

A SURVEY ON NEOPLASIA IN DOMESTIC SPECIES OVER A 40-YEAR PERIOD FROM 1935 TO 1974 IN THE REPUBLIC OF SOUTH AFRICA. II. TUMOURS OCCURRING IN SHEEP

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ABSTRACT

BASTIANELLO, STELLA S., 1982. A survey on neoplasia in domestic species over a 40-year period from 1935 to 1974 in the Republic of South Africa. II. Tumours occurring in sheep. *Onderstepoort Journal of Veterinary Research* 49, 205-209 (1982).

A survey was carried out on all ovine neoplasms recorded in the registration files of the Section of Pathology of the Veterinary Research Institute at Onderstepoort over a 40-year period from 1935 to 1974. The neoplasms were divided and tabulated into 8 groups according to body systems or tissue types.

Out of a total of 673 neoplasms, 436 (64.8%) were cases of jaagsiekte (pulmonary adenomatosis). Of the remaining 237 neoplasms, 41.3% involved the skin. Eighty per cent of the cutaneous neoplasms were squamous cell carcinomas which varied from well-differentiated to anaplastic. The majority occurred on the head, in particular on the ears, frontal region and on the eyelids or nictitating membrane. Several factors have been suggested to explain the high incidence of squamous cell carcinomas on the head.

Lymphosarcomas were the 3rd most commonly encountered tumours, whilst a significant number of hepatocellular carcinomas also occurred. A variety of tumours of connective tissue origin were recorded, the most common of which arose from fibrous tissue and cartilage.

INTRODUCTION

Although neoplasms are encountered sporadically in sheep, there has been no recent comprehensive survey undertaken in the Republic of South Africa (RSA) to indicate the types of tumours which can most likely occur. Jackson (1936) reported on the pathology and incidence of tumours encountered in the domestic animal species of the RSA for a period of 15 years up to the year 1934. He found that the majority of ovine tumours occurred on the skin or in the lymphoid tissues, or that they were of connective tissue origin. Nobel, Neumann & Klopfer (1970) recorded a high incidence of pulmonary adenomatosis and skin tumours in sheep from Israel. In the United States of America (Monlux, Anderson & Davis, 1956; Sastry & Tweihaus, 1965) and the Netherlands (Misdorp, 1967), the most common ovine neoplasm was the lymphosarcoma, whilst in England Cotchin (1960) recorded the most frequent neoplasm to be the hepatocellular carcinoma. In New Zealand the most commonly encountered ovine tumour was a carcinoma of the small intestine, followed by neoplasia of the liver and lymphoid tissue (Webster, 1966).

This survey was undertaken to compare the types of tumours encountered with those recorded previously in the RSA (Jackson, 1936) and with those occurring in other countries.

MATERIALS AND METHODS

The material for this survey was obtained from formalin-fixed tissues submitted by private or state veterinarians and stock inspectors from all parts of the RSA. During the period 1935 to 1974, the Section of Pathology of the Veterinary Research Institute (VRI) was the only veterinary laboratory to which specimens for histopathological diagnosis could be submitted. A survey over this timespan should thus give a true indication of the types of tumours which can be encountered in South African sheep.

The registration files for each year of the survey were carefully screened and all the cases diagnosed as tumours in all the domestic species were noted. The pertinent data on these cases were recorded in separate registration files. All the ovine neoplasms were tabulated into 8 groups according to body systems or tissue types. The total number of tumours in each group was recorded as well as the percentage of the whole that each group represented. When thought necessary, other tables were compiled from the data available from the daily registration files and/or report books.

For the first 15 years of the survey, the paraffin-embedded tissues of all preserved cases were routinely recut and stained with haematoxylin and eosin (HE) and examined under the light microscope. This was done to ensure that the diagnoses recorded in the registration files were correct and to obtain uniformity as regards nomenclature of the tumours. The cases for which no diagnoses could be made because of insufficient material for re-examination or insufficient data in the registration files were ignored. The tumours have been tabulated using only the present-day terminology.

