3. Chapter II

Bovine Tumors Detected at Miyakonojo Meat Inspection Office of Miyazaki Prefecture during 1974-1996

3.1 *INTRODUCTION*

Several long-term surveillance data on tumors in domestic animals have been reported not only in Europe and North American countries but also in Japan [21,23, 40,44,45,55,56]. Although Kanagawa Meat Inspection Office reported a survey on the incidence of porcine tumors, only a few surveys on cattle tumors including a regional study were reported in Japan.

A national survey on the incidence of tumors in cattle started in 1995 by National Conference of Meat inspection offices. This prompted us to conduct epidemiological and pathological surveys on the incidence of tumors in cattle slaughtered at Miyakonojo Meat Inspection Office. Our goal of this study is to compare the data examined among municipal and prefectures meat inspection offices in Kyushu.

3.2 *MATERIALS AND METHODS*

Sampling: A total of 377 tumors detected from 162,328 slaughtered cattle during 23 years (1974 to 1966) at Miyakonojo Meat Inspection Office, Miyazaki Prefecture, were examined. The cattle examined were transported from Miyakonojo city and Nishimorokata-gun in Miyazaki prefecture, and Satsunan area in Kagoshima prefecture. The number of cattle with any tumors in each year, breed, gender, and the location of the tumors were recorded, respectively. The cattle examined were divided into four groups; (1) cattle used for reproduction such as Japanese black beef cattle aged more than four

years old, (2) dairy cattle such as Holstein aged more than four years old, (3) beef cattle less than three years old, and (4) calves less than one year old.

Pathological examinations: The tumor tissues were fixed in 10% neutral buffered formalin or methanol-Carnoy's solution and embedded in paraffin. Then, paraffin sections of 4 μm were stained with hematoxylin and eosin (HE). Some selected sections were also stained with several specific stainings including periodic acid Schiff (PAS) and Azan stains. Immunostaining for the detection of antigens *in situ* was performed by avidin-biotin peroxidase complex (ABC) methods using a system kit (Vector Lab., Burlingame, CA, USA). Based on these histopathological examinations, diagnoses of the tumors were determined.

Data analysis: To compare the incidence of tumors in cattle in Kyushu, we collected the data concerning the incidence of tumors in cattle from additional five meat inspection offices in Miyazaki prefecture and 17 meat inspection offices out of Miyazaki prefecture. However, we excluded papillomas and associated tumors from the present data, since a few information were available.

3.3 *RESULTS*

Change of the incidence of tumors in cattle during 23 years examined: Tumors were detected in 377 of 162,328 (232 per 100,000) slaughtered cattle examined during 23 years (1974 to 1996) at Miyakonojo Meat Inspection Office, Miyazaki prefecture. The high incidences of tumors were recoded in 1979 (485 per 100,000), 1988 (445 per 100,000) and 1980 (441 per 100,000), respectively. In contrast, the bottoms were in 1990 (41 per 100,000) and 1984 (75 per 100,000) (Fig. 16).

Incidence of tumors among species of cattle: A total of 118,438 slaughtered cattle were inspected during 14 years (1983~1996). The details of four groups examined

were as follows; 78,843 cattle used for reproduction (66.6%), 20,313 dairy cattle (17.2%), 17,720 beef cattle (15.0%), and 1,562 calves (1.3%). The incidence of tumors detected in each four groups was as follows; 182 cattle used for reproduction (230 per 100,000), 29 dairy cattle (143 per 100,000), 12 beef cattle (68 per 100,000), and 6 calves (384 per 100,000), and 21 unrecorded cases.

Details of tumors detected: Tumors were detected in 377 of slaughtered cattle examined during 23 years including 64 mesotheliomas (Fig.17,18,19,20), 56 granulosa cell tumors (Fig.21,22,23,24), 48 bovine leukosis (Fig.25,26,27,28,29,30,31,32), 20 lung cancers (Fig.33,34,35,36), 19 liver carcinomas (Fig.37,38,39), and 17 adrenocortical adenomas (Fig.40,41,42,43) (Table 3). These six tumors occupied approximately 60% among all tumors observed.

In the figures, several autopsy cases suffering from tumors examined in the present study were introduced. Figure 44, 45 and 46 represented pheochromocytoma, figure 47, 48, 49 represented malignant melanoma and figure 50, 51, 52, 53 represented rhabdomyosarcoma and figure 54, 55 represented schwannoma.

Mesothelioma was observed in 61 Japanese black beef cattle and 4 Holstein species (mean age; 11-years-old). Among them, 43 cases were classified into epithelial type, which was characterized with tube formation and/or papillomatous proliferation, 13 cases were fibrous type with remarkable proliferation of basal body, and 8 were the mixed type.

The locations of granulosa cell tumors in the ovary were examined among 56 cases. Two cases were observed bilaterally. Sixteen were observed laterally. Although the location of the tumor was not currently recorded, 19 cases had lateral ovarian tumors. Moreover, the location of the tumors was not available in 3 cases. These 25 cases diagnosed histopathologically were classified into middle ovary follicle type (13 cases) and strip type (12 cases).

Fifty-eight bovine leukosis were 33 adult multi-centric type, 5 thymic type, and 10 unknown, respectively.

Comparative study of the incidence of tumors in cattle observed among meat inspection offices in Miyazaki prefecture: Tumors were detected in 277 of 359,416 (77 per 100,000) slaughtered cattle examined during 16 years (1978～1993) at five meat inspection offices in Miyazaki prefecture except for Miyakonojo. The incidence of tumors observed in each meat inspection office was ranging 50-159 per 100,000 heads (Table 4). Compared to the incidence of tumors at these meat inspection offices within the same period, that at Miyakonojo Meat Inspection Office was the highest (247 per 100,000). Interestingly, when the frequency of tumors at Miyakonojo and Takasaki Meat Inspection Office, a meat processing plant authorized for exportation to the USA and processing mainly beef cattle, was compared, the incidence at the former was approximately four fold higher than that at the latter. The incidence of mesotheliomas among the five meat inspection offices other than Miyakonojo was 4.73 per 100,000.

Comparative study of the incidence of tumors in cattle observed among meat inspection offices in Kyushu: Tumors were detected in 1,186 of 2,175,645 (55 per 100,000) slaughtered cattle examined during 16 years (1978～1993) at 17 meat inspection offices including municipal and prefectural facilities other than Miyazaki prefecture in Kyusyu. The highest incidence was bovine leukosis (304 cases, 13.97 per 100,000). Mesothelioma was observed in 20 cattle (0.92 per 100,000). It should be noted that the incidence of mesothelioma at Miyakonojo Meat Inspection Office during the same period was 57 cases (53.13 per 100,000).

