XII. Tumours of the lower alimentary tract

K. W. HEAD [1]

This classification is presented in two parts: (a) tumours of the gastrointestinal tract; and (b) tumours of the anal canal and margin. In the gastrointestinal tract the tumours are classified as adenoma, adenocarcinoma, and undifferentiated carcinoma, with several subtypes. Most polyps prove to be non-neoplastic, hyperplastic, or regenerative rather than adenomatous. Carcinoma of the stomach occurs mainly in dogs, but is a rare tumour in all parts of the world. Moderately differentiated, tubular adenocarcinoma of the small intestine with excessive fibrosis occurs in all six species ; in some geographical locations it may occur frequently in sheep and cattle. The adenoma/carcinoma sequence in the rectum of the dog is similar to that in man but is encountered less often. Carcinoid tumours are very rare in domestic animals. Among the soft tissue tumours, those of smooth muscle and adipose tissue are found fairly frequently and congenital mesothelioma in the peritoneum of calves occurs occasionally. Tumours of the haematopoietic and related tissues are the most common gastrointestinal neoplasms in all species and most belong to the lymphosarcoma group. Tumours of the anal canal and margin are common in the dog and 90 % of these are tumours of the hepatoid (perianal) glands.

This classification is presented in two sections. The first, covering the tumours of the gastrointestinal tract, deals with that part of the alimentary tract lined by glandular epithelium, i.e., from the junction of the squamous epithelium in the stomach or abomasum to the mucocutaneous epithelial junction at the anus (see Fig. 1 in the classification of tumours of the upper alimentary tract, p. 146 of this issue). The second section, dealing with the tumours of the anal canal and anal margin, is included for the sake of completeness but the descriptions are not comprehensive since the various types of tumour have been described previously.[a]

The decision to combine all sites in the lower alimentary tract in one classification has the advantage that the definitions are so worded that they apply to all levels of the tract. It has the disadvantage that for each tumour it is necessary to comment on the frequency of occurrence at each site for each species.

The conventions as to the use of this classification, in particular the hierarchy of the nomenclature, are as follows:

(*a*) The histological type, based on the dominant cell type and growth pattern, is used to name the tumour; if small areas of the tumour are not of this type they are mentioned subsequently.

(*b*) The grading of the degree of differentiation of the tumour is recorded using the adjectives " well " (where the tumour resembles normal tissue), " poorly " (where the normal tissue is recognized with difficulty), or " moderately ".[b]

(*c*) The stage of spread of the tumour, i.e., the deepest anatomical layer of the wall reached (mucosal, submucosal, muscular, or serosal) and the mode of growth are described.

There are considerable variations in gastrointestinal tract anatomy in the six species considered in this series (see Fig. 1 in the classification of tumours of the upper alimentary tract, p. 146 of this issue), and this will obviously be reflected in physiological differences. Likewise, at the histological level, there are differences between species, e.g., carnivores and pigs do not have Paneth's cells, and quite prominent muscle bundles are seen extending from the muscularis mucosa between the glands in the pyloric mucosa

[1] Senior Lecturer, Royal (Dick) School of Veterinary Studies, Edinburgh EH9 1QH, Scotland.

[a] See the relevant classifications in the first part of this series published in the *Bulletin of the World Health Organization*, Vol. 50, No. 1-2 (1974).

[b] See PAMUKCU, A. M. *Bulletin of the World Health Organization*, **50**: 43-52 (1974).

of the dog. Nevertheless, there are tumours that look the same and even behave in a similar fashion in different species, but caution must be exercised when comparing one species with another.

Correct diagnoses can best be achieved if the tissues to be sectioned are so oriented that those areas needed in differential diagnosis appear in the sections (compare Fig. 1 with Fig. 3 and 5). For example, polypoid tumours must be blocked so that the section passes through the stalk, which can then be examined for invasion of tissue spaces and lymph and blood vessels. Likewise, in any tumour, the blocks should be oriented at right angles to the free or luminal surface so that the lesion can be examined from mucosa to serosa (see under (*c*) above). This precise orientation of the block can best be done after the tissue has been fixed.