RESULTS

The 673 tumours encountered in sheep are given in Table 1. Additional details for some groups of tumours are set out in Tables 2-5. Micrographs of a few of the more common tumour types appear in Fig. 1-6.

The 5 tissue types most commonly neoplastic in sheep were the lung, skin, lymphoid tissue, connective tissue (fibrous tissue, cartilage, bone, muscles, peripheral nerves and adipose tissue) and the liver (Table 2). The significant ovine neoplasms could be classified into 9 specific types (Table 5).

Jaagsiekte (pulmonary adenomatosis) made up 436 (64.8%) of the 673 tumours included in this survey (Table 1). The numbers of jaagsiekte cases (Fig. 1 & 2) for the periods 1960-1964 and 1965-1969 were much higher when compared with those recorded for 1955-1959 and 1970-1974. Apart from the 436 jaagsiekte cases there were only 4 other tumours of the respiratory system. (Table 1).

When jaagsiekte is excluded, skin tumours made up 98 (41.3%) of the remaining 237 tumours (Table 1). Different types of cutaneous tumours were encountered (Table 3). Eighty per cent of the skin neoplasms were squamous cell carcinomas which could be subdivided into 3 types (Table 4). Type I, referred to as a cornu cutaneum, was proliferative in nature, formed excessive amounts of keratin and had a low grade of malignancy. Type II, with an intermediate malignancy, was both proliferative and moderately invasive and is referred to as an acanthoma. They showed well-developed keratin pearls but no excess keratinization. Type III, the anaplastic squamous cell carcinoma type, was highly malignant and invasive, and several eroded through the underlying skull bones.

TABLE 1 Tumours encountered in sheep from 1935 to 1974

Period	Skin	Connective tissues*	Respiratory system	Lymphoid tissue/ vascular system	Gastrointestinal tract	Liver	Kidney	Miscellaneous	Total
1935 to 1944	9 squamous cell carcinoma 1 basal cell tumour 1 papilloma	1 chondroma 1 rhabdomyosarcoma (heart) 1 fibrosarcoma (jaw) 1 fibrosarcoma 1 osteoma (head)	35 jaagsiekte 1 combined epidermoid/adenocarcinoma	5 lymphosarcoma 1 lymphangioma		3 hepatocellular carcinoma 1 bile duct adenoma		1 undifferentiated carcinoma	63
1945 to 1954	7 squamous cell carcinoma 2 papilloma	1 chondrosarcoma 1 lipoma	39 jaagsiekte	3 lymphosarcoma 2 thymoma	1 intestinal adenocarcinoma	1 hepatocellular carcinoma	1 renal adenocarcinoma 1 embryonal nephroma	2 undifferentiated carcinoma 2 mesothelioma	63
1955 to 1959	7 squamous cell carcinoma	1 chondrosarcoma	47 jaagsiekte	9 lymphosarcoma 1 thymoma		2 hepatocellular carcinoma		1 undifferentiated carcinoma 1 phaeochromocytoma	69
1960 to 1964	22 squamous cell carcinoma 2 papilloma 1 basal cell tumour 1 melanoma	1 chondrosarcoma 2 fibrosarcoma 1 osteosarcoma	104 jaagsiekte 1 epidermoid/carcinoma	15 lymphosarcoma 1 haemangiosarcoma	1 cystadenoma (duodenum)	1 hepatocellular carcinoma 2 cholangiocarcinoma	2 renal adenocarcinoma	1 undifferentiated carcinoma	158
1965 to 1969	17 squamous cell carcinoma 2 papilloma 1 basal cell tumour 2 melanoma	1 chondroma (rib) 3 fibroma 1 rhabdomyosarcoma 1 leiomyoma	157 jaagsiekte 1 nasal adenoma (superficial mucous membrane)	25 lymphosarcoma	2 intestinal adenocarcinoma (signet cell type) 1 adamantinoma	1 hepatic adenoma 1 bile duct adenoma	1 renal adenoma 1 fibroma	1 undifferentiated carcinoma 1 thyroid adenoma 1 pituitary adenoma 1 adrenocortical adenoma	222
1970 to 1974	16 squamous cell carcinoma 4 papilloma 2 melanoma 1 fibropapilloma	1 chondroma 1 fibrolipoma 1 neurofibrosarcoma	54 jaagsiekte 1 combined epidermoid/adenocarcinoma	12 lymphosarcoma	2 intestinal adenocarcinoma	1 fibrosarcoma 1 haemangiosarcoma		1 undifferentiated carcinoma	98
TOTAL	98	21	440	74	7	14	6	13	673