3.4 *DISCUSSION*

According to the "Report of Hygiene Administration" edited by the Division of

Statistical Analyses in the Ministry of Health and Welfare, which includes the total number of tumors observed in meat inspection offices in Japan, tumors were detected in ranging 74 to 591 (the mean 259 cases) per 100,000 slaughtered cattle examined during 20 years (1975 to 1994). Similar to that of the government data, tumors were also detected in ranging 41 to 485 (the mean 232 cases) per 100,000 slaughtered cattle in the present study. In Miyakonojo Meat Inspection Office, the incidence of tumor cases tended to alter every 6-7 years. The real reasons is unclear, however, we cannot rule out the possibility of the personal factors that were in charge of the tumor inspection.

There was higher incidence in the older breeding cattle with more times of giving birth, while in the cattle with a short breeding period the incidence was comparatively low, with no relative with the breed. We thought that older cattle commonly have the higher incidence of tumors. However, it was found that the cattle under 1 year old also showed a high incidence, which may be the result that these cattle were transported to the meat inspection office because of some diseases.

According to the research of the Miyakonojo Meat Inspection Office, tumors with the highest incidence were of mesotheliomas (64 cases, 17%), granulose cell tumor (56 cases), and bovine leukosis (48 cases), respectively. The high incidence of mesotheliomas was in accordance with the reports from Miyazaki University [44,56]. These results including our data might indicate that the incidence of mesotheliomas is higher in South Kyoshu compared to that in the other areas.

Generally, the incidence of mesotheliomas was approximately 0.22 to 1.4% of all bovine tumors, and it was also found in fetus of later pregnant period and in young calves [12,22,36]. In other adult domestic animals, mesotheliomas were also observed with a low frequency [12,22,36]. In this study, we found that the average age was 11 years old in the diseased cattle with mesotheliomas, showing a possible of postnatal cause. In

human, cases of breast mesotheliomas are frequently observed in patients with an inhaling exposure to asbestos [52]. From the present study and the data of the nationwide meat inspection office, it was found that abdominal mesotheliomas were of a high incidence in cattle. This may be because those cattle have much more frequent abdominal exposure to some carcinogens. The relationship between human mesotheliomas and asbestos has been proofed [52,60], while the tumoregenesis of bovine mesotheliomas is still unknown [22,36]. It is necessary to study the possible relationship between mesotheliomas and some substance with a similar chemical structure with asbestos, for example, the characteristic ash in South Kyushu.

Among ovary tumors, ovarian granulosa cell tumor was found to have a highest incidence in this study, which was in accordance with the reports from Saeki et al. [45]. Of which, most of the cases was of single side, with only two bilateral cases. In cattle, the inhibition of the left ovary action by the giant first stomach was reported [20], however, we did not find that this has some effects on the incidence of either the left or right ovary tumors.

Although bovine leukosis showed the highest incidence among tumors observed by the meat inspection offices in Japan [20,21], it was found to be the third one in Miyakonojo Meat Inspection. Among which, the adult multicentric type was the most one, and mostly found in Holstein breed, similar to the report of Onuma et al. [39]. Furthermore, in the research of bovine tumors in the prefectures in Kyushu during last 16 years, 304 cases of bovine leukosis were detected, among which 244 cases were found in one prefecture (260 per 100,000) (data not shown), suggesting that it is likely an endemic disease [39] occurring frequently in some specific area in Kyusyu.

3.5 *ABSTRACT*

Tumors were detected in 377 of 162,328 (232 per 100,000) slaughtered cattle examined during 23 years (1974～1996) at Miyakonojo Meat Inspection Office, Miyazaki Prefecture, including 64 mesotheliomas, 56 granulosa cell tumors, 48 bovine leukosis, 20 lung cancers,19 liver carcinomas and 17 adrenocortical adenomas. Mesothelioma was most frequently observed in Japanese black breed (11-years-old on average) and the incidence seemed to be much higher in Southern Kyushu including Miyakonojo areas than others areas of Kyushu.