The specimen should be fixed as soon as possible after death or its removal from the body so that postmortem decomposition can be kept to a minimum. Postmortem changes may lead to a loss of cytoplasmic detail. If a biopsy specimen is used, it should be placed with the submucosal or serosal surface downwards on a card and the card immersed in fixative; when the tissue has fixed flat a block can be taken with the reasonable expectation that all the glands will be cut through their long axes. The stomach should be opened along the greater curvature so that it can be laid flat for fixation and examination. The intestine should be detached from the mesentery and the lymph nodes examined at the same time; when the intestine is opened, the cut should lie at a more-or-less constant distance from the mesentery so that the relationship of the tumour to the mesentery can be appreciated in the subsequent block. Again, fixation should be on a card to prevent curving and warping, which would make the orientation of the block impossible. If the presence of a tumour is suspected before the intestine is opened, the best results are obtained by filling the affected section of intestine with fixative and immersing it in a bath of fixative. Thus, penetration of the fixative is rapid from both the serosal and the mucosal surfaces and there is no risk of rubbing off the mucosa during handling.

In addition to the taking of suitable blocks from the tumour, the normal surrounding tissue should be sampled; comparison between normal and tumour tissues are important in tumour grading. The " normal " tissue may, of course, prove to be pathological, e.g., the muscle coat may show evidence of thickening above the tumour, indicating an obstruction of some duration; it is therefore important to take blocks both above and below the tumour. The " normal " epithelium may show atrophy, which appears as dwarfing of the villi in the intestine; such changes may be pre-neoplastic in the sense that they are known to be caused by carcinogens in experimental situations. In the stomach, the presence of intestinal metaplasia should be recorded. Inflammation of the mucosa and submucosa at any level of the tract and an increase in the number of goblet cells in the small intestine are helpful in classifying a polyp as hyperplastic, regenerative, inflammatory, and non-neoplastic rather than adenomatous.

Fixation in 4% buffered formol saline and blocking in paraffin wax is adequate for most tumours. Haematoxylin and eosin staining gives a picture on which the choice of further special stains can be based. A silver stain for reticulin fibres (e.g., Gordon & Sweet's method) is useful in revealing the acinar pattern in a poorly differentiated adenocarcinoma or in an adenocarcinoma showing postmortem changes. Reticulin-fibre stains, Romanowsky stains, and toluidine blue at controlled pH are valuable in the recognition and subdivision of tumours of the haematopoietic and related tissues. Both the periodic acid-Schiff reaction for neutral mucosubstances and the alcian blue stain at pH 0.5 or pH 2.5 for acidic mucosubstances should be used. Mucin-producing gastric mucosal cells showing intestinal metaplasia and dysdifferentiated gastric carcinoma cells show a change from normal PAS positivity to a positive reaction with alcian blue. Enterochromaffin cell granules may be argentaffin or may be argyrophilic only. The argentaffin granules can reduce ammoniacal silver solution to metallic silver as in the Masson–Fontana silver method. Argyrophil granules, which are more resistant than argentaffin granules to postmortem decomposition, will reduce silver salts to metallic silver only after exposure to reducing substances, e.g., in Bodian's Protargol method. Sevier's silver method stains both types of enterochromaffin cells.

This classification is based on a study of nearly 350 cases of tumours of the gastrointestinal tract and nearly 250 cases of tumours of the anal canal and margin. The frequency with which any histological type of tumour has been seen at a particular site in a particular species will reflect (*a*) the number of specimens of the susceptible species examined, and (*b*) the existence of a particular cause at that geographical location. Adenocarcinomas of the intestine in sheep and cattle are known to be very common in

certain restricted geographical areas. In contrast, all tumours of the gastrointestinal tract of dogs and cats seem to be uncommon compared with malignancies in other sites of the body.

The species distribution of the main histological types of tumour in the Edinburgh collection is shown in Table 1. These tumours were collected over a period of 25 years and comprise the findings in a necropsy series of approximately 10 000 dogs, 5000 cats and 1000 horses. Tumours from oxen, pigs, and sheep were obtained both at necropsy and from the local abbatoir, where the standard of meat inspection is such that each animal could be considered as having undergone necropsy; the cases shown in Table 1 comprise the findings in approximately 1 million oxen and pigs and 6 million sheep.

