## 4. CHAPTERⅢ

## Bovine Tumors Detected at 6 Meat Inspection Offices in Miyazaki Prefecture during 1978-1993

#### 4.1 INTRODUCITON

On the long-term statistics for cattle tumors in Japan, some reports have been described by several universities [3,44,47,56], and by certain meat inspection offices [14, 21,23,26]. Recently, Kanagawa Meat Inspection Office has reported the results concerning the occurrence of swine tumors in the past 21 years [23]. The national scale statistical survey on tumor occurrence situation at the meat inspection offices was also carried out as of the end of 1995. However, few reports can be found for systematic analysis of tumors, which is unique to respective area as well as the reports on the comparative researches of bovine tumors between neighborhood prefectures.

We have examined the detected situation and pathological search of bovine tumors by chronological trends, breeding habitat, cattle breeding and gender in the vicinities of 6 meat inspection offices in Miyazaki prefecture. In addition, we investigated the differences of tumor incidence among 17 meat inspection offices in respective prefectures and cities in Kyushu.

### 4.2 MATERIALS AND METHODS

Out of 466,699 slaughtered cattle at 6 meat inspection offices in Miyazaki prefecture during 16 years form 1978 to 1993, 542 tumor cases were examined by chronological trends, breeding styles, gender, and organs, and followed by histopathological search. The breeds of cattle are broadly classified into Holstein including other foreign cattle and Japanese black cattle. To know the regional peculiarities, the incidence of cattle tumors at 17 meat inspection offices in respective prefectures and cities in Kyushu during the past 16 years, were compared.

Histopathological examinations were performed on paraffin sections stained with hematoxylin and eosin (HE) staining and other various special stainings. Some selected sections were employed for immunohistochemistry using an avidin-biotin-peroxidase complex (ABC) method (Vectastain PK-400, Vector Laboratories, Burlingame, CA, U.S.A.). Papillomas, which often occur as a change to a morbid state, are excluded from this study because of incomplete records.

#### 4.3 RESULTS

*Chronological trend:* Total number of slaughtered cattle in Miyazaki prefecture from 1978 to 1993 was 466,699 with average annual slaughtered number at 29,169. Among the chronological trend of detected tumors amounted to 542 cases in 16 years (0.116%), 58 cases in 1988 was the highest rate and 12 cases in 1990 was the lowest rate with average annual occurrence rate at 33.9 cases. Tumors occurrence rate per 10,000 cattle was 11.6 cases, with 22.9 cases in 1979 was the highest, and yearly decreasing trend can be seen thereafter (Fig. 56).

**Detected tumors situations by breed, gender and region:** The incidence of tumors by cattle breed and gender for 481 cases with sustaining record files, out of total 542 cases, were 329 cases for Japanese black cow (68.3%), 17 cases for steer (3.5%), 4 cases for sex unknown Japanese black, 77 cases for Holstein cow (16.0%), 19 cases for steer (3.9%), 5 cases for sex unknown Holstein, and 30 cases for unknown cattle breeding (6.2%). The incidence of tumors in each organs were 92 cases for the hematopoietic system (19.1%), 80 cases for the digestive system (16.6%), 76 cases for the genital system

(15.8%), 29 cases for the cutaneous system (6.0%), 24 cases for the respiratory system (4.9%), 23 cases for the urinary system (4.8%), 23 cases for the endocrine system (4.8%), 15 cases for the skeletal system (3.1%), and 119 cases for the other systems (24.7%, The total number of cattle slaughtered during 11 years from 1983 when the Table 5). year when Miyazaki prefecture started to collect records according to cattle breeds, to 1993, was 391,134, and they were composed of 114,682 Japanese black cow (29.3%), 106,602 steer (27.3%), 51,769 Holstein cow (13.2%), 114,208 steer (29.2%) and 3,873 the Statistically slaughtered result of these data showed that tumor occurrence others (1.0%). rate per 10,000 cattle was the highest at 23.8 cases with Japanese black cow followed by 12.7 cases with Holstein, 1.4 cases with Holstein steer, and 1.3 cases with Japanese black By the occurrence of each organ, most tumors in Japanese black cattle were found steer. in the genital and digestive systems other than 70 cases for mesothelioma and most tumors in Holstein cattle were detected for the hematopoietic system (Table 6).