Key words: cattle, meat inspection, mesothelioma, tumor

Fig.16 Change of the incidence tumors in cattle during 23 years examined

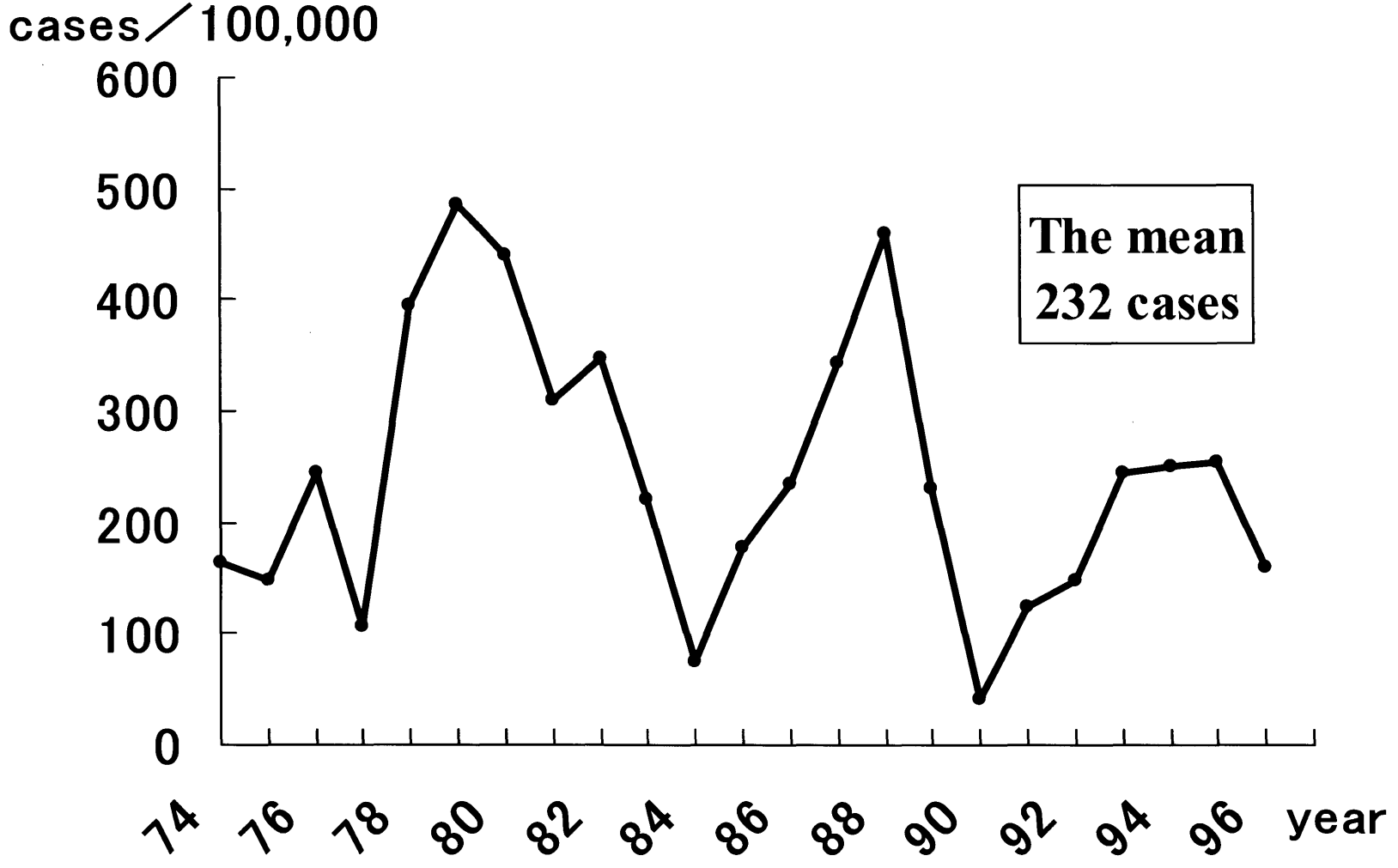


Table 3. Incidence of tumors in cattle observed among Miyakonojo Meat Inspection Office during 23 years

Classification	cases
Cutaneous system	***14***
malignant melanoma	3
melanoma	2
fibrosarcoma	3
fiborma	2
lipoma	1
squamous cell carcinoma	1
mixed tumor	1
other	1
Hematopoietic system	***51***
lyphoma	48
(adult type)	㉝
(thymic type)	⑤
hyperplasia of the spleen	3
Cardiovascular system	***1***
aortic body tumor	1
Respiratory system	***22***
lung cancer	20
(squmous cell tumor)	⑦
fibrosarcoma	2

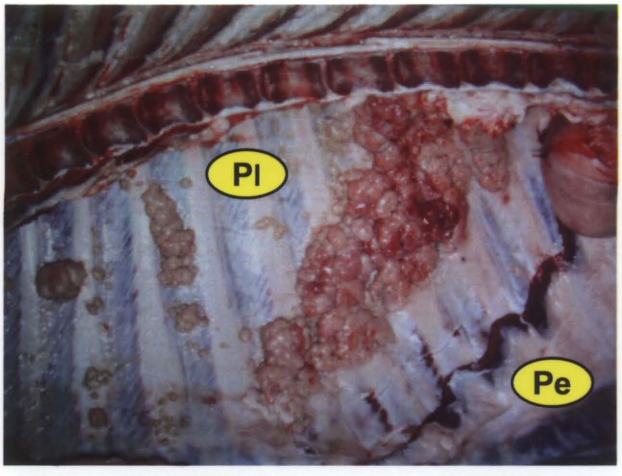
Classification	cases
Digestive system	***63***
hepatoma	19
(hepatocellulor carcinoma)	⑪
(cholangiocarcinoma)	④
liver papilloma	1
liver cell adnoma	12
hemangioma	2
fibrosarcoma	1
fibroma	2
squmous cell tumor	1
papilloma of the gall bladder	4
myxoma	1
intestinal adenoma	4
papilloma of the stomach	2
stomac hyperplastic polyp	5
hyperplasia of the pancreas	5
pancreatic carcinoma	1
adenocarcinoma	3
Urinary system	***8***
nephrobalstoma	3
renal carcinoma	1
papilloma	3
rhabdomyosarcoma	1

Classification	cases
Genital system	***71***
malignant granulosa cell tumor	9
granulosa cell tumor	47
luteoma	1
fibroma	1
leiomyoma of the uterus	7
leiomyosarcoma of the uterus	2
squmous cell tumor	2
adenoma, adenocarcinoma	2
Skeletal system	***6***
rhabdomyosarcoma	3
rhabdomyoma	1
schwannoma	1
fibroma	1
Others	***141***
malignant mesothelioma	58
mesothelioma	6
adrenocartical adenoma	17
pheochormaocytoma	4
cancer of the adrenal gland	1
thyroid adenoma	4
fibrosarcoma	1
ameloblastoma	1
mesenchymal chondrosarcoma	1
adenocarcinoma	9
unknown	39

○ include cases

Table 4. Comparsion of tumor occurrence situation with 6 meat inspection offices in Miyazaki prefecture (1978～1993)

Meat Inspection Office	meat inspection cases	tumor cases	cases per 100,000
Miyakonojo	107,283	265	247.0
Takasaki	123,182	83	67.4
Miyazaki	37,624	60	159.5
Kobayshi	41,633	51	122.5
Tsuno	113,898	57	50.0
Hyuga	43,079	26	60.4
Total	359,416	277	77.0



Pl :Pleura Pe :Peritoneum

Fig.17

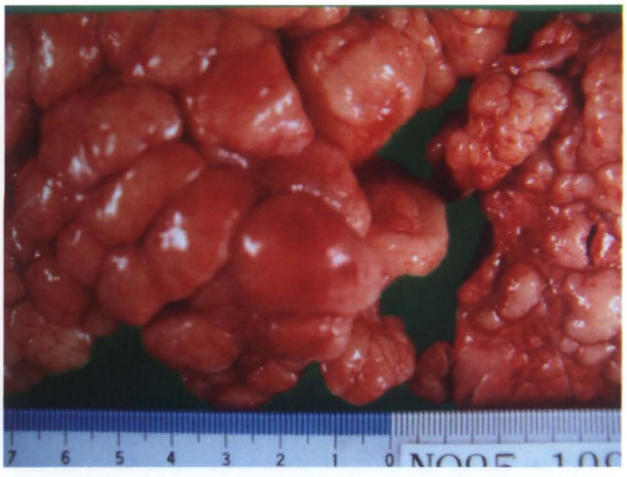


Fig.18

Fig.17 Malignant mesothelioma in a 3-year-old female Japanese black cattle, weighing about 545 kg. The neoplasm showing extend to the pleura.

Fig.18 Tumor nodules showing from gray-white to reddish-yellow colored nodules like fibrous peduncles.