Table 1. Species distribution of the main histological types of tumour in the Edinburgh material

Tumour type	Ox	Sheep	Horse	Pig	Dog	Cat	Total
Epithelial	10	108			35	13	166
Carcinoid					1		1
Smooth muscle	1				19	1	21
Other soft tissue	8		9		3	1	21
Lymphoid	3	10	6	4	79	54	156
Mast cell					1		1
Unclassified	4	4	1		12	3	24
Total	26	122	16	4	150	72	390

Fifty examples of tumours rarely seen or not yet recorded in the Edinburgh district were added to this material; for these additional specimens and for helpful discussion of the classification I am indebted to: E. C. Appleby, London, England; R. C. Giles, Washington, DC, USA; S. Larsen, Copenhagen, Denmark; L. J. Mackey, Glasgow, Scotland; W. Misdorp, Amsterdam, Netherlands; M. Murray, Glasgow, Scotland; J. Norval, Edinburgh, Scotland; H. Pearson, Bristol, England; R. F. Robinson, Indiana, USA; A. C. Rowland, Edinburgh, Scotland; Y. Shimosato, Tokyo, Japan; H. Stünzi, Zurich, Switzerland; G. Trautwein, Hanover, Federal Republic of Germany; J. G. C. Watson, Yeovil, England; E. Weiss, Giessen, Federal Republic of Germany; and C. Wray, St Boswells, Scotland. I am also most grateful to my many colleagues in the Edinburgh district without whose help I would not have had the basic material for the work. Finally, my thanks are due to Dr Basil Morson and Dr Hugh Gilmour for their critical comparison of these animal tumours with similar tumours in man, and to Mr R. C. James, Department of Veterinary Pathology, and Mr J. Paul, Medical Illustrations Service, Edinburgh for the photography.

HISTOLOGICAL CLASSIFICATION AND NOMENCLATURE OF TUMOURS OF THE LOWER ALIMENTARY TRACT

Tumours of the gastrointestinal tract

I. EPITHELIAL TUMOURS

A. ADENOMA
   1. Papillary (villous)
   2. Tubular (adenomatous polyp)
   3. Papillotubular (tubulovillous)

B. ADENOCARCINOMA
   1. Papillary adenocarcinoma
   2. Tubular adenocarcinoma
   3. Mucinous adenocarcinoma
   4. Signet-ring cell carcinoma

C. UNDIFFERENTIATED CARCINOMA

II. CARCINOID TUMOURS

A. ARGENTAFFIN TUMOURS

B. NON-ARGENTAFFIN TUMOURS

III. TUMOURS OF SOFT (MESENCHYMAL) TISSUES

A. LEIOMYOMA

B. LEIOMYOBLASTOMA

C. LEIOMYOSARCOMA

D. CAVERNOUS HAEMANGIOMA

E. LIPOMA AND LIPOMATOSIS

F. LIPOSARCOMA

G. Mesothelioma

H. Fibrosarcoma

IV. TUMOURS OF HAEMATOPOIETIC AND RELATED TISSUES

A. Lymphoid tumours
1. Multicentric
2. Localized

B. Mast cell tumours

V. SECONDARY TUMOURS

VI. UNCLASSIFIED TUMOURS

VII. TUMOUR-LIKE LESIONS

A. Hyperplastic polyp (inflammatory or regenerative polyp)

B. Porcine intestinal adenomatosis

C. Benign lymphoid polyp

D. Annular hypertrophy of muscle coats

Tumours of the anal canal and anal margin

I. EPITHELIAL TUMOURS

A. Tumours of the hepatoid (perianal) glands
1. Adenoma
2. Carcinoma
3. Tumour-like hyperplasia

B. Squamous cell carcinoma

C. Adenocarcinoma of rectal type

D. Mucoepidermoid (adenosquamous) carcinoma

E. Tumours of the anal sac glands
1. Adenoma
2. Adenocarcinoma

F. Undifferentiated carcinoma

II. TUMOURS OF THE MELANOGENIC SYSTEM

III. TUMOURS OF HAEMATOPOIETIC AND RELATED TISSUES

A. Lymphoid tumours

B. Mast cell tumours

IV. TUMOURS OF SOFT (MESENCHYMAL) TISSUES

V. UNCLASSIFIED TUMOURS

DESCRIPTION OF TUMOURS

I. EPITHELIAL TUMOURS

A. *Adenoma*

These are benign neoplasms and must be distinguished from non-neoplastic, hyperplastic polyps because the former have a premalignant significance whereas the latter do not. Adenomas must show some cellular atypia and an increase in mitotic figures when compared with the adjacent normal mucosa. The glands will show an irregular thickening of the walls owing to the formation of several layers of cells; some of these cells have enlarged nuclei and exhibit nuclear hyperchromasia. The variation in acinar shape and in nuclear/cytoplasmic size, the loss of nuclear polarity, and mitotic abnormality are not as great as in carcinoma. As the degree of atypia increases, the well organized formation of mucus in large amounts above the nucleus diminishes. There are three patterns of growth:

1. *Papillary* (*villous*) (Fig. 1, 2). This type is composed of finger-like processes covered by well differentiated epithelium and having cores of lamina propria. The tumours are more often sessile than pedunculate.