*Histopathological classification*: Histopathological classifications of 481 cases were 87 cases for lymphoma (18.1%), 74 cases for mesothelioma (15.4%), 52 cases for ovarian granulosa cell tumors (10.8%), 29 cases for hepatoma (6.0%), 18 cases for lung cancer (3.7%) and 12 cases for adrenal gland tumor (2.5%). Approximately 57% of tumors were these six tumors. The most frequently recorded tumors were 69 cases of mesothelioma in Japanese black cow (5.0 cases/10,000) followed by 49 cases of ovary granulosa cell tumor, 29 cases of bovine leukosis, 24 cases of hepatoma, 14 cases of lung cancer (including squamous cell carcinoma) and 8 cases of adrenal cortex gland tumor. In Holstein cow, 29 cases of bovine leukosis (4.7 cases/10,000) followed by 5 cases of squamous cell carcinoma, 4 cases of mesothelioma, and 4 cases of hepatoma. Then, bovine leukosis was found in 9 cases in Japanese black and 8 cases in Holstein steer (Table 6).

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*Comparison of tumor occurrence rates by meat inspection offices in Miyazaki prefecture:* The incidence of bovine tumors at 6 meat inspection offices in Miyazaki prefecture is represented in Figure 57. The highest occurrence rate of 24.7 cases/10,000, which was about 2 times higher than the other meat inspection offices, was seen at Miyakonojo Meat Inspection Office where older Japanese black and milking cows have been slaughtered. Especially, big difference of about 4 times was seen by comparing its rate with that of Takasaki Meat Inspection Office where more fattening cows were slaughtered at the plants certified to export meat to the United States (Fig. 57).

*Comparison of tumor incidence with other meat inspection offices in respective prefectures and cities in Kyushu:* The results of tumor occurrence during 16 years from 1978 to 1993 at respective prefectures and cities are represented in Table 3. Among 1,186 cases (0.055%) out of total 2,175,645 cattle, 304 cases were bovine leukosis, and 20 cases were mesotheliomas. Of 304 bovine leukosis cases, 244 were found in Oita prefecture (26 cases/10,000). At 6 meat inspection offices in Miyazaki prefecture, 542 cases (0.116%) were detected, which is about 2 times higher than those in other prefectures and cites in Kyushu. Of which, 87 cases were bovine leukosis and 74 cases were mesothelioma (Table 7).

#### 4.4 DISCUSSION

The incidence of tumors during17 years from 1975 to 1991 in Japan, according to the operational report for Sanitary Administration of the Welfare Ministry, varied from 7.1 to 53.3 cases per 100,000 swine (mean 27.7 cases) [20]. However, the number was varied in previous reports. Those were 7.3 cases per 100,000 by Kashima et al. [23], 3.3 cases by Brandly and Migaki et al.[14] in United States, and 3.8 cases by Anderson et al. [3] in England. While it is said that tumor occurrence rate in cattle is higher than that in

swine as their breeding terms are far much longer than 6 months for swine, the tumor incidence in cattle during 19 years from 1975 to 1993, as reported in the operational report for Sanitary Administration of the Welfare Ministry, were varied from 7.4 to 59.1 cases per 10,000 cattle (mean 26.3 cases). The results in this study at same period were from 3.4 to 22.9 cases (mean 11.6 cases) per 10,000 cattle, which was about half rate in cattle covering nationwide meat inspection offices investigated by the Welfare Ministry. Reasons for the lower incidence might be because Miyazaki prefecture is one of the stock breeding prefectures, 57% of slaughtered cattle is accounted by fattening cattle with shorter breeding terms. In addition, the incidence of papilloma has been excluded from the records. While the average ages by breed and gender of cattle with tumors was 11.1 years old in Japanese black cow and 2.7 years old in steer, and 6.3 years old in Holstein cow and 2.2 years old in steer. High tumor occurrence was found in higher age of Japanese black cow (23.8 cases/10,000) followed by 12.6 cases/10,000 in Holstein steer. The phenomena might be due to longer breeding period in Japanese black cow to obtain more reproduction opportunities.

Highly susceptible tumors were in bovine leukosis, mesothelioma and ovary granulosa cell tumor, respectively. Bovine leukosis is considered as highest incidence of bovine tumors according to the statistics of nationwide meat inspection offices [20]. The similar trend has been confirmed in this study and the incidental ratio of this tumor is concluded as 87 cases out of 542 samples (1.8 cases/10,000). Almost of these 87 cases were lymphocytic lymphoma, adult, and polycentric type with high incidence in Holstein cow, which accord with the reports of the meat inspection offices at most areas in Japan, with the incidental rate (mean 4.7 case/10,000). Similarly, the occurrence rate is higher in cattle with ages of 5 to 8 years (mean 6.0 years old) [59]. Of 304 cases of bovine leukosis in each prefecture or city in Kyushu, highest occurrence was found in Ohita

prefecture; 244 cases (26.3 cases/10,000) [39], suggesting wide spreading of bovine leukosis virus in this area.

Bovine mesothelioma, which is disseminated tumor in the pleura and peritoneum, rarely occurs in Japan. The tumors were found in 74 cases (1.5 cases/10,000) following to bovine leukosis. As noted in the report of Miyazaki University [44], more mesothelioma can be found in southern Kyushu at 12 cases (18.2%) out of 55 bovine The high occurrence of mesothelioma was also found (57 cases out of 74 cases) tumors. in the prefecture including the vicinities of Miyakonojo Meat Inspection Office and other surrounding areas. These findings may indicate that the tumor has peculiar occurrence in this area. Although bovine mesothelioma is said as congenial tumor and is more susceptible in calf [22,63], the result showed that much of the tumor was seen in older Japanese black cattle at mean ages of more than 10 years. Also, while pleural mesothelioma can be often found in humans [52,62], peritoneum mesothelioma was seen more frequently in cattle. The difference between humans and cattle may suggest that some exposures through digestive organ system than through respiratory system might be closely associated to the tumoregenesis of bovine peritoneal mesotheliomas. Histopathologically, as similar with Ackerman's classification [2], epithelial types with tube and cavity formation and papillary hyperplasia were seen more frequently than sarcomatous types with conspicuous substrate hyperplasia and mixed/biphasic types. While the cause of human mesothelioma has been reported for asbestos participation [52, 62] since after Wagner's report [60], the pathogenesis of bovine mesotheliomas is still unknown [63]. We have previously investigated that many cow houses in southern Kyushu used 'Shirasu' [50] instead of sawdust because of low cost, availability, and high water absorption. People in Miyakonojo and surrounding areas have kept a traditional event to scatter 'Shirasu' (volcanic ash erupted by Kirishima Big Eruption, about 20,000

years ago, similar with volcanic glass having similar chemical structure with asbestos) in the garden. We assume that 'Shirasu' might have some roles on the tumoregenesis of bovine mesotheliomas in these areas.

The third highest incidence was noted in ovarian granulosa cell tumor at 52 cases (1.1 cases/10,000), which accounted for the major ovarian tumors as in previous reports [20]. The ovary of cattle is restrained its activity due to the compression of the paunch located at left abdominal region [20]. Previously, we examined the relationship between the incidence of ovarian tumors and its regions grossly (Data not shown). In the studies, only a few cases had ovarian tumors in both sides and most tumors laterally appeared, while there was no significant difference between the left and right sides.

Concerning adrenal gland tumors, there is a report describing that the tumors in the cortex and medulla occurred in almost same frequency in 327 bovine cases with adrenal gland tumors by Wright [20]. In this study, 10 cases of all 12 adrenal gland tumors were cortical adenomas and those were found in Japanese black older cattle. Since bovine adrenocartical adenomas has been described to occur dominantly in older cattle [20], the results might be that a number of meat cattle and milking cattle were slaughtered in some of the meat inspection offices with higher occurrence rates.

In conclusion, present study has conducted the researches on the actual conditions of 6 meat inspection offices in Miyazaki prefecture and could find the characteristics of occurrence situation of cattle tumors during the 16 years in Miyazaki prefecture.

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#### 4.5 ABSTRACT

Tumors were detected in 542 cases (0.116%) of 466,699 slaughtered cattle examined during 16 years at 6 meat inspection offices in Miyazaki prefecture during 16 years from 1978 to 1993, including 87 cases of bovine leukosis, 78 cases of mesothelioma, 52 cases of ovary granulosa cell tumor, 29 cases of hepatoma, 18 cases of lung cancer, and 12 cases of adrenal grand tumor etc. By cattle breeding and by distinction of sex, Japanese black cows were detected at 23.8 cases per 10,000 with the highest rates including mesothelioma and ovary granulosa cell tumor. Holstein dairy cows were at 12.7 cases including bovine leukosis and mesothelioma. Japanese black steer and Holstein steer were only 1.3 cases and 1.4 cases respectively including bovine leukosis in both classifications. By habitat, in Miyakonojo area, more older cattles have been slaughtered, was detected with 24.7 cases per 10,000 which was about 4 times more than Takasaki, where they keep the plants certified to export meat to the United States and more fattening cattles have been slaughtered, and it shown greater differences by cattle breeding and by sexes of the slaughtered cattle. Bovine leukosis that has broken out with the highest rate at the meat inspection offices in all parts of Japan was found at equally high rate, and followed by mesothelioma which has been regarded as rate cases to arise. Especially, within the vicinities of Miyakonojo Meat Inspection Office, occurrence of mesothelioma showed very high rate at 5.3 cases of per 10,000 and gave suggestions that mesothelioma is tumors specifically susceptible to break out in Southern Kyushu.

KEY WORDS: cattle tumors, cattle breed, meat inspection, mesothelioma, Southern Kyushu.





| Breeding, sex             | Japai | iese bl  | ack      | H  | Iolstei  | Unknown |    |          |
|---------------------------|-------|----------|----------|----|----------|---------|----|----------|
| System                    | Cases | <b>우</b> | <b>♂</b> | UN | <b>우</b> | ď       | UN | breeding |
| Hematopoietic system      | 92    | 31       | 9        | 2  | 30       | 9       | 1  | 10       |
| <b>Respiratory system</b> | 24    | 20       | 1        | -  | 2        | -       | -  | 1        |
| <b>Digestive system</b>   | 80    | 61       | -        | 1  | 9        | 2       | 2  | 5        |
| Urinary system            | 23    | 15       | 1        | -  | 4        | 1       | 1  | 1        |
| Genital system            | 76    | 69       | -        | -  | 5        | -       | -  | 2        |
| Cutaneous system          | 29    | 14       | 3        | 1  | 9        | 1       | 1  | -        |
| Skeletal system           | 15    | 7        | 2        | -  | 4        | 1       | -  | 1        |
| Endocrine system          | 23    | 13       | -        | -  | 4        | 3       | -  | 3        |
| Others                    | 119   | 99       | 1        | -  | 10       | 2       | -  | 7        |
| Total                     | 481   | 329      | 17       | 4  | 77       | 19      | 5  | 30       |

 Table 5.
 Location and region of tumors detection on breeding cattles, sex

UN: Unknwon sex

| Table 6.             |       |   | Hist                        | opathologica   | l c                        | lassificat                          | ior         | n of tumors    | s found  |                  |                           |        |                             |   |   |                  |
|----------------------|-------|---|-----------------------------|--|----------------------------|-------------------------------------|-------------|----------------|--|------------------|---------------------------|--------|-----------------------------|---|---|------------------|
|                      |       |   |                             | Japanese Bla   | ck                         | _                                   |             |                |  | Hol              | stein                     |        |                             |   | Unknown   |                  |
| System               | cases |   | <u> </u>                    |  |                            | 5                                   |             | UN             | <b>우</b>   |                  | ď                         |        | UN                          |   | breeding  |                  |
| Total                | 481   |   | 329                         |  |                            | 17                                  |             | 4              | 77   |                  | 19                        |        | 5                           |   | 30  |                  |
| Hematopoietic system | 92    | lymphoma<br>other(lymph, spleen)  | 29<br>2                     |  |                            | lymphoma                            | 9           | lymphoma 2     | lymphoma<br>other(spleen)  | 29<br>1          | lymphoma<br>other(spleen) | 8<br>1 | lymphoma                    | 1 | lymphoma<br>other(spleen)   | 9<br>1           |
| Respiratory system   | 24    | lung cancer<br>squamous cell carcinoma<br>other(lung, trachea)  | 8<br>6<br>3                 | fibroma<br>fibrosarcoma  | 2<br>1                     | lung cancer                         | 1           |                | lung cancer  | 2                |                           |        |                             |   | squqmous cell<br>carcinoma  | 1                |
| Digestive syatem     | 80    | hepatocellulor carcinoma<br>cholangiocarcinoma<br>adenocarcinoma<br>adenoma<br>papilloma<br>squamous cell carcinoma | 18<br>6<br>4<br>3<br>3<br>1 | liver cell adenoma<br>hyperplastic polyp<br>fibroma<br>fibrosarcoma<br>hemagioma<br>other(liver,intestine) | 6<br>5<br>2<br>1<br>1<br>1 |                                     |             | other(liver) 1 | hepatocellulor<br>carcinoma<br>liver cell adenoma<br>pancreatic carcinoma<br>papilloma | 4<br>1<br>2<br>2 | lipoma                    | 2      | fibroma<br>other<br>(liver) | 1 | hepatocellulor<br>carcinoma<br>adenoma<br>fibroma<br>papilloma<br>other | 1<br>1<br>1<br>1 |
| Urinary system       | 23    | nephroblastoma<br>papilloma<br>hemangioma   | 2<br>4<br>3                 | renal carcinoma<br>rhabdomyosarcoma<br>other(renal,bladder)  | 1<br>1<br>4                | papilloma                           | 1           |                | nephroblastoma<br>renal carcinoma<br>other(renal,bladder)                              | 1<br>1<br>2      | papilloma                 | 1      | other<br>(bladder)          | 1 | renal carcinoma   | 1                |
| Genital system       | 76    | granulosa cell tumor<br>luteoma<br>leioma<br>squamous cell carcinoma<br>other(ovary)                                | 49<br>3<br>8<br>1<br>1      | hemangioma<br>thecoma<br>leiosarcoma<br>adenocarcinoma   | 3<br>1<br>2<br>1           |                                     |             |                | granulosa cell<br>tumor<br>leioma<br>other(ovary)                                      | 1<br>1<br>3      |                           |        |                             |   | granulosa cell<br>tumor   | 2                |
| Cutaneous system     | 29    | melanoma<br>squamous cell carcinoma<br>mixed tumor<br>other(tongue)   | 3<br>2<br>1<br>2            | fibroma<br>fibrosarcoma<br>liposarcoma   | 3<br>2<br>1                | fibroma<br>fibrosarcoma<br>melanoma | 1<br>1<br>1 | melanoma 1     | squamous cell<br>carcinoma<br>melnoma<br>other(eye,skin)                               | 5<br>2<br>2      | melanoma                  | 1      | melanoma                    | 1 |   |                  |
| Skeletal system      | 15    | rhabdomyosarcoma<br>rhabdomyoma   | 3<br>2                      | leiosarcoma<br>osteoma   | 1<br>1                     | rhabdomyoma<br>other(muscle)        | 1           |                | rhabdomyosarcoma<br>other(muscle)  | 2<br>2           | fibroma                   | 1      |                             |   | other(muscle)   | 1                |
| Endocrine system     | 23    | adrenocartical adenoma<br>pheochromaocytoma   | 8<br>2                      | thyroid adenoma<br>other(adrenal)  | 1<br>2                     |                                     |             |                | thyroid adenoma<br>adrenocartical adenoma<br>other(adrenal)                            | 2<br>1<br>1      | thyroid<br>adenoma        | 1      |                             |   | adrenocartical<br>adenoma   | 1                |
| Others               | 119   | mesothelioma<br>leiomyoma<br>other(peritoneum)  | 69<br>1<br>15               | adenocarcinoma<br>ameloblastoma  | 13<br>1                    | mesothelioma                        | 1           |                | mesothelioma<br>adenocarcinoma<br>other(peritoneum)                                    | 4 2 4            | other<br>(peritoneum)     | 2      |                             |   | other(adrenal)<br>other(peritoneum)                                     | 2<br>7           |
|                      |       | UN : Unknwon sex  |                             | no file case 61  |                            |                                     |             |                |  |                  |                           |        |                             |   |   |                  |

| Disorders   | meat inspection cases | tumor cases(%) | mesothelioma(%) | lymphoma(%)  |
|---|-----------------------|----------------|-----------------|--------------|
| 6 Meat inspection offices<br>in Miyazaki prefecture                         | 466,699               | 542(0.116)     | 74(0.0159)      | 87(0.0186)   |
| 17 Meat inspection offices<br>in respective prefecture,<br>cities in Kyushu | 2,175,645             | 1,186(0.055)   | 20(0.00092)     | 304(0.01397) |

# Table 7.Comparison of tumor occurrence situations with other meat inspection offices<br/>in respective prefectures, cities in Kyushu (1978-1993)