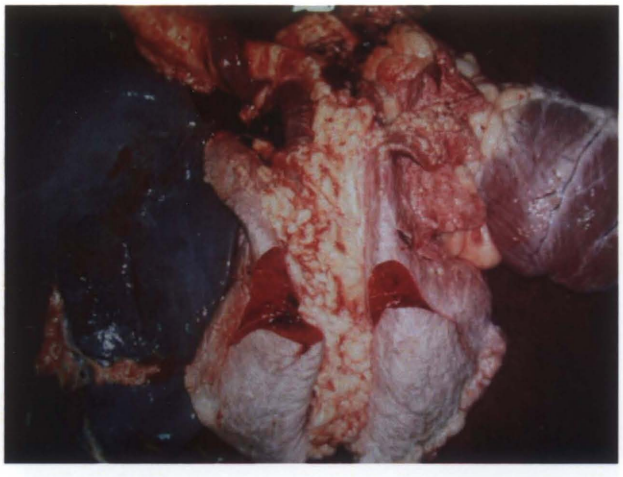


Fig.19

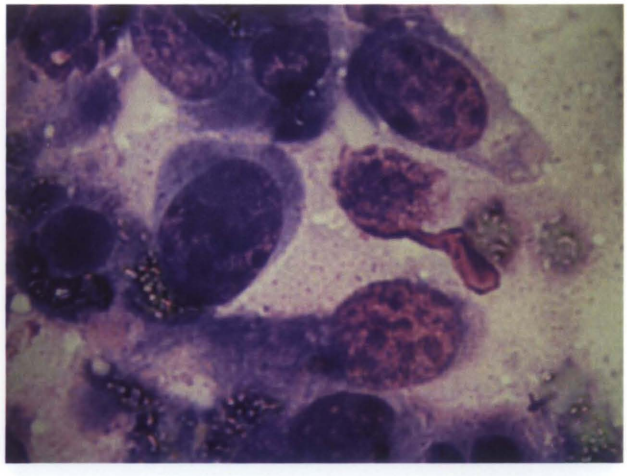


Fig.20

Fig.19 Some superficial nodules found in the parts of the diaphragm and lungs.

Fig.20 The tumor cells had moderate amount of eosinophilic cytoplasm and round to ovoid nuclei with the defined chromatin and a distinct nucleolus. Diff Quick stain. × 1000.

Fig.21

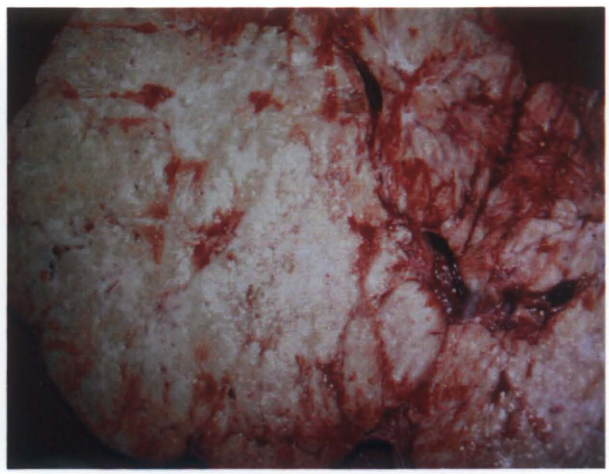


Fig.22

Fig.21 Granulose cell tumor in a 8-year-old female Japanese black cattle, weighing about 570kg. Surface view of granulosa cell tumor in the left ovary.
Fig.22 The left ovary was enlarged to approximately 30 × 17 × 13cm in size. The cut surface showing gray-white and subdividing irregular lobules.

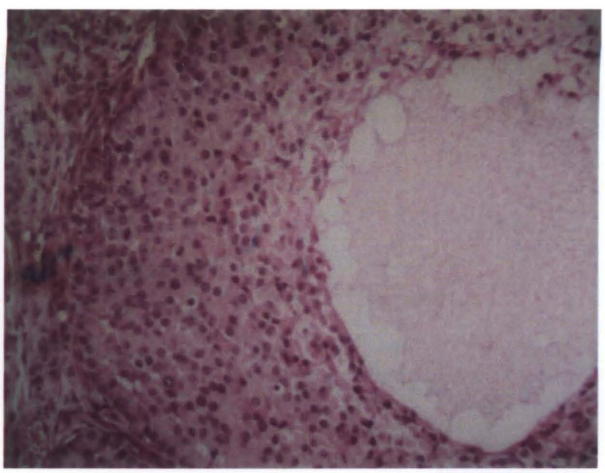


Fig.23

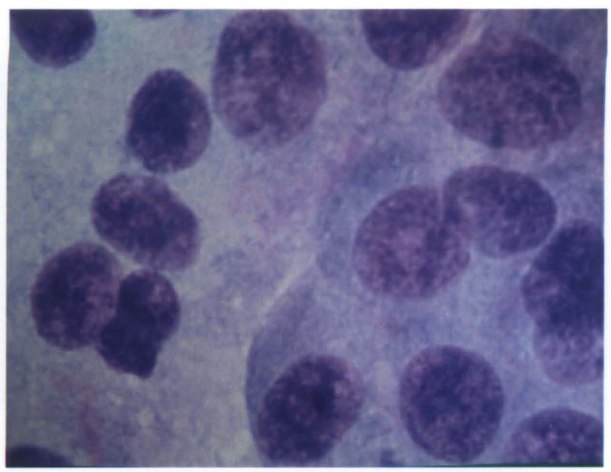


Fig.24

Fig.23 The neopastic cells were separated by connective tissue septa and follicular structure with Call-Exer body was seen in center. HE stain. × 100.
Fig.24 The tumor cells showing round or ovoid and resemble normal follicular cells, and the nuclei showing round ovoid. Diff Quick stain. × 1000.

Fig.25

Fig.26

Fig.25 and Fig.26 Bovine leukemia in a 9-year-old female Japanese black cattle, weighing about 450kg. Massive lymph node enlargements in the mesentery.