2. *Tubular* (*adenomatous polyp*) (Fig. 3, 4). In this type, branching tubules of well differentiated epithe-

lium are surrounded by lamina propria. The tumours are more often pedunculate than sessile.

3. *Papillotubular* (*tubulovillous*) (Fig. 5, 6). These are tumours showing both the above patterns.

If a benign tumour of the stomach is found, the epithelium should theoretically be characterized either as resembling superficial gastric (foveolar) epithelium or as showing various degrees of metaplasia to intestinal epithelium.

Pseudocarcinomatous invasion, which may be seen in pedunculate tumours, is thought to be due to misplaced adenomatous tissue in the submucosa caused by repeated twisting of the stalk. Within the mucosa, haemorrhage may occur into glands and the lining acinar epithelium may desquamate to mimic a tumour plug in a blood vessel.

Benign glandular tumours have been recorded in the literature at all levels of the gastrointestinal tract as rare phenomena in the dog; they have not been recorded in the other species. It would seem from the polypoid lesions that I have examined from the stomachs of dogs, from the small intestines of dogs and cats, and from the caecum of an ox, that these lesions are usually hyperplastic polyps and not true adenomas. In the large intestine of the dog, particularly in the rectum, true adenomas (mainly papillary or papillotubular) are found occasionally.

Adenocarcinomas of the small intestine of sheep may show one or more polypoid masses arising from the annular stenosing tumour. So far, no convincing cases of true adenoma of the sheep intestine without a coexisting carcinoma have been described; it is therefore not known whether the situation is comparable with that in the dog rectum, namely, the existence of benign glandular tumours some of which appear to become malignant.

Intestinal adenomatosis in pigs is morphologically, and probably etiologically, different from adenomatous polyposis coli in man, which is sometimes called adenomatosis. In this classification, therefore, porcine intestinal adenomatosis is placed in section VII (tumour-like lesions).

B. *Adenocarcinoma*

This is a malignant tumour forming tubular structures. The tumour may exhibit more than one of the patterns set out below but it is named on the basis of the predominant type. Different patterns can occur at different levels of the invasion of the wall of the stomach or intestine.

1. *Papillary adenocarcinoma*. This type has finger-like processes with a lamina propria core covered with well polarized, columnar (cylindrical) or cuboid epithelium. It may extend as polypoid masses into the lumen of the tract but true carcinomatous invasion must be seen below the muscularis mucosa. This may be in the lymph or blood vessels.

2. *Tubular adenocarcinoma* (Fig. 7–15, 20). This tumour consists of branching tubules embedded in a fibrous stroma. The epithelium may be columnar, cuboid, or flattened.

3. *Mucinous adenocarcinoma* (Fig. 16). In this type there is excessive mucin production so that the distended glands may rupture, leading to the formation of lakes of mucin in which groups of epithelial cells may be found. The mucin should constitute more than half of the tumour and be a generalized feature so that it is visible macroscopically.

4. *Signet-ring cell carcinoma* (Fig. 17–19). The tumour is mainly composed of isolated cells with mucin in their cytoplasm.

When the epithelial cells in any of these tumour patterns are producing mucosubstances, the amount and type should be noted. The mucin may appear as intracytoplasmic vacuoles filled with acid mucin, as granules of acid mucin filling the cytoplasm (as in goblet cells), or as eosinophilic cytoplasmic granules of neutral mucin with a slightly eccentric nucleus to the cell.

The stromal components of these variants of adenocarcinoma may also exhibit changes. Bone spicules may be found either in the mucosa or in the serosal regions. Infiltrating tumours may show excessive fibrosis (scirrhous carcinoma) so that the well differentiated collagenous fibrous tissue may even mask the presence of scattered sparse foci of epithelial tumour cells. The term " carcinoma *in situ* " is used when the epithelial cells show marked atypia, i.e., represent a malignant tumour that has not yet penetrated the muscularis mucosa. If the tumour infiltrates the lamina propria but not the muscularis mucosa it can give rise to lymphatic metastases by invasion of the mucosal lymphatics and should then be designated " intramucosal carcinoma " (see Fig. 20). When penetration into the submucosa has occurred, neither of these terms is appropriate; the term " superficial spreading carcinoma " may be used to indicate a tumour that has penetrated only to the submucosa but has infiltrated laterally considerable distances, often under non-neoplastic mucosa. These terms are seldom needed

in routine diagnostic oncology in the veterinary field, but early lesions of this kind are valuable in reporting, for example, the results of using dogs as experimental animals in testing the carcinogenicity of chemicals.[a]

C. *Undifferentiated carcinoma (carcinoma simplex, medullary carcinoma, solid carcinoma)*

This is a carcinoma in which no glandular structure is visible.