* Connective tissues = fibrous tissue, cartilage, bone, muscle, fat and peripheral nerves

TABLE 2 The most commonly neoplastic tissues in sheep

Body system or tissue	Number	% of 673 tumours	% of 237 tumours (jaagsiekte excluded)
Lung (jaagsiekte)	436	64,8%	—
Skin	98	14,6%	41,3%
Lymphoid tissue	74	11,0%	31,2%
Connective tissues	23	3,4%	9,7%
Liver	14	2,0%	6,0%
TOTAL	645	95,8%	88,2%

TABLE 3 The cutaneous neoplasms of the sheep

Neoplasm	Number	% of total
Squamous cell carcinoma	78	80%
Papilloma	11	11%
Melanoma	5	5%
Basal cell tumour	3	3%
Fibropapilloma	1	1%
TOTAL	98	100%

TABLE 4 The types and sites of origin of the ovine cutaneous squamous cell carcinomas

Site	Type/Grade	Number
Head (undetermined)	Cornu cutaneum	1
	Acanthoma	4
	Anaplastic type	3
Head (ocular region)	Cornu cutaneum	1
	Anaplastic type	3
Head (frontal region)	Cornu cutaneum	1
	Anaplastic type	3
Head (near nares)	Acanthoma	1
	Anaplastic type	1
Head (ear)	Cornu cutaneum	6
	Acanthoma	5
	Anaplastic type	2
Head (base of horn)	Acanthoma	1
	Anaplastic type	2
Head (eyelid)	Acanthoma	3
	Anaplastic type	4
Head (nictitating membrane)	Acanthoma	1
	Anaplastic type	1
Total (head)		43
Scrotum		1
Vulva		1
Foot		1
Site undetermined		32
GRAND TOTAL		78

TABLE 5 The most common types of ovine neoplasms

Type	Number	% of 673 tumours	% of 237 tumours (jaagsiekte excluded)
Pulmonary adenomatosis (jaagsiekte)	436	64,8%	—
Squamous cell carcinoma	78	11,6%	32,9%
Lymphosarcoma	69	10,3%	29,1%
Papilloma	11	1,6%	4,6%
Hepatocellular carcinoma	7	1,0%	2,9%
Melanoma	5	0,7%	2,1%
Fibrosarcoma	5	0,7%	2,1%
Intestinal adenocarcinoma	5	0,7%	2,1%
Fibroma	4	0,5%	1,7%
TOTAL	620	91,9%	77,5%

Forty-three of the 78 squamous cell carcinomas (Fig. 5) occurred on the head (Table 4). Nine (21%) of these were classified as cornua cutanea, 15 (35%) as acanthomas and 19 (44%) as the anaplastic type. Of the latter, 4 were extremely invasive, had eroded through the skull bones and were growing in the underlying frontal sinus, nasal cavity or arachnoid space. The sheep with the tumour in the arachnoid space exhibited nervous symptoms prior to death. Squamous cell carcinomas on the head occurred most commonly on the ear (30%), followed by the eyelid and nictitating membrane (21%). Eleven of the 13 tumours on the ear were either cornua cutanea or acanthomas.

Twenty-three connective tissue tumours, which included 5 fibrosarcomas, 4 fibromas, 1 lipoma and 1 fibrolipoma, 1 each of an osteoma and an osteosarcoma, 3 chondromas and 3 chondrosarcomas, 2 rhabdomyosarcomas, 1 leiomyoma and 1 neurofibroma, were recorded (Table 1). Fibrosarcomas were with melanomas and intestinal adenocarcinomas, the 6th most frequent type of ovine neoplasm (Table 5).

Sixty-nine of the 72 lymphoid tissue tumours were lymphosarcomas (Table 1). The lymphosarcoma was furthermore the 3rd most common type of tumour encountered (Table 5). The other 3 lymphoid tumours were thymomas. Included within this group (Table 1) were tumours of vascular origin which comprised 1 haemangiosarcoma and 1 lymphangioma.

Tumours of the gastro-intestinal tract numbered 7 in all. These included 5 intestinal adenocarcinomas (Fig. 6), 1 duodenal cystadenoma and 1 adamantinoma (Table 1).

Tumours of the liver were the 5th most common group of tumours (Table 2). Half of the 14 hepatic tumours were hepatocellular carcinomas (Fig. 3 & 4), the 5th most frequently encountered type of tumour (Table 5). The other hepatic tumours comprised 1 hepatic adenoma, 2 bile duct adenomas, 2 cholangiocellular carcinomas, 1 haemangiosarcoma and 1 fibrosarcoma.

Only 6 primary renal tumours were recorded. These included 2 renal adenocarcinomas, 1 renal adenoma, 1 embryonal nephroma and 1 fibroma (Table 1).

Tumours arising from the endocrine glands were rare, but they comprised a variety of types, including 1 adrenocortical adenoma, 1 pituitary adenoma, 1 thyroid adenoma and 1 pheochromocytoma.

DISCUSSION

This survey indicates that jaagsiekte is by far the most common neoplastic condition amongst South African sheep, accounting for 64,8% of all the neoplasms encountered. Higher numbers of jaagsiekte cases than were expected were recorded during the period 1960–1969, when Tustin (1969) conducted a nationwide survey of jaagsiekte in the RSA. As a result of his survey more cases were submitted to the VRI for histopathological diagnosis in this period than at any other time. In Israel, Nobel *et al.* (1970) recorded 89 cases of jaagsiekte out of a total of 114 tumours. In a later survey, also conducted in Israel, Nobel, Klopfer, Perl & Nyska (1979), again recorded a high incidence of jaagsiekte. Surveys in other countries make no mention of the incidence of jaagsiekte as an ovine neoplasm (Monlux *et al.*, 1956; Cotchin, 1960; Misdorp, 1967; Cordes & Shortridge, 1971). Jackson (1936) did not include jaagsiekte amongst his series of ovine neoplasms.

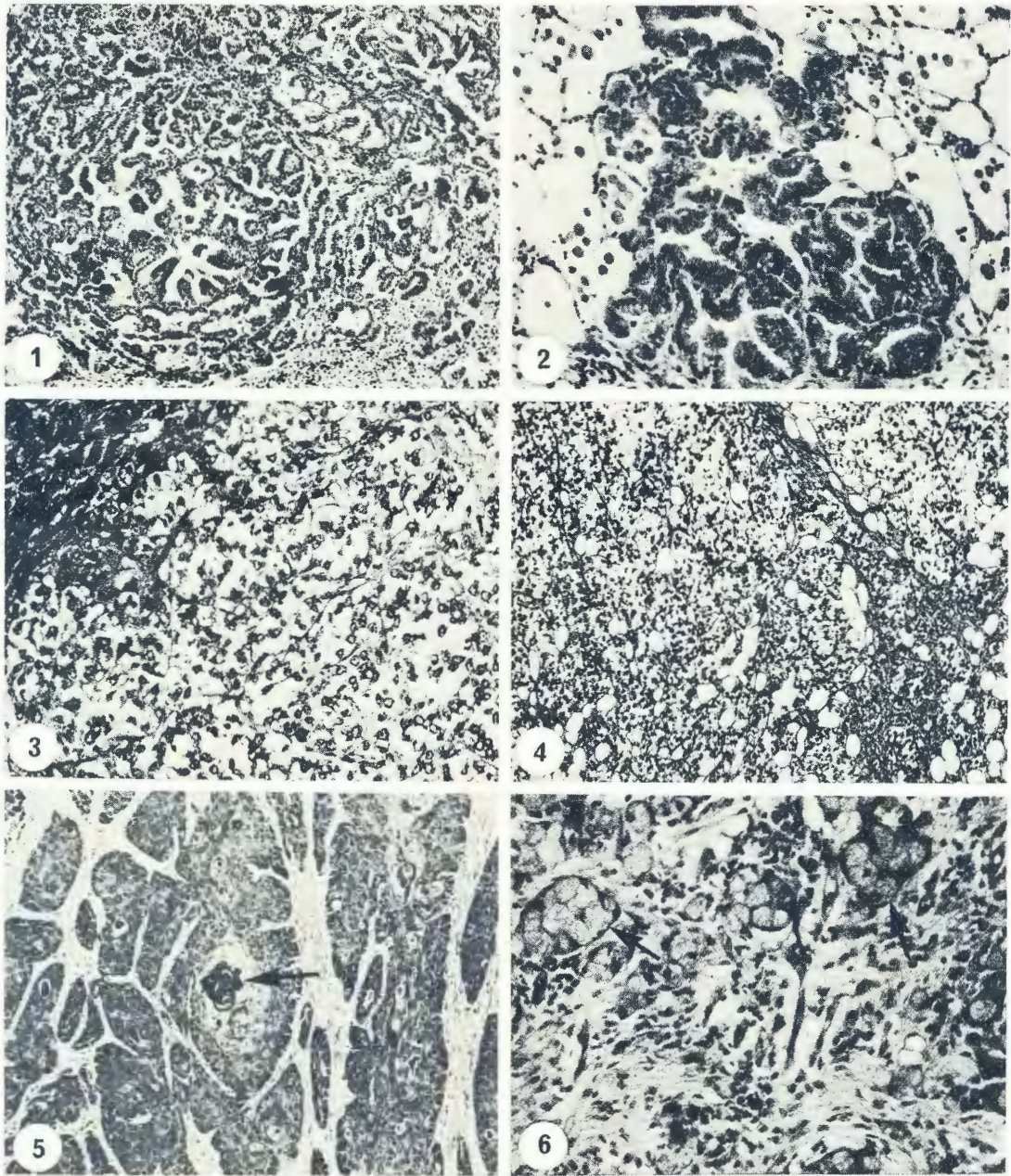


FIG. 1 Jaagsiekte (pulmonary adenomatosis). Lung with tumour nodules: HE \times 75

FIG. 2 Jaagsiekte. Epithelial cells of tumour nodule lining alveoli. Alveolar macrophages are present within lumens of unaffected alveoli: HE \times 200

FIG. 3 Hepatocellular carcinoma—clear cell type. Note capsule (arrow): HE \times 200

FIG. 4 Hepatocellular carcinoma—clear cell type. Collagen strands traversing tumour. Accumulation of fat in some of the cells: HE \times 75

FIG. 5 Squamous cell carcinoma. Note keratin pearl (arrow): HE \times 75

FIG. 6 Intestinal adenocarcinoma. Groups of mucous cells (arrows) embedded in scirrhous tissue: HE \times 200

Jaagsiekte is an important and widespread disease in the RSA and was recorded as early as 1825 (Tustin, 1969). Circumstantial evidence, such as transmission by contact and experimental transmission by means of lung secretions and tissue extracts, has pointed to a viral origin (Tustin, 1969). Since then Verwoerd, Williamson & De Villiers (1980) have shown that the aetiological agent is definitely a virus belonging to the Retroviridae. Its infectious nature could explain the high proportion of pulmonary adenomatosis neoplasms in this survey.

When jaagsiekte was excluded, the skin (41,3%), lymphoid tissue (31,2%), connective tissues (9,7%) and liver (6%) were the tissues most frequently involved. This generally corresponded to an earlier study on 39

tumours in sheep in the RSA (Jackson, 1936). According to him, 30,7% arose on the skin, 10,2% in lymphoid tissue and 10,2% in connective tissues.

Apart from the lung, the skin accounts for a high proportion of ovine neoplasms, although it appears that it is only in the RSA and Israel (Nobel *et al.*, 1970) that skin tumours account for such a high proportion of the ovine tumours. Eighty per cent of the skin neoplasms were squamous cell carcinomas. Forty-three of the 46 squamous cell carcinomas (for which the site of origin could be determined) occurred on the head and, in particular, on the ears, in the frontal region and on the nictitating membrane or eyelids. Squamous cell carcinomas of the skin also occurred preferentially on the head of sheep in India (Sastry, 1959; Damodaran & Parthasarathy, 1972) and Australia (Vandegraaff, 1976).

The cutaneous squamous cell carcinomas of the head could be classified into 3 grades, namely, cornu cutaneum, acanthoma and anaplastic, with low, intermediate and high malignancy rates respectively. The anaplastic tumours were very invasive, eroding through the skull bones into the underlying nasal and cranial cavities. In one sheep, nervous symptoms caused by penetration of the tumour into the cranial cavity were recorded.

Several factors may have influenced the high incidence of cutaneous squamous cell carcinoma of the head. These include breed and age of the animals, the regions where sheep are reared, and farming practices which involve sheep being exposed for prolonged periods to the ultraviolet rays of the sun. The majority of South African sheep are woolbreed Merinos. Most of them are raised under extensive conditions in the Karoo where the sunlight is intense for long periods of the year. The Merino is a white breed with little melanin pigment, and the face and ears are not covered by wool. Consequently, the latter sites are most exposed to the ultraviolet irradiation of sunlight and susceptible to the development of squamous cell carcinoma. According to Anderson & Skinner (1961), squamous cell carcinoma of the skin in humans is more common on exposed parts of the body, in light-skinned people, and in parts of the world where sunlight is more intense. They noted a similar situation with ocular squamous cell carcinoma in Hereford cattle in which the incidence of this tumour was higher in regions having intense sunlight, and in older cows with little pigment around the eyes. Whitehead (1967) noted squamous cell carcinomas on the head and, in particular, on the ears of white-haired cats. The aetiology of the ovine squamous cell carcinoma is still unknown. One could speculate that a virus is involved, the effect of which is enhanced by ultraviolet irradiation and lack of pigment as in ocular squamous cell carcinomas of cattle.

The lymphoid tissue was the 3rd most frequently affected tissue, with 69 out of the 72 tumours being lymphosarcomas. The lymphosarcoma as a specific tumour type was the 3rd most commonly encountered type. When jaagsiekte was excluded, lymphosarcomas accounted for 29.1% of all the tumours. The aetiology of ovine lymphosarcomas is believed to be a virus the same as or closely related to the bovine C-type virus which causes lymphosarcoma and leukaemia in cattle. Hoss & Olson (1974) induced the development of lymphosarcomas in sheep by the inoculation of this bovine C-type virus. The viral aetiology could explain the relatively high incidence of lymphosarcoma in sheep.

The connective tissue tumours accounted for a low percentage of neoplasms in sheep in the RSA. Most numerous amongst this group were benign or malignant varieties arising either from fibrous tissue or cartilage.

Hepatic tumours accounted for only 2% of the total number of tumours included in this survey. Half of the hepatic tumours were hepatocellular carcinomas. This is in contrast to the situation in Great Britain where hepatocellular carcinomas were the most common tumour amongst sheep (Cotchin, 1960), and in New Zealand and Netherlands where hepatic tumours were the 2nd most frequently encountered group amongst sheep (Webster, 1966; Misdorp, 1967).

Only 5 intestinal adenocarcinomas were encountered in this survey. This, too, is in contrast to the situation in New Zealand, where carcinoma of the small intestine is

the most prevalent ovine tumour (Dodd, 1960; Webster 1966; Cordes & Shortridge, 1971; Ross, 1980). This tumour amongst New Zealand sheep is believed to be induced by several factors (Ross, 1980).

Tumours of the respiratory system (excluding pulmonary adenomatosis), blood vessels, lymphatics, endocrine organs and kidney as well as mesotheliomas were extremely rare amongst South African sheep.

ACKNOWLEDGEMENTS

The author would like to thank the Photography Department for the photographs, Mrs A. M. Coetzer for typing the manuscript, the technical staff of the Section of Pathology for preparing the histological material and Mr J. N. Baldwin for his assistance.

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