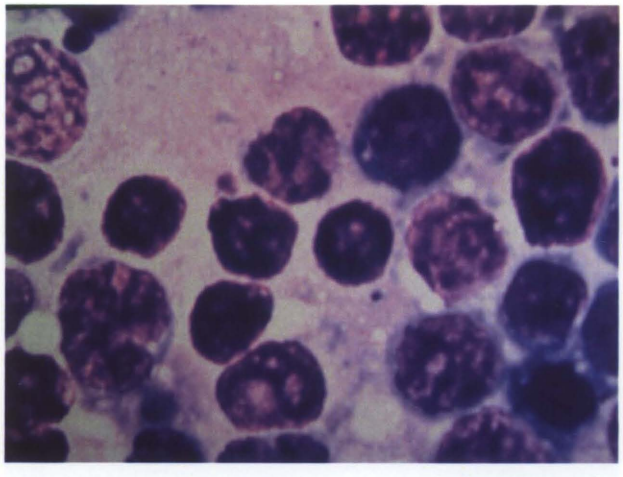


Fig.27

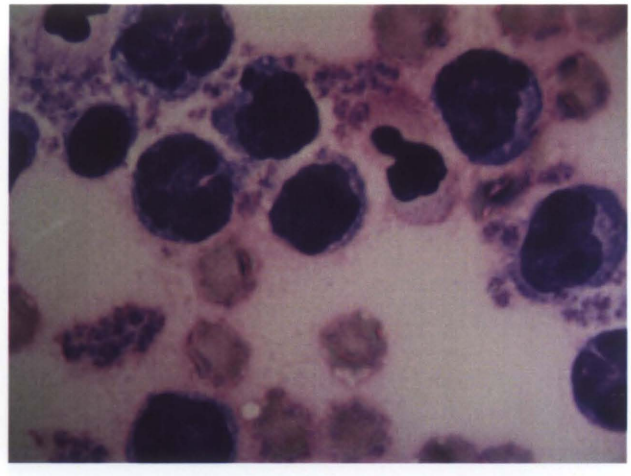


Fig.28

Fig.27 Tumor mass touch impression. Diff Quick stain. × 1000.
Fig.28 Blood aspirate. Observe the lymphoid cells are large with fine chromatin and obvious nucleoli. Giemsa stain. × 1000.

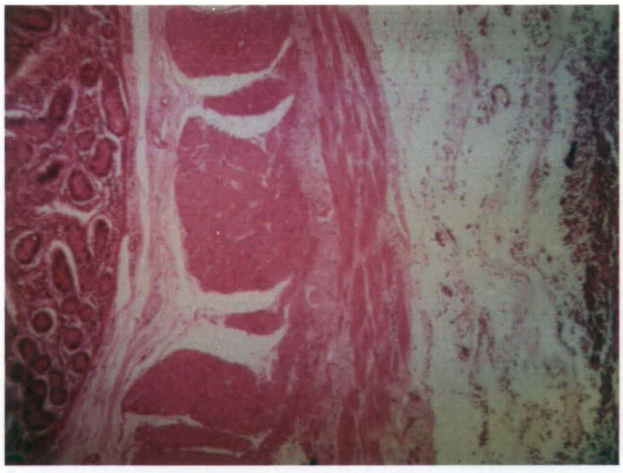


Fig.29

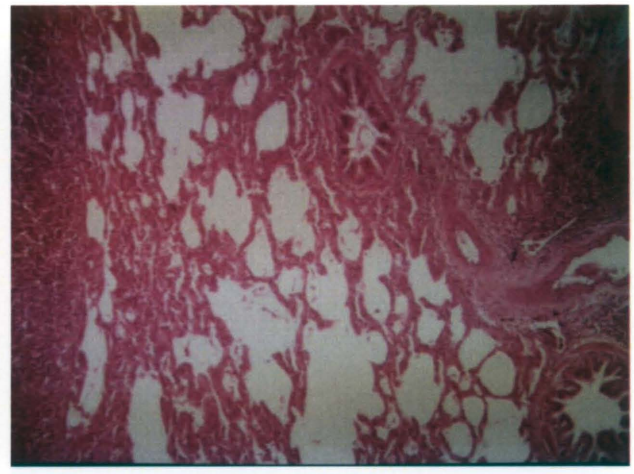


Fig.30

Fig.29 Bovine leukemia. Infiltration of tumor cells in the small intestine. HE Stain. × 40.

Fig.30 Infiltration of tumor cells in the lung. HE Stain. × 40.

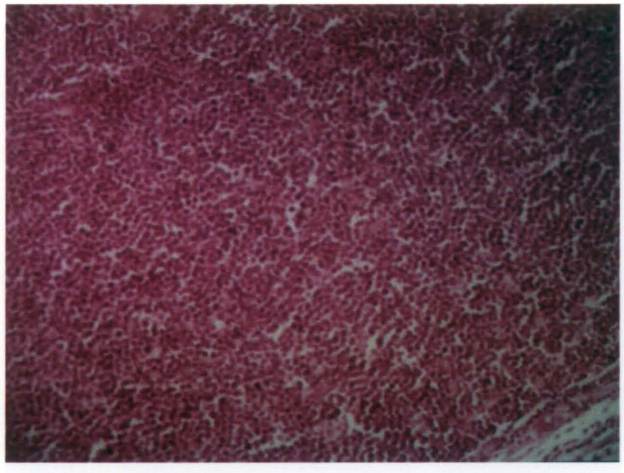


Fig.31

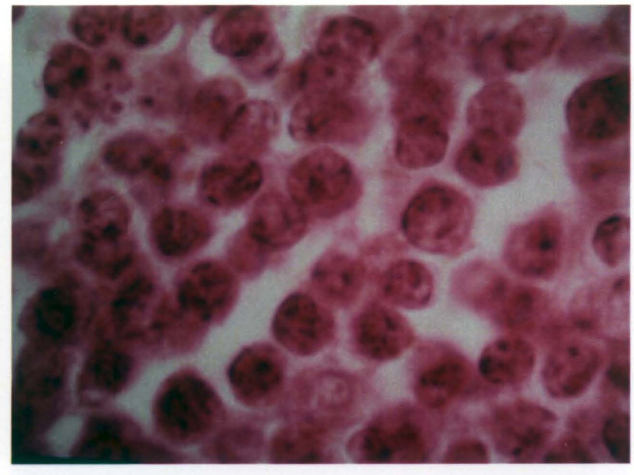


Fig.32

Fig.31 Infiltration of tumor cells in the pulmonary lymph node. HE Stain. × 100.

Fig.32 The neoplasmaes of pulmonary node. HE Stain. × 1000.

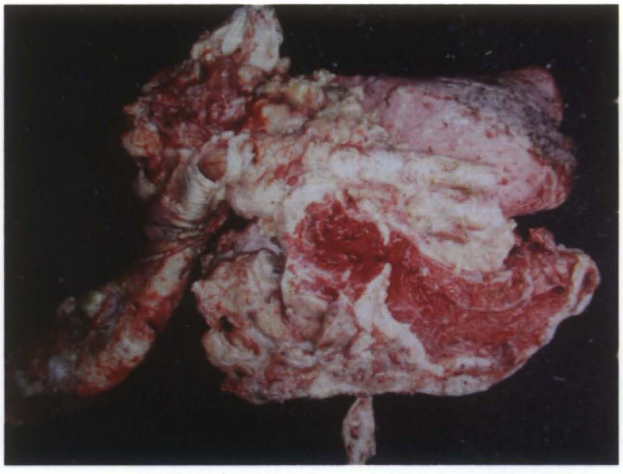


Fig.33

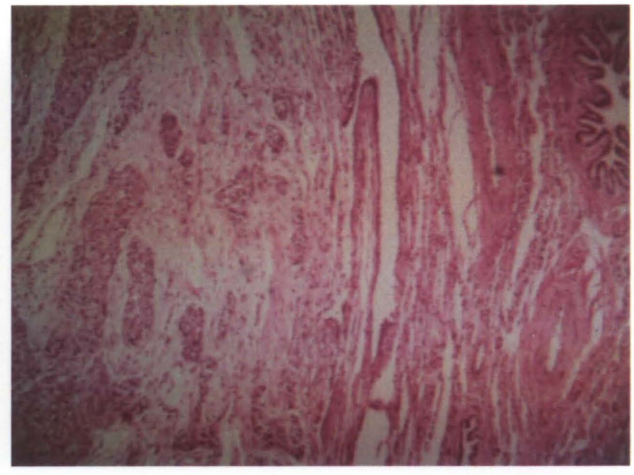


Fig.34

Fig.33 Lung cancer in a 9-year-old female Japanese black cattle, weighing about 400kg. Diffuse mass of carcinoma in the right and left lungs. Metastastic lesions of the neoplastic cells were found in the premediastinal lymph nodes.

Fig.34 The tumor separating by connective tissue from normal lung tissue. HE stain. ×40.

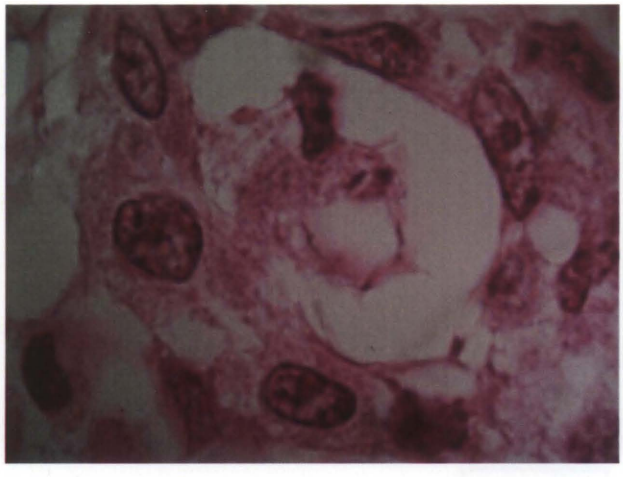


Fig.35

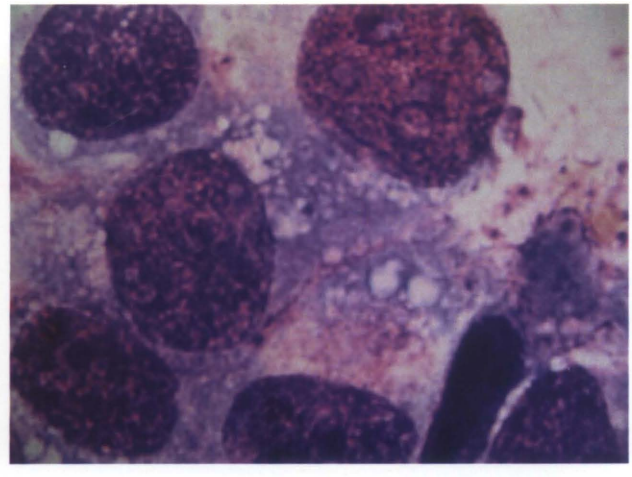


Fig.36

Fig.35 The neoplastic tissue showing cuboidal cells form alvolar like structures. HE stain. ×1000.

Fig.36 The tumor cells showing large, and obvious or ovoid, and tumor nuclei showing round or ovoid. The tumor mass touch impression. Diff Quick stain. ×1000.

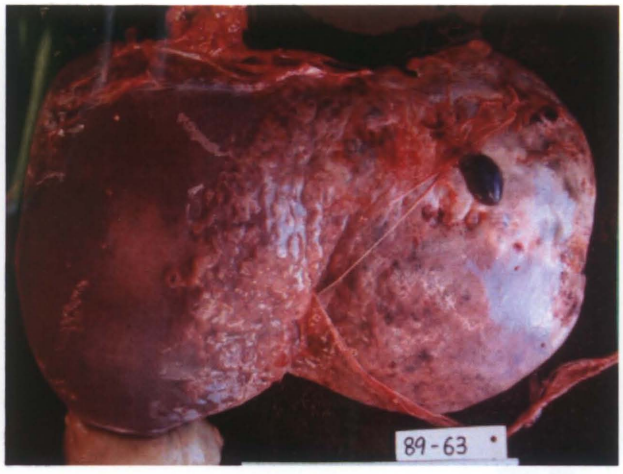


Fig.37

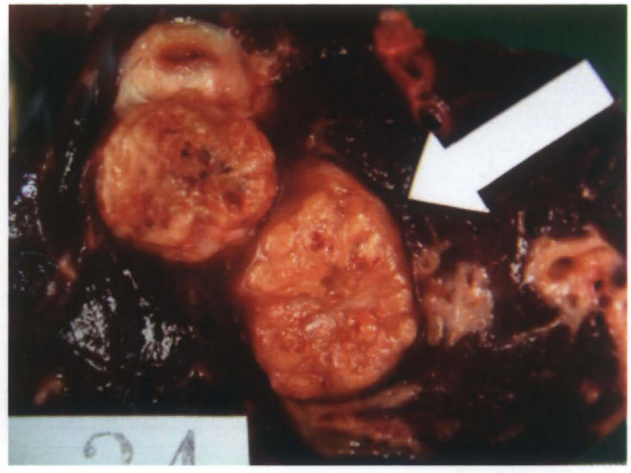


Fig.38

Fig.37 and Fig.38 Hepatocellulor carcinoma in a 10-year-old female Japanese black cattle, weighing about 450kg. Diffuse mass in the liver. The cut surface showing distinguished from the surrounding liver because of their pale color.

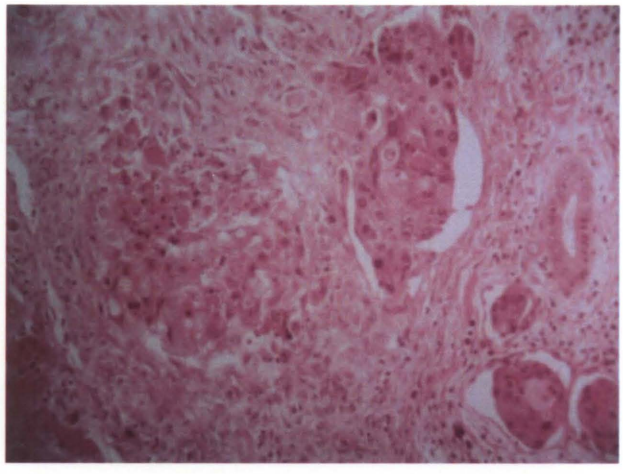


Fig.39

Fig.39 The neoplastic tissue showing form pseudoglandular structures. The tumor cells had moderate amount of eosinophilicc cytoplasm and round nuclei with the defined chromatin. HE stain. × 100.

Fig.40

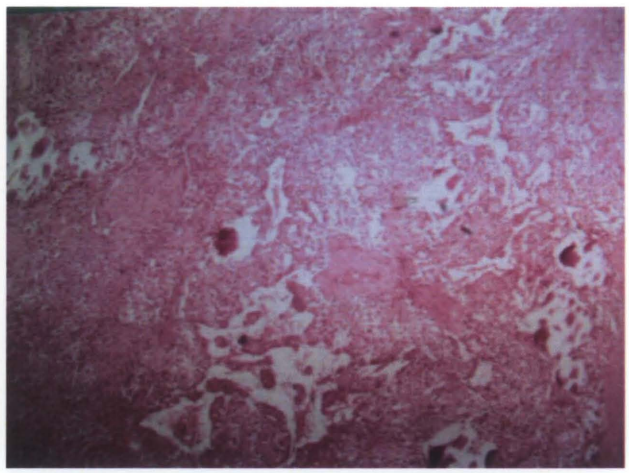


Fig.41

Fig.40 Adrenocortical adenoma in a 5-year-old female Japanese-black cattle, weighing about 450kg. Surface view in the right side of the adrenal gland. The tumor was enlarged to approximately 34 × 23 × 11cm in size, and cut surface showing dark red collared .

Fig.41 The tumor have some calcification. HE stain. × 40.

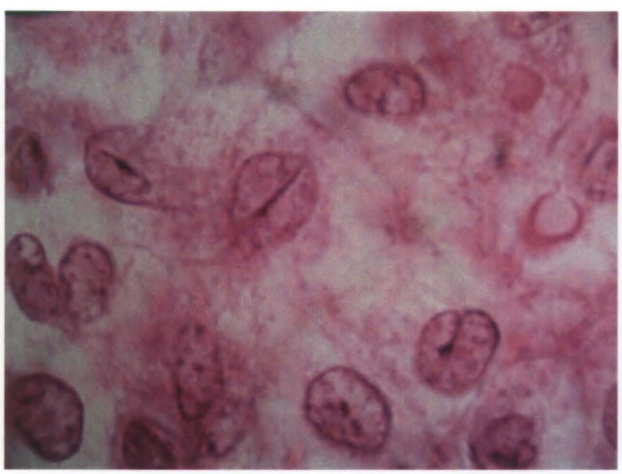


Fig.42

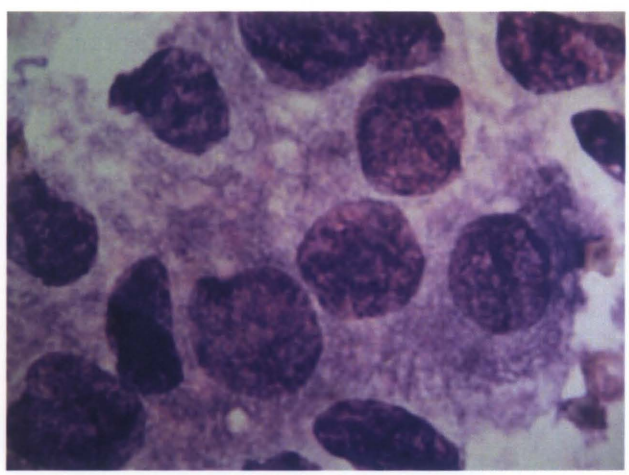


Fig.43

Fig.42 The tumor cells had moderate amount of cytoplasm, and showing like coffee bean. HE stain. × 1000.

Fig.43 The smear of the tumor mass. Diff Quick stain. × 1000.

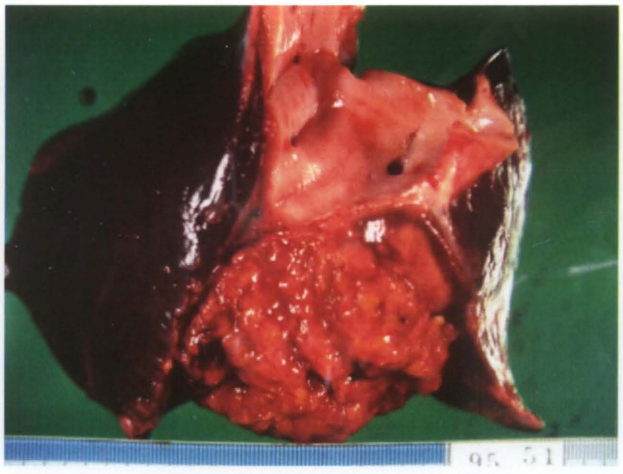


Fig.44

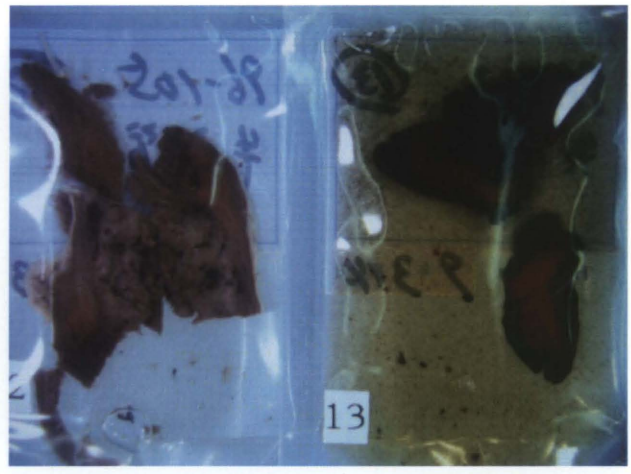


Fig.45

Fig.44 Pheochromocytoma in a 8-year-old female Holstein cattle, weighing about 550kg. Surface view in the right side of the adrenal gland The tumor was enlarged to approximately 6 × 5 × 5cm in size, and cut surface showing yellow brown.
Fig.45 The formalin liquid changes to yellow brown from clean color.

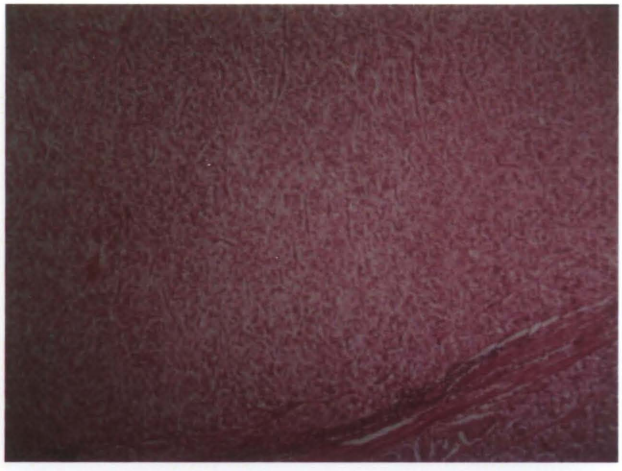


Fig.46

Fig.46 The tumor cells showing vary cells from small cuboidal to polyhedral, similar to those in normal adrenal medulla.
The tumor cells showing positive for Grimelius' silver stain. HE stain. × 40.

Fig.47

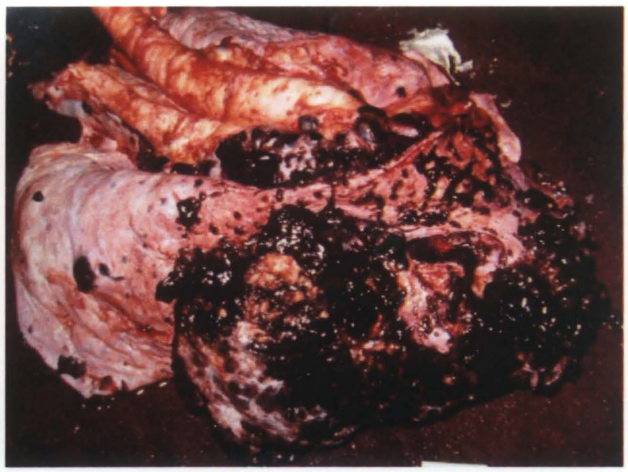


Fig.48

Fig.47 Malignant melanoma in left shoulder skin of a 5-year-old female Holstein cattle, weighing about 540kg. The tumor was enlarged to approximately 7 × 7 × 4cm in size.

Fig.48 Metastasis of the malignant melanoma to right lung showing multiple black nodules.

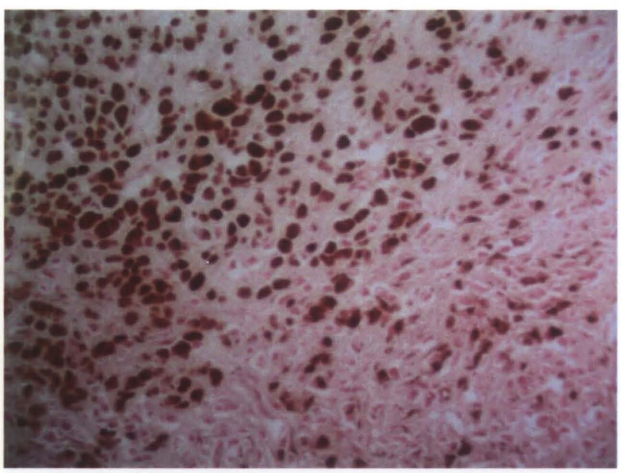


Fig.49

Fig.49 Junctional melanocytoma showing nests of melanocyotes at the lung. HE stain. × 40.

Fig.50

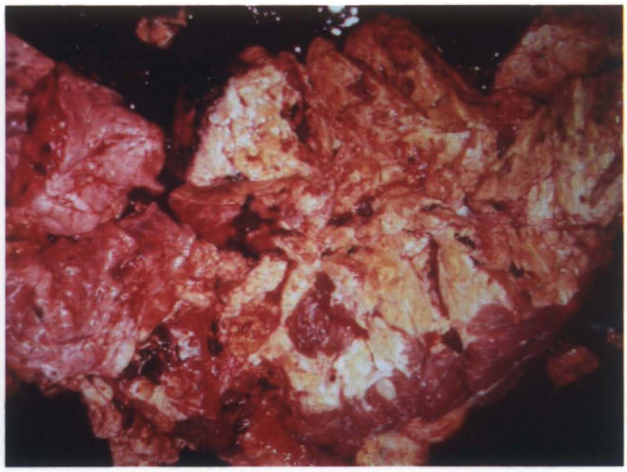


Fig.51

Fig.50 Rhabdomyosarcoma in the neck muscles of a 10-year-old female Japanese black cattle, weighing about 380kg.

Fig.51 The neoplasm shape line demarcation from normal skeleton maculae the cut surface showing gray-white.

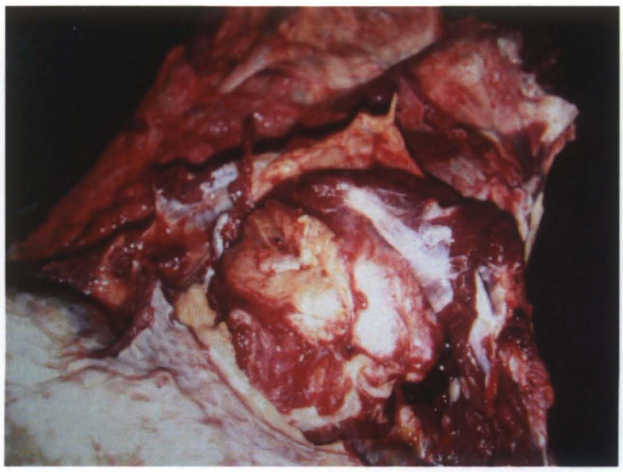


Fig.54

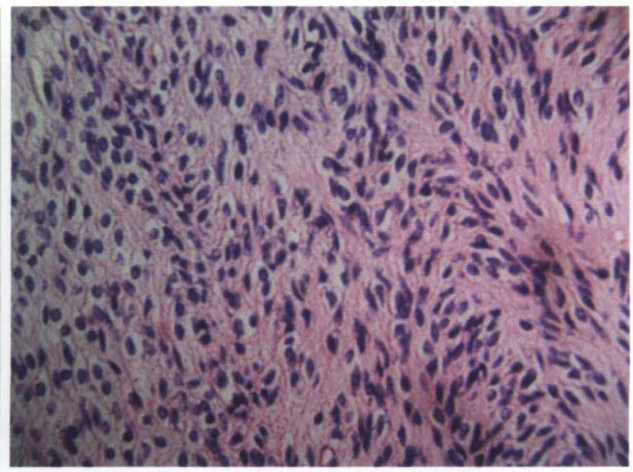


Fig.55

Fig.54 Schwannoma in a 13-year-old female Japanese black cattle, weighing about 450kg. The neoplasm showing skeletal muscles.
The tumor was enlarged to approximately 20 × 15 × 15cm in size and cut surface showing gray-white collar.

Fig.55 The neoplastic cells showing antoni type-A tissue patterns.
HE stain. ×200.