Another approach to classification that is related to the geographical prevalence of gastric carcinoma in man is as follows:

Intestinal type. The cells resemble intestinal columnar epithelial cells lying in tubules with prominent brush borders. The nuclei are basal (i.e., well polarized), goblet cells may be seen, and the edge of the tumour is well demarcated.

Diffuse type. This comprises small rounded cells with a poorly developed tubular pattern and an ill-defined edge because of infiltrative growth. Many but not all of the cells are of signet-ring pattern.

Intermediate type. The tumour is composed either of equal amounts of the two above types or of solid carcinoma, i.e., of cells packed closely together with only occasional acini but having a well defined boundary at the invasive edge.

Carcinomas of the stomach are reported to account for 1% of all malignant neoplasms of dogs. They are seen somewhat less frequently in cats. The author has seen a few examples in oxen and sheep but not in horses or pigs. Because the dog is most often involved, one might expect to see a wide range of histological types. In fact, they form a rather monotonous group of poorly differentiated signet-ring cell adenocarcinomas with excessive fibrosis; they are often ulcerated and show wide lateral invasive growth. This corresponds to the diffuse type of gastric carcinoma in man, which is the sporadic form of the disease; this is interesting, since up to one-third of the cases in one series of dog tumours showed intestinal metaplasia in the adjacent areas of the stomach.

In some localities, carcinoma of the small intestine can be extremely common in oxen and sheep over three years of age. These tumours occur occasionally in older animals of other species but are not found in the pig. Prevalence in the dog is slightly lower than that of gastric carcinoma but in the cat, this site is more often affected than either the stomach or the large intestine. The jejunum is the commonest site for this tumour in the dog, sheep, and ox but in the cat, the ileum is more often involved. Macroscopically, the lesions are nearly always annular and stenosing; histologically, they are usually moderately to poorly differentiated, tubular adenocarcinomas, often with excessive fibrosis.

Carcinoma of the large intestine occurs more often in old dogs than in any of the other species. It is more common than carcinoma of the stomach but is still a relatively rare tumour. The rectum is involved more often than the colon or the caecum. The situation is similar in the cat, except that the small intestine is more often a tumour site than the large intestine. In sheep and oxen, the age distribution is similar to that of the small intestinal adenocarcinoma; the lesions usually involve the spiral colon rather than the rectum. As with tumours of the small intestine in ruminants, precancerous lesions are unknown but in dogs, carcinomas may develop from adenomas. In the colon, the tumour is annular and stenosing whereas in the rectum it may be plaque-like and ulcerated or polypoid. In the dog, tumours of the large intestine show a considerable range of histological patterns, unlike carcinomas of the stomach and small intestine.

Although some types of animal tumour may have excessive mucin production, mucinous adenocarcinomas as defined here have yet to be reported.

Metastasis to the drainage lymph nodes is common. The liver may be thus affected but metastasis to the lung is rarely seen before clinical signs have led to euthanasia of the affected animal. Especially with adenocarcinoma of the small intestine, extensive transcoelomic deposits on the flanks and diaphragm with accompanying excessive fibrosis and ascites may divert attention from the small, apparently insignificant primary tumour in the intestine and lead to a diagnosis of mesothelioma.

The histological patterns described above are not constantly related to the macroscopic form of the tumour. Plaque-like ulcerating and annular stenosing tumours are more often scirrhous than nodular or fusiform tumours.

II. CARCINOID TUMOURS (Fig. 21–24)

These tumours are composed of uniform, small-to-medium sized cells, sometimes with ill-defined

[a] See SHIMOSATO, Y. ET AL. *Journal of the National Cancer Institute*, **47**: 1053-1070 (1971).

cytoplasmic boundaries. The nuclei are round and uniform in size and seldom show mitoses. The cells are arranged in sheets, cords, and clusters with peripheral palisading of the cells and sometimes poorly-formed acini. These tumours of enterochromaffin cells show acidophilic granules in well-fixed sections stained with H & E.

A. *Argentaffin tumours*

In this type, the cells have the ability to reduce ammoniacal silver solutions to metallic silver.

B. *Non-argentaffin tumours*

In this type, the cells do not give the argentaffin reaction but may be argyrophilic, i.e., they may show granules with silver impregnation methods in which reducers are used.

Argentaffin carcinoids have occasionally been reported from the small and large intestines of the dog, from the colon of the cat, and from the jejunum of the ox. The author has seen a non-argentaffin but argyrophilic carcinoid in the stomach of a dog. In the few carcinoid tumours of domestic animals studied, the arrangement into packets has not been as discrete as in the classical human tumour and the cells have not resembled carcinoma cells so closely.

These tumours arise deep in the mucosa but rapidly spread to the submucosa, and may appear to be primary submucosal tumours. The muscularis mucosa must be followed to find the primary site in the deep mucosa.

III. TUMOURS OF SOFT (MESENCHYMAL) TISSUES [a]

A. *Leiomyoma* (Fig. 25)

This tumour is composed of interlacing bundles of eosinophilic, spindle-shaped cells that are surrounded by reticulin fibres and have long nuclei with blunt ends. Mitotic figures are rarely found. A prominent nuclear palisading resembling that found in neurilemoma may be demonstrated, but myofibrils may be present.

B. *Leiomyoblastoma*

This tumour is composed of round or polygonal cells with non-staining cytoplasm around the nucleus. Few mitotic figures are seen. Myofibrils are not found but the cells sometimes become elongated to resemble smooth muscle cells. The tumour clearly arises in the muscle coat of the wall of the tract.

[a] For further details see WEISS, E. *Bulletin of the World Health Organization*, **50**: 101-110 (1974).

C. *Leiomyosarcoma* (Fig. 26–28)

It is impossible to lay down clear-cut criteria for distinguishing this type from leiomyoma. One should look for greater numbers of cells and mitotic figures; some of the mitotic figures are abnormal. Varying numbers of non-striated myofibrils may be demonstrated and cellular pleomorphism, including tumour giant cells, may be found.

Leiomyoblastoma has been seen only rarely in the dog. Leiomyoma and leiomyosarcoma are found at all levels of the tract in both the dog and the cat. In the dog, leiomyoma is more common in the stomach than carcinoma, with which it sometimes coexists. The rectum is the commonest site in the large intestine of the dog. The small tumours found incidentally at routine necropsy clearly originate from within the muscle coats and not from the muscularis mucosa.

D. *Cavernous haemangioma*

This tumour has occasionally been recorded in most of the species. It is of interest that malignant haemangioendothelioma does not seem to occur in the alimentary tract, even in Alsatian dogs, which commonly develop this type of tumour at other sites.

E. *Lipoma and lipomatosis*

Lipomas rarely occur in the wall of the gastrointestinal tract but more frequently arise from the mesentery and retroperitoneal fat. These tumours in the horse are often pedunculate, and twisting of the stalk may lead to necrosis in the tumour.

In high-fat-yielding cattle over two years of age, particularly the Channel Islands breeds of Jersey and Guernsey, a progressive deposition of mature fat cells with broad fibrous bands forming irregular lobules may be seen in the omentum, mesentery, and retroperitoneum and surrounding the intestine. The ileum and colon, when involved, may have up to 10 cm of fat and fibrous tissue between the serosa and the muscle coat. Late in the disease, fat necrosis and dystrophic calcification of these masses may occur. The condition is called lipomatosis or fibrolipomatosis. It may not be a true tumour and certainly does not metastasize, but it seems to be progressive until the animal dies or is slaughtered.

F. *Liposarcoma*

This is a very rare tumour of the small intestine of dogs.

G. *Mesothelioma* (Fig. 29–32)

These tumours, arising from the mesothelial lining of the coelomic cavities (especially the pleura and peritoneum), consist of a variable mixture of epithelioid and spindle cell elements. When the cells form tubules or solid cords of epithelioid cells the tumours resemble transcoelomic metastases of a carcinoma. When the tumours are composed of spindle cells in a fibrillary matrix they resemble fibromas or fibrosarcomas. Mitotic figures are rare.

Mesotheliomas may be solitary or multiple; the multiple form is called the " diffuse form " because the multiple nodules are present over wide areas of the parietal and visceral surfaces and tend to become confluent. Such extensive lesions are accompanied by ascites or hydrothorax.

Mesotheliomas are rare but occur in the diffuse form in the peritoneum of calves, including fetuses; for this reason they are considered to be congenital. Some tumours show islands of cartilage within the fibroblastic tissue.

Mesotheliomas have been reported from old cows and bitches. When making such a diagnosis one must eliminate the possibility of transcoelomic metastasis from ovarian, uterine, or intestinal carcinomas and, in the case of the bitch, lymphatic spread through the chest or abdominal wall from a mammary carcinoma. Similarly, the proliferative peritonitis sometimes associated with parasitosis and traumatic ruminitis/reticulitis/omasitis in cattle and sheep can superficially resemble a mesothelioma.

H. *Fibrosarcoma*

Occasional fibrosarcomas have been recorded in most of the species. This group includes the so-called " spindle cell sarcomas ". If a tumour is so poorly differentiated that there are no regions with spindle-shaped nuclei set in a fibrillary matrix that gives a positive staining reaction for collagen, the tumour should be placed in *Unclassified tumours*.

IV. TUMOURS OF HAEMATOPOIETIC AND RELATED TISSUES [a]

A. *Lymphoid tumours*

As can be seen from Table 1, these tumours are common in all six species. They are found at all levels of the tract but occur mainly in the small intestine, sometimes as one focus, sometimes as several widely separated lesions, and occasionally as a diffuse thickening of most of the gastrointestinal tract. The involvement may be restricted to the alimentary tract and drainage lymph node or the tract may be involved as part of a multicentric, more generalized systemic disease. Most of the tumours are lymphosarcomas but some are tumours of immunoglobulin-forming cells. The tumour cells grow in rows between the muscle bundles so that when these atrophy the reticulin fibres remain in parallel rows.

B. *Mast cell tumours*

Indisputable primary mast cell tumours of the gastrointestinal tract are rare. The author's attention was drawn to a mesenchymal tumour in the intestine of cats composed of large rounded cells. The cytoplasm of these cells shows PAS-positive granules that are sometimes faintly toluidine blue metachromatic. Direct silver nitrate reduction, diazo coupling, and the ferric ferricyanide reaction normally used to identify enterochromaffin granules do not show these tumours to be carcinoids; they may be poorly differentiated or degranulated mast cell tumours.

V. SECONDARY TUMOURS (Fig. 16)

This category includes: (*a*) tumours that have metastasized from another site in the intestinal tract, either by retrograde lymphatic or venous dissemination or by colonization from the lumen; and (*b*) metastases of tumours from some other site in the body as part of a generalized arterial dissemination.

VI. UNCLASSIFIED TUMOURS

These are primary tumours of the alimentary tract that cannot be placed in any of the above categories.

VII. TUMOUR-LIKE LESIONS

A. *Hyperplastic polyp* (*inflammatory or regenerative polyp*) (Fig. 33–36)

This is a sessile or pedunculate polypoid non-neoplastic lesion that should be distinguished from adenoma. In the stomach, the epithelium of such polyps is foveolar and in the large intestine, it has fewer goblet cells than normal epithelium. Although the glands in the polyp are hyperplastic, they closely resemble those in the adjacent mucosa both in morphology and in frequency of mitotic figures.

[a] For further details see JARRETT, W. F. & MACKEY, L. J. *Bulletin of the World Health Organization*, **50**: 21-34 (1974).

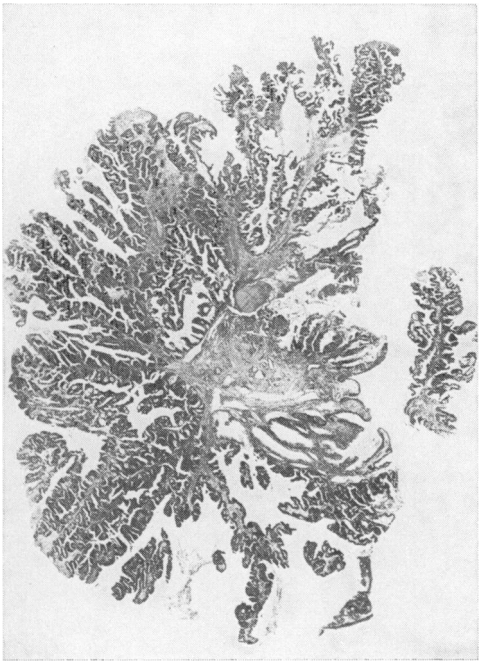

Fig. 1. Papillary adenoma, "pinch biopsy", terminal rectum (11-year-old terrier bitch). *Edinburgh.*

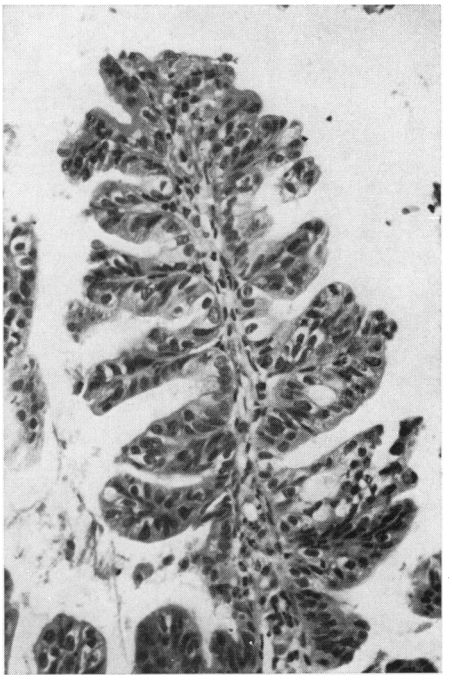

Fig. 2. Papillary adenoma. High power of Fig. 1.

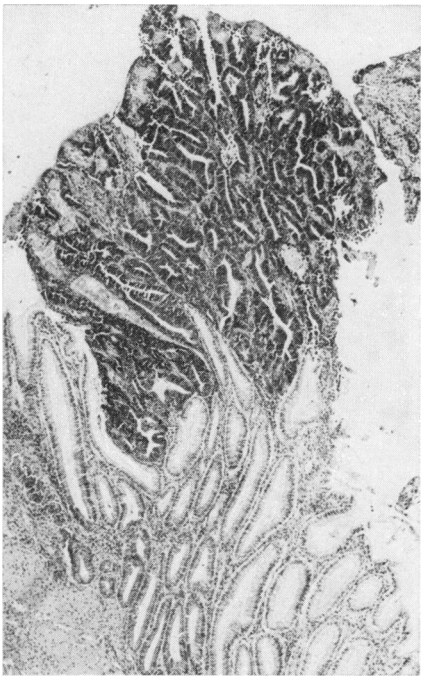

Fig. 3. Tubular adenoma, terminal rectum (12-year-old terrier dog). *Edinburgh.*

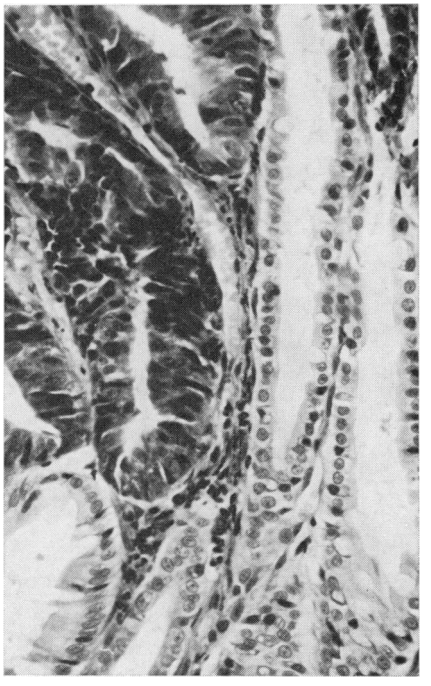

Fig. 4. Tubular adenoma. High power of centre of Fig. 3. Compare tumour (top left) with normal tissue (bottom right).

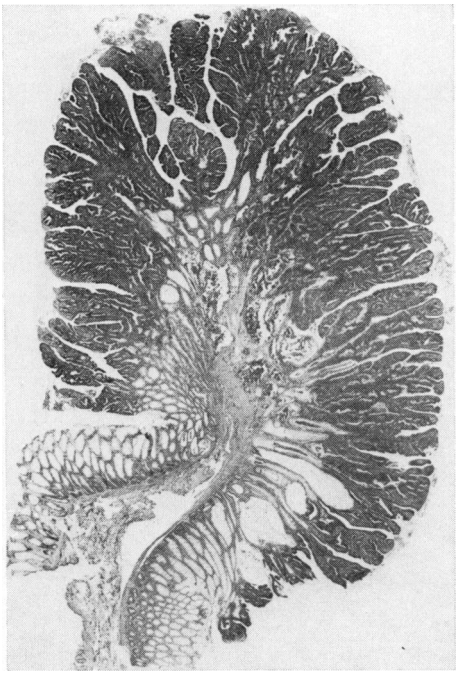

Fig. 5. