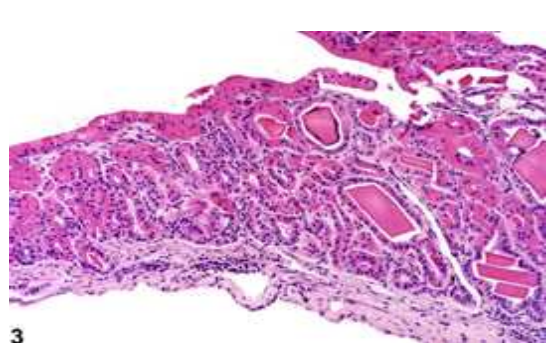
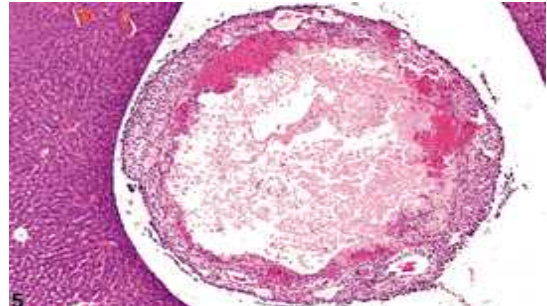
## Bone Marrow - Pigment (색소)



Low amounts of golden brown pigment in bone marrow in a male B6C3F1 mouse from a subchronic study.

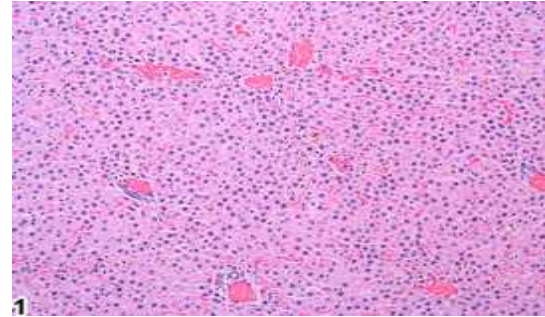
## 4. 간담도계

### 1) 담낭

Gallbladder, Epithelium - Hyperplasia (증생)	
	Epithelial hyperplasia—arrows indicate papillary hyperplasia in a male B6C3F1 mouse from a chronic study.
Gallbladder - Hyaline Droplet Accumulation (유리질 소적 축적)	
	Hyaline droplet accumulation with extracellular crystalline material in the gallbladder in a male B6C3F1 mouse from a chronic study.
Gallbladder - Inflammation (염증)	
	Gallbladder inflammation in a female B6C3F1 mouse from a 28-day study.

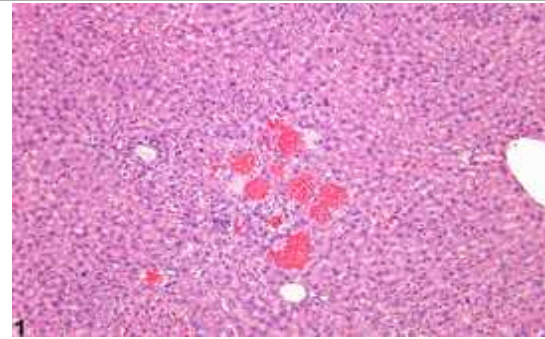
## 2) 간

## Liver - Atrophy (위축)



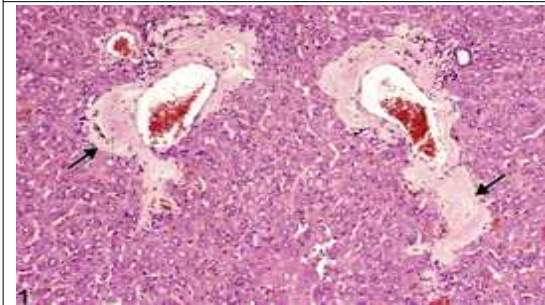
Atrophy in a female F344/N rat from a subchronic study.

## Liver - Angiectasis (혈관확장)



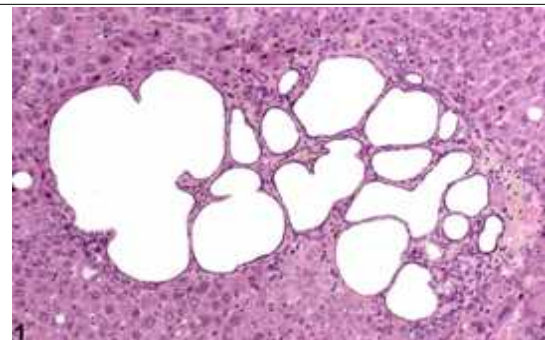
Angiectasis in a female F344/N rat from a chronic study.

## Liver - Amyloid (아밀로이드)



Amyloid (arrows) in a male Swiss-Webster mouse from a chronic study.

# Liver, Bile Duct - Cyst (낭포)



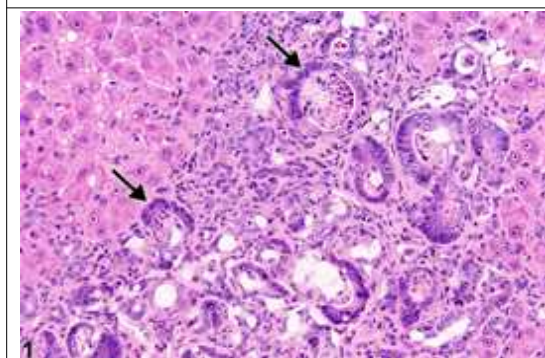
Bile duct cysts in a female Harlan Sprague-Dawley rat from a chronic study.

# Liver, Bile Duct - Hyperplasia (증생)



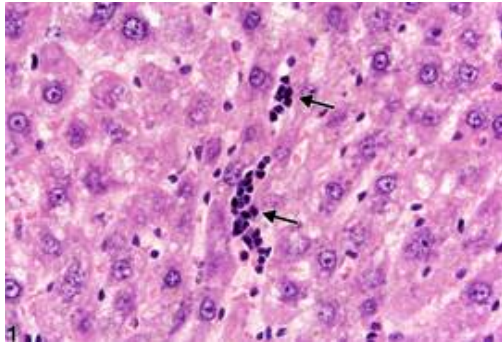
Bile duct hyperplasia in a female F344/N rat from a subchronic study.

# Liver - Cholangiofibrosis (담관섬유증)



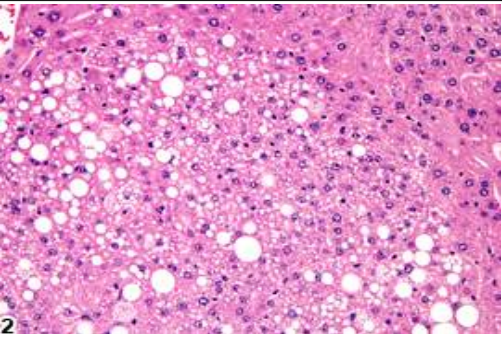
Cholangiofibrosis—arrows indicate incompletely lined proliferating bile ducts in a female Harlan Sprague-Dawley rat in a chronic study.

## Liver - Extramedullary Hematopoiesis (골수외조혈)



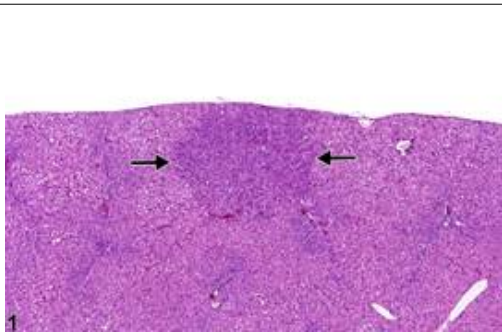
Extramedullary hematopoiesis—arrows indicate erythroid cells in a female Harlan Sprague-Dawley rat from a chronic study.

## Liver - Fatty Change (지방변성)



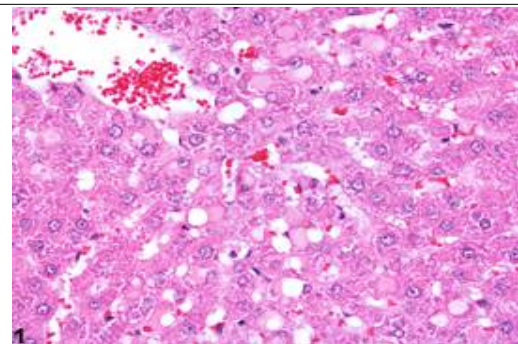
Fatty change—focal fatty change in a B6C3F1 male mouse from a chronic study.

## Liver - Focus (병소, = Focus of cellular alteration 세포변이 병소)



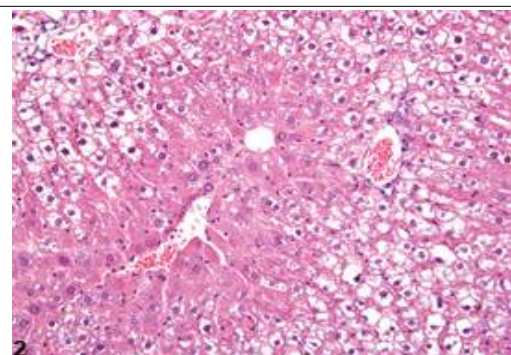
Basophilic focus (arrows) in a male F344/N rat from a subchronic study.

Liver, Hepatocyte - Cytoplasmic Inclusions (간세포 세포질 봉입체)



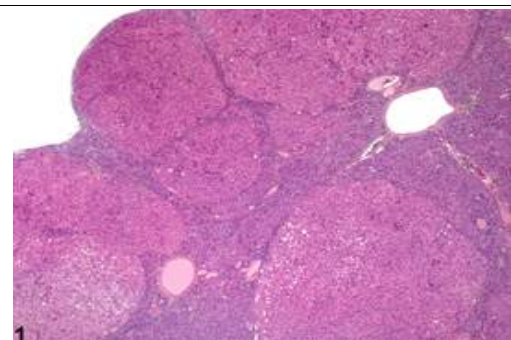
Cytoplasmic inclusions in a male F344/N rat from a subchronic study.

Liver, Hepatocyte - Glycogen Accumulation and Depletion (간세포 당 축적, 고갈)



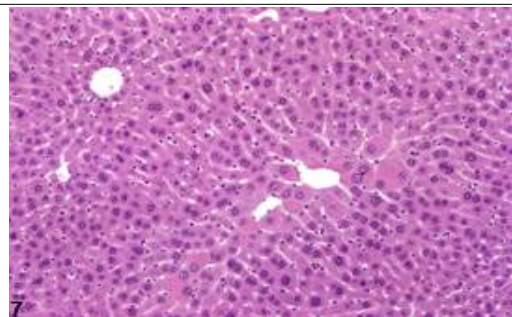
Glycogen accumulation-normal mobilization of glycogen from centrilobular area in a male B6C3F1 mouse from a subchronic study.

Liver, Hepatocyte - Hyperplasia, Nodular (결절성 간세포 증생)



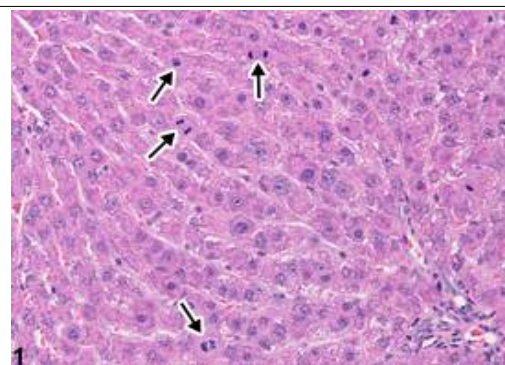
Nodular hyperplasia in a female Harlan Sprague-Dawley rat from a chronic study.

## Liver, Hepatocyte - Hypertrophy (간세포 비대)



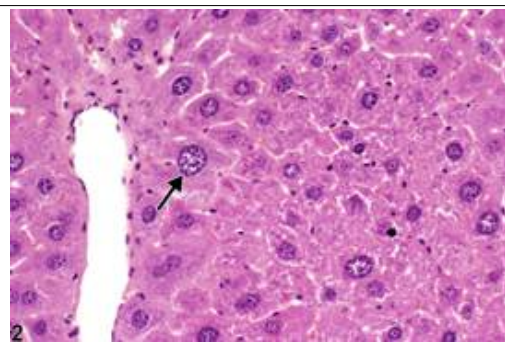
Hepatocyte hypertrophy in a male B6C3F1 mouse from chronic study.

## Liver, Hepatocyte - Increased Mitosis (간세포 분열 증가)



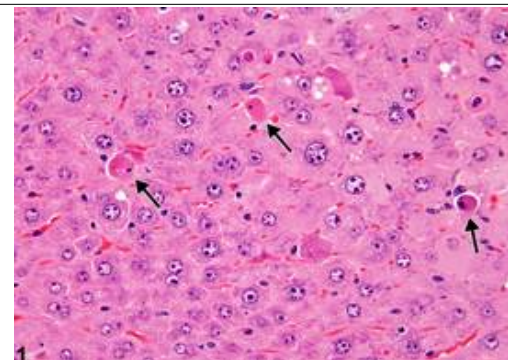
Increased mitosis (arrows) in a male F344/N rat from an acute repeated-dose study.

## Liver, Hepatocyte - Karyomegaly (거대 간세포)



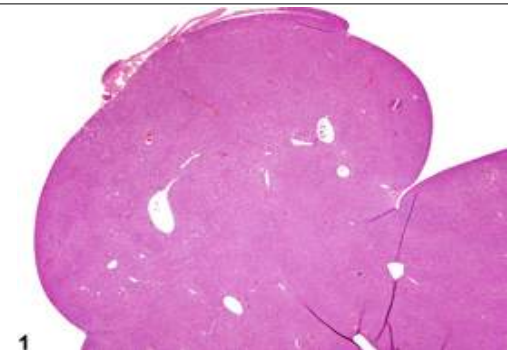
Karyomegaly in a female B6C3F1 mouse from a subchronic study. Arrow indicates enlargement of hepatocyte cytoplasm and nucleus.

Liver, Hepatocyte - Necrosis, Single Cell (단일 간세포 괴사)



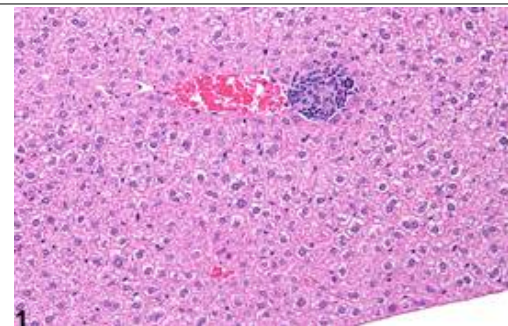
Single-cell necrosis (arrows) in a male B6C3F1 mouse from subchronic study.

Liver - Hepatodiaphragmatic Nodule (간횡격막 결절)



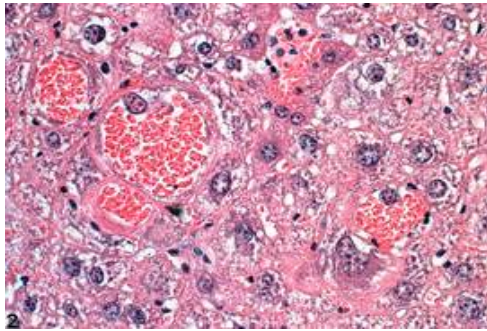
Hepatodiaphragmatic nodule in a female F344/N rat from a subchronic study.

Liver - Inflammation (염증)



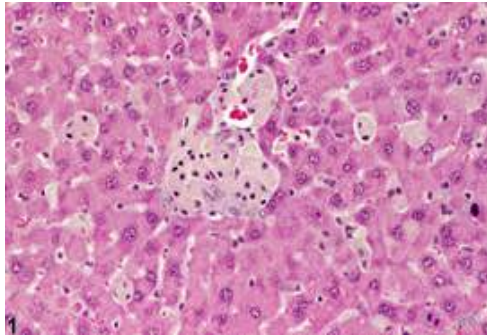
Focal inflammation in a female B6C3F1 mouse from a subchronic study.

## Liver - Intrahepatocellular Erythrocytes (간세포내 적혈구)



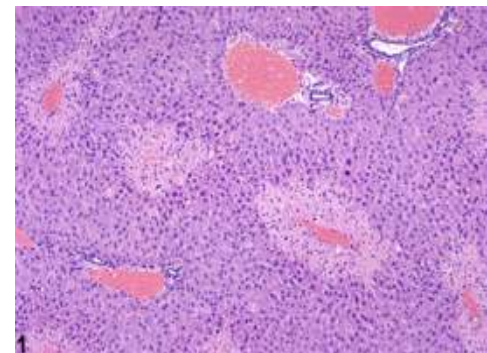
Intrahepatocellular erythrocytes in a B6C3F1 mouse from a 2-year study.

## Liver, Kupffer Cell - Hyperplasia (Kupffer 세포 증생)



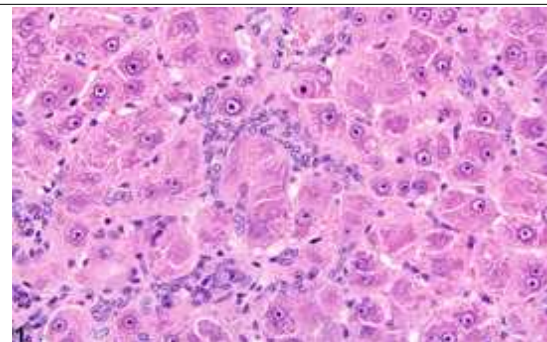
Kupffer cell hyperplasia in a female F344/N rat from a subchronic study.

## Liver - Necrosis (괴사)



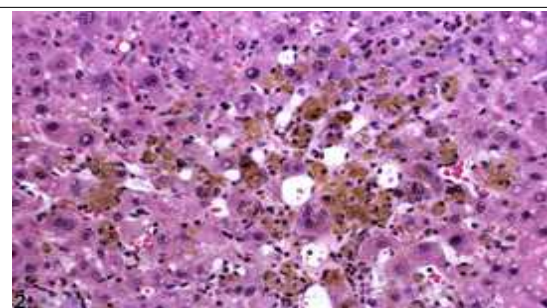
Necrosis-sharply demarcated centrilobular necrosis in a male B6C3F1 mouse from a subchronic study.

Liver, Oval Cell - Hyperplasia (Oval 세포 증생)



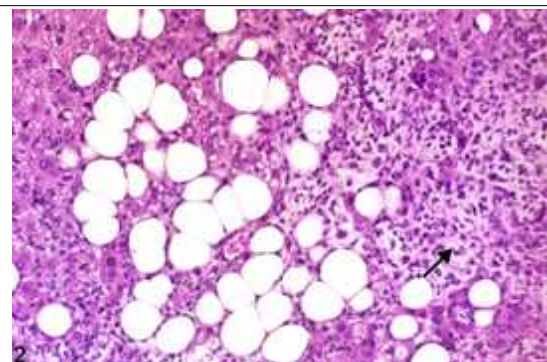
Oval cell hyperplasia in a female Harlan Sprague-Dawley rat from a chronic study.

Liver - Pigment (색소)



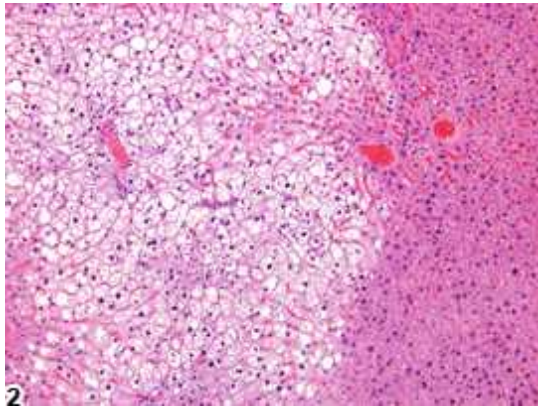
Pigment in hepatocytes in a male Harlan Sprague-Dawley rat from a chronic study.

Liver, Stellate Cell - Hyperplasia (위성세포 증생)



Stellate cell hyperplasia-arrow indicates stellate cells with a spindloid morphology in a female B6C3F1 mouse from a chronic study.

## Liver - Tension Lipidosis (건 지방증)

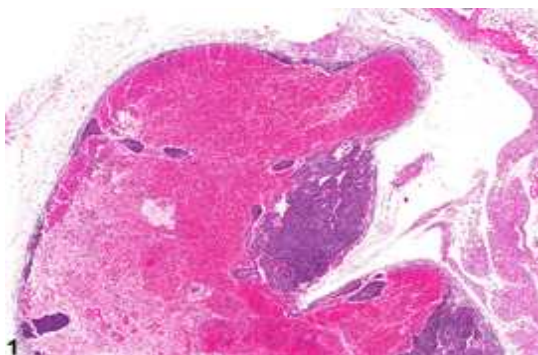


Tension lipidosis in a male B6C3F1 mouse from a chronic study.

## 5. 면역계

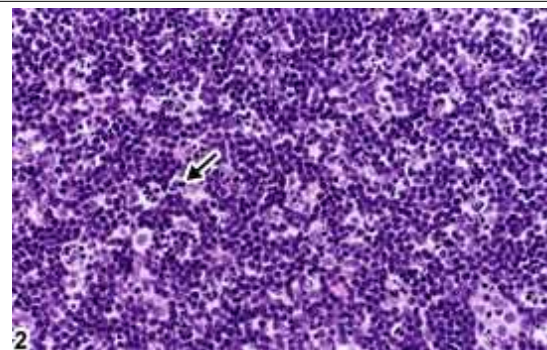
## 1) 림프절

## Lymph Node - Angiectasis (혈관확장)



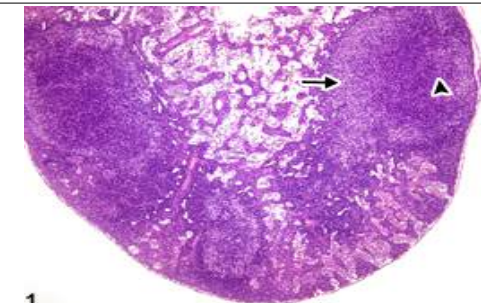
Lymph node - Angiectasis in a female B6C3F1/N mouse from a chronic study. The lymph node architecture is distorted by a markedly distended vessel.

### Lymph Node - Apoptosis, Lymphocyte (임파구 세포자멸)



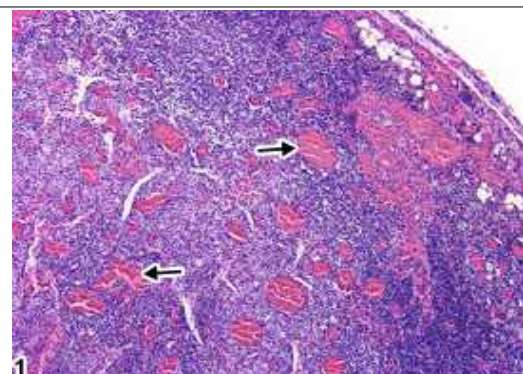
Lymph node - Apoptosis, Lymphocyte in a female B6C3F1/N mouse from a subchronic study (higher magnification of Figure 1). Tingible-body macrophages contain fragments of apoptotic lymphocytes (apoptotic bodies) (arrow).

### Lymph Node - Atrophy (위축)



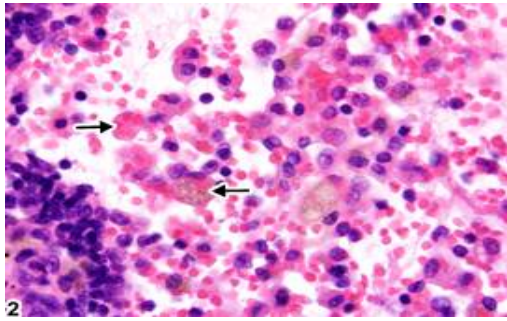
Lymph node - Atrophy in a female F344/N rat from a subchronic study. With early lymph node atrophy, paracortical lymphocytes are depleted (arrow), and number and size of follicles are decreased (arrowhead).

### Lymph Node - Congestion (충혈)



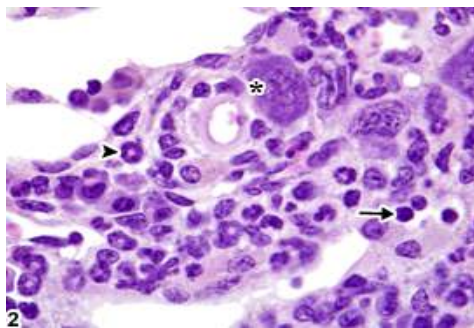
Lymph node - Congestion in a female B6C3F1/N mouse from a chronic study. Numerous vessels are expanded by an excessive accumulation of blood (arrows).

## Lymph Node - Erythrophagocytosis (적혈구포식증)



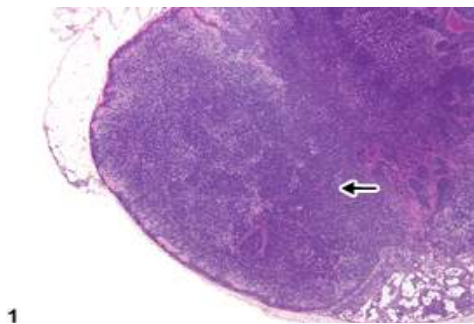
Lymph node - Erythrophagocytosis in a female F344/N rat from a chronic study. Macrophages within the medullary sinus contain variable numbers of erythrocytes and/or pigment within their cytoplasm (arrows).

## Lymph Node - Extramedullary Hematopoiesis (수질외 조혈)



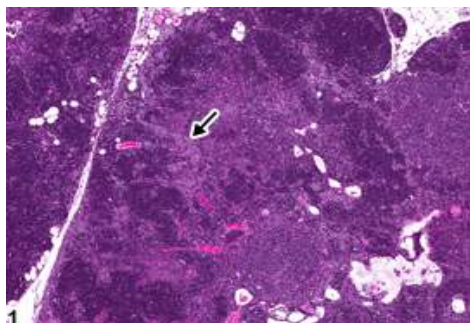
Lymph node - Extramedullary hematopoiesis in a female B6C3F1/N mouse from a chronic study. Hematopoietic cells include erythroblasts (arrow), immature granulocytes (arrowhead), and megakaryocytes (asterisk).

## Lymph Node - Hyperplasia, Lymphocyte (임파구 증생)



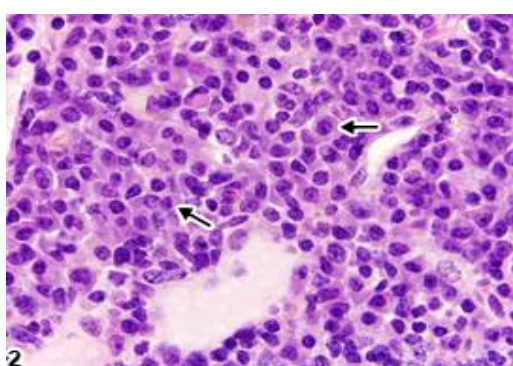
Lymph node - Hyperplasia, Lymphocyte in a male F344/N rat from a subchronic study. The lymph node paracortex is expanded by increased numbers of lymphocytes (arrow).

### Lymph Node - Hyperplasia, Mast Cell (비만세포 증생)



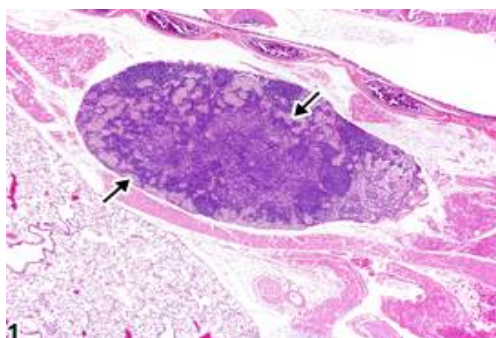
Lymph node - Hyperplasia, Mast cell in a female B6C3F1/N mouse from a chronic study. Mast cells are increased within the lymph node parenchyma (arrow).

### Lymph Node - Hyperplasia, Plasma Cell (형질세포 증생)



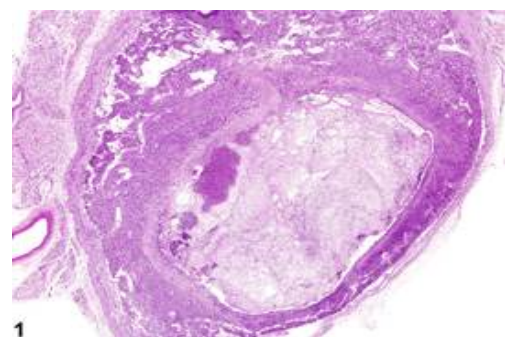
Lymph node - Hyperplasia, Plasma cell in a control female B6C3F1/N mouse from a chronic study. Plasma cells (arrows) are present within the medullary cords.

### Lymph Node - Infiltration, Cellular, Histiocyte (조직구 침투)



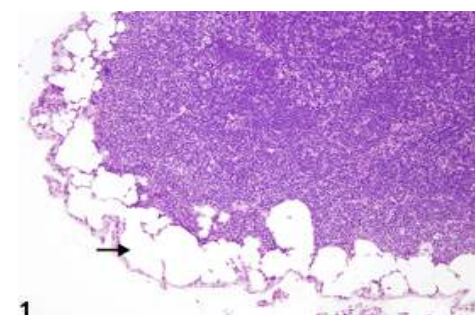
Lymph node - Infiltrate, Cellular, Histiocyte in a male Harlan Sprague Dawley rat from a subchronic study. Increased numbers of histiocytes are present within the paracortical and subcapsular sinuses (arrows).

## Lymph Node - Inflammation (염증)



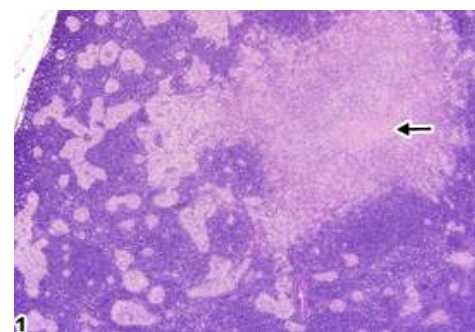
Lymph node - Inflammation, Suppurative in a male F344/N rat from a chronic study. Lymph node is focally expanded by a suppurative exudate.

## Lymph Node - Lymphatic Sinus, Ectasia (임파동 확장)



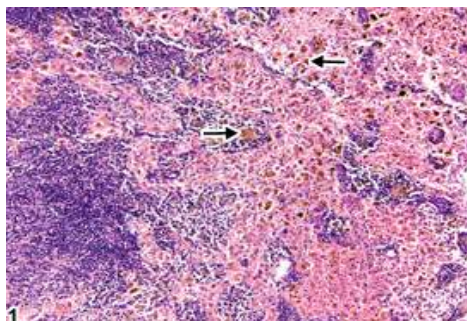
Lymph node - Lymphatic sinus, Ectasia in a treated female F344/N rat from a subchronic study. Subcapsular sinuses are ectatic (arrow).

## Lymph Node - Necrosis (괴사)



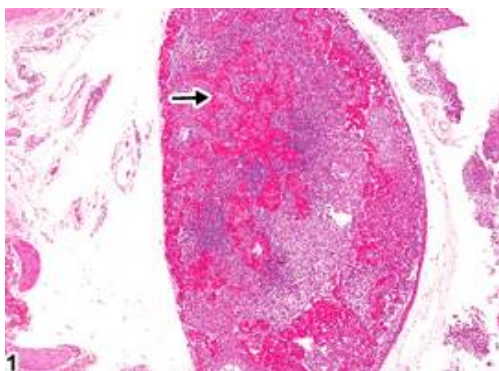
Lymph node - Necrosis in a treated male Harlan Sprague-Dawley rat from a subchronic study. A central focus of necrotic cellular debris (arrow) is evident.

### Lymph Node - Pigment (색소)



Lymph node, Medullary sinuses - Pigment in a male Harlan Sprague-Dawley rat from a chronic study. Macrophages within the medullary sinuses contain intracytoplasmic golden-brown pigment suggestive of hemosiderin (arrows).

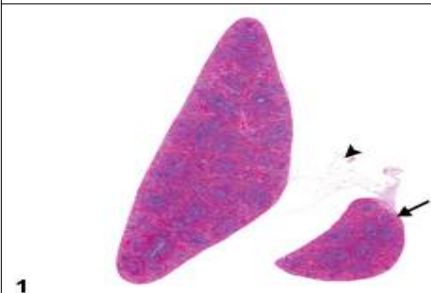
### Lymph Node - Sinus Erythrocytosis (임파동 적혈구증다증)



Lymph node - Sinus erythrocytosis in a female B6C3F1/N mouse from a chronic study. The lymphatic sinuses (arrow) of this lymph node are markedly dilated by numerous extravasated erythrocytes.

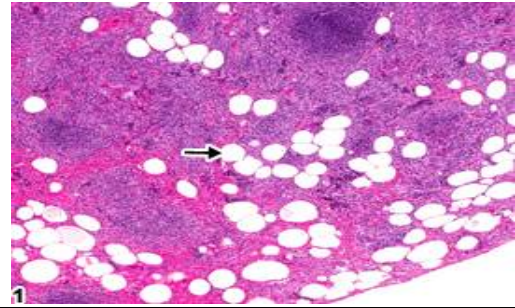
## 2) 비장

### Spleen - Accessory Spleen (보조 비장)



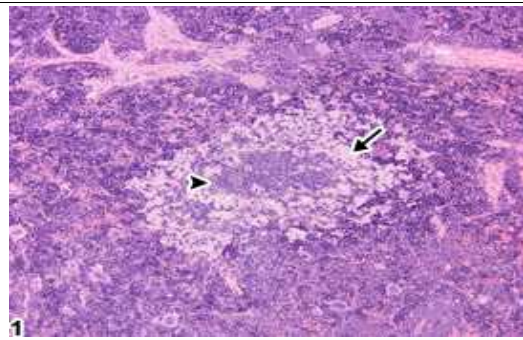
Spleen - Accessory in a male B6C3F1/N mouse from a chronic study. A nodule of splenic tissue (accessory spleen) (arrow) is connected to the spleen via a mesenteric attachment (arrowhead).

## Spleen - Adipocyte Metaplasia (지방세포 화생)



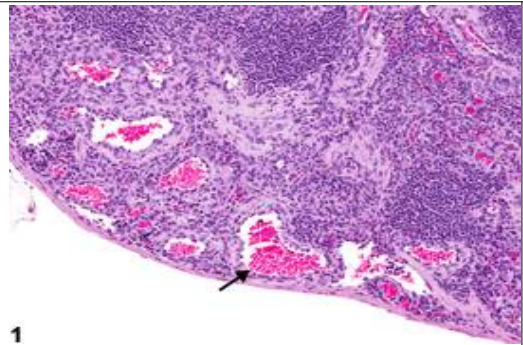
Spleen - Adipocyte metaplasia in a female F344/N rat from a chronic study. Well-differentiated adipocytes (arrow) are present multifocally within the splenic red pulp.

## Spleen - Amyloid (아밀로이드)



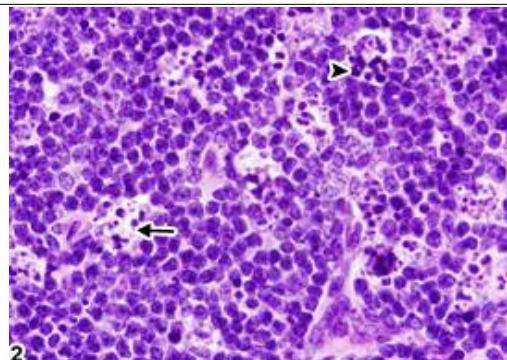
Spleen - Amyloid in a male B6C3F1/N mouse from a chronic study. Amyloid protein (arrow) surrounds and infiltrates the white pulp, which is atrophied (arrowhead).

## Spleen - Angiectasis (혈관 확장)



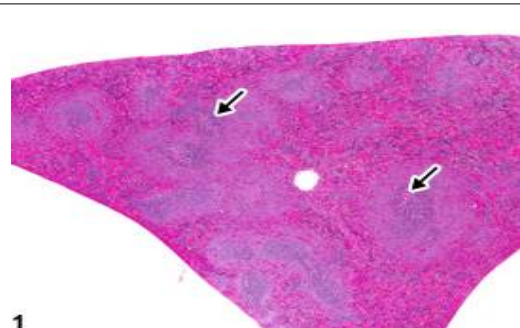
Spleen - Angiectasis in a female B6C3F1/N mouse from a chronic study. Multiple variably sized blood-filled spaces lined by endothelium (arrow) are present within the splenic parenchyma.

Spleen - Apoptosis, Lymphocyte (임파구 세포소멸)



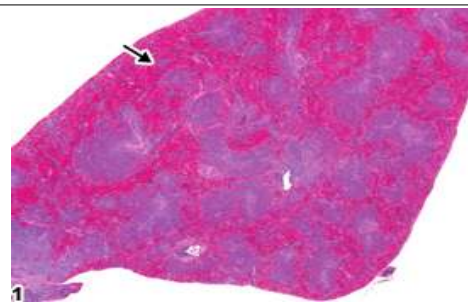
Spleen - Apoptosis, Lymphocyte in a female B6C3F1/N mouse from a subchronic study. Tingible body macrophages (arrow) contain intracytoplasmic fragments of apoptotic lymphocytes (apoptotic bodies) (arrowhead).

Spleen - Atrophy (위축)



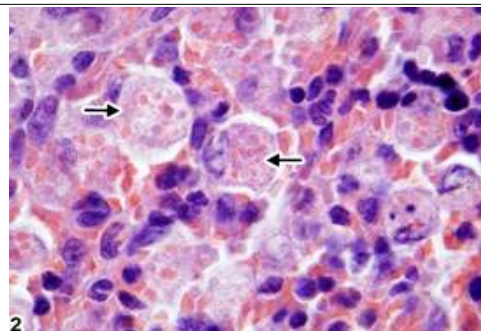
Spleen, White pulp - Atrophy in a female F344/N rat from a subchronic study. Overall area and cellularity of the white pulp (periarteriolar lymphatic sheaths and follicles) are decreased (arrows), although the marginal zones appear to be within normal limits.

Spleen - Congestion (충혈)



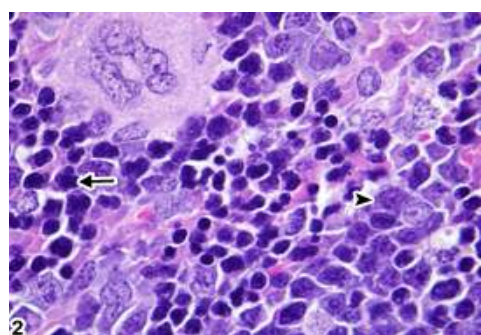
Spleen - Congestion in a female F344/N rat from a chronic study. The red pulp sinusoids are moderately distended by erythrocytes (arrow).

## Spleen - Erythrophagocytosis (적혈구탐식)



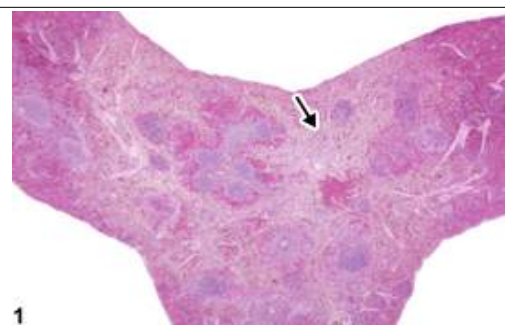
Spleen - Erythrophagocytosis in a male B6C3F1/N mouse from a chronic study. Macrophages contain intracytoplasmic erythrocytes and eosinophilic cellular debris (arrows).

## Spleen - Extramedullary Hematopoiesis (수질외 조혈)



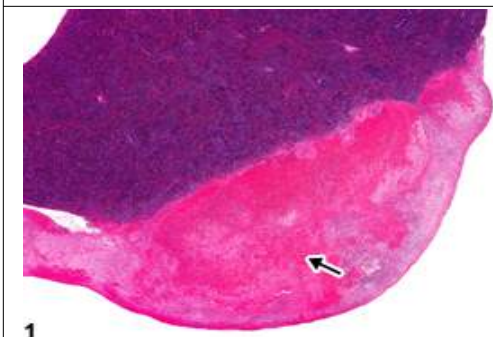
Spleen, Red pulp - Extramedullary hematopoiesis, Increased in a treated male B6C3F1/N mouse from a chronic study (higher magnification of Figure 1). Extramedullary hematopoiesis in this case includes increased numbers of erythroid (arrow) and myeloid (arrowhead) precursor cells.

## Spleen - Fibrosis (섬유증)



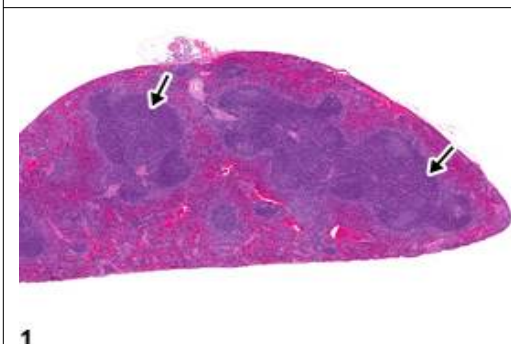
Spleen, Parenchyma - Fibrosis in a male F344/N rat from a chronic study. The splenic red pulp is contracted by fibrous connective tissue (arrow).

Spleen - Hemorrhage (출혈)



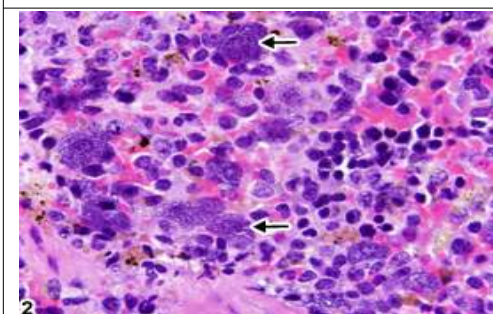
Spleen - Hemorrhage in a female Harlan Sprague-Dawley rat from a chronic study. A focal accumulation of extravasated erythrocytes resulted in protrusion of the splenic capsule (arrow).

Spleen - Hyperplasia, Lymphocyte (임파구 증생)



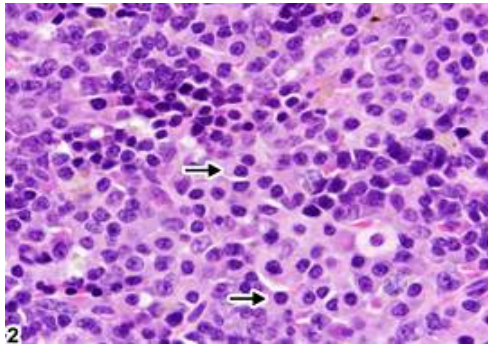
Spleen - Hyperplasia, Lymphocyte in a male B6C3F1/N mouse from a chronic study. The splenic white pulp is expanded by increased numbers of normal lymphocytes (arrows).

Spleen - Hyperplasia, Mast Cell (비만세포 증생)



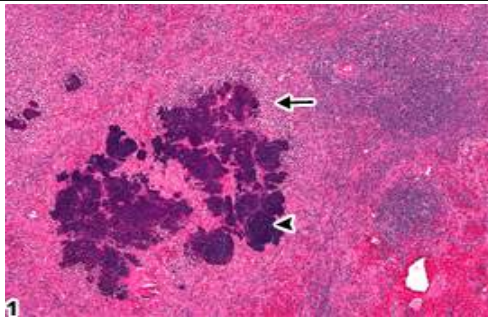
Spleen - Hyperplasia, Mast cell in a female B6C3F1/N mouse from a chronic study. Clusters of well-differentiated mast cells (arrows) are intermixed with other red pulp cellular components.

## Spleen - Hyperplasia, Plasma Cell (형질세포 증생)



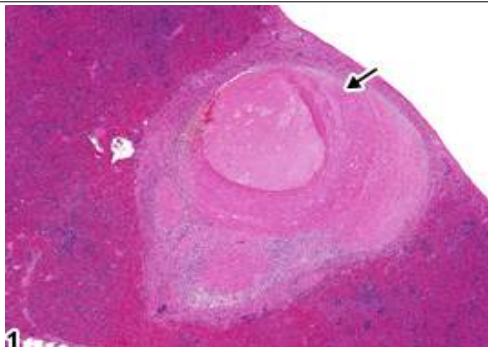
Spleen - Hyperplasia, Plasma cell in a female B6C3F1/N mouse from a chronic study. Plasma cells (arrow) are round to oval with a high nucleus-to-cytoplasm ratio, typically eccentric nucleus with heterochromatin in a characteristic cartwheel or clock face arrangement, and a pale perinuclear region with a Golgi

## Spleen - Inflammation (염증)



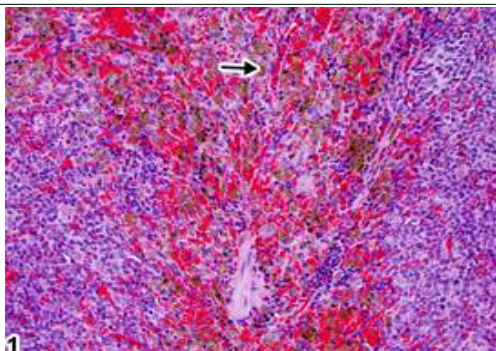
Spleen - Inflammation, Suppurative in a male F344/N rat from a chronic study. Suppurative inflammation (arrow) borders a large focus of bacteria (arrowhead) within the splenic red pulp.

## Spleen - Necrosis (괴사)



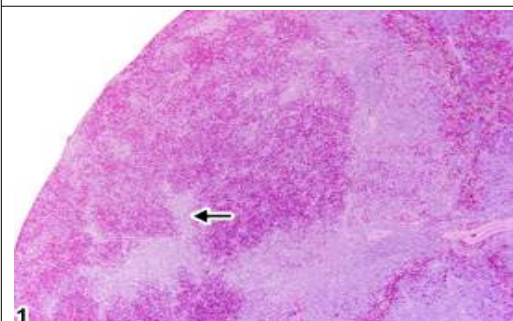
Spleen - Necrosis in a male F344/N rat from a chronic study. A large necrotic focus (arrow) is present with the spleen.

### Spleen - Pigment (색소)



Spleen - Pigment in a male F344/N rat from a chronic study. Multifocal macrophages with intracytoplasmic dark-brown granular pigment (arrow) are present within the splenic red pulp.

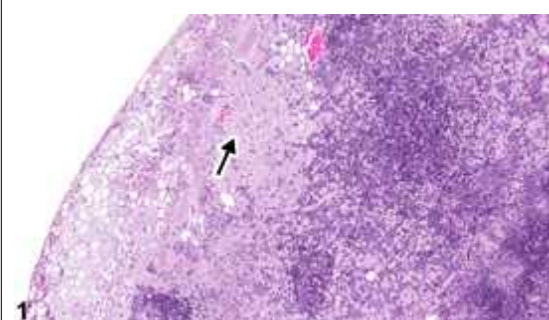
### Spleen, Red Pulp - Hyperplasia, Stromal (적수 기질 증생)



Spleen, Red pulp - Hyperplasia, Stromal cell in a female F344/N rat from a chronic study. Intersecting, irregular bundles and bands of stromal cells (arrow) infiltrate the splenic red pulp.

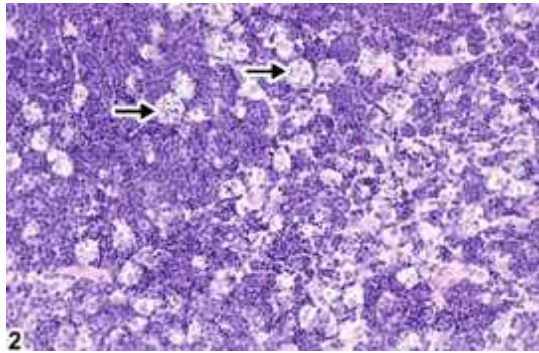
## 3) 흉선

### Thymus - Amyloid (아밀로이드)



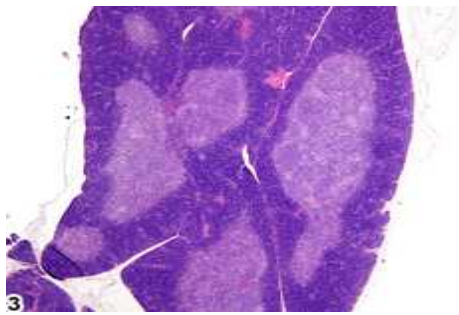
Thymus - Amyloid in a female B6C3F1/N mouse from a chronic study. Normal thymic architecture has been disrupted by deposition of amyloid protein (arrow).

## Thymus - Apoptosis, Lymphocyte (임파구 세포소멸)



Thymus - Apoptosis, Lymphocyte in a female B6C3F1/N mouse from a subchronic study. Tingible-body macrophages (arrows) contain intracytoplasmic fragments of apoptotic lymphocytes (apoptotic bodies).

## Thymus - Atrophy (위축)



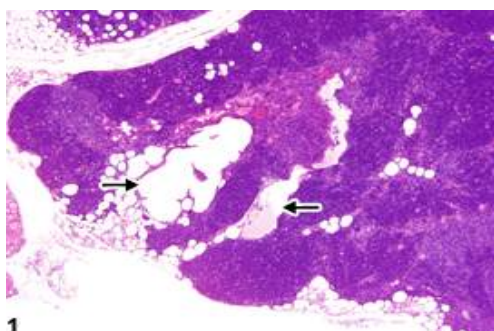
Thymus - Atrophy in a treated female F344/NTac rat from a subchronic study. The cortex, showing minimal atrophy, is thinner and more irregular compared with normal.

## Thymus - Atypical Hyperplasia Lymphocyte (비전형 임파구 증생)



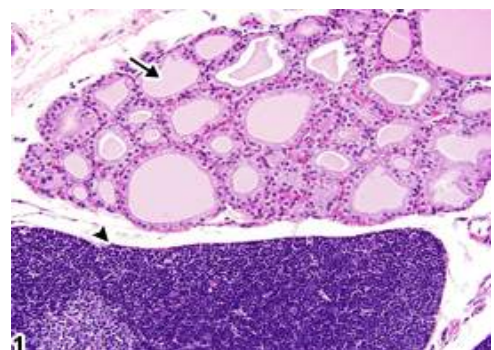
Thymus - Atypical hyperplasia, Lymphocyte in a female p53+/- (C57Bl/6) mouse from a subchronic study. When atypical lymphocyte hyperplasia is unilateral, the affected lobe (arrow) is typically smaller than the unaffected lobe.

### Thymus - Cyst (낭포)



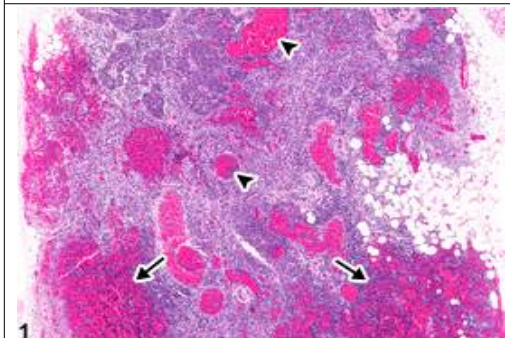
Thymus - Cyst, Multiple in a female F344/N rat from a chronic study. Multiple cysts (arrows) are present within the thymus.

### Thymus - Ectopic Tissue (이소성 조직)



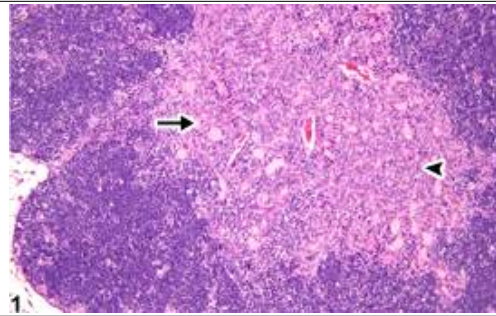
Thymus - Ectopic tissue, Thyroid in a control male Harlan Sprague-Dawley rat from a subchronic study. A structurally normal fragment of thyroid tissue (arrow) is adjacent to the thymus (arrowhead).

### Thymus - Hemorrhage (출혈)



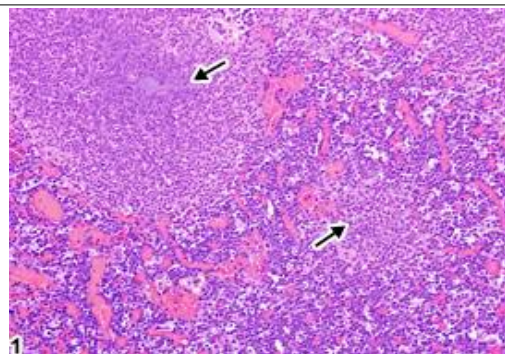
Thymus - Hemorrhage in a male F344/N rat from a chronic study. Multifocal to coalescing areas of hemorrhage are present within this involuted thymus (arrows). Numerous vessels are also congested (arrowheads).

## Thymus - Hyperplasia, Epithelial (상피세포 증생)



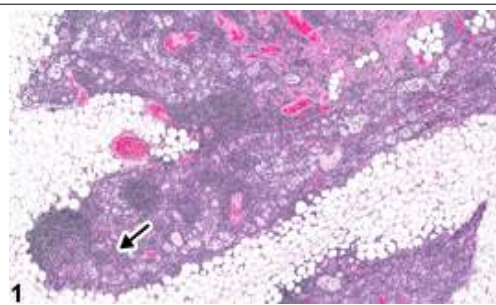
Thymus - Hyperplasia, Epithelial in a male B6C3F1 mouse from a chronic study. Hyperplastic epithelial cells form tubules (arrow) and cords (arrowhead) within the thymus medulla.

## Thymus - Inflammation (염증)



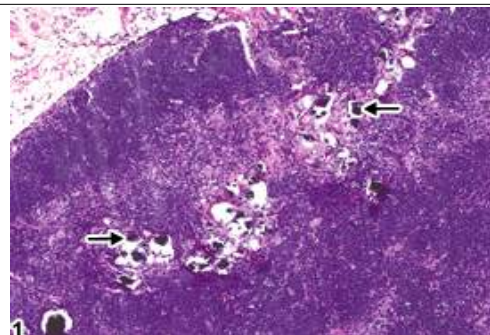
Thymus - Inflammation, Suppurative in a female B6C3F1/N mouse from a chronic study. Multifocal, discrete regions of suppurative exudate (abscesses) are present (arrows).

## Thymus - Involution (퇴화)



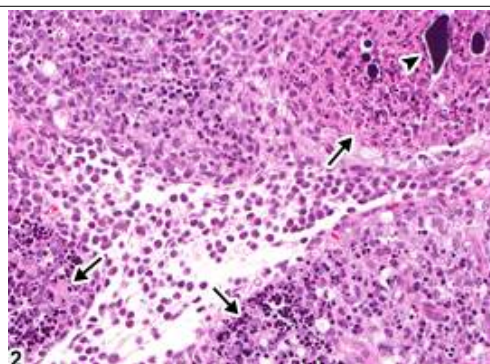
Thymus - Involution in a female Harlan Sprague-Dawley rat from a chronic study. The lymphocyte density is significantly decreased (arrow), and the corticomedullary junction is indistinct. Adipocytes infiltrate the capsule.

### Thymus - Mineralization (무기질 침착)



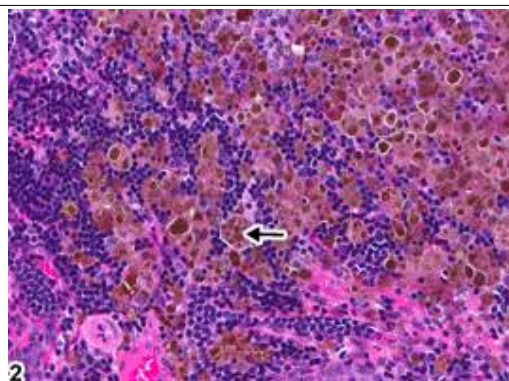
Thymus - Mineralization in a male B6C3F1/N mouse from a chronic study. Multiple mineralized foci (arrows) are present within the thymic medulla.

### Thymus - Necrosis, Lymphocyte (임파구 괴사)



Thymus - Necrosis, Lymphocyte in a male Harlan Sprague-Dawley rat from a subchronic study. Lymphocyte necrosis (arrows) is accompanied by eosinophilic cytoplasmic debris, basophilic nuclear debris, mineral (arrowhead), and inflammation.

### Thymus - Pigment (색소)

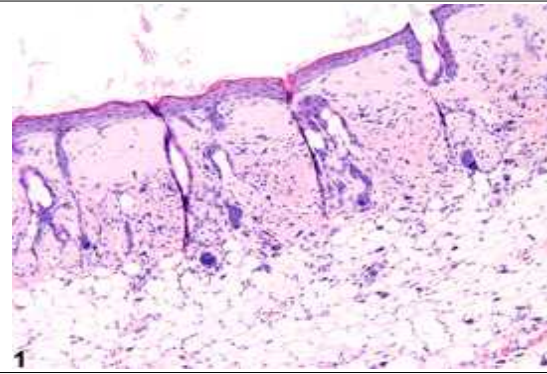


Thymus - Pigment in a female F344/N rat from a chronic study (higher magnification of Figure 1). Numerous macrophages contain intracytoplasmic dark brown granular pigment (arrow).

## 6. 피부

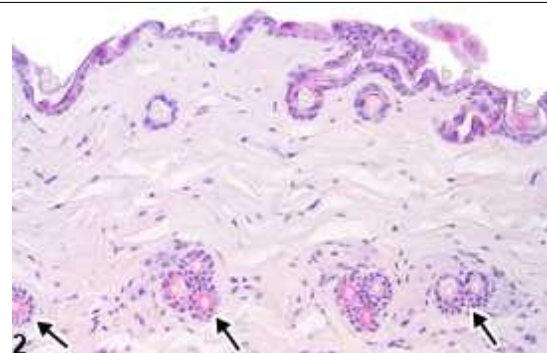
## 1) 피부

## Skin - Amyloid (아밀로리드)



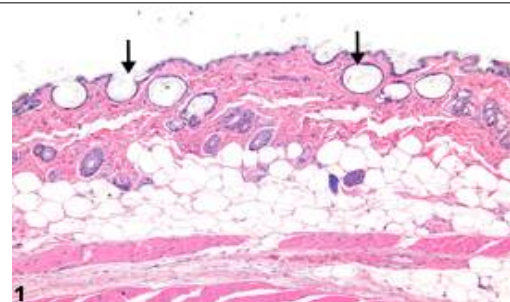
Amyloid-accumulations of amorphous, eosinophilic, extracellular material in a female Swiss CD-1 mouse from a chronic study.

## Skin - Atrophy (위축)



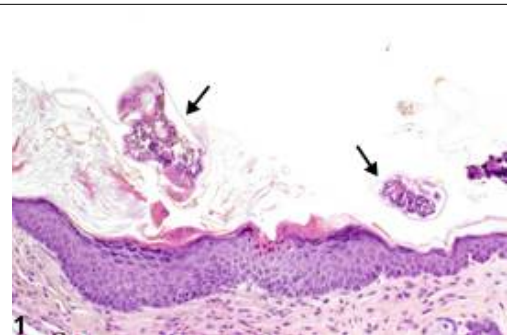
Adnexal atrophy-smaller and reduced numbers of pilosebaceous units (arrows) in a male B6C3F1 mouse from a chronic study.

## Skin, Hair Follicle - Dilatation and Cyst (털 소낭, 확장과 낭포)



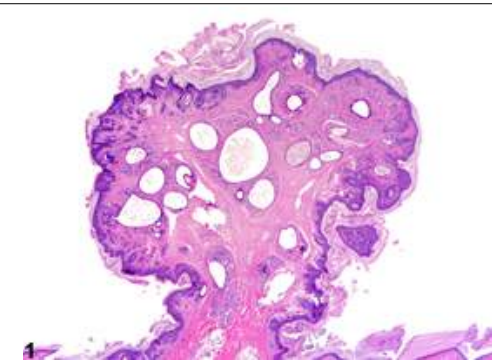
Hair follicle dilatation-ectatic hair follicles with intraluminal keratin (arrows) in a male B6C3F1 mouse from a chronic study.

### Skin - Ectoparasites (체외 기생충)



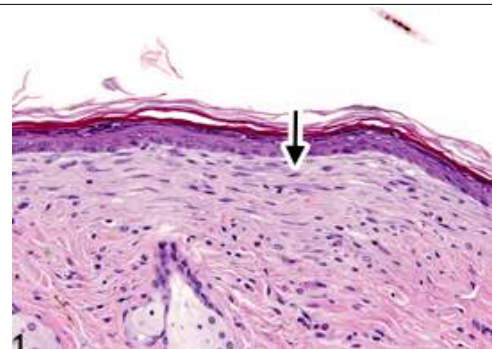
Ectoparasites-arthropod ectoparasites (arrows) with epidermal hyperplasia and hyperkeratosis and dermal inflammation in a female B6C3F1 mouse from a chronic study.

### Skin - Fibroadnexal Hamartoma (과오종)



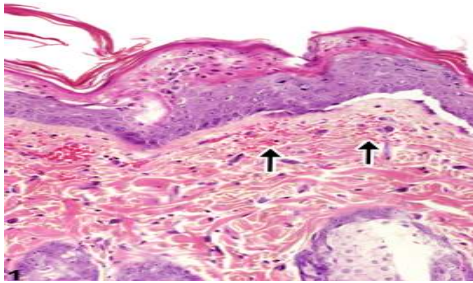
Fibroadnexal hamartoma-exophytic growth composed of dilated hair follicles and overlying hyperplastic epithelium in a female F344/N rat from a chronic study.

### Skin - Fibrosis (섬유증)



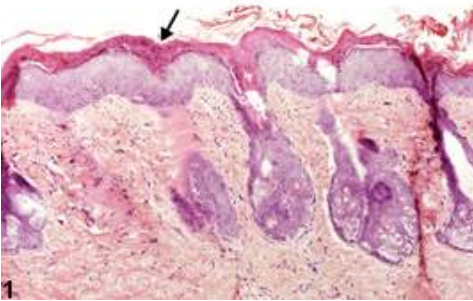
Fibrosis-increase of fibrous connective tissues in the dermis (arrow) in a male B6C3F1 mouse from a 2-year study.

## Skin - Hemorrhage (출혈)



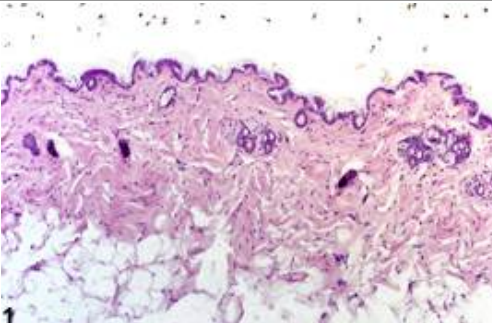
Hemorrhage-extravascular erythrocytes within the dermis (arrows) in a male F344/N rat from a subchronic study.

## Skin - Hyperkeratosis (각막비후증)



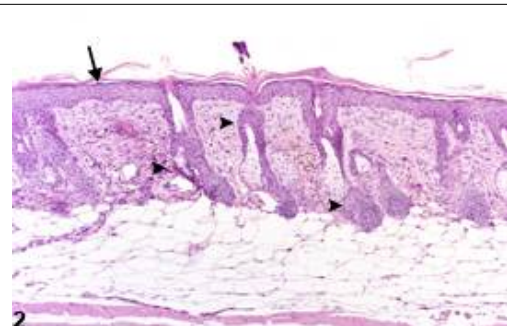
Hyperkeratosis-parakeratotic hyperkeratosis (arrow) in a male F344/N rat from a subchronic study.

## Skin - Hyperplasia (증생)



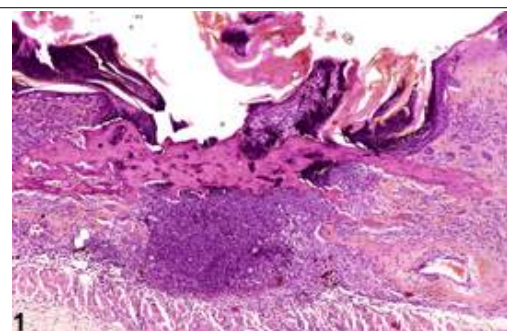
Normal skin in a male B6C3F1 mouse from a 90-day study.

### Skin - Hyperplasia (증생)



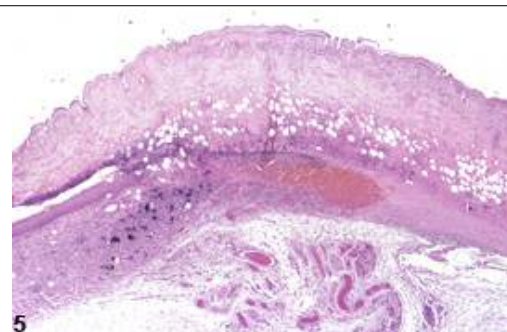
Epithelial hyperplasia-increased numbers of squamous cells in the epidermis (arrow) and follicular epithelium (arrowheads) in a female B6C3F1 mouse from a 90-day study.

### Skin - Inflammation (염증)



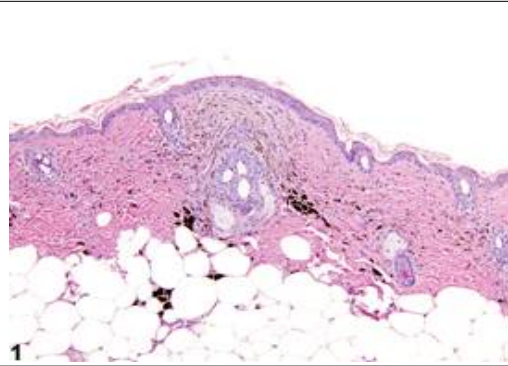
Acute inflammation-dense infiltrations of neutrophils and osseous metaplasia in a male B6C3F1 mouse from a chronic study.

### Skin - Necrosis (괴사)



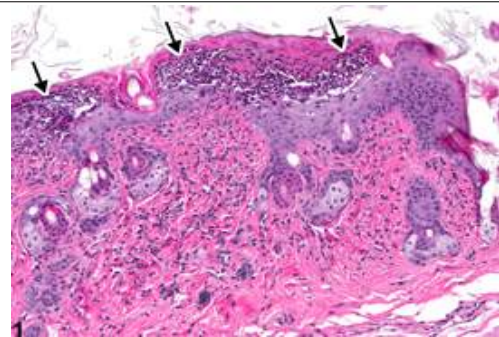
Skin necrosis-transmurular necrosis of the epidermis, dermis, and subcutis in a male B6C3F1 mouse from a 90-day study.

## Skin - Pigment (색소)



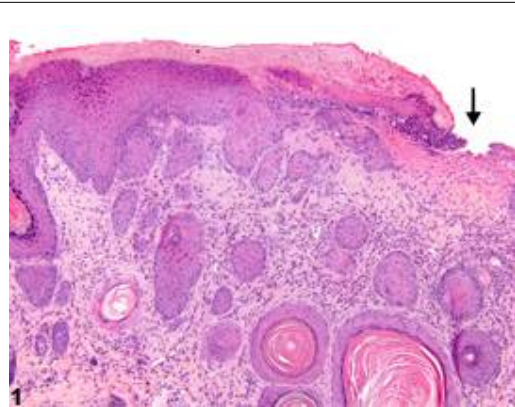
Pigment-accumulation of pigment-laden cells in the dermis in a male B6C3F1 mouse from a chronic study.

## Skin - Pustule (농포)



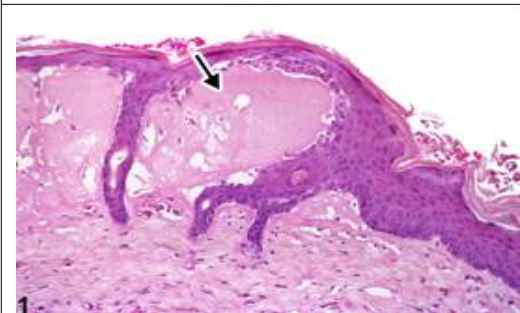
Pustule-accumulations of neutrophils with the stratum corneum (arrows) in a male B6C3F1 mouse from a subchronic study.

## Skin - Ulcer and Erosion (궤양, 부식)



Ulcer-loss of the epidermis, with adjacent epidermal hyperplasia and underlying inflammation (arrow), in a male B6C3F1 mouse from a chronic study.

## Skin - Vesicle (소낭)

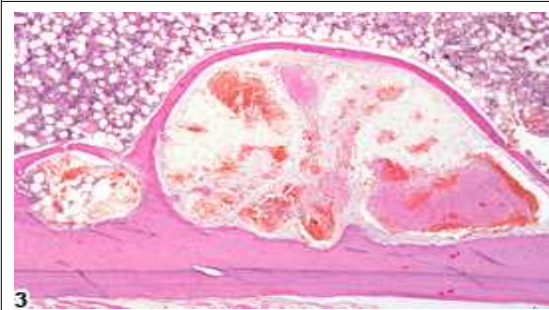


Vesicle-subepidermal cystlike space that contains serous fluid (arrow) in a female B6C3F1 mouse from an 80-week study.

## 7. 근골격계

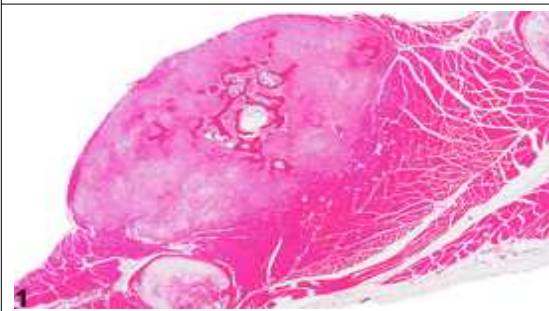
### 1) 뼈

## Bone - Cyst (낭포)



Bone - Cyst in a male F344/N rat from a chronic study. The cyst contains large amounts of hemorrhage.

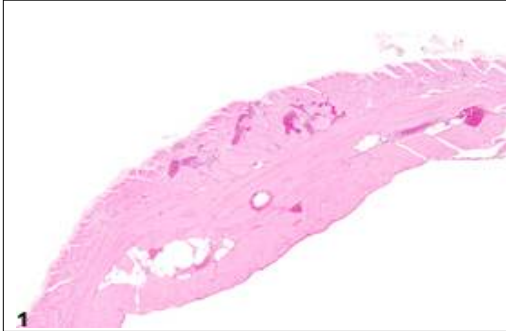
## Bone - Callus (가골)



Bone - Callus in a male Wistar rat from a chronic study. There is callus formation surrounding a rib, characterized by a marked proliferative fibrous connective tissue response and bony remodeling.

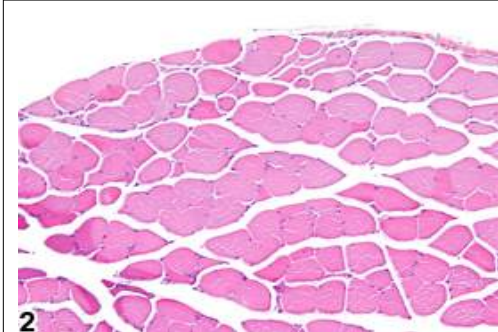
## 2) 뼈 근육

## Skeletal Muscle - Angiectasis (혈관확장)



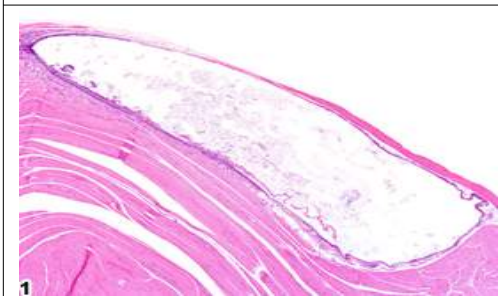
Skeletal muscle - Angiectasis in a male B6C3F1/N mouse from a chronic study. Note the dilated endothelial-lined vessels filled with blood.

## Skeletal Muscle - Atrophy (위축)



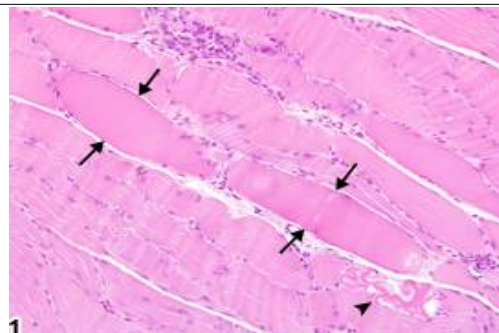
Skeletal muscle - Atrophy in a male B6C3F1/N mouse from a subchronic study. Note the reduction in myofiber diameter of the affected fibers (top) compared with the more normal myofibers along the bottom.

## Skeletal Muscle - Cyst (낭포)



Skeletal muscle - Cyst in a female F344/N rat from a chronic study. A thin-walled epithelium-lined cyst is present within skeletal muscle.

### Skeletal Muscle - Degeneration (변성)



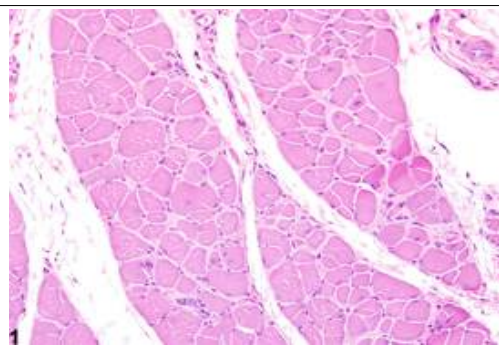
Skeletal muscle-Degeneration in a male Harlan Sprague-Dawley rat from a subchronic study. A central myofiber is swollen and hypereosinophilic (arrows), and a fragmented segment of another fiber (arrowhead) demonstrates segmental degeneration.

### Skeletal Muscle - Edema (부종)



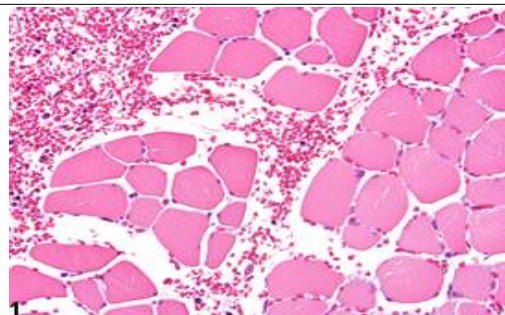
Skeletal muscle - Edema in a male F344/N rat from a chronic study. Muscle fibers and muscle bundles are separated by expanded interstitial spaces filled with pale pink material.

### Skeletal Muscle - Fibrosis (섬유화)



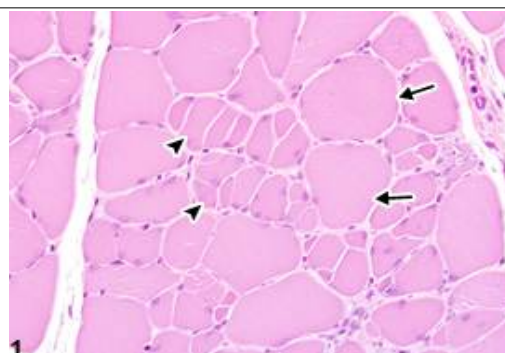
Skeletal muscle - Fibrosis in a male Harlan Sprague-Dawley rat from a subchronic study. Early change consists of increased perimysial deposits of pale eosinophilic material (immature collagen).

## Skeletal Muscle - Hemorrhage (출혈)



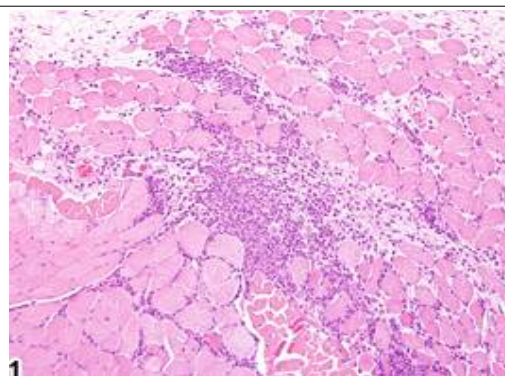
Skeletal muscle - Hemorrhage in a male F344/N rat from a chronic study. Free erythrocytes and circulating leukocytes are present adjacent to and between muscle bundles.

## Skeletal Muscle - Hypertrophy (비대)



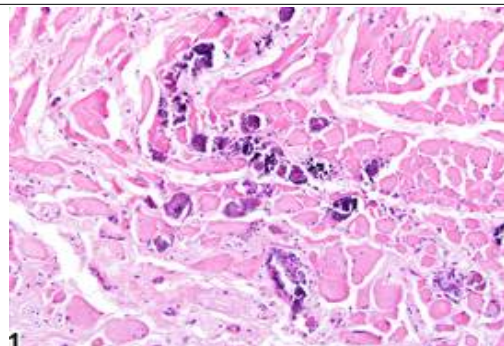
Skeletal muscle - Hypertrophy in a male Harlan Sprague-Dawley rat from a subchronic study. Large, hypertrophic fibers (arrows) are adjacent to longitudinally split muscle fibers (arrowheads).

## Skeletal Muscle - Inflammation (염증)



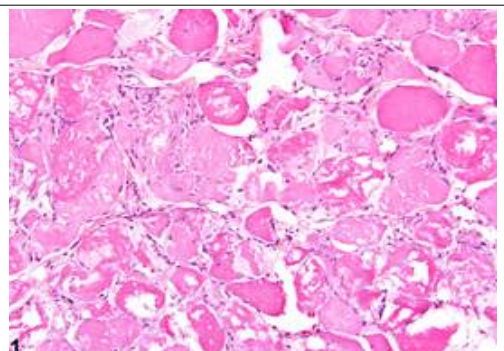
Skeletal muscle - Inflammation, Acute in a female Swiss CD-1 mouse from a chronic study. A neutrophilic infiltrate has led to necrosis and loss of muscle fibers.

### Skeletal Muscle - Mineralization (무기질 침착)



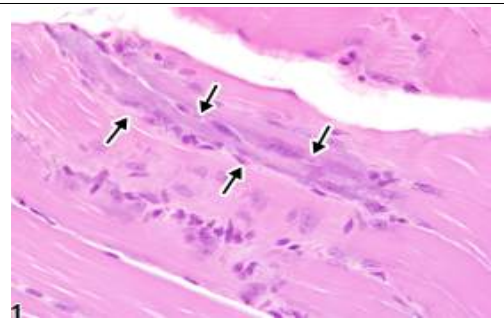
Skeletal muscle - Mineralization in a male F344/N rat from a chronic study. Multiple deposits of deeply basophilic mineral are present in damaged muscle fibers.

### Skeletal Muscle - Necrosis (괴사)



Skeletal muscle - Necrosis in a male F344/N rat from a chronic study. This cross section of skeletal muscle exhibits an extensive, highly fragmented and vacuolated collection of muscle fibers; some are hypereosinophilic, and others are pale.

### Skeletal Muscle - Regeneration (재생)

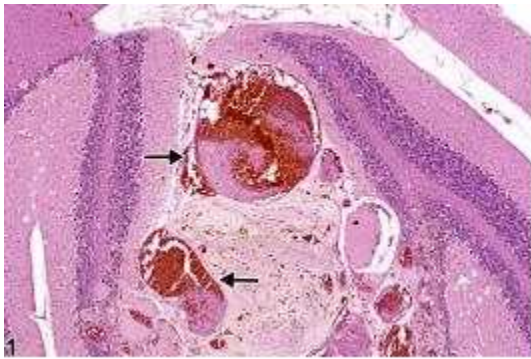


Skeletal muscle - Regeneration in a male Harlan Sprague-Dawley rat from a subchronic study. Myoblasts and cytoplasmic basophilia (arrows) characterize regeneration of a previously damaged muscle fiber.

## 8. 신경계

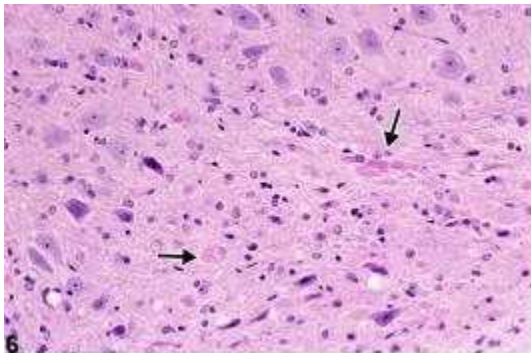
## 1) 뇌

## Brain - Angiectasis (혈관확장)



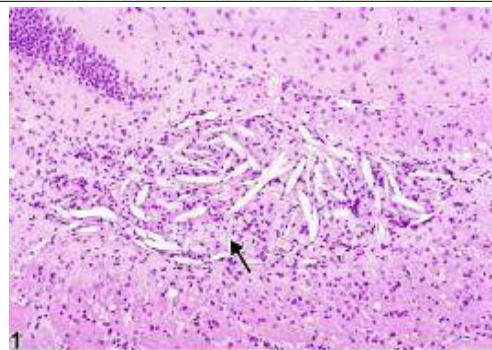
Brain - Incidental angiectasis in a cerebellar vein in a female F344/N rat from a chronic study. The arrows identify ectatic veins containing thrombi.

## Brain - Axonopathy (축삭병증)



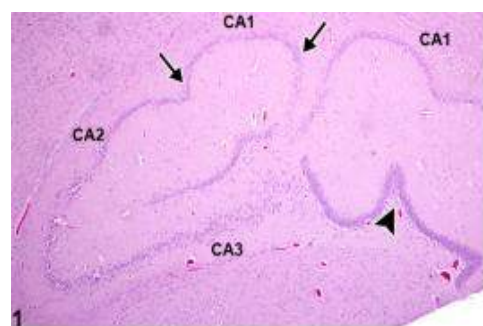
Axonal spheroids (arrows) in brain parenchyma in a male B6C3F1 mouse from a subchronic study.

### Brain - Cholesterol clefts (콜레스테롤열)



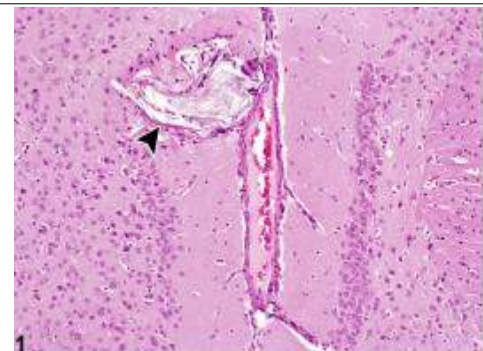
Cholesterol clefts in a male B6C3F1 mouse from a chronic study.

### Brain - Dysplasia (형태이상)



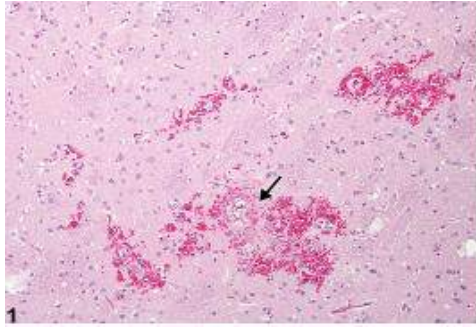
Incidental hippocampal dysplasia in a female F344/N rat from a 2-year study. Note the abnormal undulation of the CA1 region (arrows) and the distortion of the dentate gyrus (arrowhead).

### Brain - Epidermoid Cyst (유포피낭포)



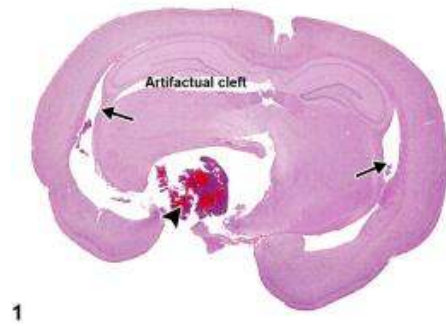
Brain, cingulate cortex-incidental epidermoid cyst (arrowhead) in a male B6C3F1 mouse from a chronic study.

## Brain - Hemorrhage (출혈)



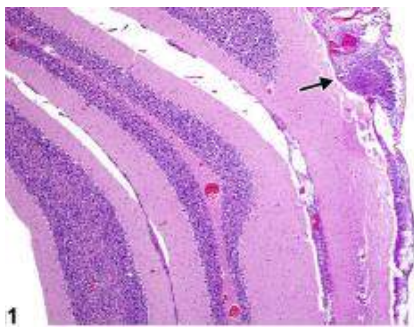
Brain hemorrhage in a male F344/N rat from a chronic study. Note the accumulation of extravasated red blood cells around capillaries and the transudation of protein-rich fluid (arrow).

## Brain - Hydrocephalus (뇌수종)



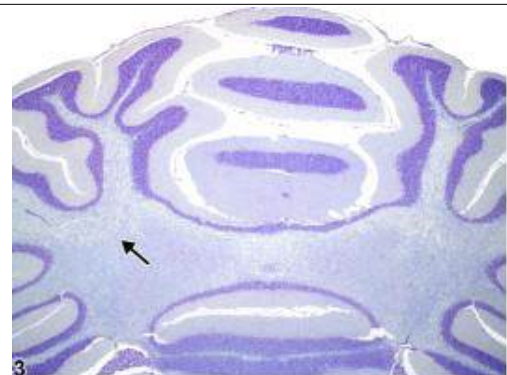
An example of bilateral noncommunicating, obstructive hydrocephalus of the lateral ventricles (arrows) in a male F344/N rat from a chronic study. It is secondary to a pituitary neoplasm (arrowhead) compressing and distorting the diencephalon while obstructing the ventral aspect of the third ventricle.

## Brain - Inflammation (염증)



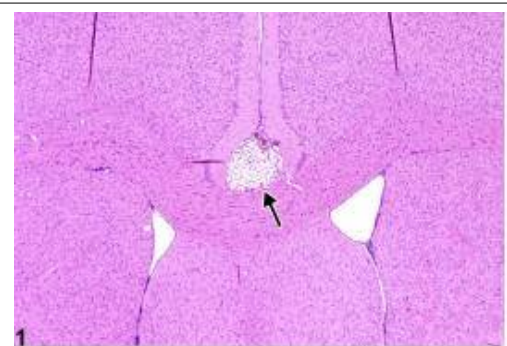
Brain, cerebellum, leptomeninges—accumulation of acute inflammatory cells (arrow) in the leptomeninges of the cerebellum, subsequent to septicemia, resulting in acute suppurative meningitis, in a female B6C3F1 mouse.

### Brain - Interamyelinic Edema (미엘린 내 부종)



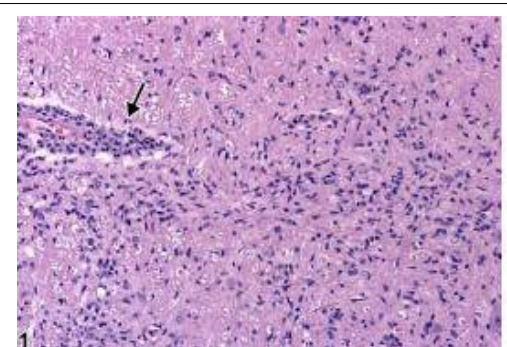
Brain, cerebellum-morphologic features of toxin-induced intramyelinic edema in white matter (arrow) stained with Luxol fast blue and cresyl violet in a rat.

### Brain, Leptomeninges (연막)- Hamartoma (과오종), Lipomatous



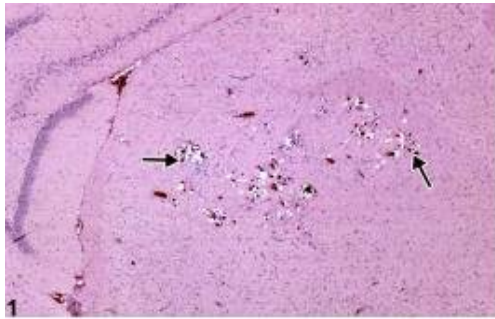
Leptomeningeal lipomatous hamartoma in an untreated male B6C3F1 mouse from a 2-year study. The arrow identifies the location of the lipomatous mass.

### Brain - Microgliosis (미세아교세포증)



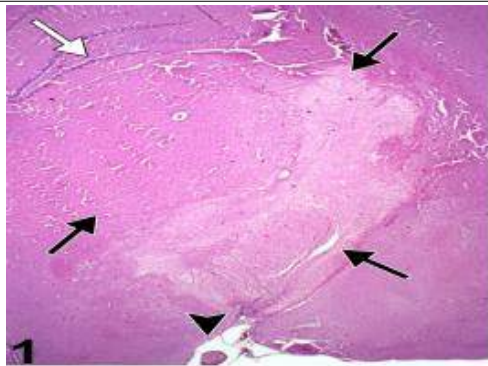
Microgliosis adjacent to an inflammatory mononuclear perivascular cuff (arrow) in a female F344/N rat from a chronic study. Note the many elongated, irregular nuclei of typical microglial cells.

## Brain - Mineralization (무기질 침착)



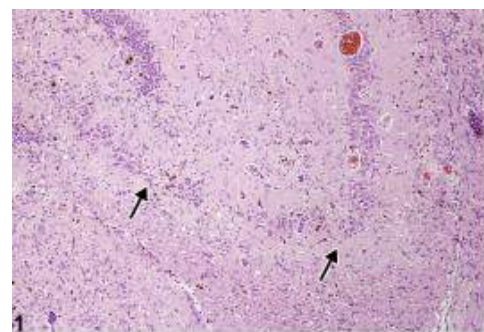
Incidental thalamic mineralization in a female F344/N rat from a 16-week study. The arrows identify focal mineral deposits.

## Brain - Necrosis (괴사)



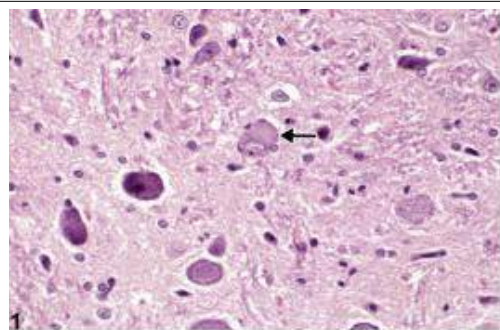
Appearance of a thalamic infarct at low magnification, identified by pallor within the zone of the black arrows, in an F344/N rat. The dentate gyrus of the hippocampus is identified by a white arrow. This infarct was the result of an arterial embolus (arrowhead).

## Brain, Neuron - Cell Loss (신경세포 손실)



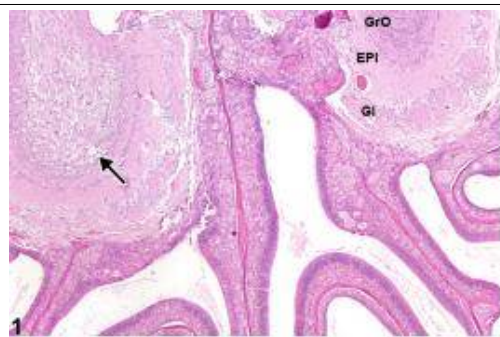
Neuronal cell loss in a female F344/N from a 2-year study. Note the loss of neurons in CA3 region of the hippocampus (arrows).

### Brain, Neuron - Chromatolysis (염색질용해)



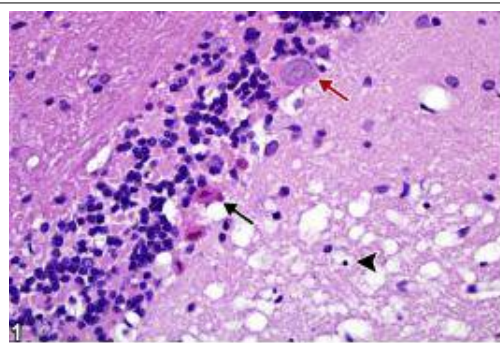
Neuronal central chromatolysis in a male F344/N rat from a 90-day study. The arrow identifies the affected neuron with typical features of cytoplasmic pallor and eccentricity of the nucleus.

### Brain, Neuron - Degeneration (변성)



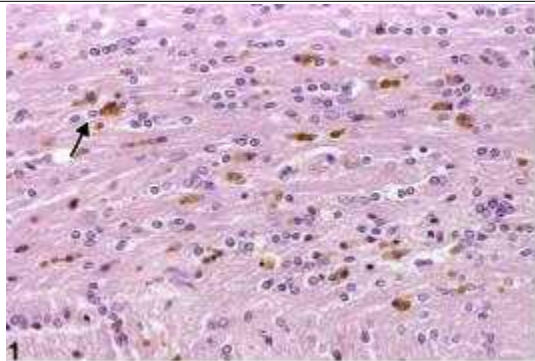
Olfactory bulb neuronal degeneration in a female B6C3F1 mouse from a chronic study. The arrow indicates the vacuolation and neuronal degeneration of the olfactory bulb. Gl, glomerular layer; EPI, external plexiform layer; GrO, internal granule cell layer.

### Brain, Neuron - Necrosis (괴사)



Neuronal necrosis in a male F344 rat from an acute inhalation study. The black arrow identifies acute eosinophilic necrosis. By contrast, the red arrow identifies a relatively normal neuron, and the arrowhead identifies a pyknotic nucleus amid associated vacuolation of the neuropil.

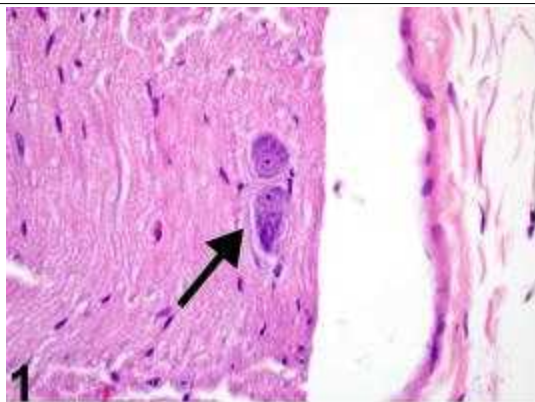
## Brain - Pigment (색소)



Pigment. A site of former hemorrhage (arrow) in the corpus callosum in a female F344/N rat from a chronic study. Multiple brown-pigmented hemosiderin-laden macrophages are present.

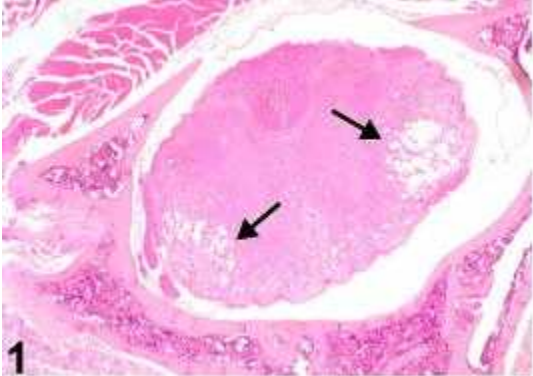
## 2) 신경

## Nerve - Ectopic Neuron (이소성 신경)



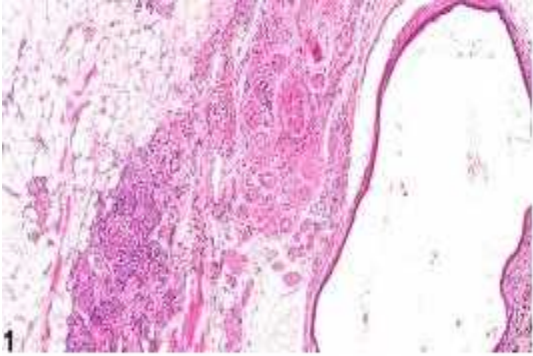
Ectopic neurons (arrow) in the sciatic nerve in a male Sprague-Dawley rat from a 30-week study.

### 3) 척수

Spinal Cord - Demyelination (탈수초)	
	<p>Mouse spinal cord depicting bilateral demyelination of the lateral columns (arrows) in a mouse (age, strain, and gender unknown).</p>

## 9. 암컷 생식기계

### 1) 음핵선

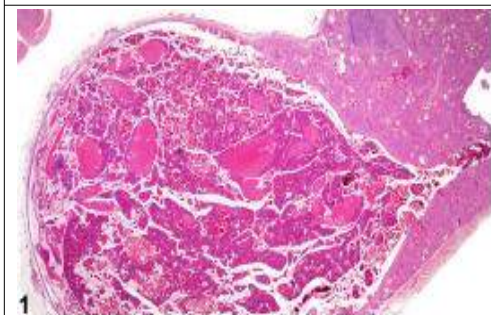
Clitoral Gland - Angiectasis (혈관확장)	
	<p>Clitoral gland - Angiectasis in a female B6C3F1/N mouse from a chronic study. Variably sized and shaped channels are distributed throughout the clitoral gland.</p>

## Clitoral Gland - Atrophy (위축)



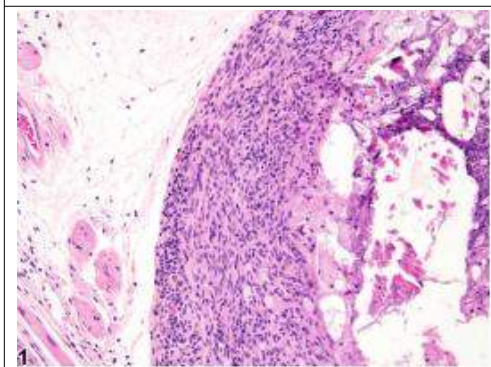
Clitoral gland - Atrophy, Unilateral in a female B6C3F1/N mouse from a chronic study. The gland on the left is atrophied, while the gland on the right is within normal limits.

## Clitoral Gland, Duct - Dilation (확장)



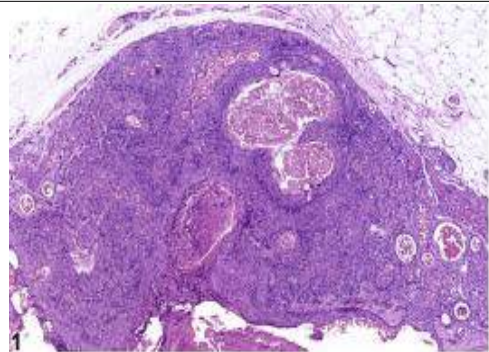
Clitoral gland, Duct - Dilation, Marked in a female Sprague-Dawley rat from a chronic study. The central duct is markedly dilated and filled with eosinophilic material.

## Clitoral Gland - Fibrosis (섬유화)



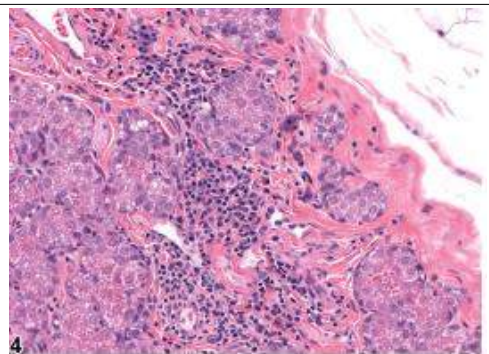
Clitoral gland - Fibrosis in a female B6C3F1/N mouse from a chronic study. Immature fibrous tissue effaces the clitoral gland stroma.

### Clitoral gland - Hyperplasia (증생)



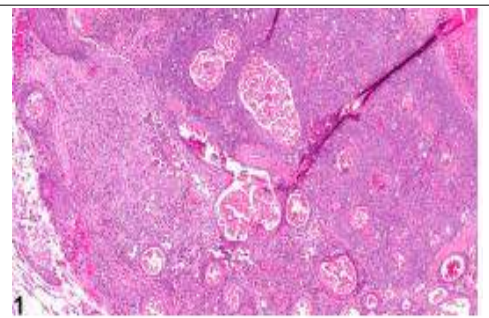
Clitoral gland - Hyperplasia in a female F344/N rat from a chronic study. An area of acinar hyperplasia is sharply demarcated from the adjacent clitoral gland; dilated ducts are also evident.

### Clitoral Gland - Infiltration Cellular (세포 침윤)



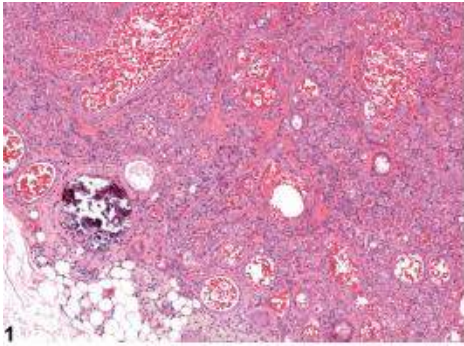
Clitoral gland - Infiltration cellular, Lymphocyte and Plasma cells in a female F344/N rat from a chronic study. An infiltration of lymphocytes and plasma cells is present in the stroma.

### Clitoral Gland - Inflammation (염증)



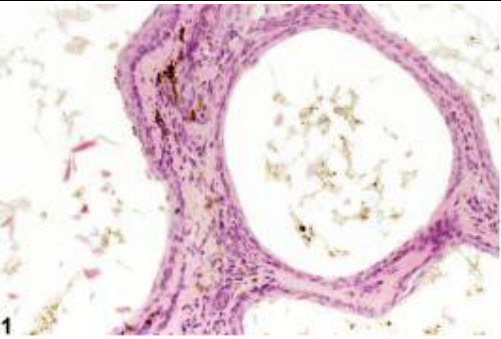
Clitoral gland - Inflammation, Chronic active in a female F344/N rat from a chronic study. An infiltration of lymphocytes, neutrophils, and macrophages is present in the gland parenchyma and around the ducts.

## Clitoral Gland - Mineralization (무기질침착)



Clitoral gland - Mineral in a female F344/N rat from a chronic study. There is focal mineralization within a clitoral gland duct.

## Clitoral Gland - Pigment (색소)



Clitoral gland - Pigment in a female B6C3F1/N mouse from a chronic study. Pigment is evident in the stroma adjacent to dilated ducts.

## 2) 난소

## Ovary - Amyloid (아밀로이드)



Ovary - Amyloid in a female Swiss CD-1 mouse from a chronic study. There are prominent deposits of pale amyloid.

### Ovary - Angiectasis (혈관확장)



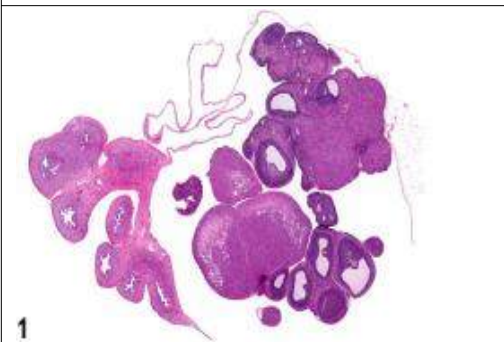
Ovary - Angiectasis, in a female F344/N rat from a chronic study. Dilated, enlarged vascular channels are present throughout the ovarian parenchyma.

### Ovary - Atrophy (위축)



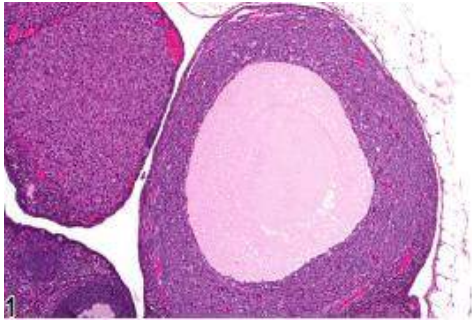
Ovary - Atrophy in a female F344/N rat from a chronic study. The ovary is small and lacking follicles and corpora lutea.

### Ovary, Bursa - Cyst (활액 낭포)



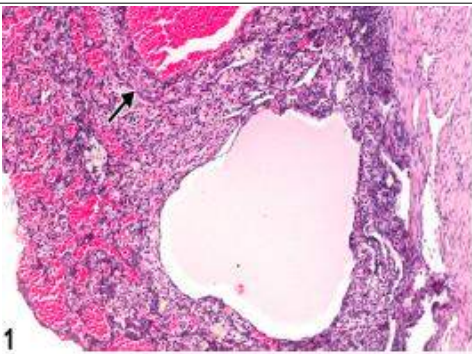
Ovary, Bursa - Cyst in a female F344/N rat from a subchronic study. A large cyst encompasses the ovary.

## Ovary, Corpus Luteum - Cyst (황체 낭포)



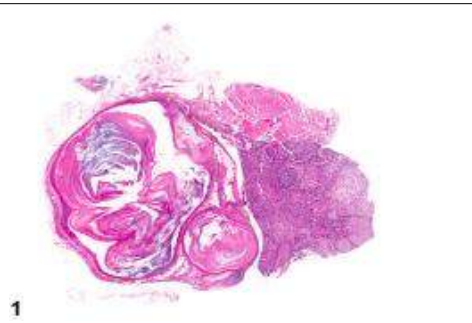
Ovary, Corpus luteum - Cyst in a female F344/N rat from a subchronic study. The cyst is thick walled and fluid filled, and a secondary follicle lined by dark basophilic granulosa cells is present in the adjacent parenchyma.

## Ovary - Cyst (낭포)



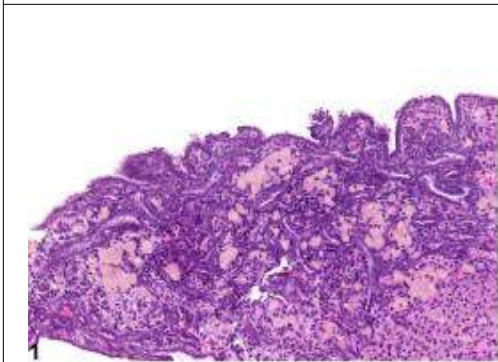
Ovary - Cyst in a female B6C3F1/N mouse from a chronic study. The cyst is adjacent to a hematocyst (arrow), which contains blood.

## Ovary - Cyst, Epithelial (상피 낭포)



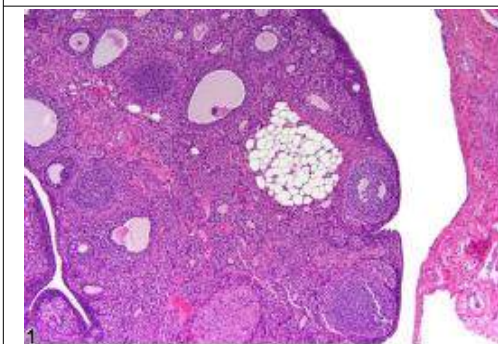
Ovary - Cyst, Epithelial in a female B6C3F1/N mouse from a chronic study. The cyst is compressing adjacent ovarian parenchyma.

Ovary - Epithelium, Hyperplasia (상피 증생)



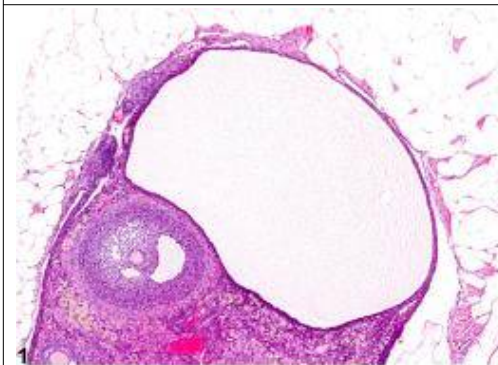
Ovary, Epithelium - Hyperplasia, in a female F344/N rat from a chronic study. There is proliferation of the surface epithelium of the ovary.

Ovary - Fatty Change (지방 변성)



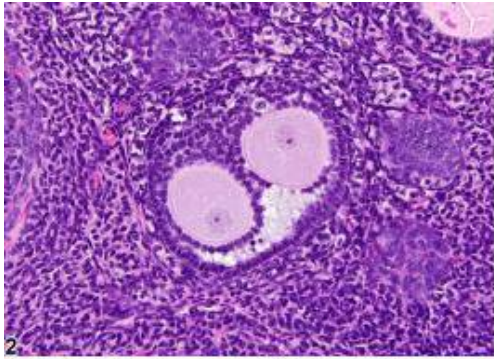
Ovary - Fatty change in a female F344/N rat from a subchronic study. There is focal accumulation of adipocytes in the ovarian parenchyma.

Ovary, Follicle - Cyst (난포 낭포)



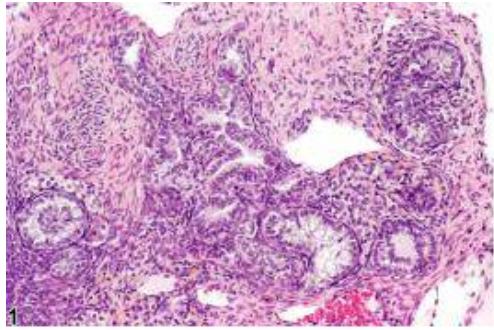
Ovary, Follicle - Cyst in a female B6C3F1/N mouse from a chronic study. A large ovarian follicular cyst appears as a distended fluid-filled space lacking an oocyte.

## Ovary, Follicle - Polyovular (다란성 난포)



Ovary, Follicle - Polyovular in a female B6C3F1/N mouse from a subchronic study. One follicle contains two oocytes, in contrast to the adjacent follicles shown in Figure 1.

## Ovary - Hyperplasia, Sertoliform (세르토리형 증생)



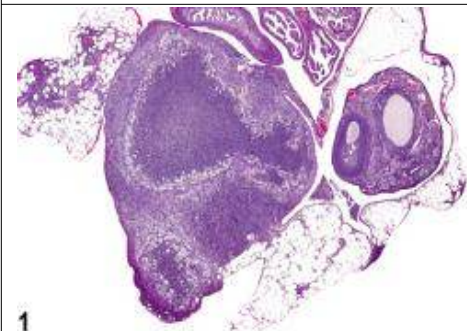
Ovary - Hyperplasia, Sertoliform in a female F344/N rat from a chronic study. The hyperplastic tubules are adjacent to the hilus of the ovary.

## Ovary - Infiltration Cellular (세포 침윤)



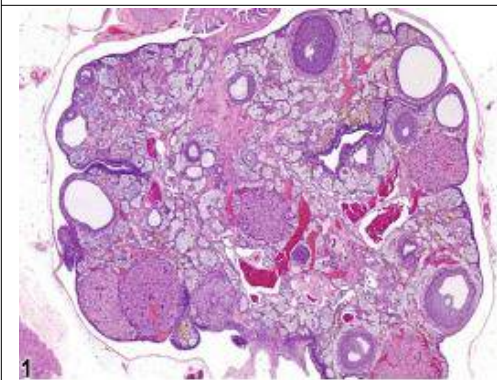
Ovary - Infiltration cellular, Macrophage in a female B6C3F1/N mouse from a chronic study. Macrophages have infiltrated the interstitium of the ovary.

Ovary - Inflammation (염증)



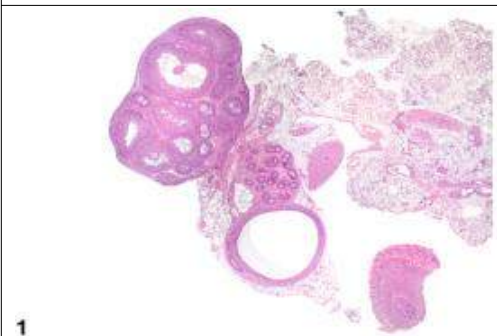
Ovary - Inflammation, Suppurative in a female B6C3F1/N mouse from a chronic study. Large focal accumulations of intact and degenerating neutrophils are present in the ovary.

Ovary, Interstitial Cell - Hyperplasia (간질세포 증생)



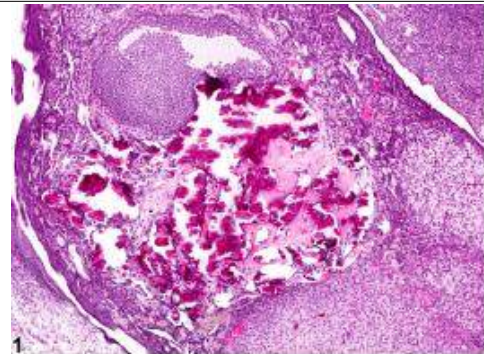
Ovary, Interstitial cell - Hyperplasia in a female F344/N rat from a subchronic study. Clusters of pale interstitial cells are interspersed among follicles.

Ovary - Mesonephric Duct Remnant (중신관 잔류)



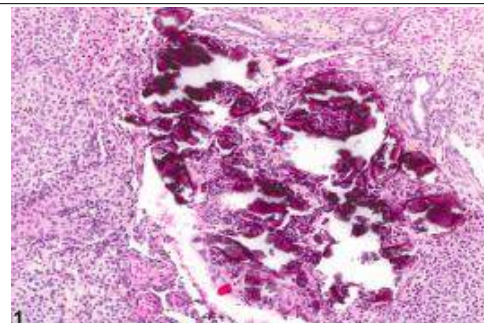
Ovary - Mesonephric duct remnant in a female Wistar Han rat pup from a subchronic study. The cluster of tubules is present in the periovarian tissue.

## Ovary - Metaplasia, Osseous (골화생)



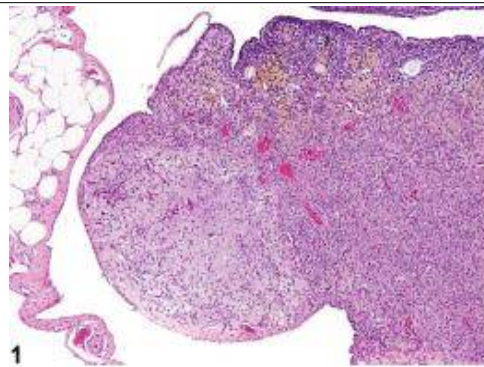
Ovary - Metaplasia, Osseous in a female B6C3F1/N mouse from a chronic study. An area of osteoid is present in the ovarian parenchyma.

## Ovary - Mineral (무기질)



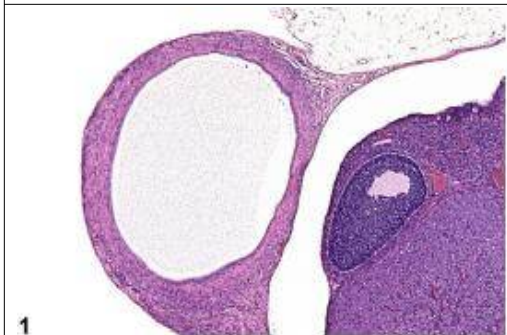
Ovary - Mineral in a female B6C3F1/N mouse from a chronic study. Mineral deposition is present in the ovarian parenchyma.

## Ovary - Necrosis (괴사)



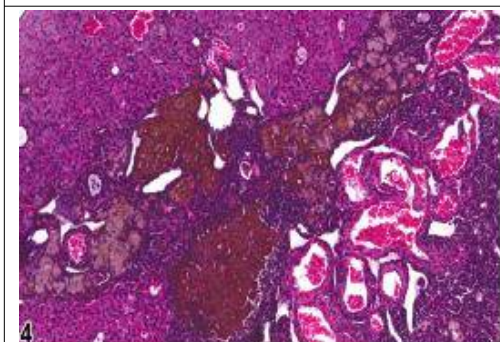
Ovary - Necrosis in a female F344/N rat from a chronic study. The necrotic ovarian tissue is sharply demarcated from the adjacent ovary.

### Ovary, Paraovarian Tissue - Cyst (부난소낭포)



Ovary, Paraovarian tissue - Cyst in a female F344/N rat from a subchronic study. There is a large fluid-filled space in the mesovarium.

### Ovary - Pigment (색소)




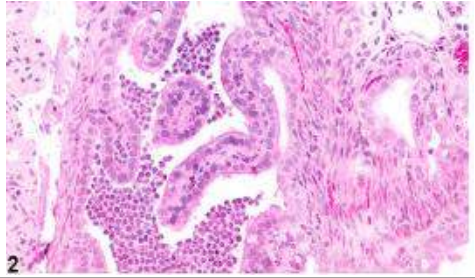
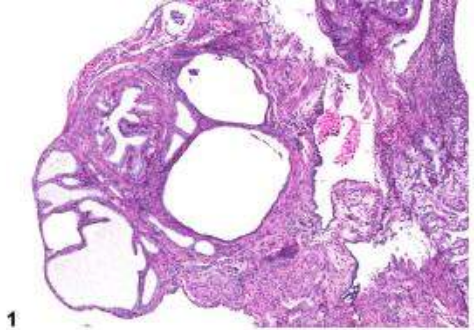
Ovary - Pigment in a female B6C3F1/N mouse from a chronic study. There is brown pigment in the interstitial cells of the ovary.

### Ovary - Thrombosis (혈전)

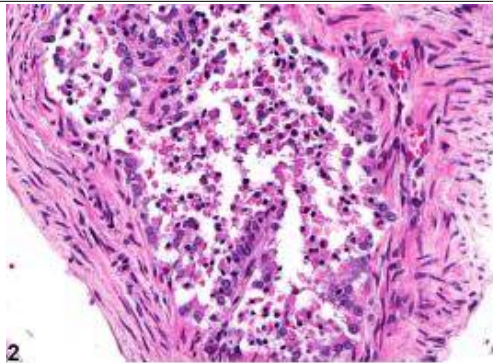


Ovary - Thrombosis in a female B6C3F1/N mouse from a chronic study. A large thrombus occupies the majority of an ovary.

## 3) 난관

<p>Oviduct - Atrophy (위축)</p> 	<p>Oviduct - Atrophy in a female B6C3F1/N mouse from a chronic study. The fimbria in the infundibulum are small and collapsed (arrow) and the folds of epithelium in the isthmus are blunted (asterisk).</p>
<p>Oviduct - Inflammation (염증)</p> 	<p>Oviduct - Inflammation, Acute in a female B6C3F1/N mouse from a chronic study. There are many neutrophils in the oviduct lumen.</p>
<p>Oviduct - Mesonephric Duct Remnant (중신관 잔류)</p> 	<p>Oviduct - Mesonephric duct remnant in a female B6C3F1/N mouse from a chronic study. Multiple cross sections of cystic structures are adjacent to the oviduct.</p>

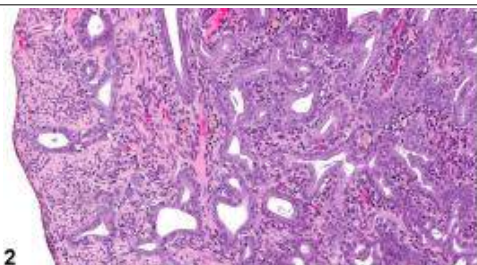
#### Oviduct - Necrosis (괴사)



Oviduct - Necrosis in a female Harlan Sprague-Dawley rat from a chronic study. There is sloughing of necrotic epithelial cells into the lumen of the oviduct.

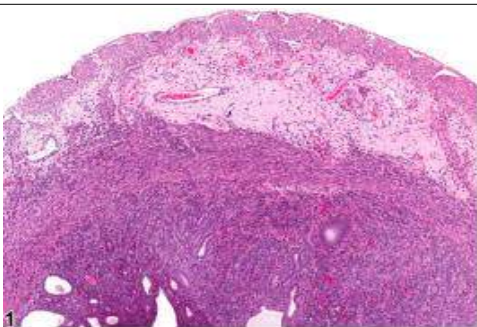
#### 4) 자궁

#### Uterus - Adenomyosis (선근종증)



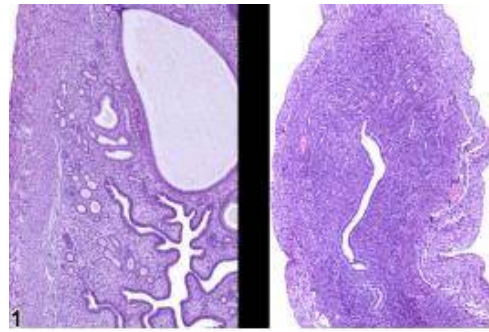
Uterus - Adenomyosis in a female Harlan Sprague-Dawley rat from a chronic study. There are well-differentiated glands within the myometrium.

#### Uterus - Amyloid (아밀로이드)



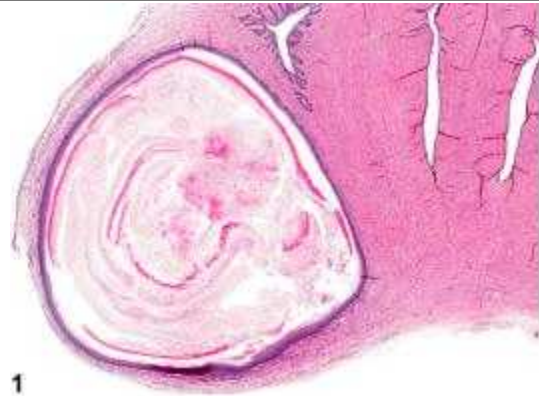
Uterus - Amyloid deposition in a female Swiss Webster mouse from a chronic study. There is an amorphous, eosinophilic, pale-staining material in the myometrium.

## Uterus - Atrophy



Uterus - Atrophy in a female B6C3F1/N mouse from a subchronic study (right image; left image is control). The uterus of the treated animal (right) is atrophic compared with that of a control animal (left). Image provided courtesy of Dr. R. Miller.

## Uterus, Cervix - Cyst, Squamous (자궁경 편평상피 낭포)



Uterus, Cervix - Cyst, Squamous in a female F344/N rat from a chronic study. There is a cyst lined by squamous epithelium adjacent to the uterine cervix.

## Uterus - Decidual Reaction (탈락막 반응)



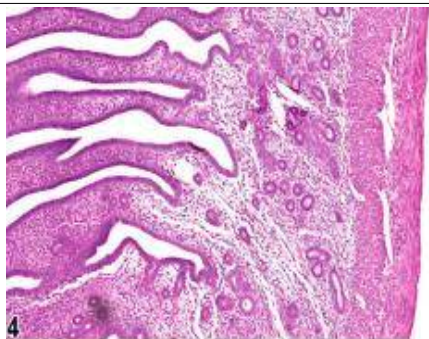
Uterus - Decidual reaction in a female F344/N rat from a chronic study. There is an area of decidual reaction in the uterus.

### Uterus - Dilation (확장)



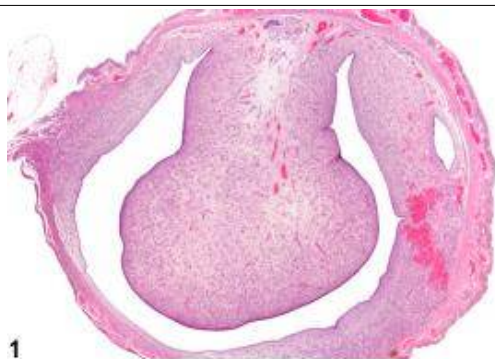
Uterus - Dilation of the uterine lumen in a female B6C3F1/N mouse from a chronic study. There is dilation of the uterine horn.

### Uterus - Edema (부종)



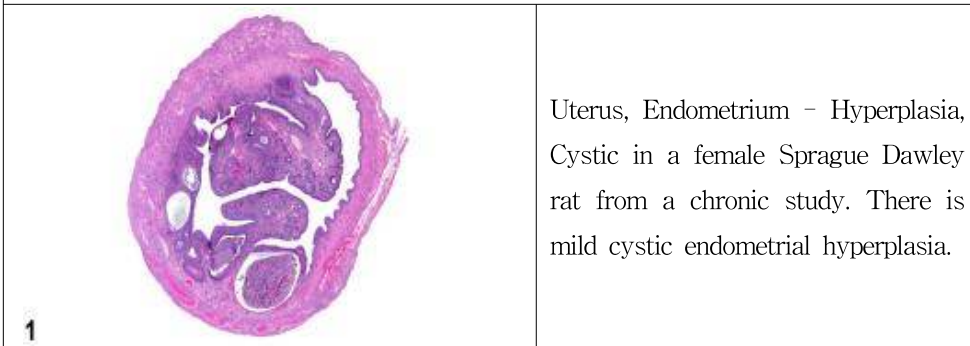
Uterus - Edema in a female B6C3F1/N mouse from a chronic study. There is edema of the endometrium characterized by an increase in the intercellular spaces.

### Uterus - Endometrial Stromal Polyp (자궁내막 기질 폴립)

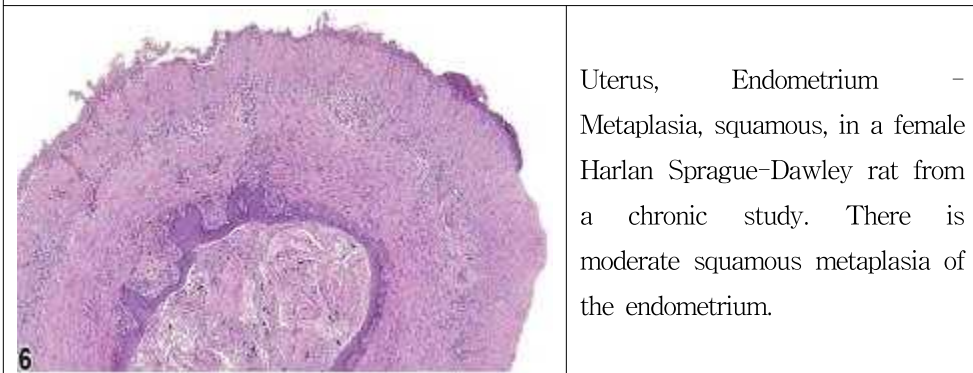


Uterus - Endometrial stromal polyp in a female Sprague-Dawley rat from a chronic study. A pedunculated polyp is present in the uterine lumen

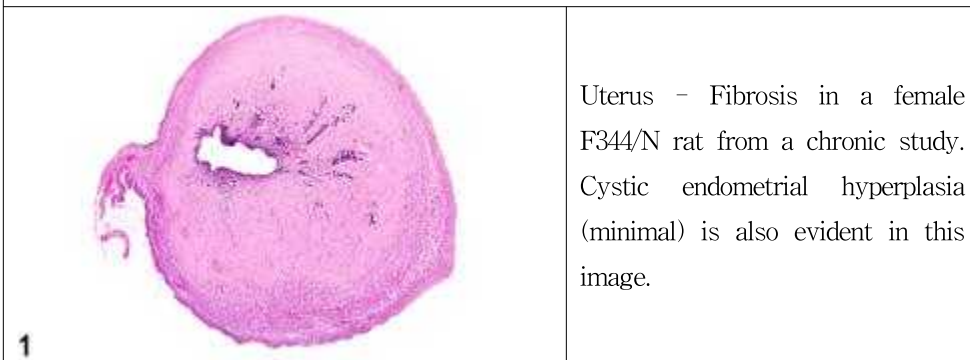
### Uterus, Endometrium - Hyperplasia, Cystic



### Uterus, Endometrium - Metaplasia, Squamous (편평상피 화생)



### Uterus - Fibrosis (섬유화)

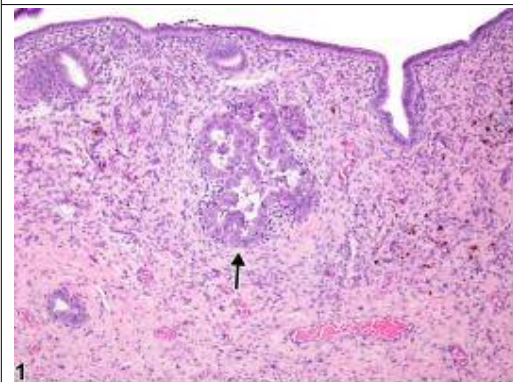


Uterus - Hemorrhage (출혈)



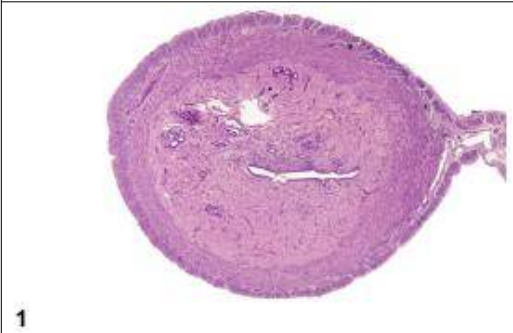
Uterus - Hemorrhage in a female F344/N rat from a chronic study. There is accumulation of blood in the uterine lumen.

Uterus - Hyperplasia, Atypical (비정형 자궁내막 증생)



Uterus, Endometrium - Hyperplasia, Atypical in a female Wistar Han rat from a chronic study. The glandular epithelium projects into the glandular lumen (arrow), forming multiple thickened infoldings and projections.

Uterus - Hyperplasia, Stromal (기질 증생)



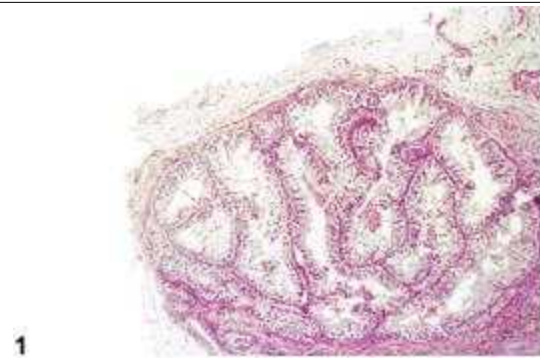
Uterus - Hyperplasia, Stromal in a female F344/N rat from a chronic study. There is stromal hyperplasia of the endometrium with concomitant thickening of uterine wall.

## Uterus - Inflammation (염증)



Uterus - Inflammation, Suppurative in a female B6C3F1/N mouse from a chronic study. An area of suppurative inflammation is present in the myometrium, with many degenerating neutrophils.

## Uterus - Mesonephric Duct Remnant (중신관 잔류)



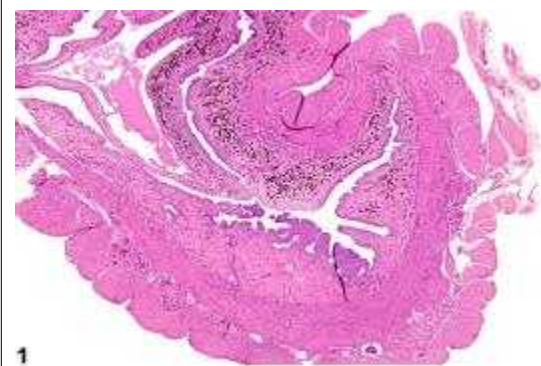
Uterus - Mesonephric duct remnant in a female Osborne Mendel rat from a chronic study. Tubules lined by pseudostratified columnar epithelium and smooth muscle are adjacent to the uterus.

## Uterus - Necrosis (괴사)



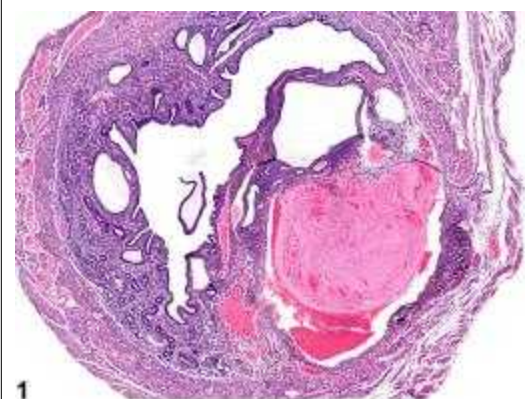
Uterus - Necrosis in a female F344/N rat from a chronic study. Fibrosis and mineralization are present in the necrotic uterine tissue.

Uterus - Pigment (색소)



Uterus - Pigment in a female F344/N rat from a chronic study. There is brown pigment in the endometrium.

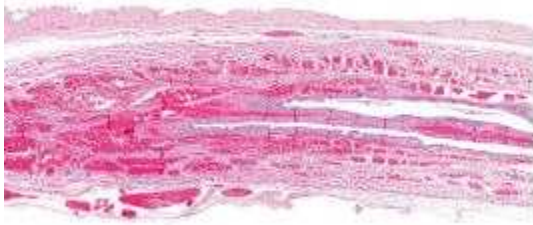
Uterus - Thrombus (혈전)



Uterus - Thrombus in a female B6C3F1/N mouse from a chronic study. A large thrombus is evident in the myometrium.

## 5) 질

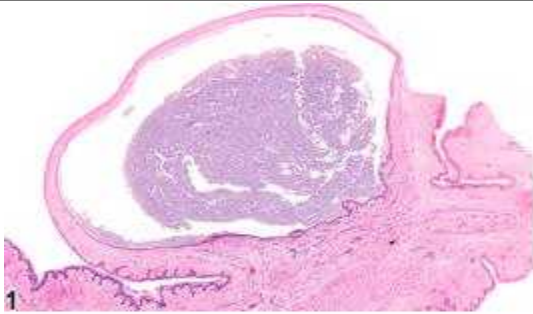
## Vagina - Angiectasis (혈관확장)



1

Vagina - Angiectasis in a female F344/N rat from a chronic study. Dilated blood vessels are present in the wall of the vagina.

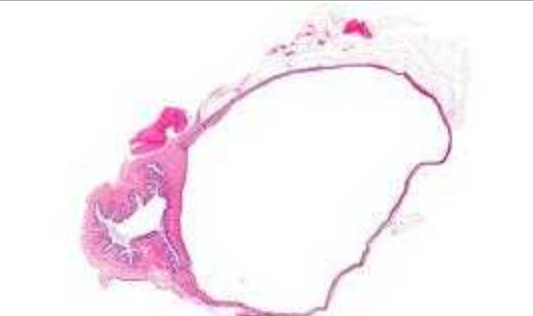
## Vagina - Cyst (낭포)



1

Vagina - Cyst in a female F344/N rat from a chronic study. A prominent thin-walled cyst is present in the vaginal wall.

## Vagina - Dilation (확장)



1

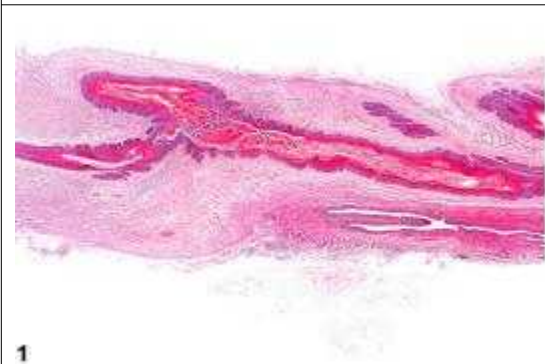
Vagina - Dilation in a female F344/N rat from a chronic study. There is dilation of the vagina.

Vagina, Epithelium - Hyperplasia (상피세포 증생)



Vagina, Epithelium - Hyperplasia in a female B6C3F1/N mouse from a chronic study. There is a focal area of basal cell hyperplasia.

Vagina - Fibrosis (섬유화)



Vagina - Fibrosis in a female B6C3F1/N mouse from a chronic study. Increased fibrous tissue is present in the vagina wall.

Vagina - Hypertrophy, Stromal (기질 증대)



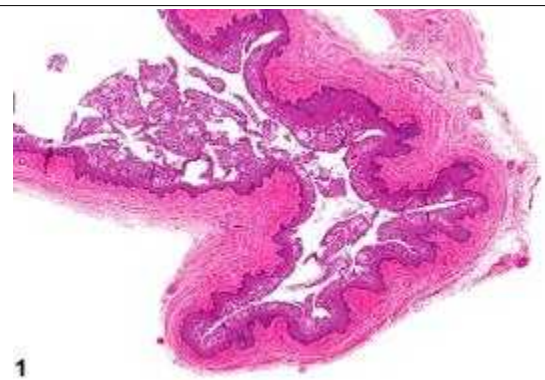
Vagina - Hypertrophy, Stromal in a female F344/N rat from a chronic study. Thickening of the wall of the vagina is due to stromal hypertrophy.

## Vagina - Inflammation (염증)



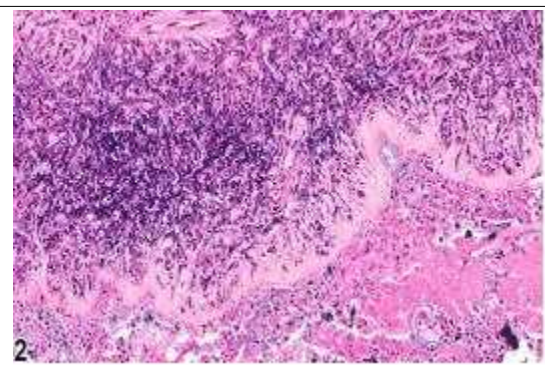
Vagina - Inflammation, Chronic active in a female B6C3F1/N mouse from a chronic study. Chronic active inflammation is present in a focal area of epithelial erosion.

## Vagina - Mucification (점액 분비기)



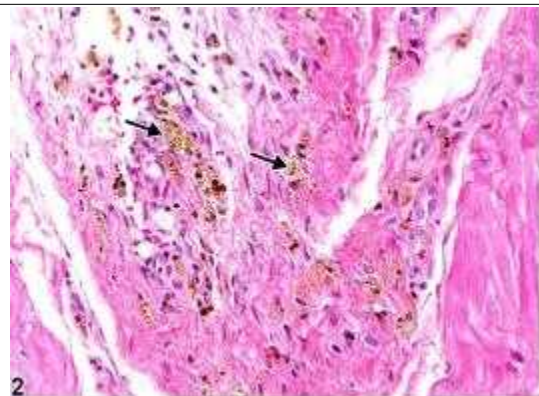
Vagina - Mucification in a female Harlan Sprague-Dawley rat from a chronic study. The epithelium of the vagina is superficially mucified.

## Vagina - Necrosis (괴사)



Vagina - Necrosis, Epithelial in a female Harlan Sprague-Dawley rat from a chronic study. There is necrosis of the vagina and an associated inflammatory response.

### Vagina - Pigment (색소)



Vagina - Pigment in a female F344/N rat from a chronic study. There is golden brown pigment in the cells and interstitium of the vagina (arrows).

### Vagina - Ulcer (꺾양)

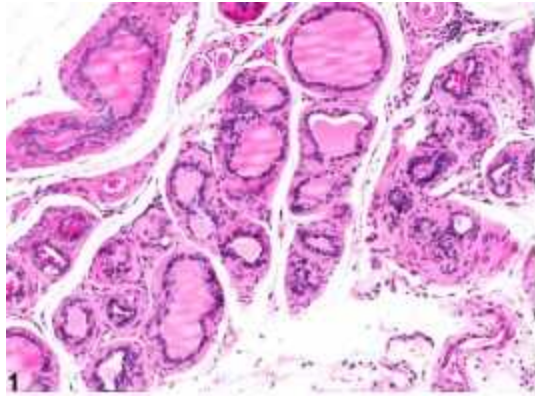


Vagina - Ulcer in a female Harlan Sprague-Dawley rat from a chronic study. There is a focal area of ulceration of the vagina epithelium.

## 10. 수컷 생식기계

## 1) 응고선

## Coagulating Gland - Atrophy (위축)



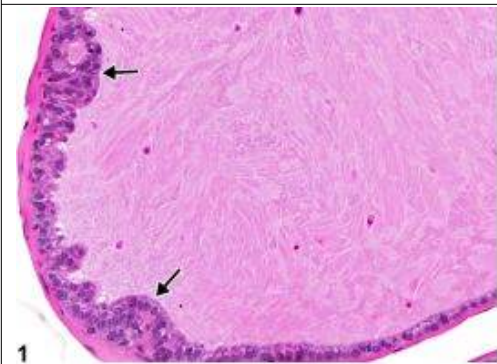
Coagulating Gland - Atrophy.  
Atrophy of the coagulating gland  
in a male B6C3F1 mouse from a  
chronic study.

## Coagulating Gland - Dilation, Acinar (선방 확장)



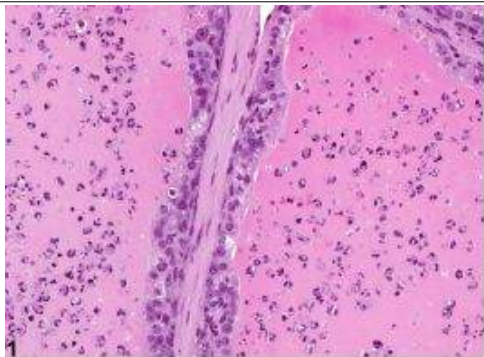
Coagulating Gland - Dilation,  
Acinar. Acinar dilation of the  
coagulating gland in a male  
B6C3F1 mouse from a chronic  
study.

### Coagulating Gland - Hyperplasia (증생)



Coagulating Gland - Hyperplasia. Arrows indicate bulging of hyperplastic epithelium into the acinar lumen in a male B6C3F1 mouse from a chronic study.

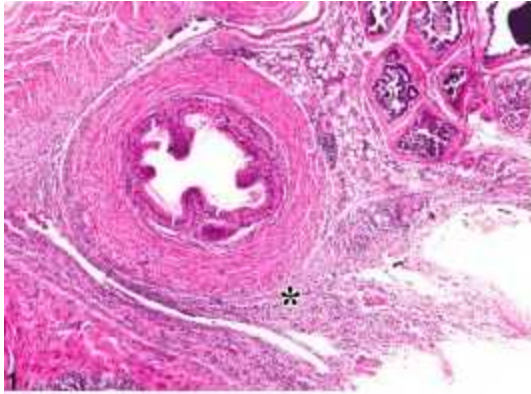
### Coagulating Gland - Inflammation (염증)



Coagulating Gland - Inflammation. Acute inflammation in a male B6C3F1 mouse from a chronic study.

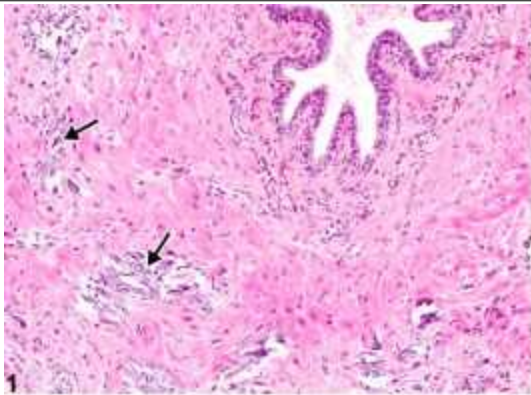
## 2) 정관

## Ductus Deferens - Inflammation (염증)



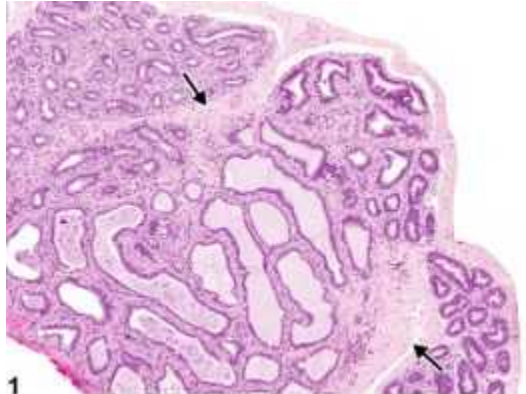
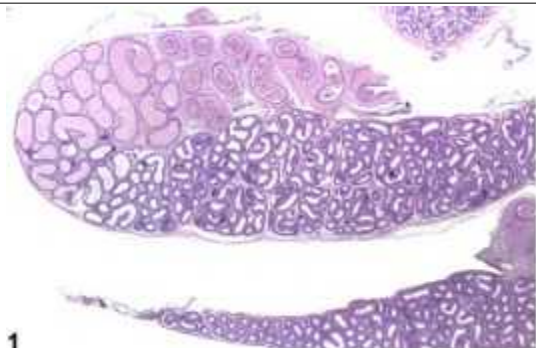

Ductus Deferens - Inflammation. Asterisk indicates infiltration of inflammatory cells in the muscle and surrounding tissue in a male B6C3F1 mouse from a chronic study.

## Ductus Deferens - Mineralization (무기질침착)

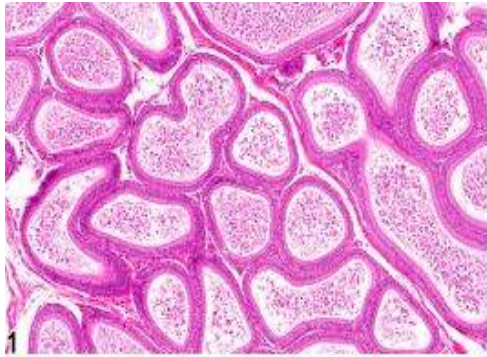


Ductus Deferens - Mineralization. Arrows indicate granular to amorphous mineral deposits in a male B6C3F1 mouse from a chronic study.

### 3) 부고환

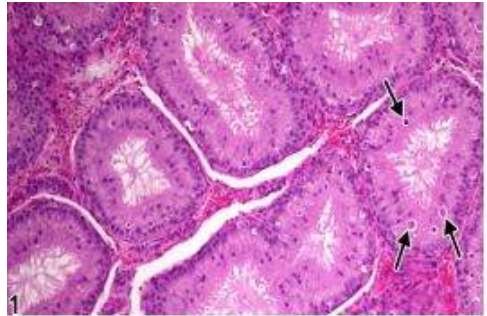
Epididymis - Amyloid (아밀로이드)	
	<p>Epididymis - Amyloid. Amyloid deposits in the interstitium (arrows) in a male B6C3F1 mouse from a chronic study.</p>
Epididymis, Duct - Atrophy (위축)	
	<p>Epididymis, Duct - Atrophy. Decreased diameter of empty ducts in the body and tail of the epididymis in a male F344/N rat from a subchronic study.</p>
Epididymis, Duct - Dilation (확장)	
	<p>Epididymis, Duct - Dilation. Segmental dilation of ducts in the epididymis of a rat.</p>

## Epididymis, Duct - Exfoliated Germ Cell (박리된 생식세포)



Epididymis, Duct - Exfoliated Germ Cell. Sloughed testicular germ cells and cellular debris in the epididymal ducts in a male F344/N rat from a subchronic study.

## Epididymis, Epithelium - Apoptosis (세포자멸사)



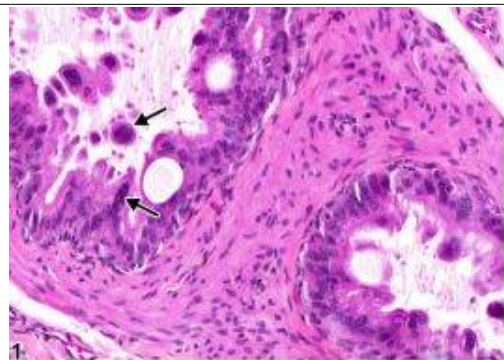
Epididymis, Epithelium - Apoptosis. Numerous apoptotic cells (arrows) are present in the epididymal epithelium of a rat. (Photograph courtesy of D. Creasy.)

## Epididymis, Epithelium - Degeneration (변성)



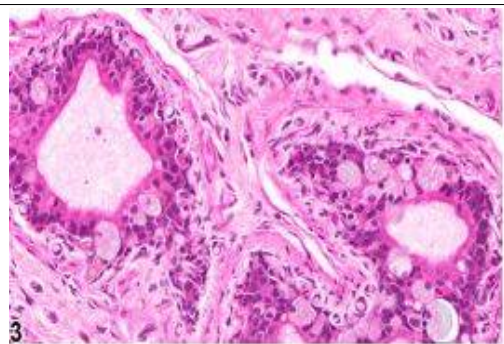
Epididymis, Epithelium - Degeneration. Sloughed epididymal epithelium in the duct lumen in a B6C3F1 mouse from a chronic study

Epididymis, Epithelium - Karyomegaly (거대핵)



Epididymis, Epithelium - Karyomegaly. Atypical enlarged nuclei (arrows) in the epididymal epithelium in a male B6C3F1 mouse from a chronic study.

Epididymis, Epithelium - Vacuolation (공포)



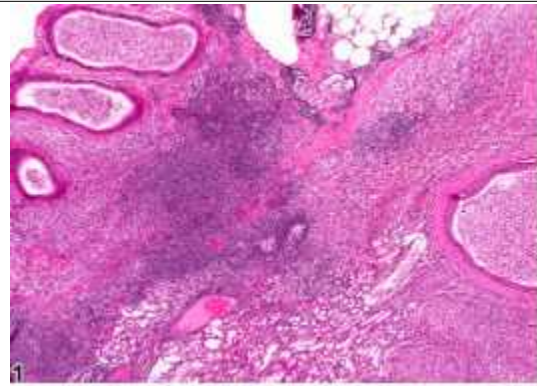
Epididymis, Epithelium - Vacuolation. Numerous macrovesicular cytoplasmic vacuoles are present in the ductal epithelium in a male F344/N rat from a chronic study.

Epididymis - Hypospermia (정자감소증)



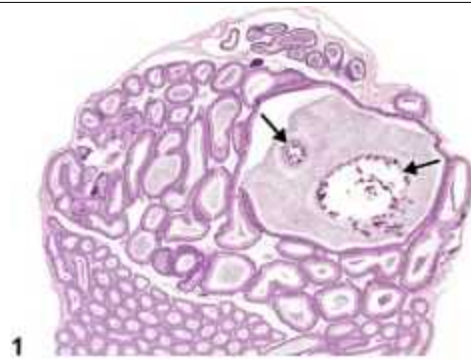
Epididymis - Hypospermia. A reduced number of sperm in the epididymis in a male B6C3F1 mouse from a subchronic study.

## Epididymis - Inflammation (염증)



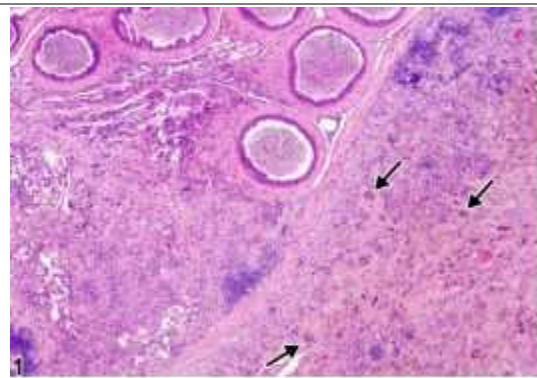
Epididymis - Inflammation. Chronic inflammation with lymphoid aggregates in the epididymis in a male B6C3F1 mouse from a chronic study.

## Epididymis - Spermatocele (정액류)



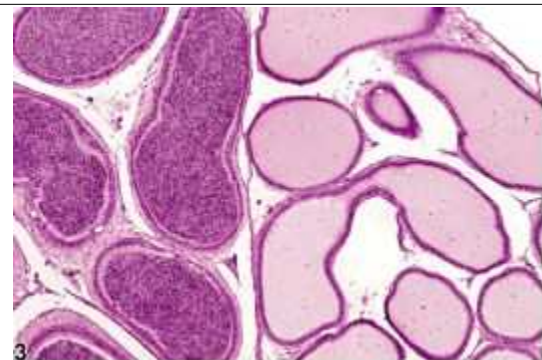
Epididymis - Spermatocele. A sperm-filled dilated duct in the head of the epididymis, with focal areas of mineralization (arrows), in a male B6C3F1 mouse from a subchronic study.

## Epididymis - Sperm Granuloma (정자 육아종)



Epididymis - Sperm Granuloma. Giant cells are present in the sperm granuloma (arrows) in a male B6C3F1 mouse from a chronic study.

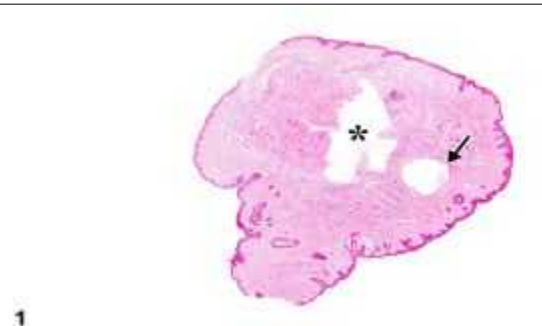
### Epididymis - Sperm Stasis (정자 정체)



Epididymis - Sperm Stasis. Sperm stasis is present on the left and ducts without sperm on the right in a male B6C3F1 mouse from a subchronic study.

## 4) 음경

### Penis - Fibrosis (섬유화)



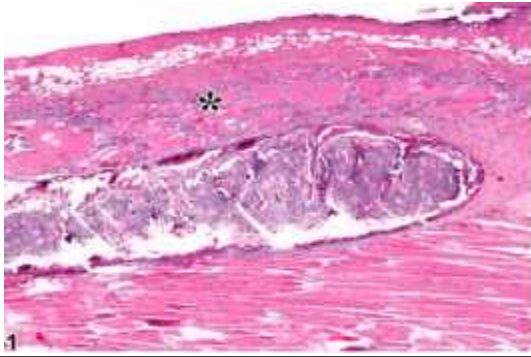
Penis - Fibrosis. The large space (asterisk) is an artifact. The urethra is markedly dilated (arrow) in a male B6C3F1 mouse from a chronic study.

### Penis, Epithelium - Hyperplasia (상피 증생)



Penis, Epithelium - Hyperplasia. Arrow indicates papillary proliferation of squamous epithelium in a male B6C3F1 mouse from a chronic study.

## Penis - Inflammation (염증)



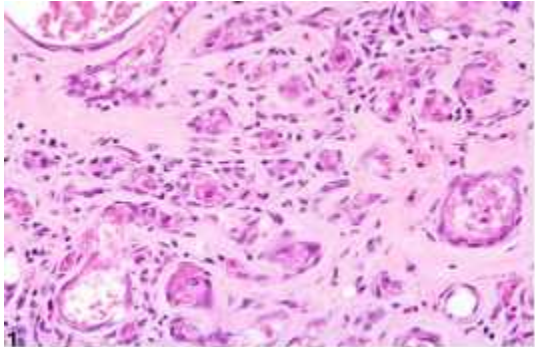
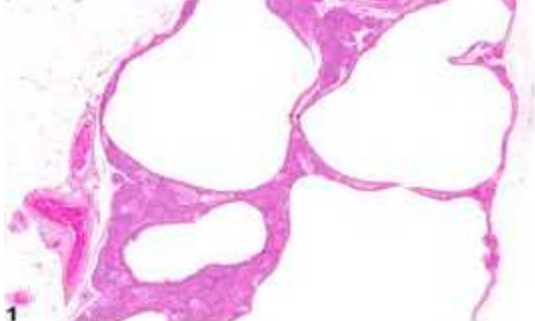
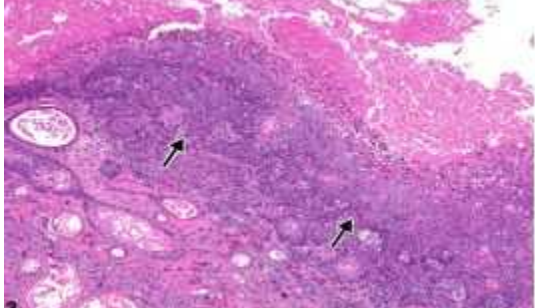
Penis - Inflammation. Asterisk indicates chronic inflammation in a male B6C3F1 mouse from a chronic study.

## Penis, Prepuce - Inflammation (표피 염증)

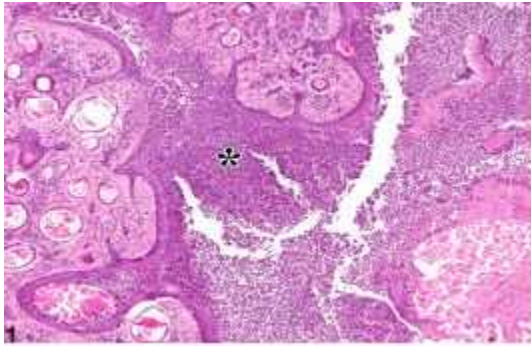


Prepuce - Inflammation. Asterisk indicates acute inflammation associated with necrosis of overlying epithelium (arrow) in a F344/N rat from a chronic study.

## 5) 표피선

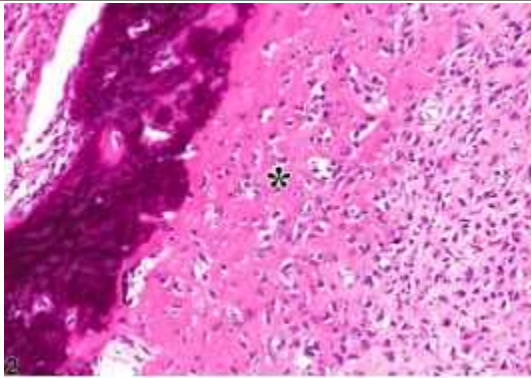
Preputial Gland - Atrophy (위축)	 <p>Preputial Gland - Atrophy in a male F344/N rat from a chronic study. There are small collections of epithelial cells surrounded by thick bands of fibrosis.</p>
Preputial Gland, Duct - Dilation (확장)	 <p>Preputial Gland, Duct - Dilation. Ductular dilation in a male B6C3F1 mouse from a subchronic study.</p>
Preputial Gland - Hyperplasia (증생)	 <p>Preputial Gland, Duct - Hyperplasia. Arrows indicate hyperplastic squamous epithelium with an anastomosing trabecular pattern in a male F344/N rat from a chronic study.</p>

## Preputial Gland - Inflammation (염증)



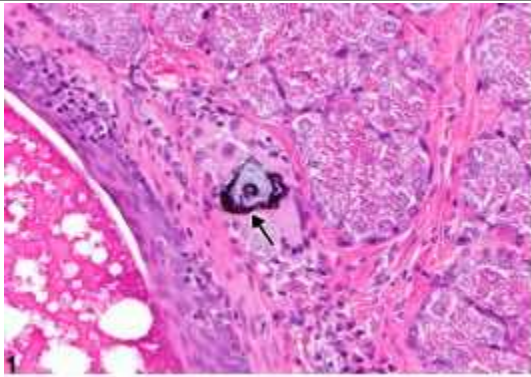
Preputial Gland - Inflammation. Asterisk indicates cellular exudates in a male F344/N rat from a chronic study.

## Preputial Gland - Metaplasia, Osseous (골화생)



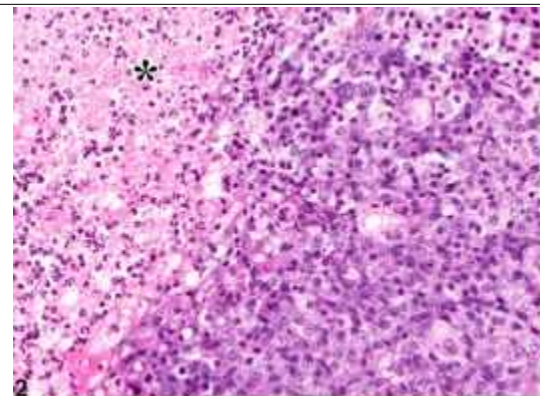
Preputial Gland - Metaplasia, Osseous. Asterisk indicates osteoid formation with deep basophilic staining of mineralized osteoid in a male F344/N rat from a chronic study.

## Preputial Gland - Mineralization (무기질침착)



Preputial Gland - Mineralization. Arrow indicates mineral deposits in a male F344/N rat from a subchronic study.

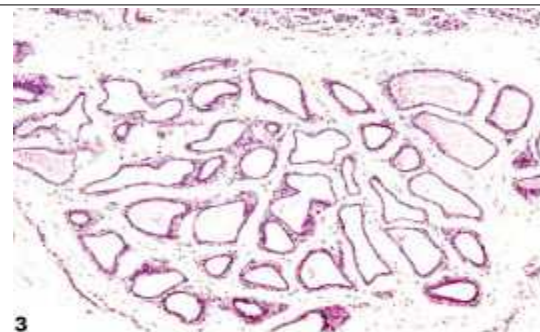
Preputial Gland - Necrosis (괴사)



Preputial Gland - Necrosis. Asterisk indicates accumulation of cellular, pyknotic, and karyorrhectic debris from a male F344/N rat in a chronic study.

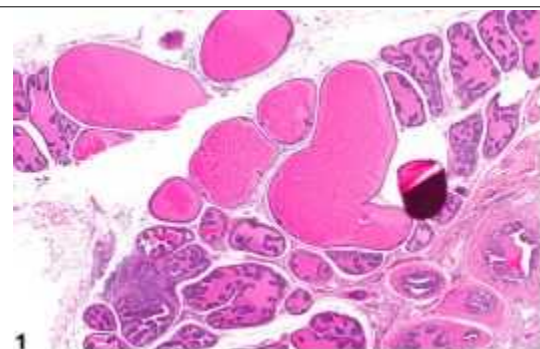
6) 전립선

Prostate, Acinus - Atrophy (위축)



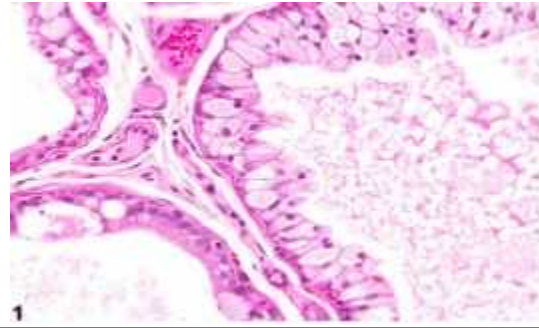
Prostate, Acinus - Atrophy. Decreased acinar size and absence of secretion are evident in this prostate in a male F344/N rat from a subchronic study.

Prostate, Acinus - Dilation (확장)



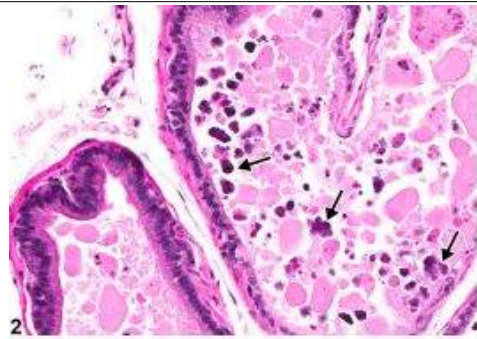
Prostate, Acinus - Dilation. Acinar dilation in a male F344/N rat from a chronic study.

## Prostate, Epithelium - Degeneration (변성)



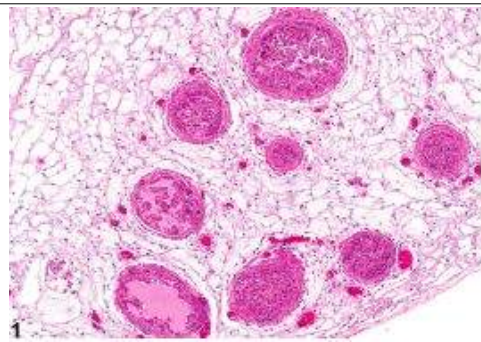
Prostate, Epithelium - Degeneration. Degeneration of the epithelium in the prostate in a male F344/N rat from a chronic study.

## Prostate, Acinus - Secretory alteration (concretions) (결석)



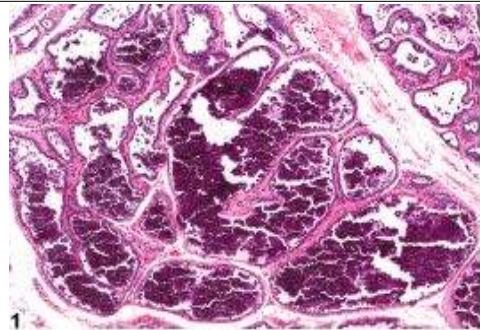
Prostate, Acinus - Secretory Alteration. Mineralization of some concretions (arrows) in a male F344/N rat from a chronic study.

## Prostate - Edema (부종)



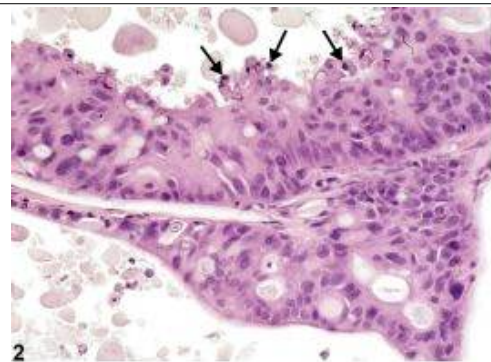
Prostate - Edema. Edema of the prostate from a male F344/N rat in a chronic study.

Prostate - Mineralization (무기질침착)



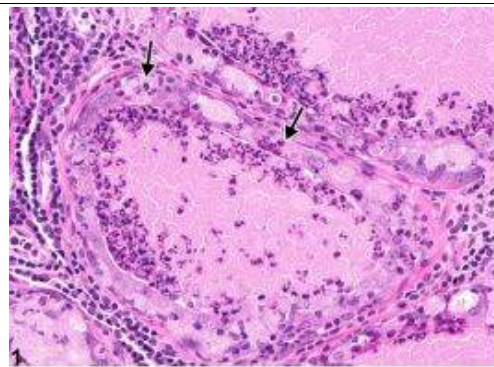
Prostate - Mineralization. Mineralization of the prostate in a male Osborne-Mendel rat from a chronic study.

Prostate, Epithelium - Hyperplasia (증생)



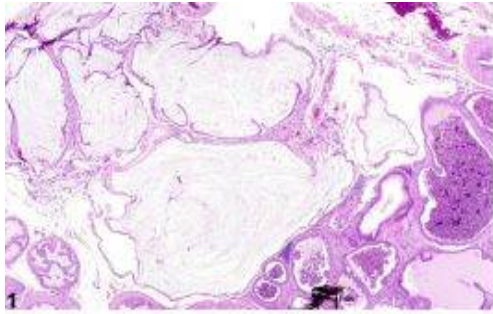
Prostate, Epithelium - Hyperplasia. Higher magnification of Figure 1. Proliferative epithelial cells have formed a thickened lining of the affected acini, and there is evidence of associated apoptosis (arrows) in a male F344/N rat from a chronic study.

Prostate - Inflammation (염증)



Prostate - Inflammation. Arrows indicate neutrophils passing through the acinar mucosa in a male F344/N rat from a chronic study.

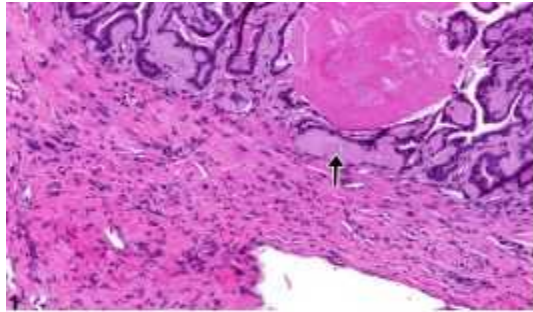
## Prostate, Acinus - Cyst (낭포)



Prostate, Acinus - Cyst, Mucinous.  
Mucinous cyst in a male F344/N rat  
from a chronic study.

## 7) 정낭

## Seminal Vesicle - Amyloid (아밀로이드)



Seminal Vesicle - Amyloid.  
Arrow indicates amyloid deposits  
in a male B6C3F1 mouse from a  
chronic study.

## Seminal Vesicle - Atrophy (위축)



Seminal Vesicle - Atrophy.  
Atrophy of the seminal vesicle in  
a male B6C3F1 mouse from a  
subchronic study.

### Seminal Vesicle - Dilation (확장)

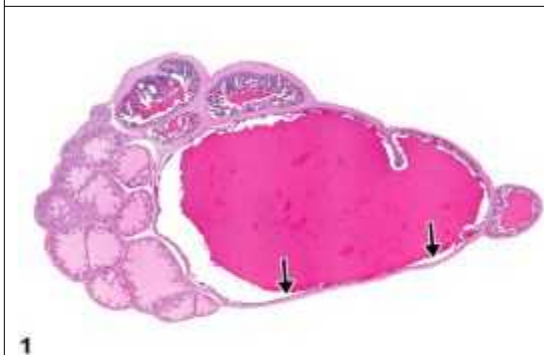
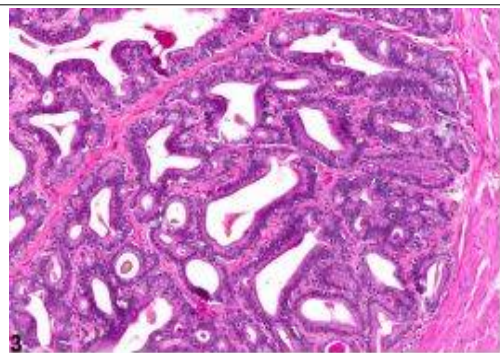


Image of dilation in the seminal vesicle from a male F344/N rat in an chronic study

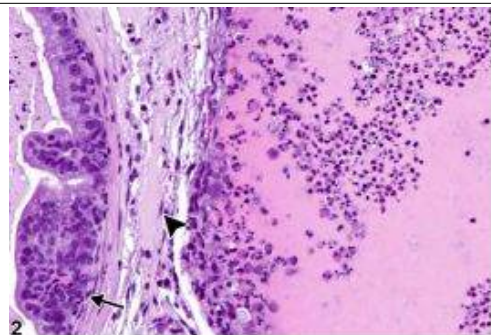
Seminal Vesicle - Dilation. Arrows indicate flattened epithelium in the distended acinus in a male F344/N rat from a chronic study.

### Seminal Vesicle, Epithelium - Hyperplasia (상피세포 증생)



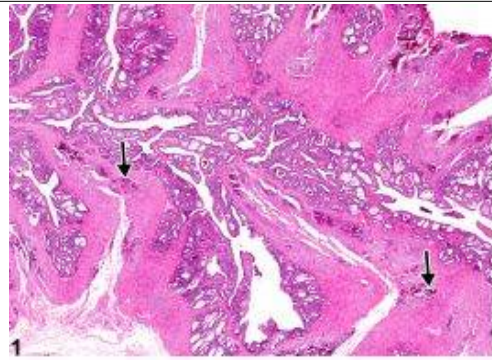
Seminal Vesicle, Epithelium - Hyperplasia. Hyperplasia of seminal vesicle epithelium in a male F344/N rat from a chronic study.

### Seminal Vesicle - Inflammation (염증)



Seminal Vesicle - Inflammation. Arrow indicates an area of hyperplasia, and arrowhead points to epithelial necrosis in a male B6C3F1 mouse from a chronic study.

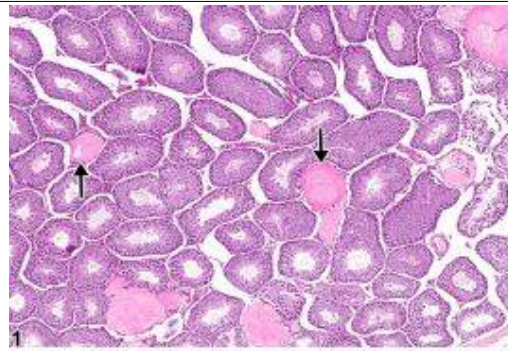
## Seminal Vesicle - Mineralization (무기질침착)



Seminal Vesicle - Mineralization. Arrows indicate multifocal mineral deposits in a male F344/N rat from a chronic study.

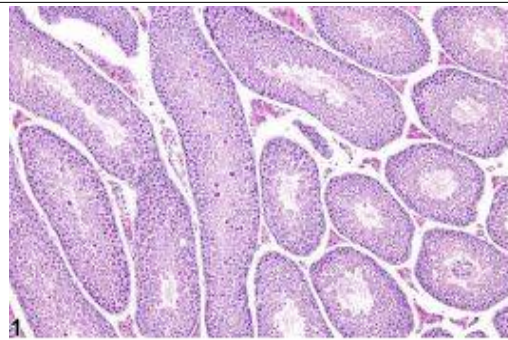
## 8) 고환

## Testis - Amyloid (아밀로이드)



Testis - Amyloid in a male B6C3F1 mouse from a chronic study. There are perivascular accumulations of homogenous, eosinophilic material in the interstitium (arrows).

## Testis - Atypical Residual Bodies (비정형 잔류물)



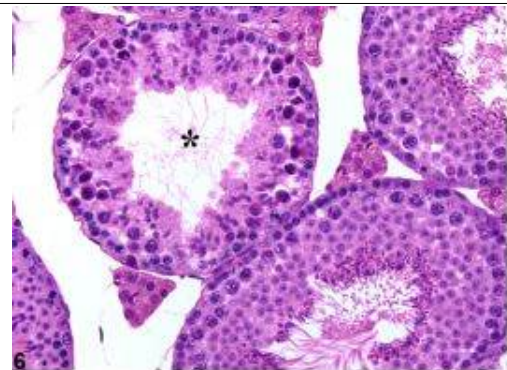
Testis - Atypical residual bodies in a B6C3F1 mouse from a subchronic study. Seminiferous tubules show atypical residual bodies.

### Testis - Fibrosis (섬유화)



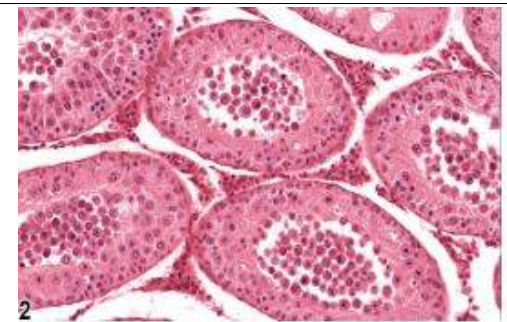
Testis - Fibrosis in a male Swiss CD-1 mouse from a chronic study. Fibrosis (asterisk) with extension into the tunica albuginea.

### Testis, Germ Cell - Degeneration (종자세포 변성)



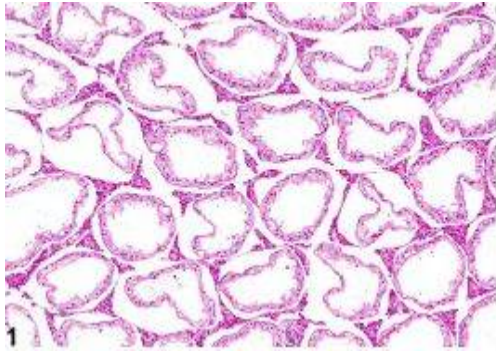
Testis, Germ cell - Degeneration in a male BALB/c mouse 12 hours after exposure. Germ-cell-specific degeneration of pachytene spermatocytes in a stage X tubule (asterisk).

### Testis, Germ Cell - Exfoliation (종자세포 탈락)



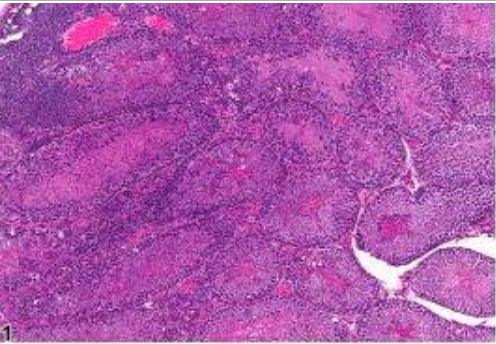
Testis, Germ cell - Exfoliation in a male Harlan Sprague-Dawley rat. Higher magnification of Figure 1 showing germ cells in seminiferous tubule lumens.

### Testis, Germinal Epithelium - Atrophy (종자상피 위축)



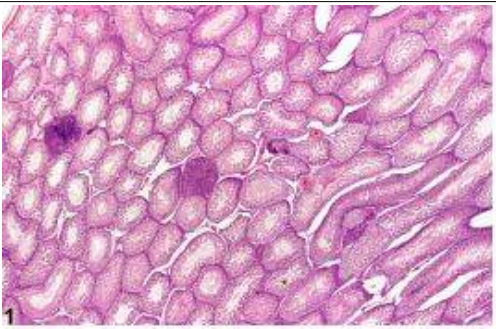
Testis, Germinal epithelium - Atrophy in a male F344/N rat from a subchronic study. Seminiferous tubules are lined only by Sertoli cells.

### Testis - Inflammation (염증)



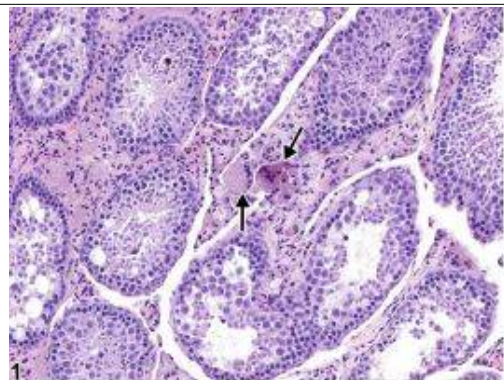
Testis - Inflammation in a male B6C3F1 mouse from a chronic study. Acute inflammation of the testis.

### Testis, Interstitial Cell - Hyperplasia (간질세포 증생)



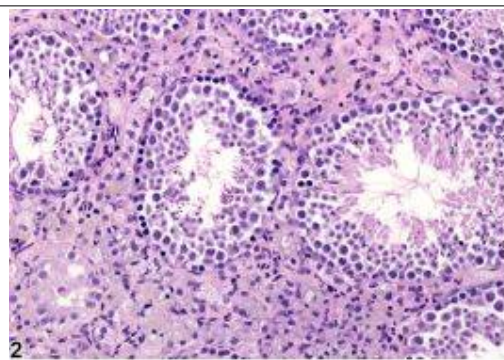
Testis, Interstitial cell - Hyperplasia in a male F344/N rat from a chronic study. Two focal areas of hyperplasia are present in the testis.

### Testis, Interstitial Cell - Syncytial Cells (간질세포 합포체)



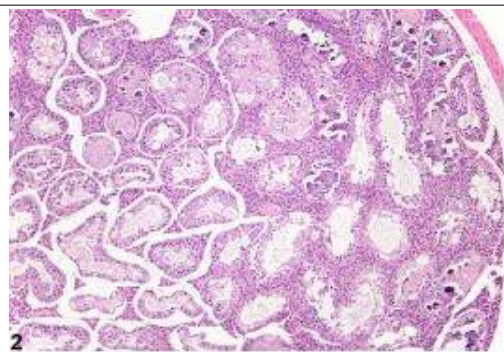
Testis, Interstitial cell - Vacuolation in a male FVB/N transgenic mouse from a chronic study. There are interstitial syncytial cells (arrows).

### Testis, Interstitial Cell - Vacuolation (간질세포 공포)



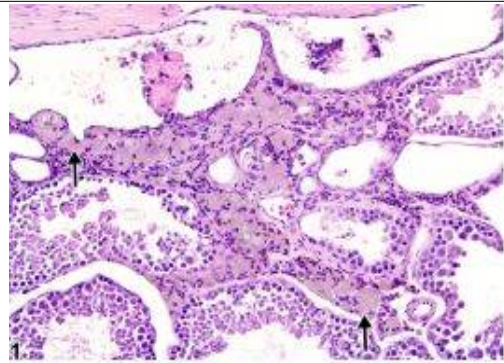
Testis, Interstitial cell - Vacuolation in a male FVB/N transgenic mouse from a chronic study. This higher magnification of Figure 1 shows the vacuolation of interstitial cells.

### Testis - Mineralization (무기질 침착)



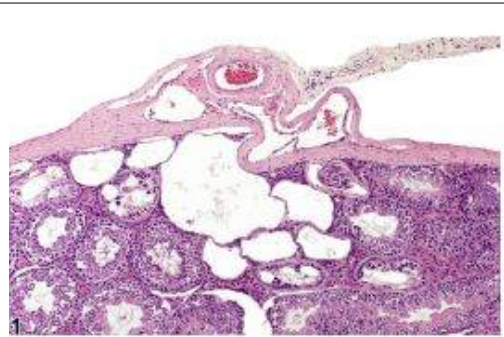
Testis - Mineralization in a male B6C3F1 mouse from a subchronic study. Mineralization involving seminiferous tubules.

## Testis - Pigment (색소)



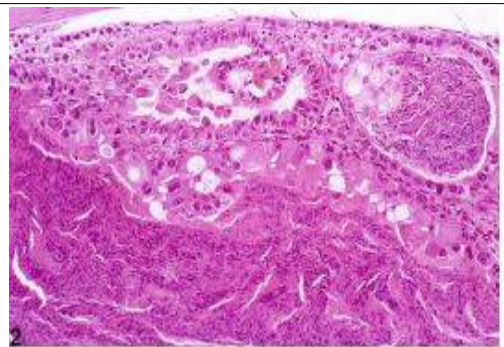
Testis - Pigment in a male B6C3F1 mouse from a chronic study. Intracytoplasmic accumulation of ceroid (lipofuscin) pigment (arrows) in interstitial cells.

## Testis, Rete Testis - Dilation (고환그물 확장)



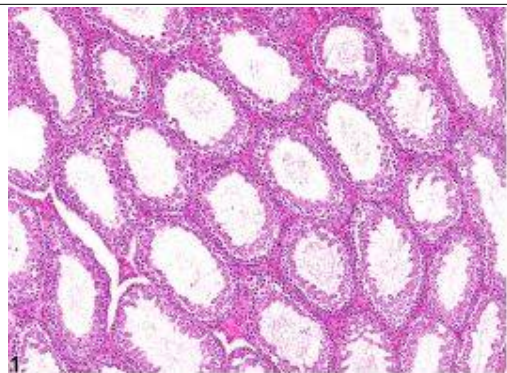
Testis, Rete testis - Dilation in a male B6C3F1 mouse from a chronic study. The rete testis is dilated.

## Testis, Rete Testis - Hyperplasia (고환그물 증생)



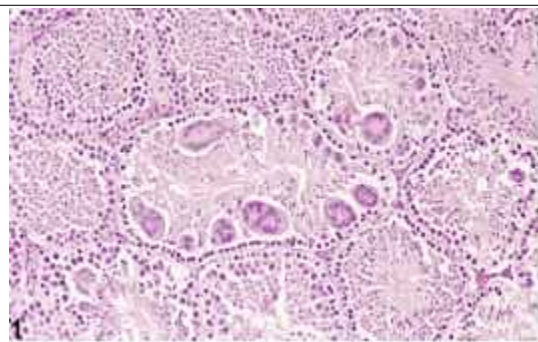
Testis, Rete testis - Hyperplasia in a male CD1 mouse. Hyperplasia of the lining epithelium of the rete testis.

Testis, Seminiferous Tubule - Dilation (정세관 확장)



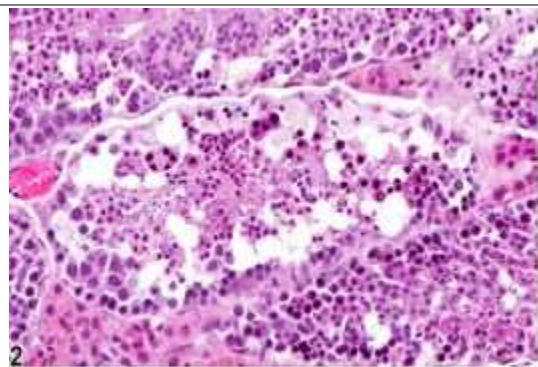
Testis, Seminiferous tubule - Dilation in a male B6C3F1 mouse from a chronic study. These seminiferous tubules are dilated.

Testis, Seminiferous Tubule - Giant Cells (거대 세포)



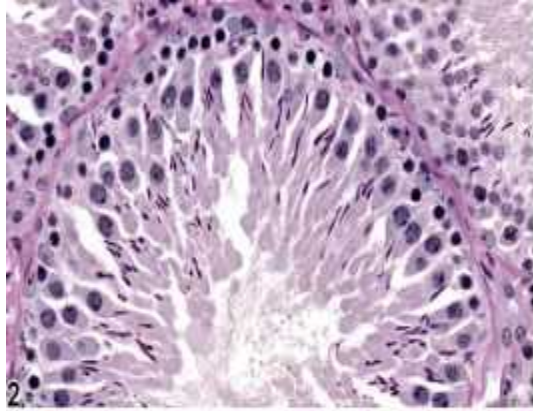
Testis, Seminiferous tubule - Giant cells in a male B6C3F1 mouse from a subchronic study. These cells are associated with germ cell degeneration.

Testis, Seminiferous Tubule - Necrosis (정세관 괴사)



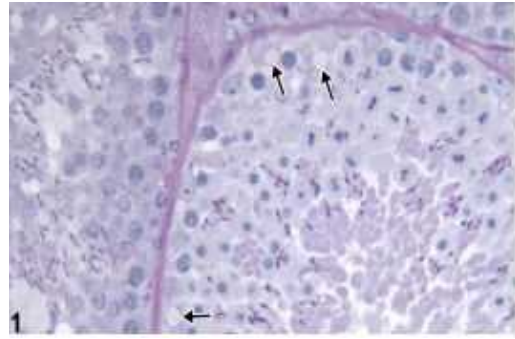
Testis, Seminiferous tubule - Necrosis in a male Swiss Webster mouse from a chronic study. This higher magnification of Figure 1 shows that both germ cells and Sertoli cells are undergoing necrosis.

### Testis, Seminiferous Tubule - Retention, Spermatid (정자세포 저류)



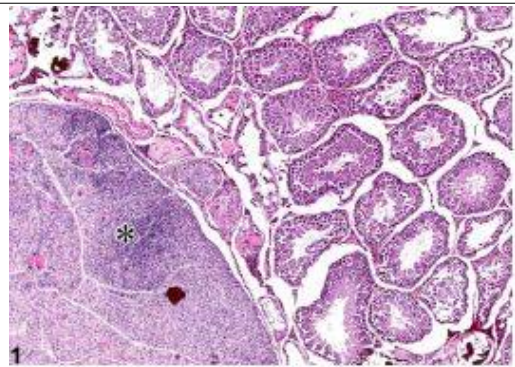
Testis, Seminiferous tubule - Retention, Spermatid in a male Sprague-Dawley rat. Retention of elongated spermatids in the basal region of a stage XII seminiferous tubule.

### Testis, Seminiferous Tubule - Vacuolation (정세관 공포)



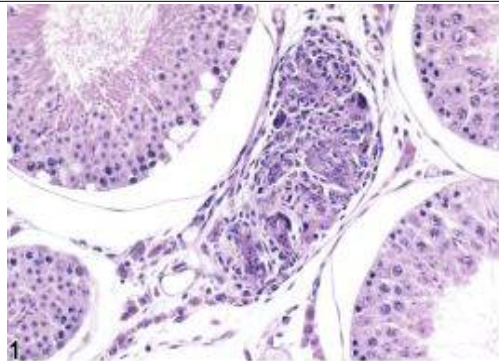
Testis, Seminiferous tubule - Vacuolation in a male Harlan Sprague-Dawley rat from a reproductive and continuous breeding study. Vacuolation in basal Sertoli cell cytoplasm (arrows). PAS stain.

### Testis - Spermatocele (정액류)



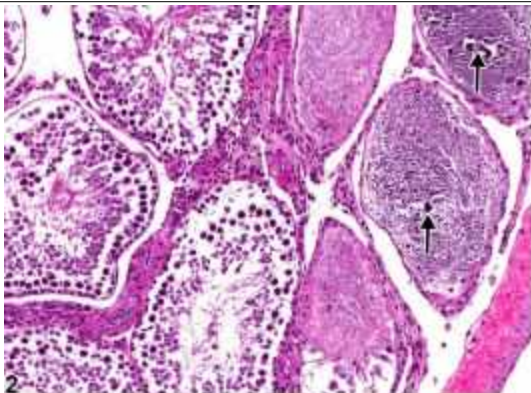
Testis - Spermatocele in a male B6C3F1 mouse from a chronic study. There is a large spermatocele in the testis (asterisk).

### Testis - Sperm Granuloma (정자 육아종)



Testis - Sperm granuloma in a male hamster. Though this example of a sperm granuloma is from a hamster, its appearance in a mouse or rat would be the same.

### Testis - Sperm Stasis (정자 정체)

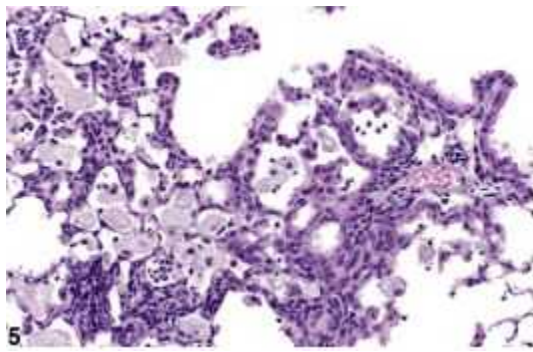


Testis - Sperm stasis in a male F344/N rat from a chronic study. Arrows indicate focal mineralization of sperm.

## 11. 호흡기계

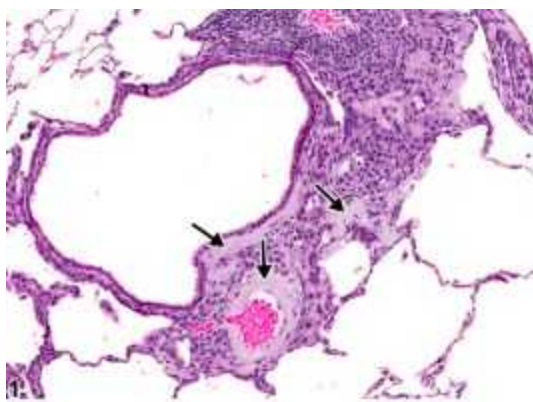
## 1) 폐

## Lung, Alveolar/Bronchiolar Epithelium - Hyperplasia (증생)



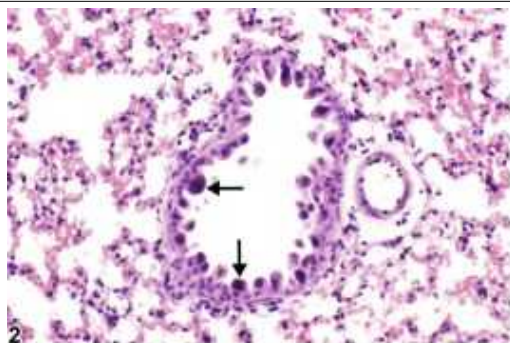
Lung, Alveolar epithelium - Hyperplasia in a male B6C3F1/N mouse from a chronic study (higher magnification of Figure 4). Large, foamy macrophages, neutrophils, and lymphocytes are associated with the alveolar epithelial hyperplasia.

## Lung - Amyloid (아밀로이드)



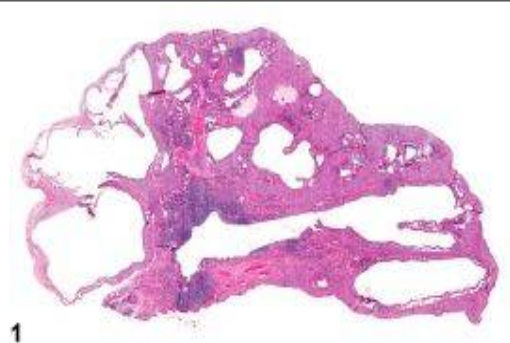
Lung - Amyloid in a female B6C3F1/N mouse from a chronic study. There is perivascular and peribronchiolar amyloid deposition (arrows).

Lung - Atypia, Cellular (비정형 세포)



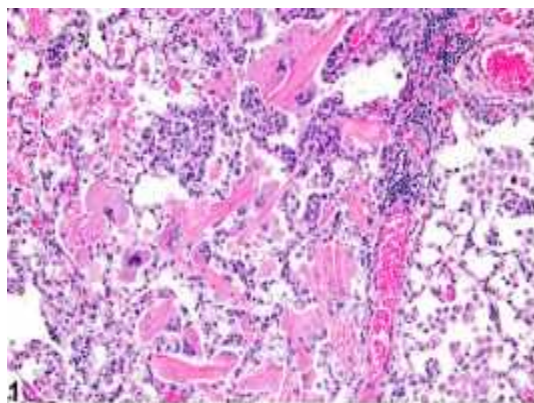
Lung, Alveolar epithelium - Atypia, Cellular in a male B6C3F1/N mouse from a subchronic study. Atypical cells (arrows) have enlarged nuclei and may be binucleated.

Lung - Bronchiectasis (기관지확장증)



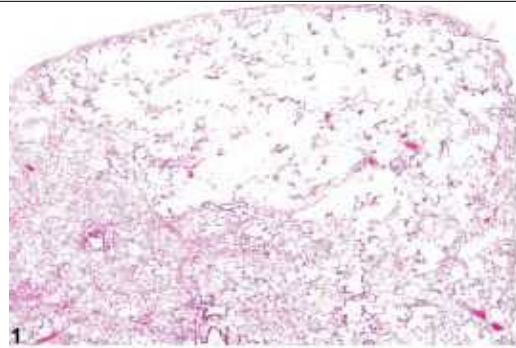
Lung - Bronchiectasis in an F344/N rat. The airways are markedly dilated.

Lung - Crystals (결정)



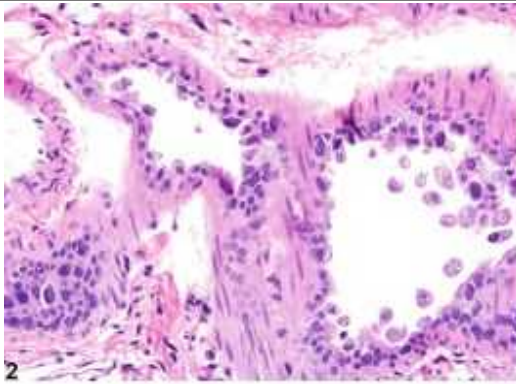
Lung - Crystals in a male B6C3F1/N mouse from a chronic study. Acicular, eosinophilic crystals and associated granulomatous inflammation are present in the alveoli.

## Lung - Emphysema (폐기종)



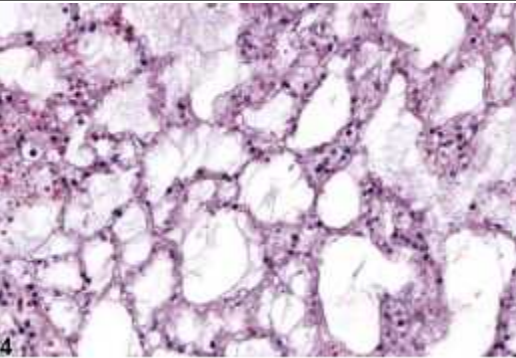
Lung - Emphysema in a male F344/N rat from a chronic study. The alveolar septa are absent in a region of the lung, creating one large airspace.

## Lung, Epithelium - Degeneration (변성)



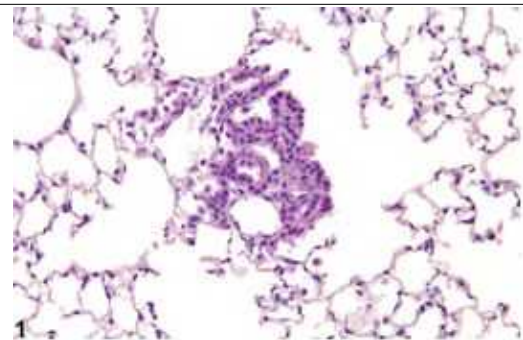
Lung, Epithelium, Bronchiole - Degeneration in a male B6C3F1/N mouse from a subchronic study. The epithelial cells are vacuolated and sloughing and have lost their cilia, but there is little necrotic debris or inflammation.

## Lung, Epithelium - Necrosis (괴사)



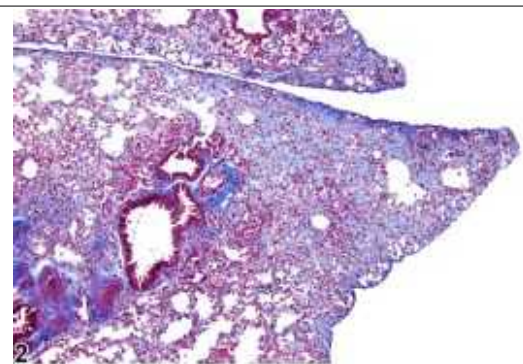
Lung, Epithelium, Alveolus - Necrosis in a female F344/N rat from a subchronic study. In this focal lesion, there is loss of epithelial and interstitial cells.

Lung, Epithelium, Alveolus - Hyperplasia (증생)



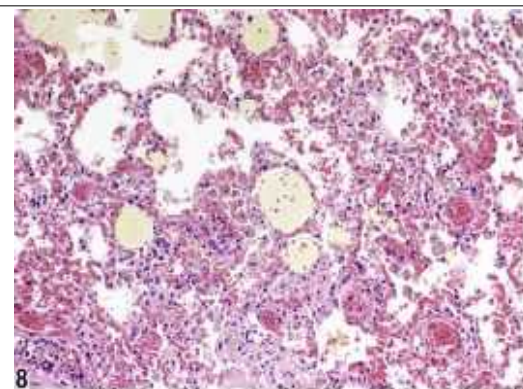
Lung, Epithelium, Alveolus - Hyperplasia in a male B6C3F1/N mouse from a chronic study. There is a small proliferation of alveolar epithelial cells with no inflammation.

Lung - Fibrosis (섬유화)



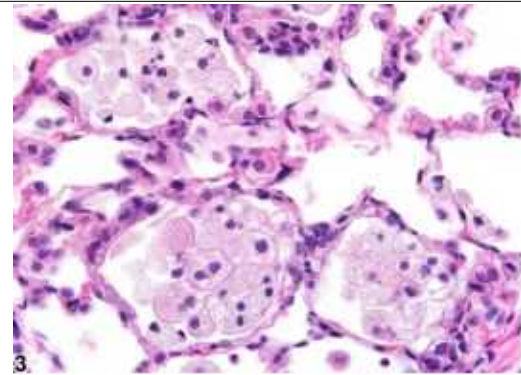
Lung - Fibrosis in a mouse. The blue staining indicates interstitial fibrosis. Masson's trichrome stain.

Lung - Foreign Body (이물체)



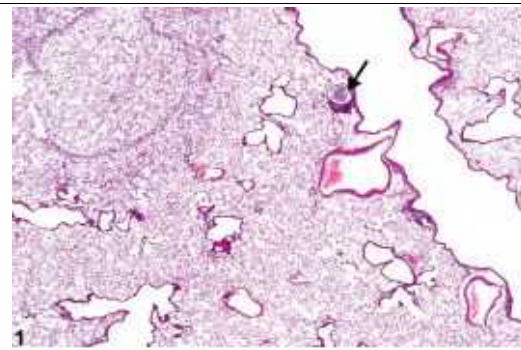
Lung, Alveolus - Foreign body in a female F344/N rat from a chronic study. Corn oil from a gavage accident is present in the alveoli, with acute inflammation and hemorrhage.

## Lung - Foreign Material (이물질)



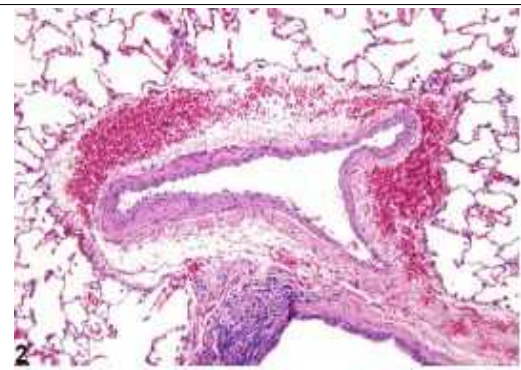
Lung, Alveolus - Foreign material in a male Harlan Sprague-Dawley rat from a subchronic study. The brown to black material within the macrophages is considered to be the test agent.

## Lung, Glands - Cyst (낭포)



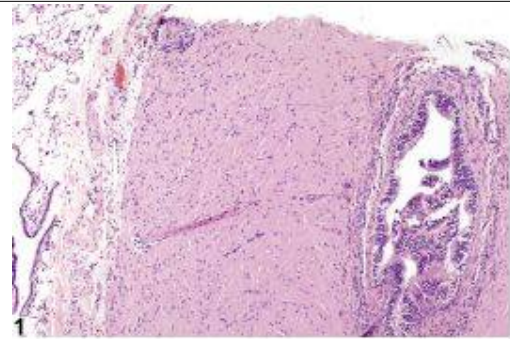
Lung, Glands - Cyst in a male B6C3F1/N mouse from a chronic study. There is a small cyst adjacent to a bronchus (arrow).

## Lung - Hemorrhage (출혈)



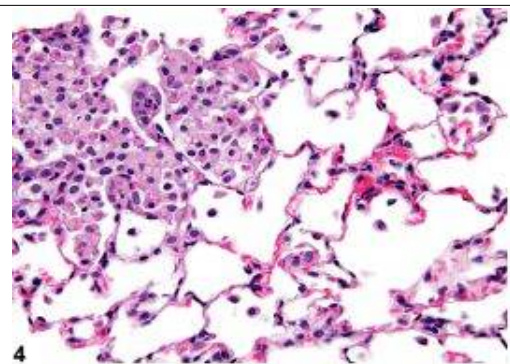
Lung - Hemorrhage in a male F344/N rat from a chronic study (same animal as in Figure 1). Erythrocytes are present in the perivascular space around a pulmonary vein.

Lung - Hypertrophy, Smooth Muscle (평활근 비대)



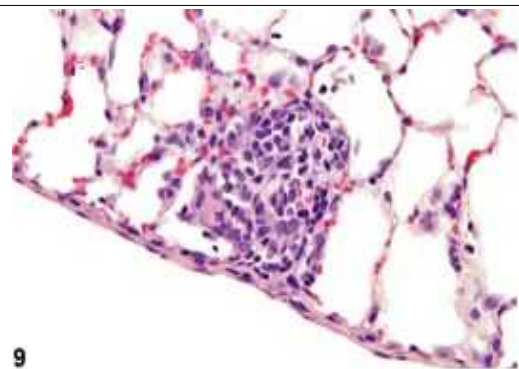
Lung, Bronchiole, Smooth muscle - Hypertrophy in a male F344/N rat from a chronic study. The smooth muscle around this bronchiole is markedly thickened; there is concurrent epithelial hyperplasia.

Lung - Infiltration Cellular, Histiocyte (조직구 침투)



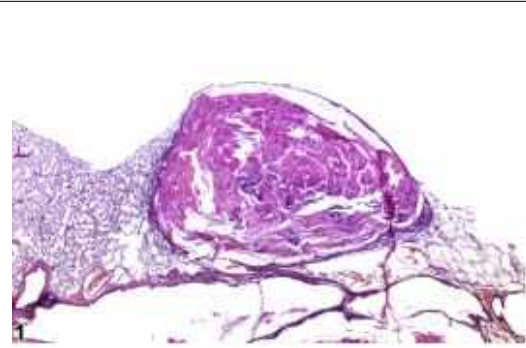
Lung - Infiltration cellular, Histiocyte in a control male F344/NTac rat from a subchronic study. Many of the alveolar macrophages in this focal accumulation contain variably sized vacuoles.

Lung - Inflammation (염증)



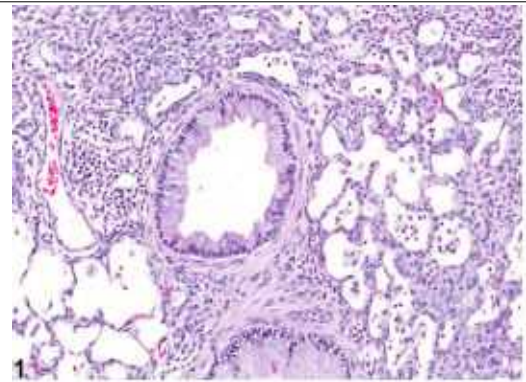
Lung - Inflammation, Chronic in a male F344/N rat from a subchronic study. These focal, subpleural lesions are a common background finding.

## Lung - Keratinizing Cyst (각질화 낭포)



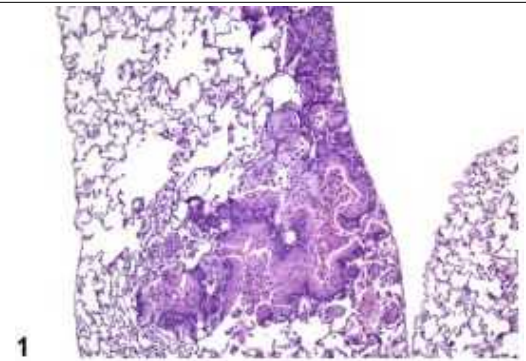
Lung - Keratinizing cyst in a male F344/N rat from a chronic study. There is a large cyst filled with keratin.

## Lung - Metaplasia, Goblet Cell (배상세포 화생)



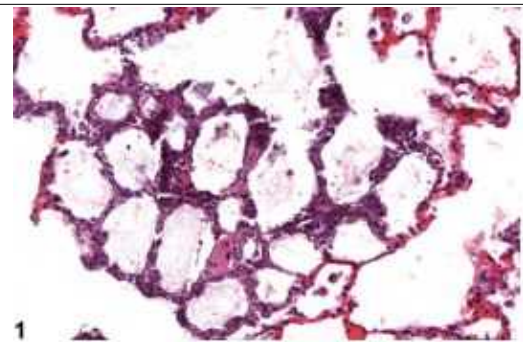
Lung, Bronchiole - Metaplasia, Goblet cell from a male Sprague-Dawley rat in an acute study. The majority of the cells in this airway are goblet cells. Image provided courtesy of Dr. J. Bonner.

## Lung - Metaplasia, Squamous (편평세포 화생)



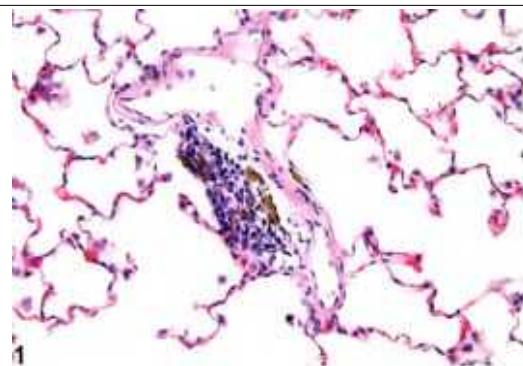
Lung, Alveolus - Metaplasia, Squamous in a female Harlan Sprague-Dawley rat from a subchronic study. The normal alveolar epithelium has been replaced by squamous epithelium.

### Lung - Mineral (무기질)



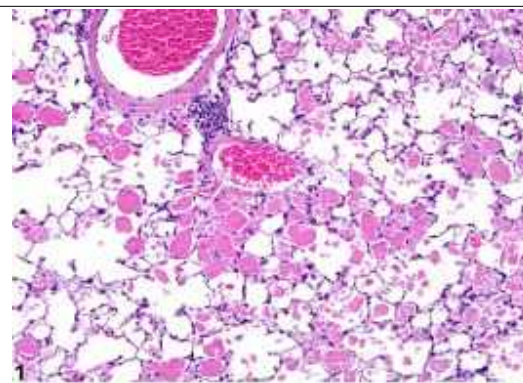
Lung, Interstitium - Mineral in a male F344/N rat from a chronic study. Deeply basophilic material is present within the expanded alveolar septa.

### Lung - Pigment (색소)



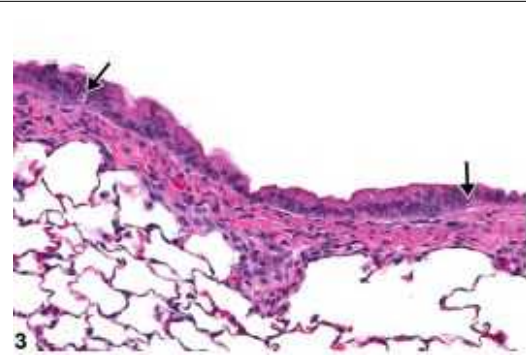
Lung, Alveolus - Pigment in a female Harlan Sprague-Dawley rat from a chronic study. The pigment is most likely hemosiderin and is contained within macrophages.

### Lung - Proteinosis (단백질증)



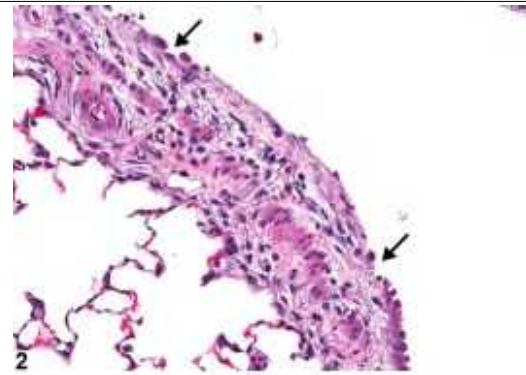
Lung, Alveolus - Proteinosis in a male B6C3F1/N mouse from a chronic study. There is amorphous, brightly eosinophilic material (proteinosis) within the alveoli.

## Lung - Regeneration (재생)



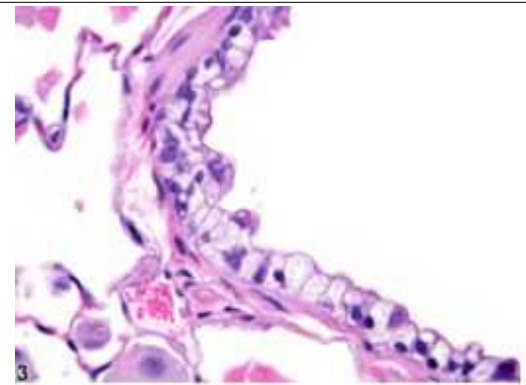
Lung, Bronchiole - Regeneration in a male Wistar Han rat from an acute study. The scattered necrotic cells in the epithelium (arrows) suggest that this hyperplastic response is associated with regeneration secondary to previous damage.

## Lung - Ulceration (궤양)



Lung, Bronchus - Ulceration in a male Wistar Han rat from an acute study. Some early regenerative changes are visible in the adjacent epithelium (arrows).

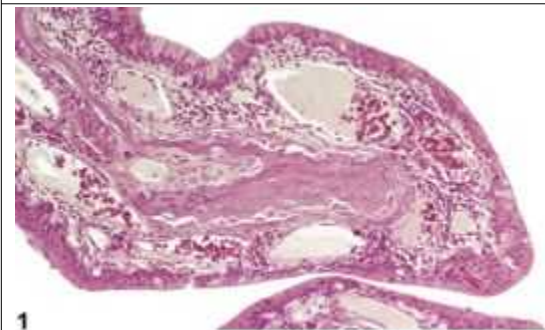
## Lung - Vacuolization, Cytoplasmic (세포질 공포)



Lung, Bronchiole - Vacuolization, Cytoplasmic in a female B6C3F1/N mouse from a chronic study. The bronchiolar epithelial cells contain clear, intracytoplasmic vacuoles.

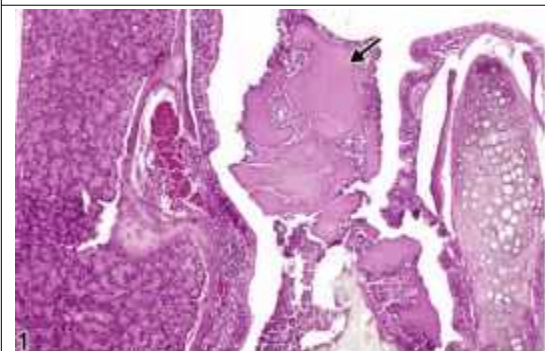
## 2) 비강

### Nose, Bone - Periosteal Proliferation (골막 증식)



Nose, Bone - Periosteal proliferation in a male F344/N rat from a chronic study. The thickening of the trabecular bone and increased number of osteoblasts are accompanied by inflammation and vascular dilation.

### Nose - Concretion (결석)



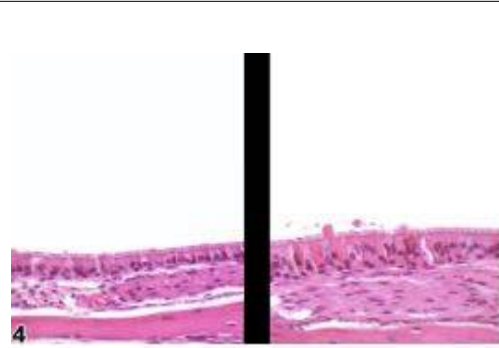
Nose - Concretion in a male B6C3F1/N mouse from a chronic study. Laminated eosinophilic material mixed with inflammatory cells is present in the meatus (arrow).

### Nose - Eosinophilic Material (호산성 물질)



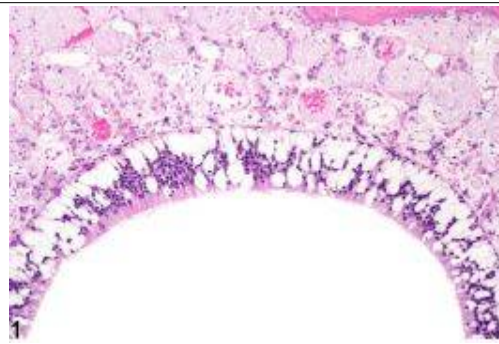
Nose - Eosinophilic material in a male B6C3F1/N mouse from a chronic study. There is bilateral accumulation of an eosinophilic material in the lamina propria of the ventral nasal septum.

## Nose, Epithelium - Accumulation, Hyaline Droplet (초자적 축적)



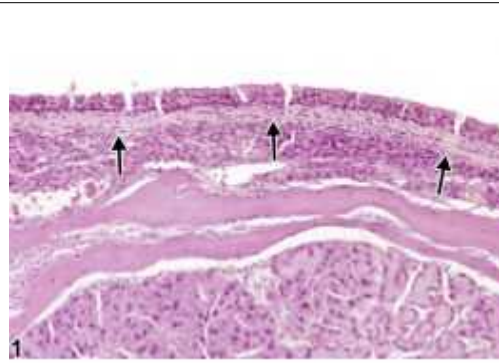
Nose, Respiratory epithelium - Accumulation, Hyaline droplet in a treated female B6C3F1/N mouse (right) and a normal control female B6C3F1/N mouse from a subchronic study (left). Hyaline droplet material is present in the respiratory epithelial cells lining the nasopharyngeal duct from the treated mouse (right) but not in the control mouse (left).

## Nose, Epithelium - Degeneration (변성)



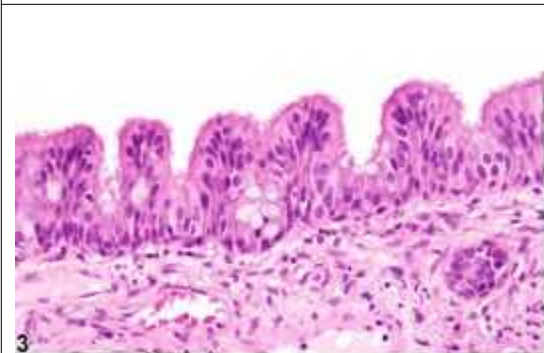
Nose, Olfactory epithelium - Degeneration in a male F344/N rat from a chronic study. Numerous vacuoles are present in the olfactory mucosa.

## Nose, Epithelium - Fibrosis (섬유화)



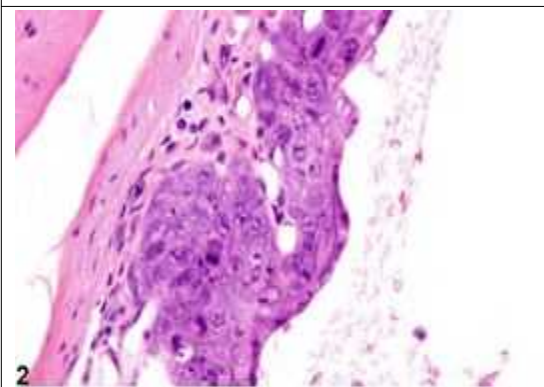
Nose, Transitional epithelium - Fibrosis in a female B6C3F1/N mouse from a chronic study. Eosinophilic fibrillar material expands the lamina propria, separating the epithelium from the glands in the lamina propria.

Nose, Epithelium - Hyperplasia (상피 증생)



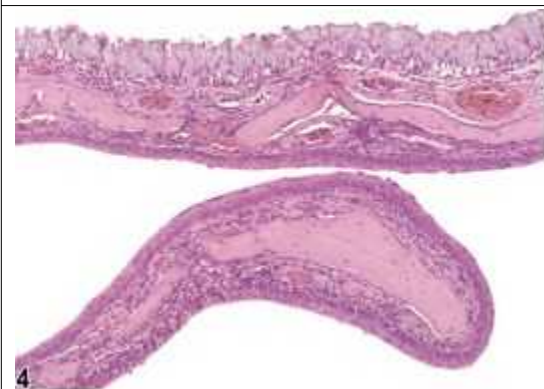
Nose, Respiratory epithelium - Hyperplasia in a female Harlan Sprague-Dawley rat from a chronic study. The thickened proliferative epithelial surface is arranged in regular folds.

Nose, Epithelium - Hyperplasia, Atypical (비정형 상피 증생)



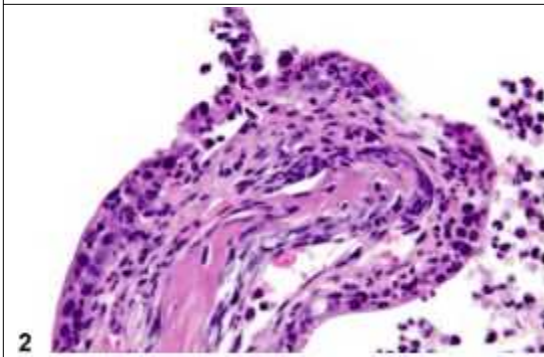
Nose, Respiratory epithelium - Hyperplasia, Atypical in a female B6C3F1/N mouse from a chronic study. Proliferation of atypical and poorly organized epithelium is present on the turbinate.

Nose, Epithelium - Metaplasia, Squamous (편평상피 화생)



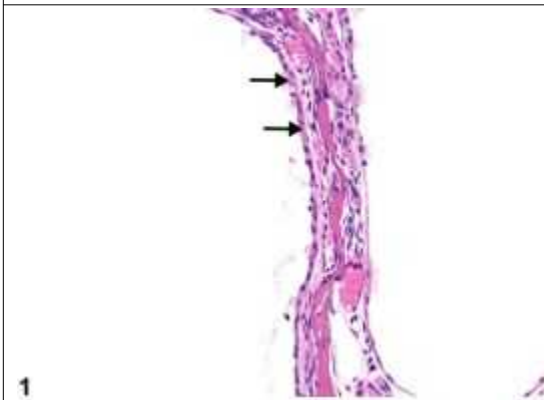
Nose, Respiratory epithelium - Metaplasia, Squamous in a male F344/N rat from a chronic study. The respiratory epithelium on the turbinate and the transitional epithelium on the tip of the turbinate have been replaced by squamous epithelium.

## Nose, Epithelium - Necrosis (상피 괴사)



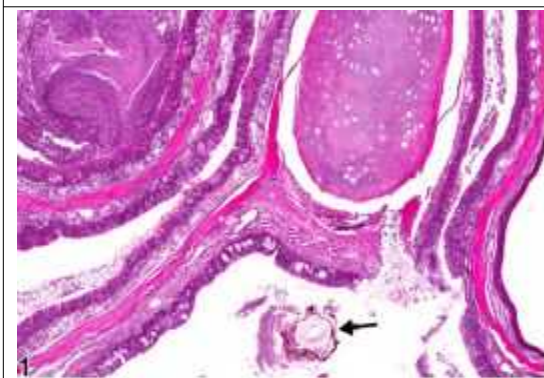
Nose, Transitional epithelium - Necrosis in a female B6C3F1/N mouse from a chronic study. Necrotic epithelium is characterized by prominent pyknosis, with evidence of exfoliation; acute inflammation is also present.

## Nose, Epithelium - Regeneration (재생)



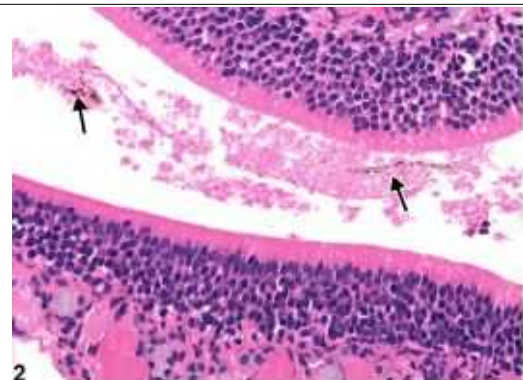
Nose, Respiratory epithelium - Regeneration in a female B6C3F1/N mouse from a chronic study. A thin layer of epithelium is covering an area where the respiratory epithelium was previously lost (arrows).

## Nose - Foreign Body (이물체)



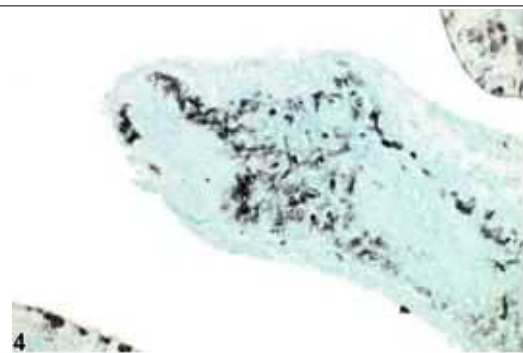
Nose - Foreign body in a female F344/N rat from a chronic study. There is hair fragment in the nasopharyngeal duct (arrow).

### Nose - Foreign Material (이물질)



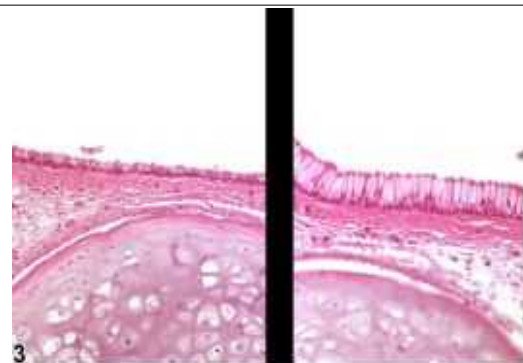
Nose - Foreign material in a female F344/NTac rat from an acute study. The dark brown particulate material (arrows) is associated with proteinaceous material.

### Nose - Fungus (균류)



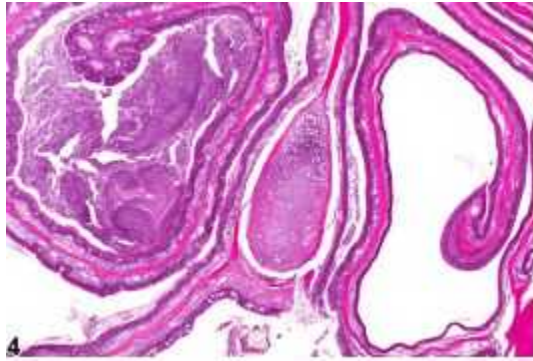
Nose - Fungus in a male F344/N rat from a chronic study. Silver staining techniques, such as this Gomori's methenamine silver stain, highlight the fungal organisms.

### Nose - Hyperplasia, Goblet Cell (배상세포 증생)



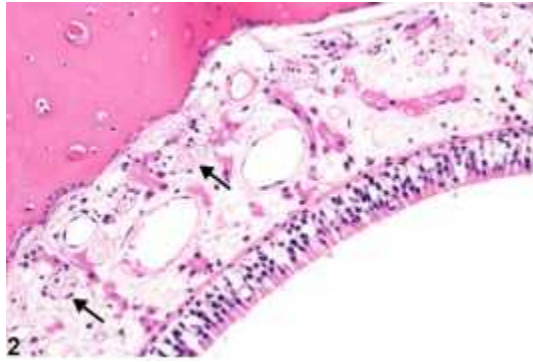
Nose, Respiratory epithelium - Hyperplasia, Goblet cell (right) and normal respiratory epithelium (left) of the nasopharyngeal duct in a male F344/N rat from a subchronic study. Image provided courtesy of Dr. R. Miller.

## Nose - Inflammation (염증)



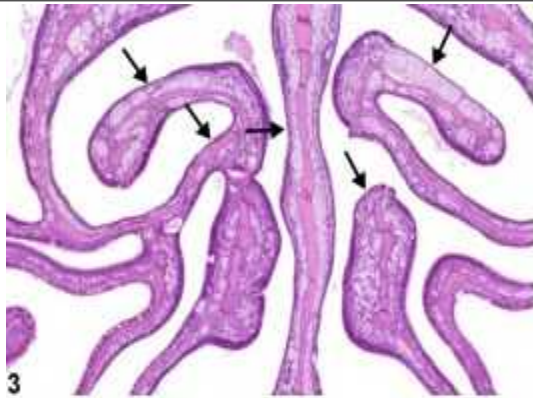
Nose, Olfactory epithelium - Inflammation, Suppurative in a female F344/N rat from a chronic study. There is a proliferative epithelial reaction to the suppurative inflammation in the ventral nasal cavity.

## Nose, Nerve - Atrophy (신경 위축)



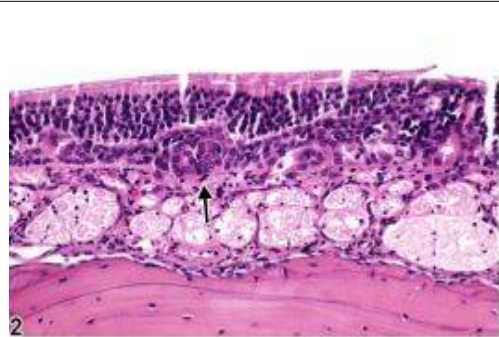
Nose, Nerve - Atrophy in a female F344/N rat from a subchronic study. The olfactory nerves in the lamina propria are decreased in size and number (arrows), and there is loss of cells in the olfactory epithelium.

## Nose, Olfactory Epithelium - Atrophy (후각상피 위축)



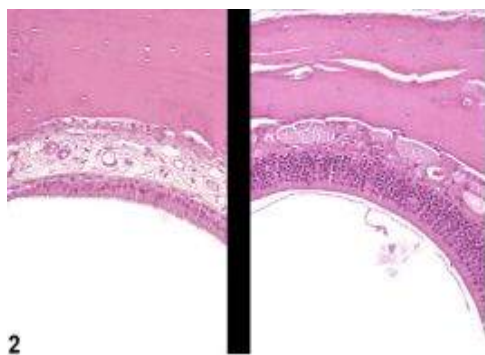
Nose, Olfactory epithelium - Atrophy in a male F344/N rat from a chronic study. The olfactory epithelium is thin in multiple areas (arrows).

Nose, Olfactory Epithelium - Hyperplasia, Basal Cell (기저세포 증생)



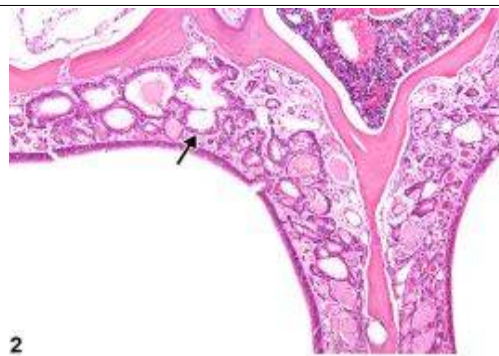
Nose, Olfactory epithelium - Hyperplasia, Basal cell in a male F344/N rat from a subchronic study. A focal area of proliferation of basal epithelial cells (arrow) is present in the olfactory mucosa.

Nose, Olfactory Epithelium - Metaplasia, Respiratory (호흡상피 화생)



Nose, Olfactory epithelium - Metaplasia, Respiratory in a treated male B6C3F1/N mouse (left) and normal olfactory epithelium from a control male B6C3F1/N mouse from a subchronic study (right). The olfactory epithelium of the treated mouse has been replaced by respiratory epithelium.

Nose, Olfactory Epithelium, Glands - Hyperplasia (후각상피 선 증생)



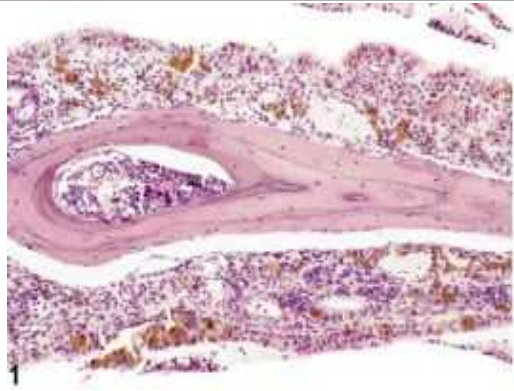
Nose, Olfactory epithelium, Glands - Hyperplasia in a male B6C3F1/N mouse from a chronic study. Many of the hyperplastic Bowman's glands are dilated (arrow).

## Nose, Olfactory Epithelium, Glands - Metaplasia, (후각상피 선 화생)



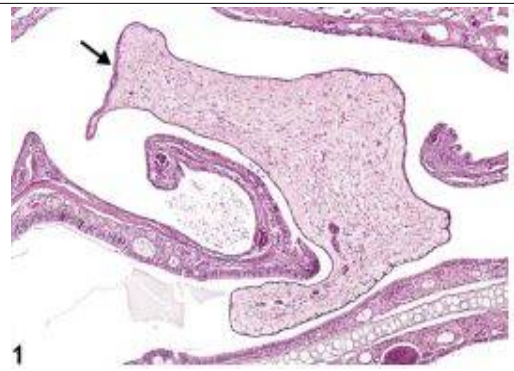
Nose, Olfactory epithelium, Glands - Metaplasia, Squamous in a male F344/N rat from a chronic study. The Bowman's glands are dilated and lined by squamous epithelium.

## Nose - Pigment (색소)



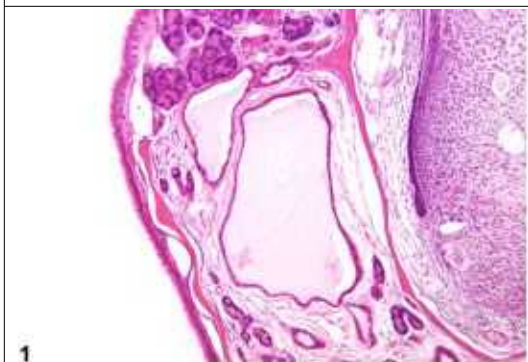
Nose, Respiratory epithelium - Pigment in a female B6C3F1/N mouse from a subchronic study. The mucosa and lamina propria of the turbinate contain pigment deposits.

## Nose - Polyp, Inflammatory (용종 염증)



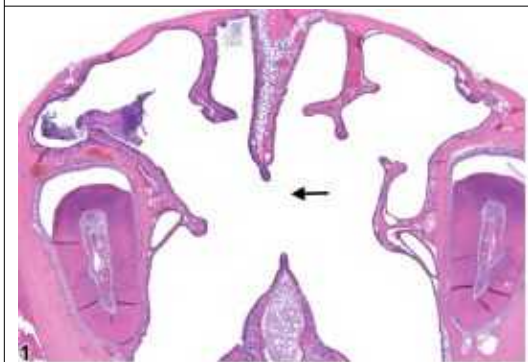
Nose - Polyp, Inflammatory in a male B6C3F1/N mouse from a chronic study. The attachment of the epithelial-lined, proliferative, connective tissue polyp (arrow) to the mucosa is not present in this section.

Nose, Respiratory Epithelium, Glands - Dilation (호흡상피 선 확장)



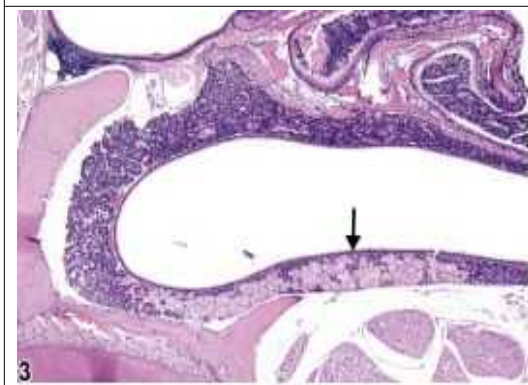
Nose, Respiratory epithelium, Glands  
- Dilation in a male B6C3F1/N mouse from a chronic study. The glands in the respiratory mucosa are dilated and contain pale eosinophilic material.

Nose, Septum - Perforation (천공)



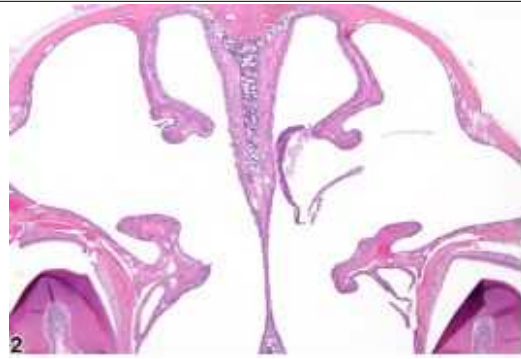
Nose, Septum - Perforation in a female B6C3F1/N mouse from a chronic study. A perforation is present in the nasal septum (arrow).

Nose, Steno's Glands - Degeneration (변성)



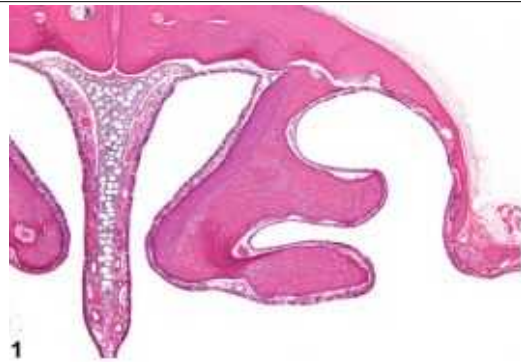
Nose, Steno's glands - Atrophy in a male B6C3F1/N mouse from a subchronic study. Focal atrophy is characterized by a localized loss of glandular acini (arrow).

## Nose, Turbinate - Atrophy (비갑개 위축)



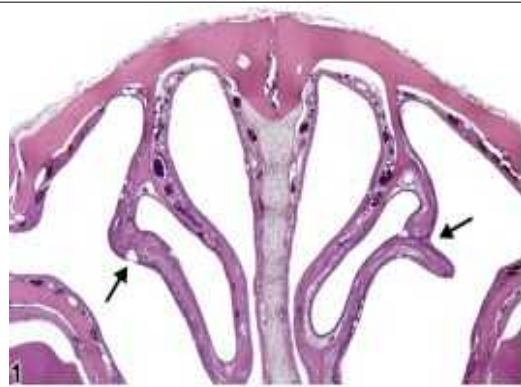
Nose, Turbinate - Atrophy in a male B6C3F1/N mouse from a subchronic study. The size of the turbinates is decreased compared with normal turbinates

## Nose, Turbinate - Hyperostosis (비갑개 골비대증)



Nose, Turbinate - Hyperostosis in a male B6C3F1/N mouse from a chronic study. Thickening of the turbinate bone is present.

## Nose - Synechia (유착)

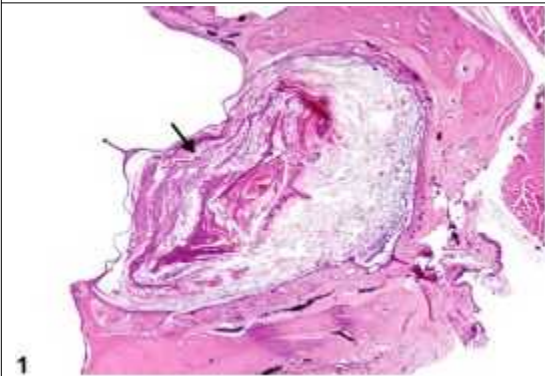


Nose, Turbinate - Synechia in a male F344/N rat from a subchronic study. There are adhesions of the tips of the nasal turbinates to each other (arrows).

## 12. 감각계

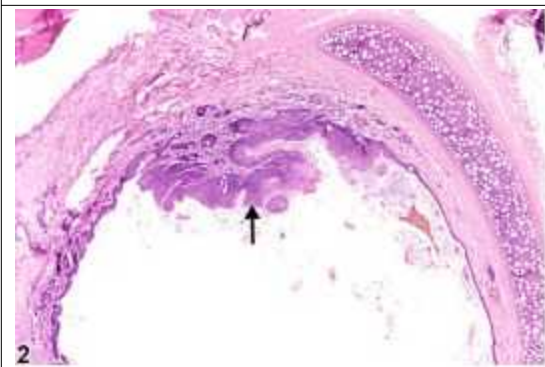
### 1) 귀

#### Ear, Canal - Dilation (관 확장)



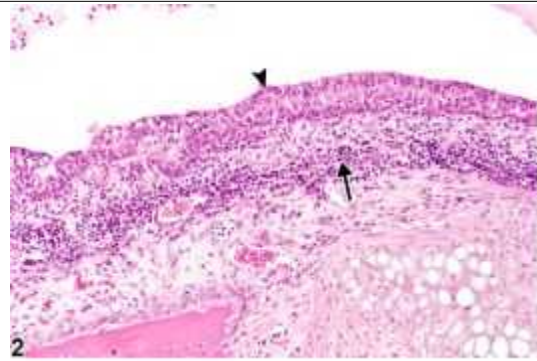
Ear, Canal - Dilation in a male Fischer 344/N rat from a chronic study. Dilation of the external ear canal (arrow), characterized by plugs of sloughed keratin lamellae, cerumen, and necrotic debris that occludes and distends the canal.

#### Ear, Epithelium - Hyperplasia (상피 증생)



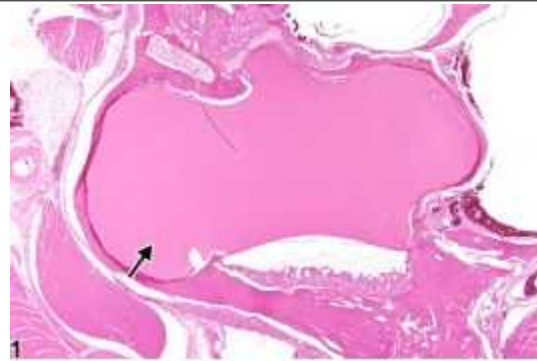
Ear, Epithelium - Hyperplasia in a male Fischer 344/N rat from a chronic study. The exophytic, papillary projections of squamous epithelium in the external ear canal (arrow) represent focal hyperplasia.

## Ear - Inflammation (염증)



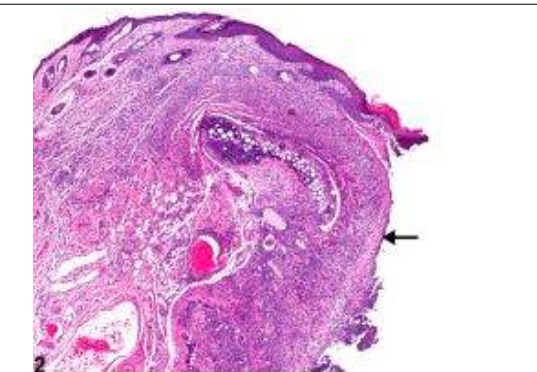
Ear - Inflammation, Chronic active in a male Fischer 344/N rat from a chronic study. There are neutrophils and mononuclear cells in the lamina propria (arrow) extending into the hyperplastic epithelium (arrowhead) lining the tympanic cavity.

## Ear - Proteinaceous fluid (단백질 액)



Ear, Middle ear - Proteinaceous fluid in a male Fischer 344/N rat from a chronic study. There is acellular, eosinophilic, proteinaceous fluid in the tympanic cavity of the middle ear.

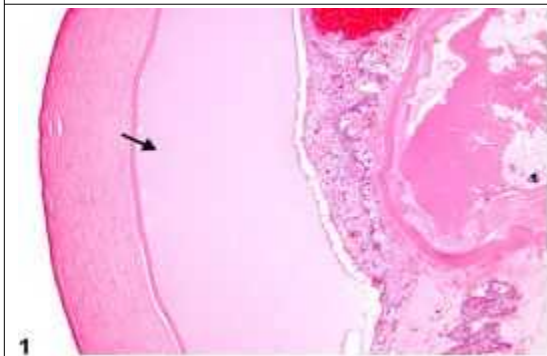
## Ear - Ulcer (궤양)



Ear - Ulcer in a male Swiss CD-1 mouse from a chronic study (higher magnification of Figure 1). There is an ulcer (arrow) of the external ear canal epithelium.

## 2) 눈

### Eye - Anterior chamber - Proteinaceous fluid (단백질 액)



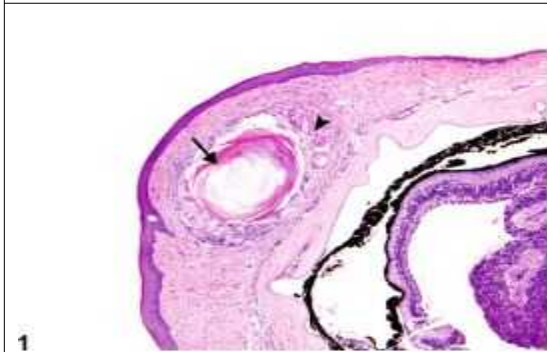
Eye, Anterior chamber - Proteinaceous fluid in a female F344/N rat from a chronic study. Anterior chamber proteinaceous fluid (arrow) is characterized by accumulations of homogeneous pale eosinophilic material that contains few if any inflammatory cells.

### Eye, Conjunctiva - Edema (결막 부종)



Eye, Conjunctiva - Edema in a female F344/N rat from a chronic study. There is diffuse swelling of the bulbar conjunctiva (arrows) due to accumulation of fluid; inflammatory cells are also present.

### Eye, Cornea - Cyst (각막 낭포)



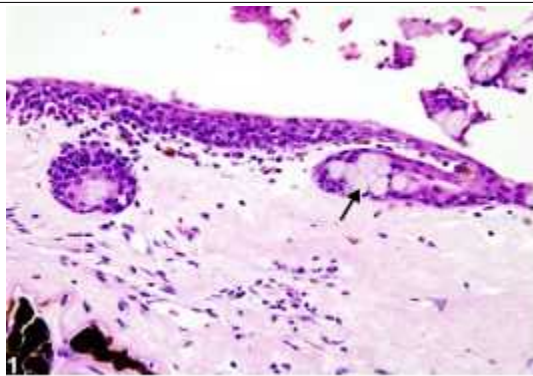
Eye, Cornea - Cyst in a male B6C3F1 mouse from a chronic study. There is a corneal epithelial inclusion cyst (arrow) filled with keratin-like material with secondary granulomatous inflammation (arrowhead).

### Eye, Cornea - Edema (각막 부종)



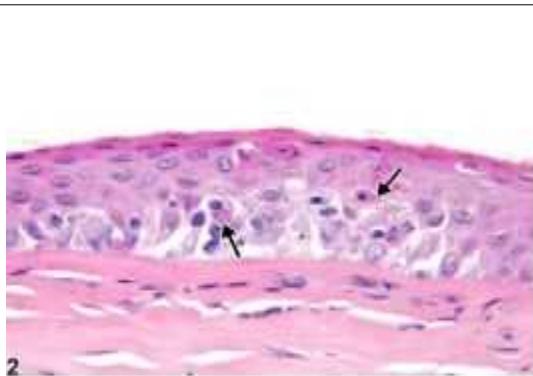
Eye, Cornea - Edema in a female F344/N rat from a chronic study. Corneal edema (asterisk) is characterized by marked thickening of the corneal stroma due to accumulation of eosinophilic proteinaceous fluid

### Eye, Cornea - Metaplasia, Goblet Cell (각막 배상세포 화생)



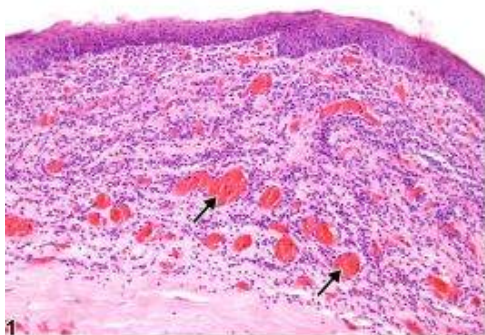
Eye, Cornea - Metaplasia, Goblet cell in a female B6C3F1 mouse from a chronic study. There are clusters of cells similar to normal conjunctival goblet cells in the corneal epithelium (arrow).

### Eye, Cornea - Necrosis (각막 괴사)



Eye, Cornea - Necrosis in a female F344/N rat from a chronic study. Shrunken, hypereosinophilic, necrotic cells (arrows) are present in the hyperplastic corneal epithelium.

Eye, Cornea - Neovascularization (각막 혈관신생)



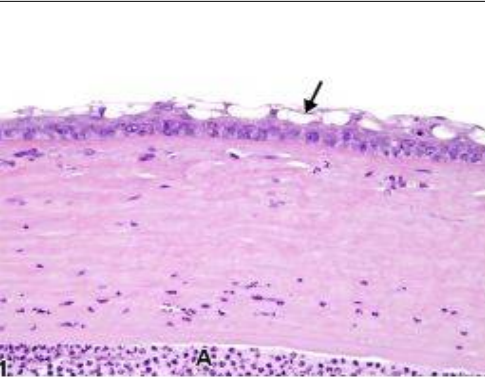
Eye, Cornea - Neovascularization in a male F344/N rat from a chronic study. There are multiple small blood vessels in the stroma (arrows) with concurrent inflammation and epithelial hyperplasia

Eye, Cornea - Ulcer (각막 궤양)



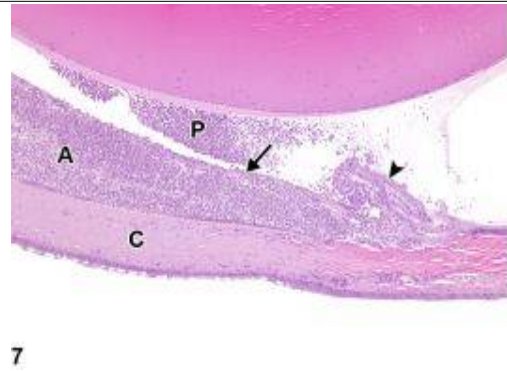
Eye, Cornea - Ulcer in a male B6C3F1 mouse from a subchronic study. There is denudation of all layers of the corneal epithelium (arrow).

Eye, Cornea - Vacuolation, Cytoplasmic (각막 세포질 공포)



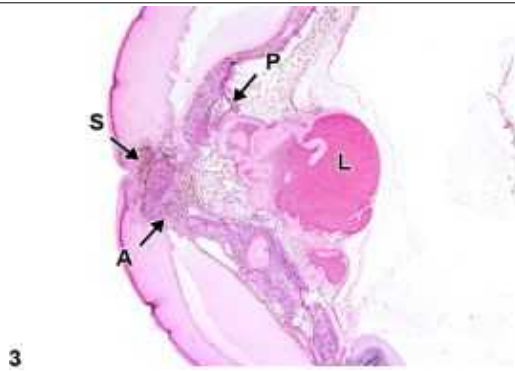
Eye, Cornea - Vacuolation, Cytoplasmic in a male F344/N rat from a chronic study. There are clear discrete vacuoles (arrow) in the corneal epithelial cells and inflammatory cells in the anterior chamber (A).

### Eye - Inflammation (염증)



Eye, Iris - Inflammation, Acute and Eye, Ciliary body - Inflammation, Acute in a male F344/N rat from a chronic study. There are abundant inflammatory cells in the iris and ciliary body; inflammatory cells are also present in the anterior chamber (A), posterior chamber (P), and cornea (C).

### Eye, Iris - Synechia (홍채 유착)



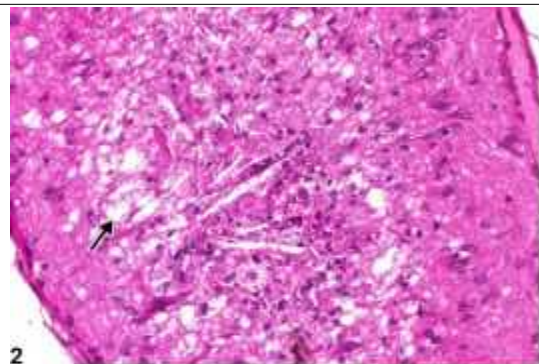
Eye, Iris - Synechia in a male F344/NTac rat from a subchronic study. There are concurrent anterior (A) and posterior (P) iridial synechiae, partial protrusion of the iris into the corneal stroma (staphyloma) (S), and a cataractous lens (L).

### Eye, Lens - Cataract (백내장)



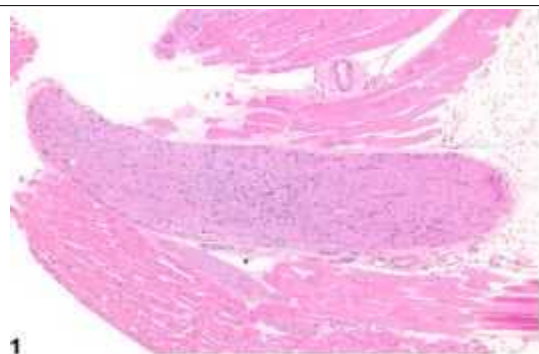
Eye, Lens - Cataract in a female F344/N rat from a chronic study. There are lens fibers with separation, swelling, granularity, condensation, fragmentation, and disruption of the normally orderly configuration.

### Eye, Optic Nerve - Degeneration (시신경 변성)



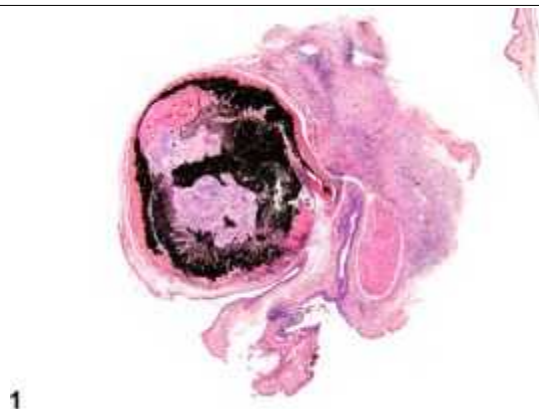
Eye, Optic nerve - Degeneration in a female B6C3F1 mouse from a chronic study. There are scattered clear vacuoles (arrow) in the optic nerve.

### Eye, Optic Nerve - Gliosis (시신경아교증)



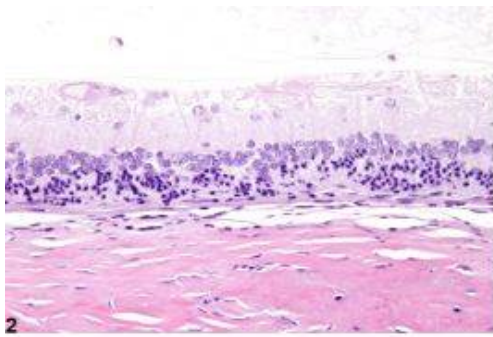
Eye, Optic nerve - Gliosis in a male B6C3F1 mouse from a chronic study. There is a diffuse increase in number of glial cells in the optic nerve.

### Eye - Phthisis Bulbi (안구위축)



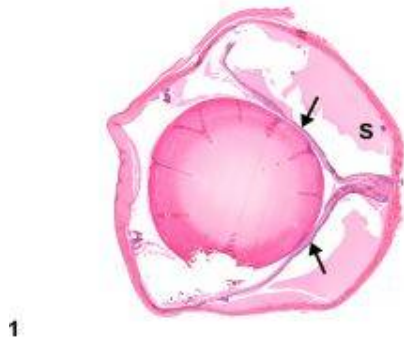
Eye - Phthisis bulbi in a female B6C3F1 mouse from a chronic study. Phthisis bulbi ("end-stage" eye) is characterized by prominent shrinkage of the globe with marked structural displacement and disorganization

### Eye, Retina - Degeneration (망막 변성)



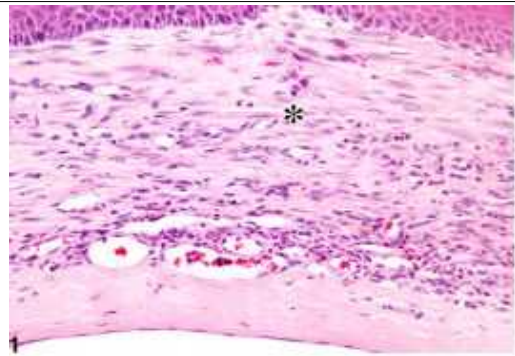
Eye, Retina - Degeneration in a male F344/N rat from a chronic study. Mild retinal degeneration, featuring loss of rod and cone photoreceptor processes, single-cell necrosis of outer nuclear layer photoreceptor cells, hypocellularity and disorganization of the inner and outer nuclear layers, and narrowing or absence of the plexiform layers.

### Eye, Retina - Detachment (망막 박리)



Eye, Retina - Detachment in a female F344/N rat from a chronic study. The retina is detached from the posterior fundus, remaining attached only at the optic disc and the ora ciliaris retinae, resulting in the classic "Y-shaped" configuration, and there is proteinaceous fluid in the subretinal space (S).

### Eye, Cornea - Fibrosis (각막 섬유화)



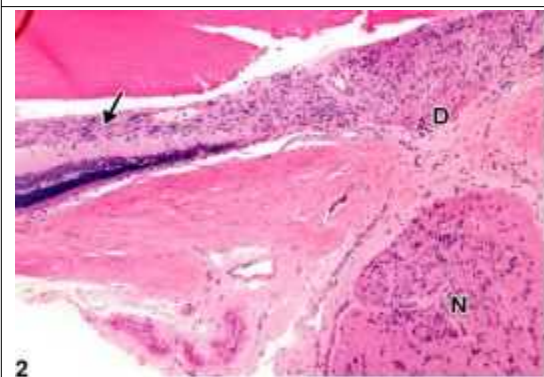
Eye, Cornea - Fibrosis in a male B6C3F1 mouse from a chronic study. The normal orderly collagen lamellar architecture is replaced by coarse, irregular bundles of collagen fibers.

Eye, Retina - Dysplasia (망막 형성이상)



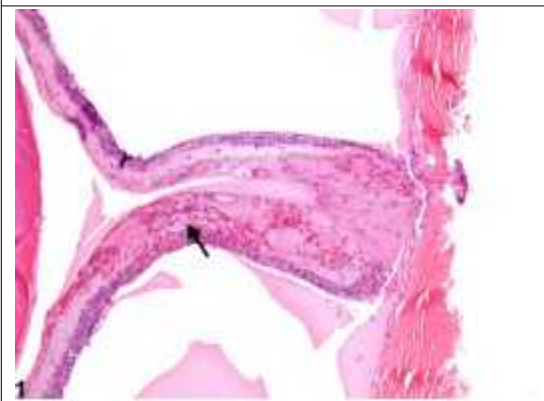
Eye, Retina - Dysplasia in a female B6C3F1 mouse from a chronic study. There are focal infoldings or rosette-like formations of the retinal layers (arrow)

Eye, Retina - Gliosis (망막 신경아교증)



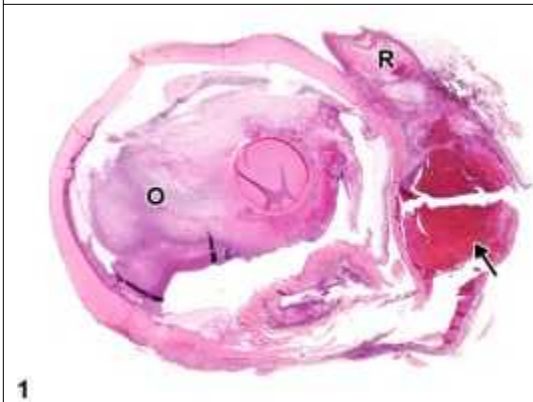
Eye, Retina - Gliosis in a female F344/N rat from a chronic study. There are increased numbers of glial cells in the nerve fiber layer (arrow), optic disc (D), and optic nerve (N).

Eye, Retina - Hemorrhage (망막 출혈)



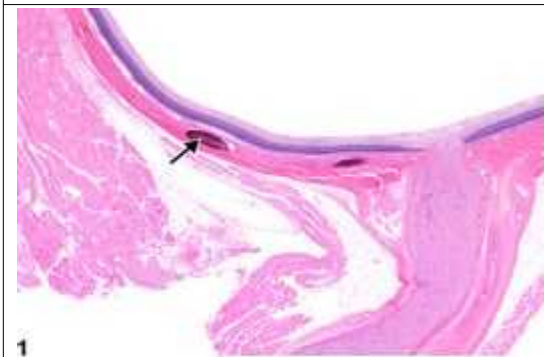
Eye, Retina - Hemorrhage in a female F344/N rat from a chronic study. There are extravasated blood cells (arrow) in a detached and degenerate retina.

### Eye, Retrobulbar - Hemorrhage (안구 후부 출혈)



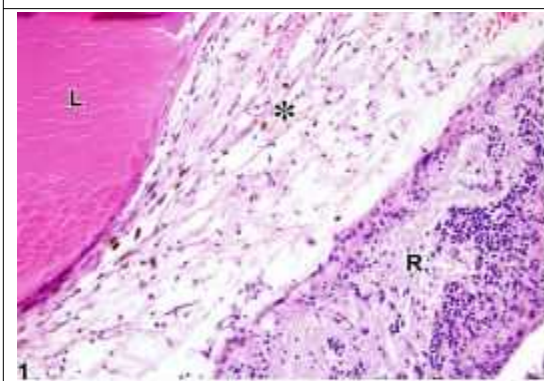
Eye, Retrobulbar - Hemorrhage in a male F344/N rat from a chronic study. There is hemorrhage (arrow) of the retrobulbar region; retrobulbar (R) and ocular (O) inflammation is also present.

### Eye, Sclera - Metaplasia, Osseous (공막 골화생)



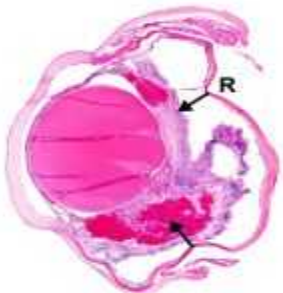
Eye, Sclera - Metaplasia, Osseous in a male F344/N rat from a chronic study. There are two foci of focal osseous metaplasia (arrow) in the sclera.

### Eye, Vitreous - Fibrosis (유리체 섬유화)




Eye, Vitreous - Fibrosis in a male F344/N rat from a chronic study. There is loose fibrous connective tissue (asterisk) in the vitreous space between a cataractous lens (L) and a detached, degenerate retina (R).

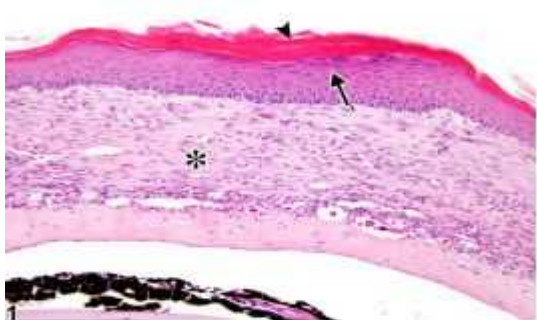
### Eye, Vitreous - Hemorrhage (유리체 출혈)

 <p>1</p>	<p>Eye, Vitreous - Hemorrhage in a male F344/N rat from a chronic study. There are intravitreal accumulations of extravasated blood cells (arrow) with retinal detachment and degeneration (R).</p>
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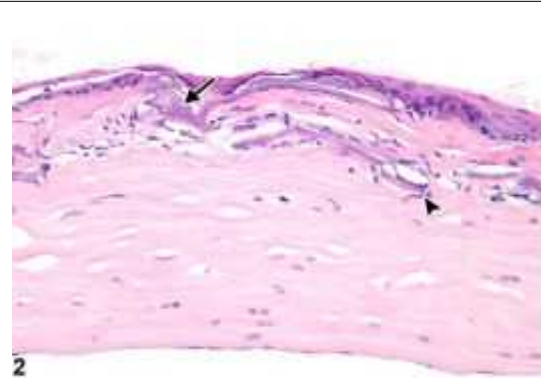
### Eye, Vitreous - Proteinaceous Fluid (유리체 단백질 액)

 <p>1</p>	<p>Eye, Vitreous - Proteinaceous fluid in a male F344/N rat from a subchronic study. There is homogeneous pale eosinophilic material (asterisk) with few inflammatory cells posterior to the lens; there is also retinal detachment and degeneration (arrow) and proteinaceous fluid in the subretinal space (S).</p>
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### Eye, Cornea - Hyperplasia, Squamous (각막 편평상피 증생)

 <p>1</p>	<p>Eye, Cornea - Hyperplasia, Squamous in a male B6C3F1 mouse from a chronic study. There are increased cell layers of the corneal epithelium (arrow) and superficial hyperkeratosis (arrowhead) with inflammation in the underlying stroma (asterisk).</p>
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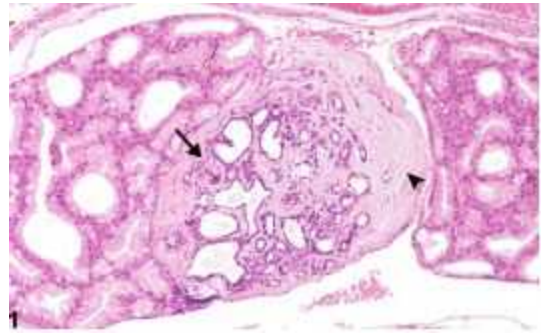
### Eye, Cornea - Mineralization (각막 무기질침착)



Eye, Cornea - Mineralization in a female B6C3F1 mouse from a chronic study. There are irregular basophilic deposits (arrow) in the stroma with concurrent stromal granulomatous inflammation (arrowhead).

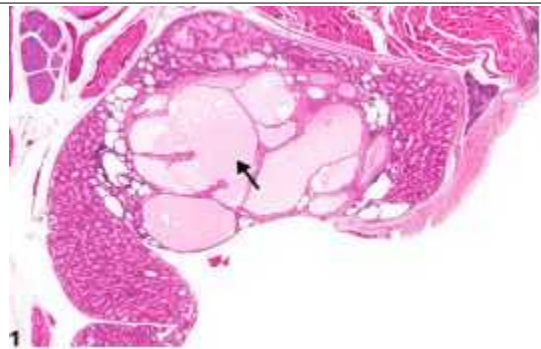
### 3) 하드리안선

#### Harderian Gland - Atrophy (위축)



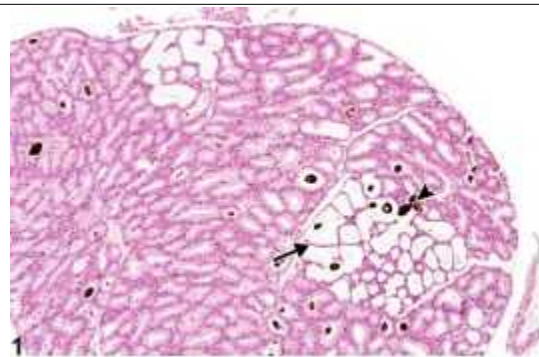
Harderian gland - Atrophy in a female B6C3F1 mouse from a chronic study. The alveoli are shrunken, tortuous and lined by variably flattened epithelial cells (arrow), and there is concurrent interstitial fibrosis (arrowhead).

#### Harderian Gland - Cyst (낭포)



a chronic study. Cysts (arrow) consisting of large, widely distended, multiloculated spaces filled with variable amounts of pale amorphous secretory material.

### Harderian Gland - Dilation (확장)



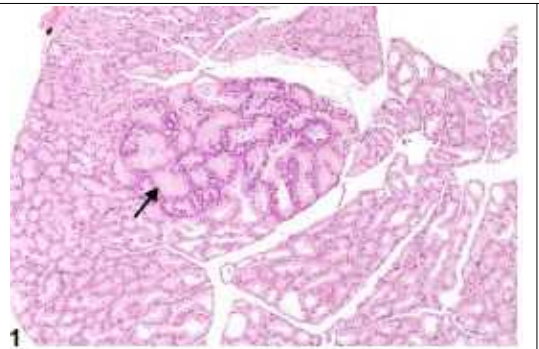
Harderian gland - Dilatation in a male B6C3F1 mouse from a chronic study. There are focal clusters of alveoli with dilated lumens lined by slightly flattened epithelial cells (arrow) some of which contain intraluminal porphyrin-pigment (arrowhead).

### Harderian Gland - Hemorrhage (출혈)



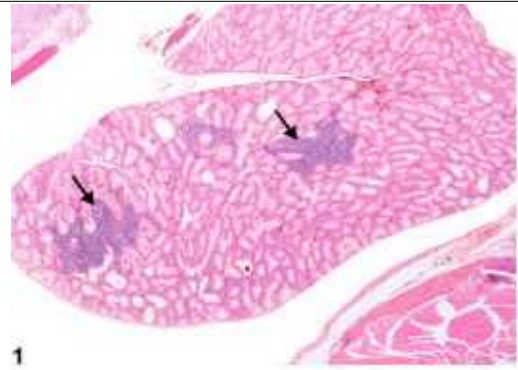
Harderian gland - Hemorrhage in a male Fischer 344\N rat from a chronic study. There are abundant extravasated blood cells in the Harderian gland.

### Harderian Gland - Hyperplasia (증생)



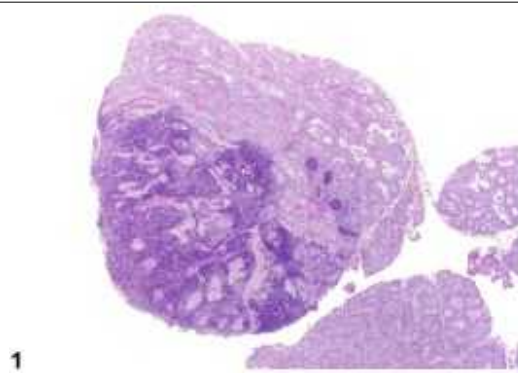
Harderian gland - Hyperplasia in a male B6C3F1 mouse from a chronic study. There is a well-demarcated focus of alveoli that doesn't compress the adjacent tissue.

## Harderian Gland - Infiltration Cellular, Mononuclear Cell (단핵세포 침윤)



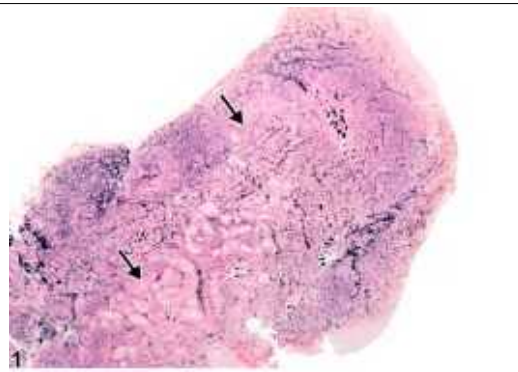
Harderian gland - Infiltration cellular, Mononuclear cell in a female B6C3F1 mouse from a chronic study. Focal interstitial clusters of mononuclear cells (arrows) in the Harderian gland.

## Harderian Gland - Inflammation (염증)



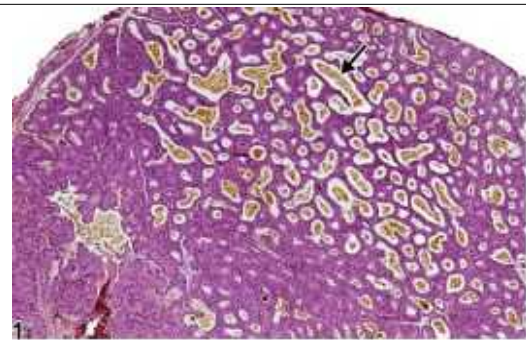
Harderian gland - Inflammation, Chronic active in a female Sprague-Dawley rat from a chronic study. Numerous inflammatory cells are present in the interstitium and alveoli with destruction of the acinar tissue.

## Harderian Gland - Necrosis (괴사)



Harderian gland - Necrosis in a male B6C3F1 mouse from a chronic study. Large areas are effaced and replaced by necrotic cell debris (arrows).

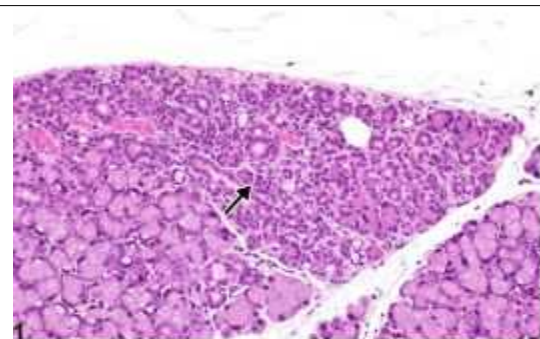
#### Harderian Gland - Pigment (색소)



Harderian gland - Pigment in a female F344/N rat from a subchronic study. There are golden to dark brown amorphous clumps or laminated concretions of pigment (likely porphyrin) in the acinar lumens (arrow).

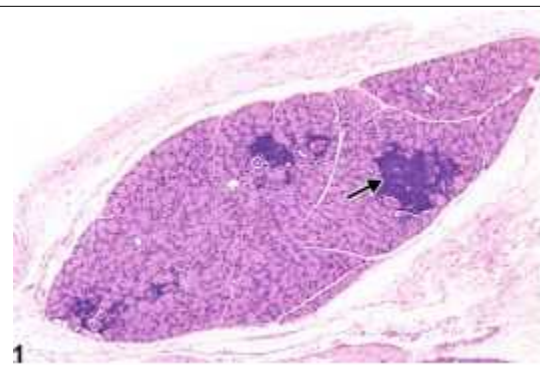
#### 4) 누선

#### Lacrimal Gland - Atrophy (위축)



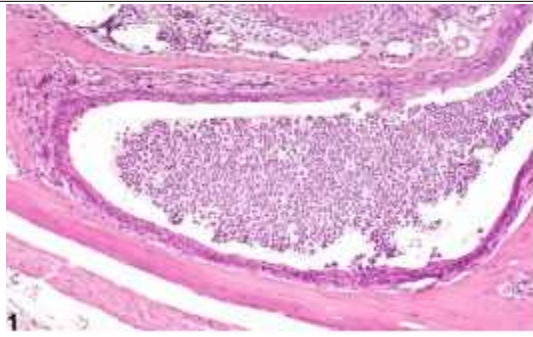
Lacrimal gland - Atrophy in a male B6C3F1 mouse from a chronic study. Atrophy (arrow) is characterized by a focus of shrunken acini lined by small, low cuboidal to flattened cells with increased fibrous stroma.

#### Lacrimal Gland - Infiltration Cellular, Mononuclear Cell (단핵세포 침윤)



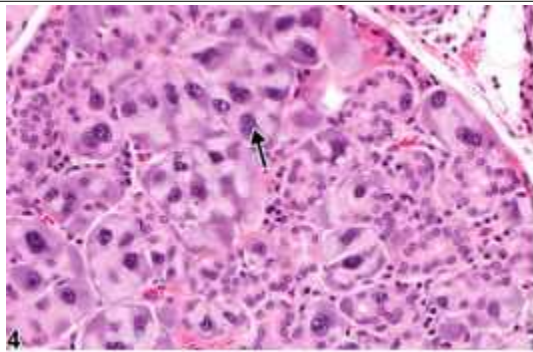
Lacrimal gland - Infiltration cellular, Mononuclear cell in a male B6C3F1 mouse from a chronic study. Variably sized interstitial foci of mononuclear cells (mainly lymphocytes) (arrow) are present in the lacrimal gland.

## Lacrimal Gland - Inflammation (염증)



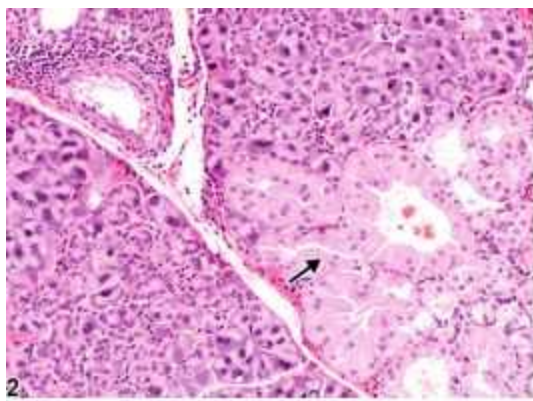
B6C3F1 mouse from a chronic study. Acute inflammation is characterized by predominantly neutrophil accumulations in the lacrimal gland duct.

## Lacrimal Gland - Karyomegaly (거대핵)



Lacrimal gland - Karyomegaly in a male Osborne-Mendel rat from a chronic study. Karyomegaly is characterized by acinar cells with enlarged nuclei (arrow), which are often pleomorphic.

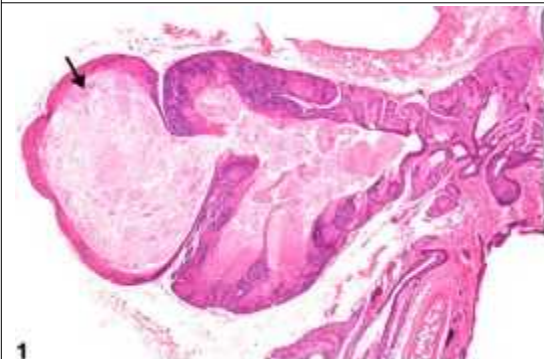
## Lacrimal Gland - Metaplasia, Harderian (하드리안 화생)



Lacrimal gland - Metaplasia, Harderian in a male Osborne-Mendel rat from a chronic study (higher magnification of Figure 1). Metaplasia, Harderian (arrow) is characterized by tubules lined by cuboidal cells with pale, foamy to vacuolated cytoplasm resembling Harderian gland alveoli.

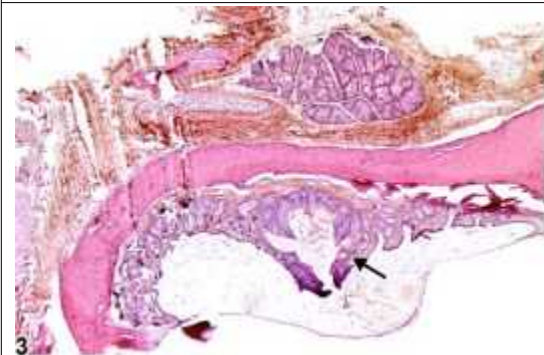
## 5) Zymbal 선

### Zymbal's Gland, Duct - Cyst (낭포)



Zymbal's gland, Duct - Cyst in a female F344/N rat from a chronic study. The Zymbal's gland duct is markedly distended (arrow).

### Zymbal's Gland - Hyperplasia (증생)



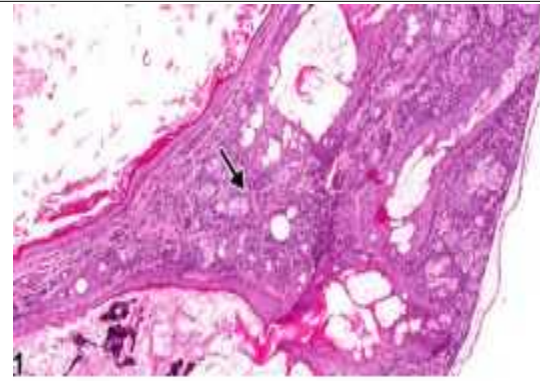
Zymbal's gland - Hyperplasia in a male Fischer 344/N rat from a chronic study. There is an increase in the number of sebaceous acini with slight lobular architectural distortion and compression of adjacent tissue (arrow in the diffuse Zymbal's gland tissue in the external ear canal).

### Zymbal's Gland - Hypertrophy (증대)



Zymbal's gland - Hypertrophy in a male F344/N rat from a chronic study. There are clusters of enlarged epithelial cells (arrows).

## Zymbal's Gland - Inflammation (염증)

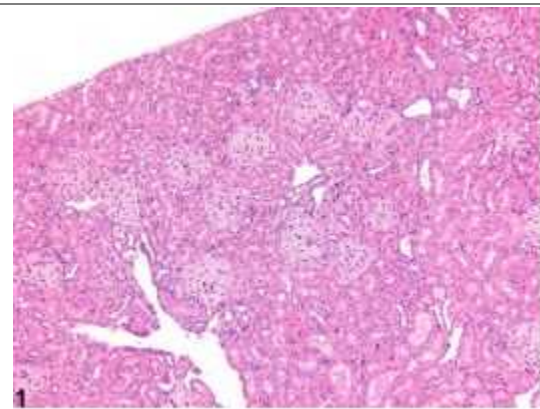


Zymbal's gland - Inflammation, Chronic in a male Tg.AC (FVB/N) homozygous mouse from a subchronic study. Chronic inflammation (arrow) in the Zymbal's gland.

## 13. 비뇨기계

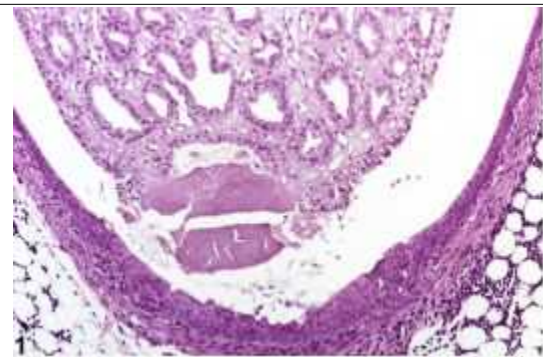
## 1) 신장

## Kidney - Amyloid (아밀로이드)



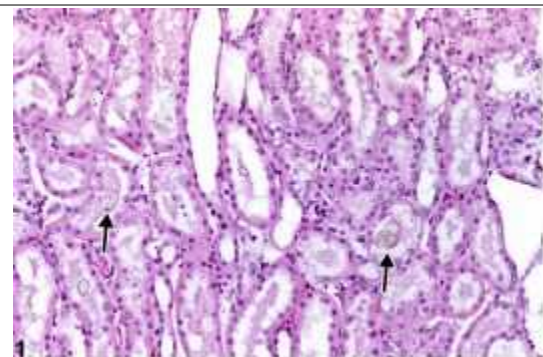
Kidney, Glomerulus - Amyloid in a female B6C3F1 mouse from a chronic study. Glomeruli contain a pale, amorphous, eosinophilic material identified as amyloid.

### Kidney - Calculus (결석)



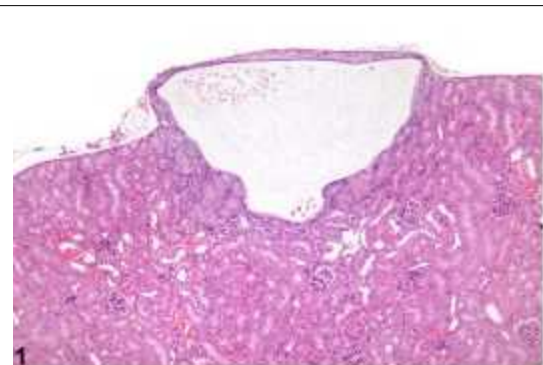
Kidney - Calculus in a female F344/N rat from a chronic study. A small calculus is present near the tip of the renal papilla.

### Kidney - Crystal (결정체)



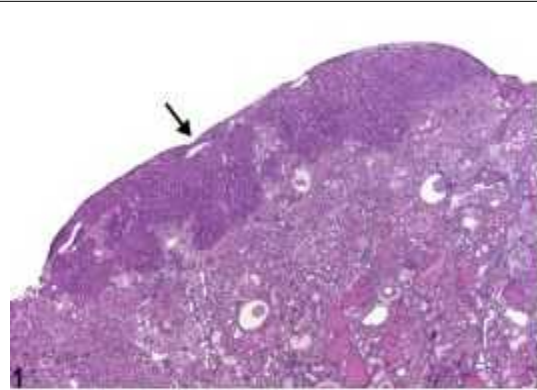
Kidney, Renal tubule - Crystals in a male B6C3F1 mouse from a chronic study. There are crystals (arrows) within tubule lumens.

### Kidney - Cyst (낭포)



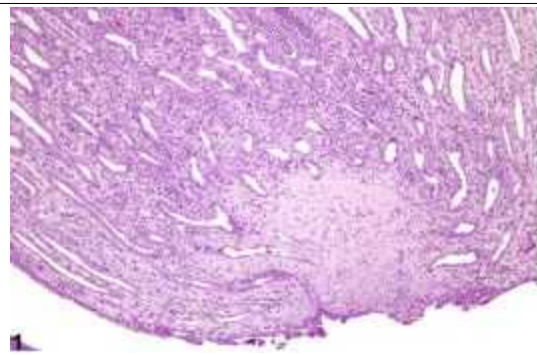
Kidney, Renal tubule - Cyst in a male Tg.Ac (FVB/N) hemizygous mouse from a subchronic study. A spontaneous cortical cyst lined by flattened cells is present.

## Kidney - Ectopic Tissue (이소성 조직)



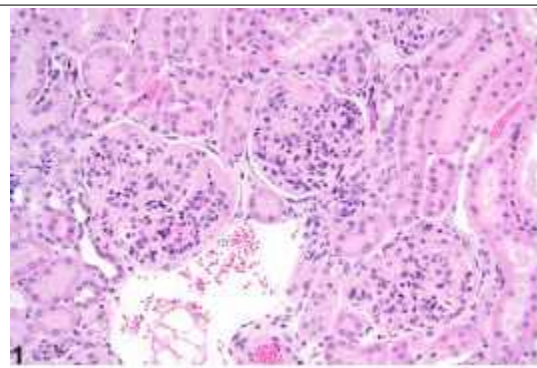
Kidney - Ectopic tissue, Liver in a female F344/N rat from a chronic study. Ectopic liver (arrow) involves the capsule of the kidney.

## Kidney - Fibrosis (섬유화)



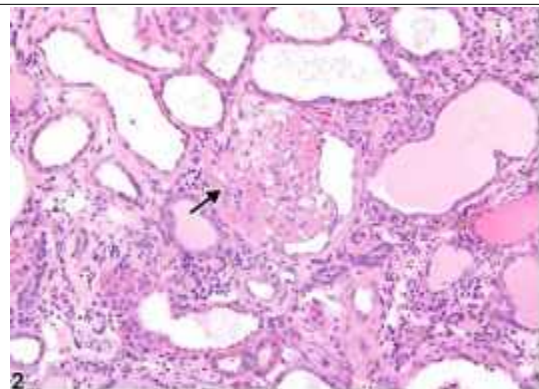
Kidney - Fibrosis in a female F344/N rat from a chronic study. A focal area of fibrosis is present in the distal renal papilla.

## Kidney - Glomerulonephritis (사구체신염)



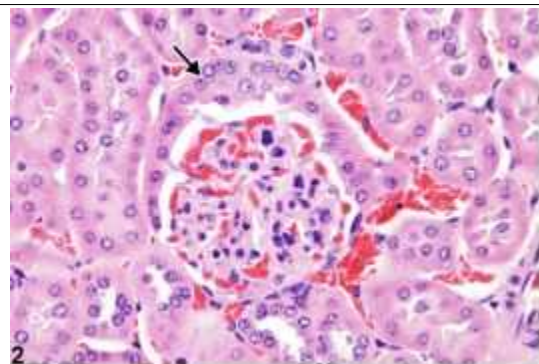
Kidney - Glomerulonephritis in a female B6C3F1 mouse from a chronic study. Glomerulonephritis is characterized by enlarged glomeruli with increased cellularity and mesangial expansion.

### Kidney - Glomerulosclerosis (사구체경화증)



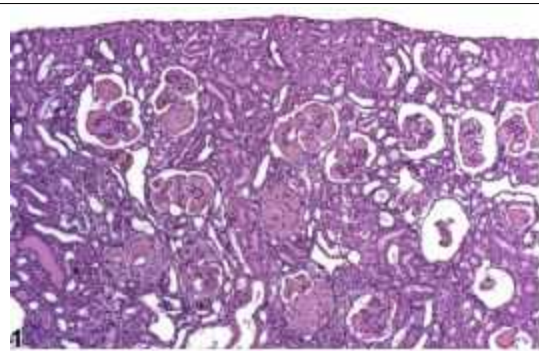
Kidney - Glomerulosclerosis in a male Wistar Han rat from a chronic study. Affected glomeruli often have adhesions (arrow) between the glomerular tuft and Bowman's capsule.

### Kidney, Glomerulus - Metaplasia (사구체 화생)



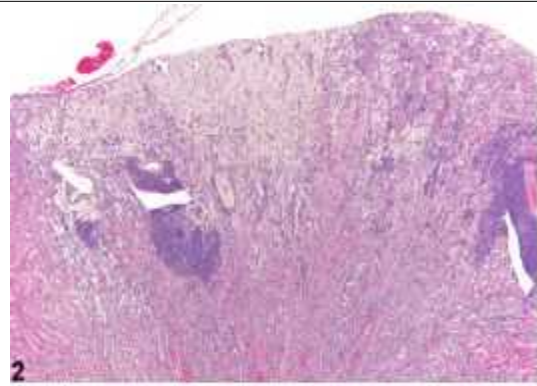
Kidney, Glomerulus - Metaplasia in a female B6C3F1 mouse from a chronic study. Metaplasia is characterized by a change from the flattened parietal epithelium to cuboidal epithelium (arrow).

### Kidney - Hyaline Glomerulopathy (유리질 사구체병증)



Kidney - Hyaline glomerulopathy in a female B6C3F1 mouse from a chronic study. Hyaline glomerulopathy is characterized by enlargement of the glomerular tufts by eosinophilic material.

## Kidney - Infarct (경색)



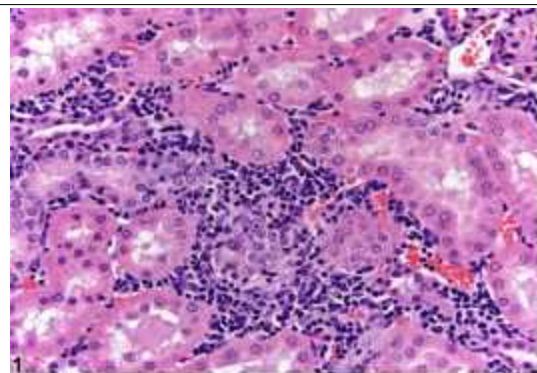
Kidney - Infarct in a female B6C3F1 mouse from a chronic study. This infarct has a prominent area of basophilic inflammatory cellularity associated with an infarcted area.

## Kidney - Inflammation (염증)



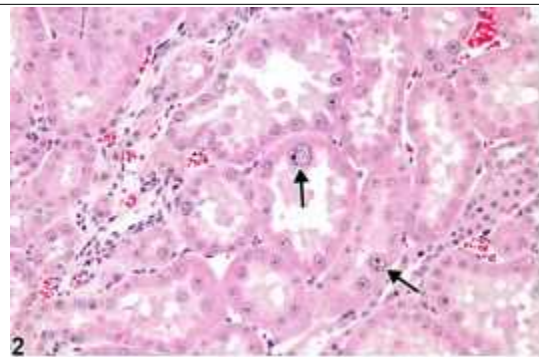
Kidney, Renal Pelvis - Inflammation, Chronic in a female F344/N rat from a chronic study. Inflammation involves the renal pelvis with infiltrates of inflammatory cells in the pelvis and peripelvic tissue; note the hyperplasia of the papillary epithelium and urothelium.

## Kidney, Interstitium - Infiltration, Cellular (세포침윤)



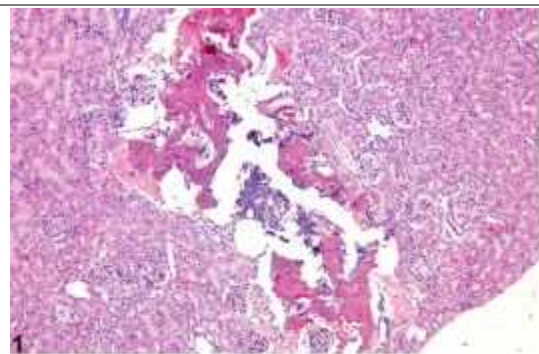
Kidney, Interstitium - Infiltration, Cellular, Lymphocyte in a rat. There are relatively small numbers of lymphocytes in the renal cortical interstitium, with little to no tissue damage.

### Kidney - Karyomegaly (거핵세포)



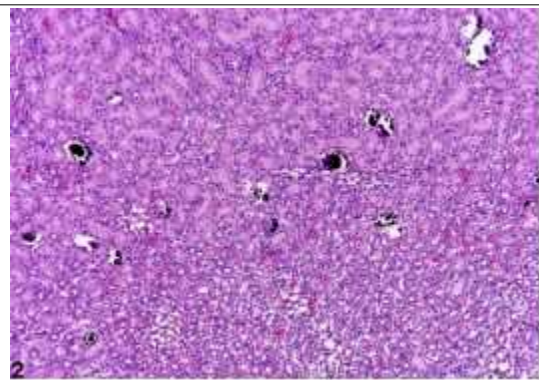
Kidney - Karyomegaly in a male F344/N rat from a subchronic study. Karyomegaly is present in several tubular epithelial cells.

### Kidney - Metaplasia, Osseous (골 화생)



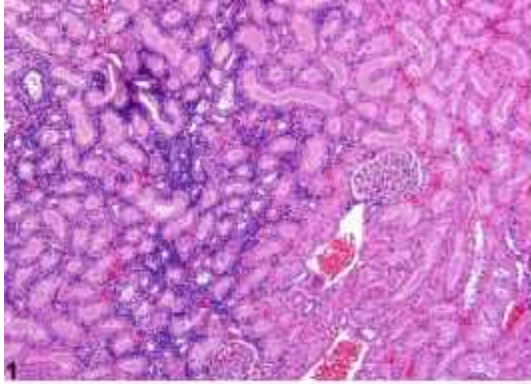
Kidney - Metaplasia, Osseous in a female B6C3F1 mouse from a chronic study. An area of mature bone and associated hematopoietic cells is present in the renal cortex.

### Kidney - Mineralization (무기질침착)



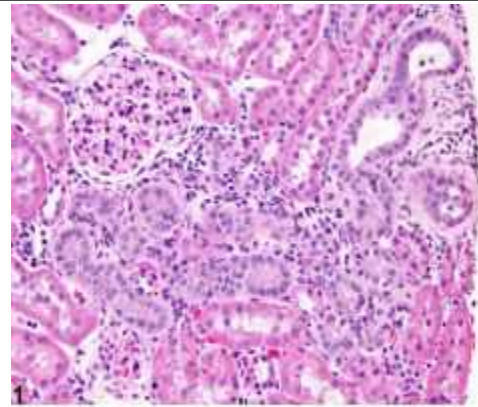
Kidney - Mineralization in a female Sprague-Dawley rat from an acute study. Mineralization is commonly observed in the area of the outer stripe and inner stripe of the outer medulla.

## Kidney - Nephroblastematosi (신아세포종증)



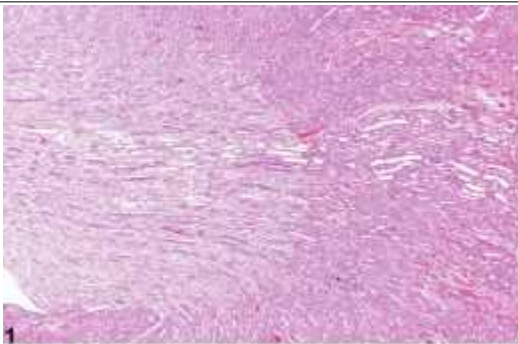
Kidney - Nephroblastematosi in a female Harlan Sprague-Dawley rat from a subchronic study. An area of dense basophilic cellularity can be seen in the renal cortex.

## Kidney - Nephropathy, Chronic Progressive (만성진행성 신증)



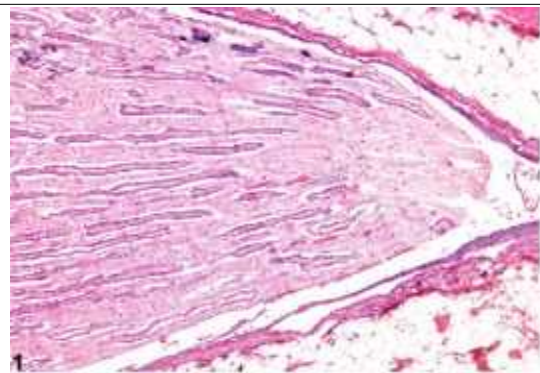
Kidney - Nephropathy, Chronic progressive in a male F344/N rat from a subchronic study. The early cases of chronic progressive nephropathy (CPN) occur as focal to multifocal areas of tubule basophilia with or without hyaline (protein) casts.

## Kidney - Nephropathy, Obstructive (폐색성 신증)



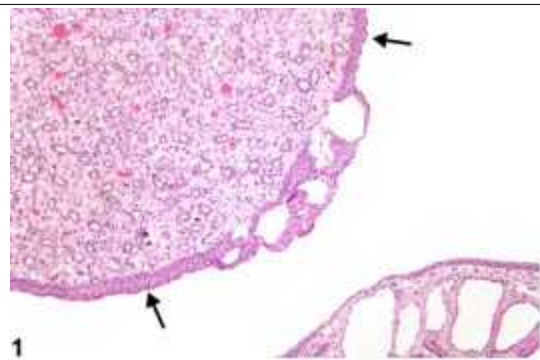
Kidney - Nephropathy, Obstructive in a female F344/N rat from a chronic study. Dilated tubules extending from the renal papilla into the cortex are characteristic of obstructive nephropathy.

### Kidney, Papilla - Necrosis (유두 괴사)



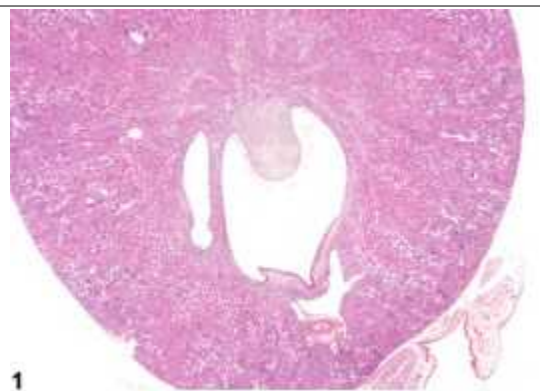
Kidney, Papilla - Necrosis in a male F344/N rat from a chronic study. Early necrosis of the papilla shows loss of cellular detail and staining affinity.

### Kidney, Papilla, Epithelium - Hyperplasia (유두 상피 증생)



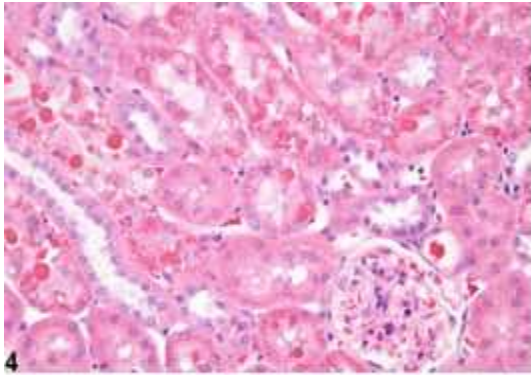
Kidney, Papilla, Epithelium - Hyperplasia in a male F344/N rat from a chronic study. The epithelium is thickened (arrows), and there are large clear spaces within the hyperplastic epithelium.

### Kidney, Pelvis - Dilation (신우 확장)



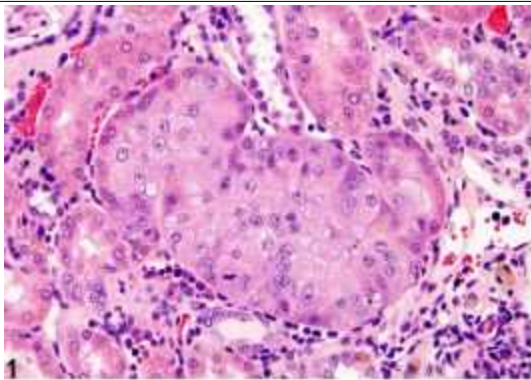
Kidney, Pelvis - Dilation in a male B6C3F1 mouse from a chronic study. Dilation of the renal pelvis is accompanied by atrophy of the renal papilla.

## Kidney, Renal Tubule - Accumulation, Hyaline Droplet (세뇨관 초자 축적)



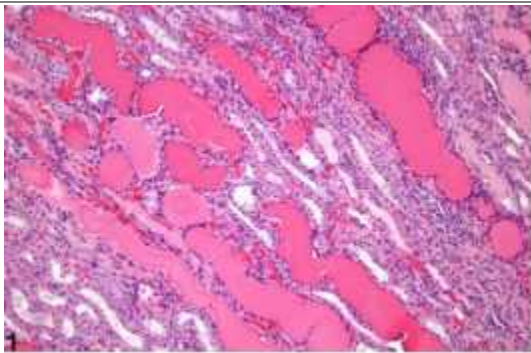
Kidney, Renal tubule - Accumulation, Hyaline droplet in a male F344/N rat from a subchronic study. Increased number and size of hyaline droplets associated with chemically induced increase in alpha 2u-globulin.

## Kidney, Renal Tubule - Atypical Tubule Hyperplasia (비정형 세뇨관 증생)



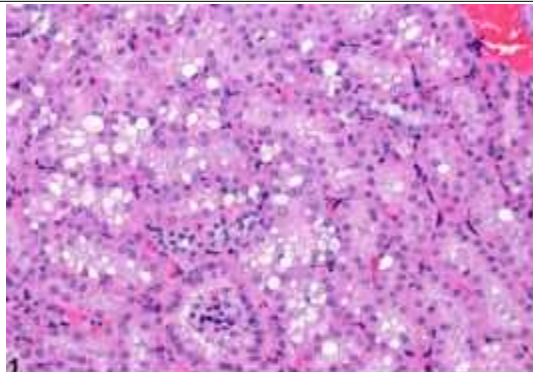
Kidney, Renal tubule - Atypical tubule hyperplasia in a male F344/N rat from a chronic study. Atypical tubule hyperplasia is confined to one tubule and is characterized by an increase in cellularity and cell size, cytoplasmic basophilia, nuclear enlargement, and circumferential expansion.

## Kidney, Renal Tubule - Cast (세뇨관 캐스트)



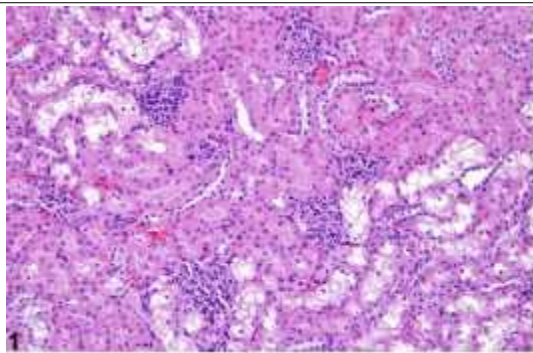
Kidney, Renal tubule - Cast in a male F344/N rat from a chronic study. Linear, hyaline (protein) casts are present in the medullary tubules.

Kidney, Renal Tubule - Cytoplasmic Alteration (세뇨관 세포질 변화)



Kidney, Renal tubule - Normal in a male B6C3F1 mouse from a chronic study. Numerous clear cytoplasmic vacuoles are present in renal tubule cells.

Kidney, Renal Tubule - Degeneration (세뇨관 변성)



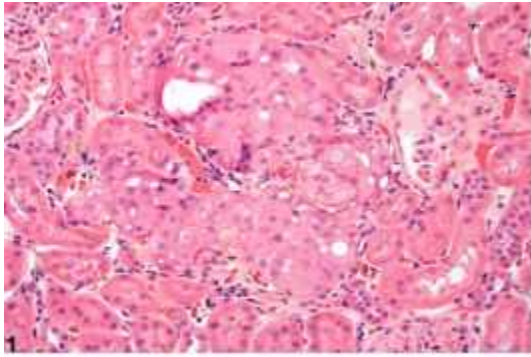
Kidney, Renal tubule - Degeneration in a male Tg.Ac (FVB/N) hemizygous mouse from a subchronic study. The degeneration of cortical tubule epithelial cells is characterized by vacuolation of the cytoplasm and pyknosis of the nuclei.

Kidney, Renal Tubule - Dilation (세뇨관 확장)



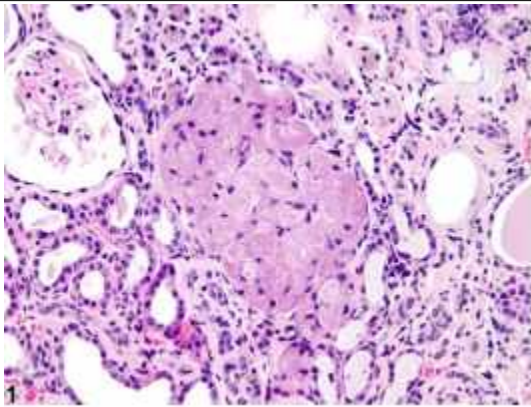
Kidney, Renal tubule - Dilation in a male F344/N rat from a chronic study. Tubule dilation is present throughout the outer stripe of the outer medulla, extending into the cortex.

## Kidney, Renal Tubule - Hyperplasia, Amphophilic-Vacuolar (세뇨관 양염색성공포)



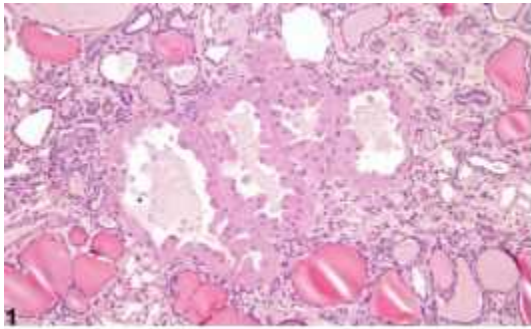
Kidney, Renal tubule - Hyperplasia, Amphophilic-vacuolar in a female F344/N rat from a chronic study. There is a small focus of hyperplastic tubule cells with amphophilic and vacuolated cytoplasm.

## Kidney, Renal Tubule - Hyperplasia, Oncocytic (세뇨관 종양세포 증생)



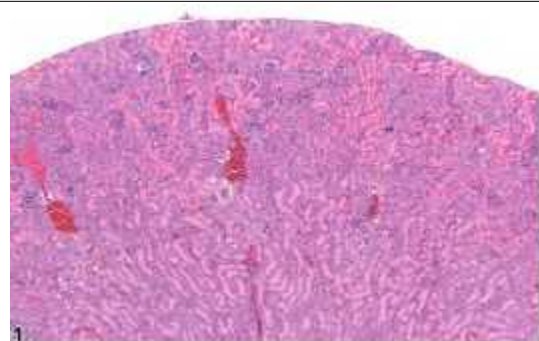
Kidney, Renal tubule - Hyperplasia, Oncocytic in a male F344/N rat from a chronic study. Oncocytic hyperplasia represents an increased number of tubule epithelial cells characterized by cytoplasmic enlargement due to the presence of lightly staining, finely granular cytoplasm and centralized nuclei (oncocytes).

## Kidney, Renal Tubule - Hypertrophy (세뇨관 비대)



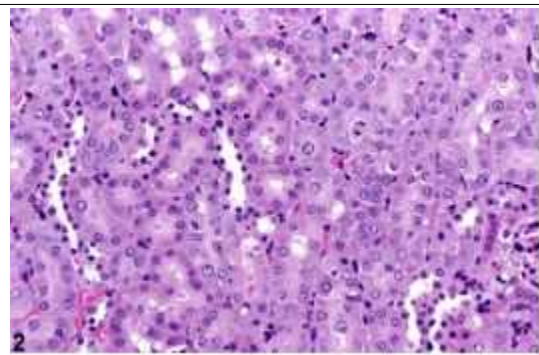
Kidney, Renal tubule - Hypertrophy in a male F344/N rat from a chronic study. These hypertrophied tubular epithelial cells with an increased amount of amorphous, eosinophilic cytoplasm and small, round, dense nuclei are associated with chronic progressive nephropathy.

### Kidney, Renal Tubule - Necrosis (세뇨관 괴사)



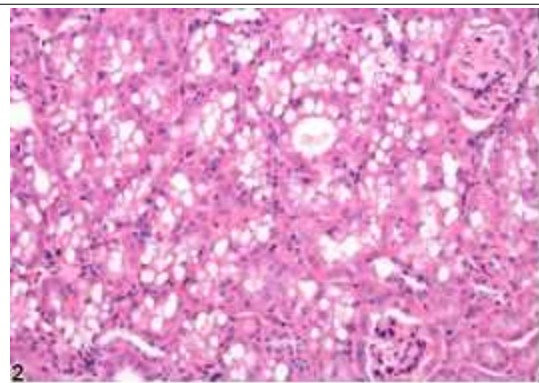
Kidney, Renal tubule - Necrosis in a female B6C3F1 mouse from a chronic study. Diffuse tubule necrosis appears as lighter-staining, more eosinophilic tubules.

### Kidney, Renal Tubule - Regeneration (세뇨관 재생)



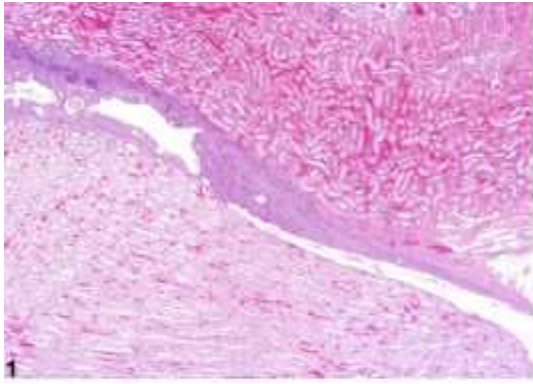
Kidney, Renal tubule - Regeneration in a male rat from an acute study. Regeneration following acute tubule epithelial injury is characterized by flattened epithelium and tubule epithelial cell basophilia and is accompanied by nuclear crowding.

### Kidney, Renal Tubule - Vacuolation, Cytoplasmic (세뇨관 세포질 공포)



Kidney, Renal tubule - Vacuolation, Cytoplasmic in a treated male B6C3F1 mouse from a chronic study. Numerous clear vacuoles are present in the cytoplasm of renal tubule epithelial cells.

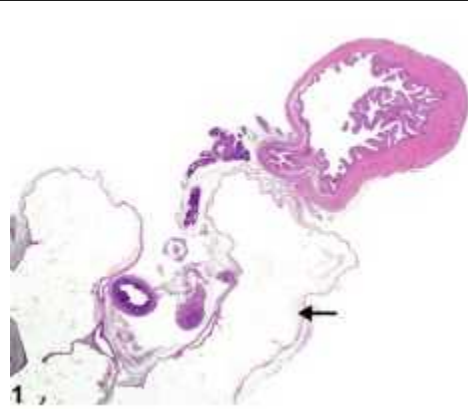
## Kidney, Urothelium - Hyperplasia (요로상피 증생)



Kidney, Urothelium - Hyperplasia in a male F344/N rat from a chronic study. A focus of urothelial hyperplasia is present in the renal pelvis adjacent to the renal papilla.

## 2) 요로

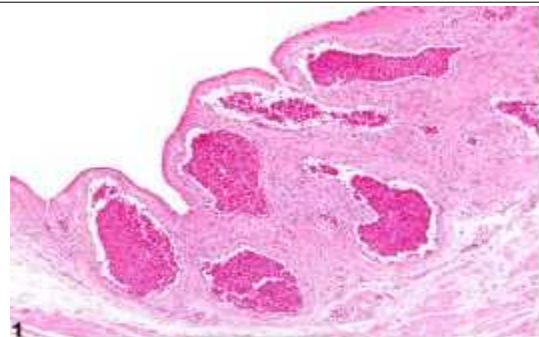
## Ureter - Dilation (확장)



Greatly dilated ureter (arrow) of probable familial origin from a male mouse.

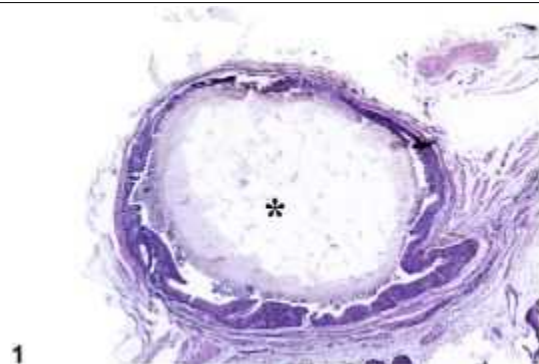
### 3) 방광

#### Urinary Bladder - Angiectasis (혈관확장)



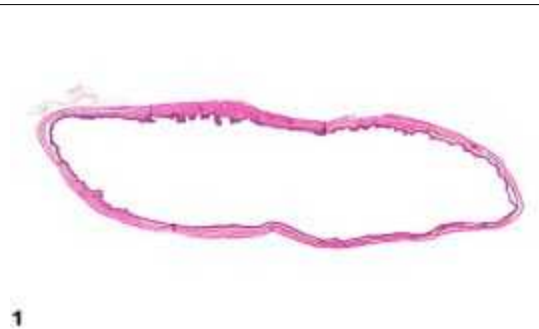
Angiectasis. Dilated blood vessels within a fibrous stroma in the urinary bladder submucosa from a female B6C3F1 mouse in a chronic study.

#### Urinary Bladder - Calculus/Crystal (결석, 결정체)



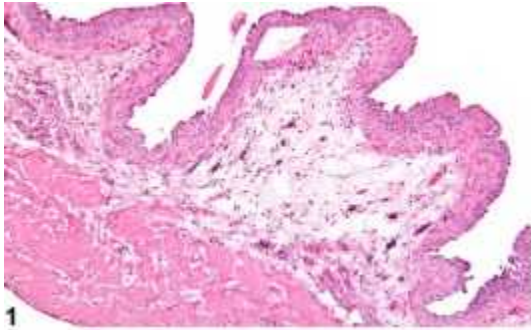
A calculus (asterisk) fills the entire bladder lumen from a male F344/N rat in a chronic study.

#### Urinary Bladder - Dilation (확장)



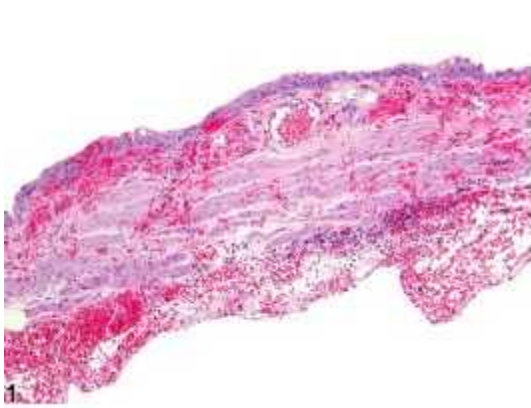
Dilation of the urinary bladder with focal to diffuse flattening of urothelium, from a male B6C3F1 mouse in a chronic study.

## Urinary Bladder - Edema (부종)



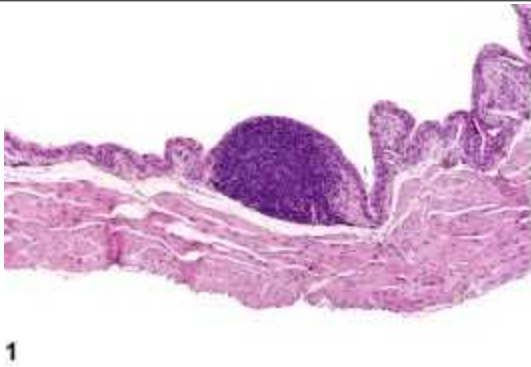
A focal area of edema in the urinary bladder submucosa from a female B6C3F1 mouse in a chronic study.

## Urinary Bladder - Hemorrhage (출혈)



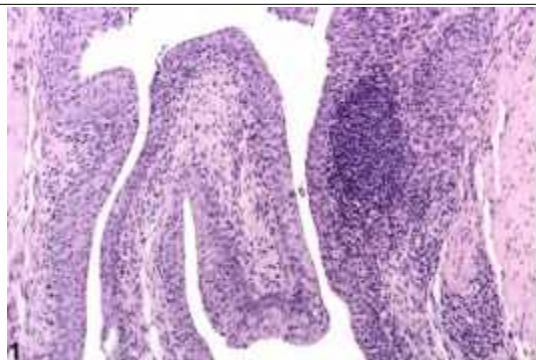
Hemorrhage associated with inflammation, from a female F344/N rat in a chronic study.

## Urinary Bladder - Infiltration Cellular, Lymphocyte (임파구 침투)



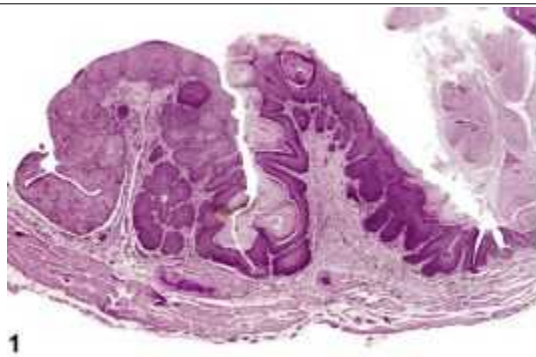
Infiltrative cellular, lymphocyte-focal lymphoid aggregate underlying the urothelium from a female B6C3F1 mouse in a chronic study.

### Urinary Bladder - Inflammation (염증)



Chronic-active inflammation involving the urothelium and subepithelial layers from a male F344/N rat in a chronic study.

### Urinary Bladder - Metaplasia (화생)



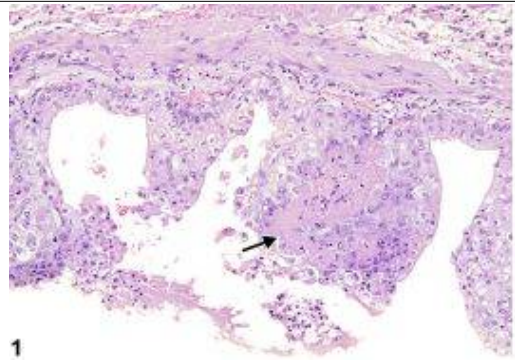
Diffuse squamous metaplasia and keratinization of hyperplastic urothelium from a female F344/N rat in a subchronic interim study.

### Urinary Bladder - Mineralization (무기질 침착)



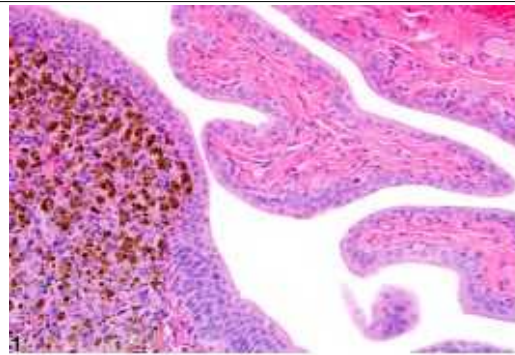
Focal basophilic deposits of serosal mineralization from a male F344/N rat in a chronic study.

## Urinary Bladder - Necrosis (괴사)



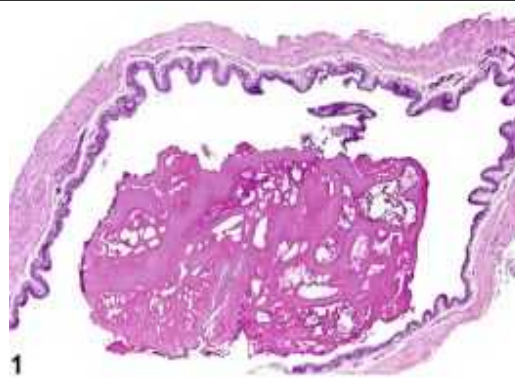
An area of urothelial necrosis (arrow) associated with acute inflammation from a male F344/N rat in a chronic study.

## Urinary Bladder - Pigment (색소)



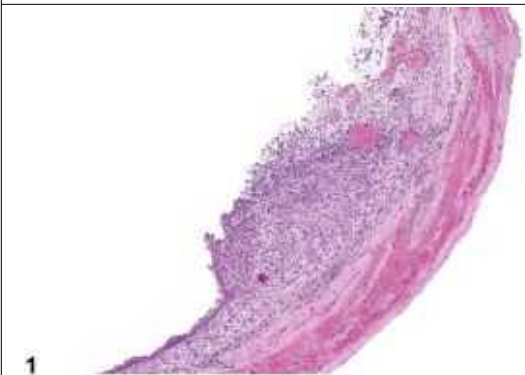
Pigment—a focal area of hemosiderin from a female F344/N rat in a chronic study.

## Urinary Bladder - Proteinaceous Plug (단백질 플러그)



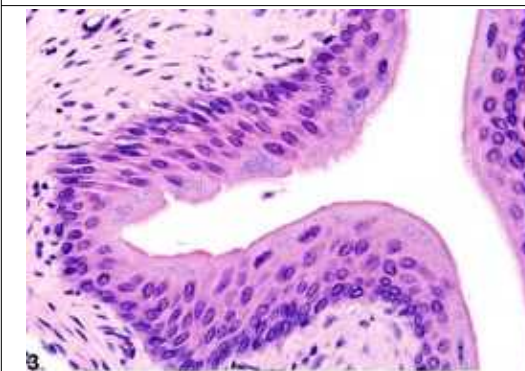
An eosinophilic amorphous proteinaceous plug in the bladder lumen from a male B6C3F1 mouse in a chronic study.

### Urinary Bladder - Ulcer (궤양)



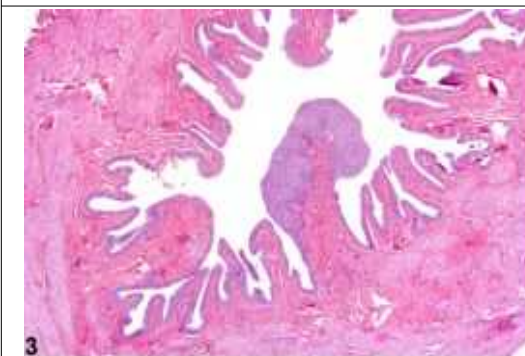
A focal ulcer of the urothelium, with inflammation of the underlying submucosa and muscularis layers, from a male B6C3F1 mouse in a chronic study.

### Urinary Bladder, Urothelium - Cytoplasmic Granules (세포질 과립체)



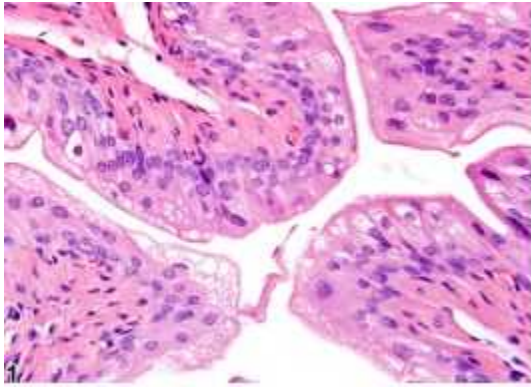
Cytoplasmic granules - basophilic granules present in the urothelium from a male B6C3F1 mouse in a 28-day study.

### Urinary Bladder, Urothelium - Hyperplasia (요로상피 증생)



Urothelial hyperplasia (nodular) from a male F344/N rat in a chronic study.

## Urinary Bladder - Vacuolation, Cytoplasmic (세포질 공포)



Cytoplasmic vacuolation: clear vacuoles are present in urothelial "umbrella" cells from a male B6C3F1 mouse in a 28-day study.



## <<연 구 진>>

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## <<연 구 기 간>>

2016. 1. 1 ~ 2016. 11. 30



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**-별첨-**

(2016-연구원-1250)

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발 행 일 : 2016년 11월  
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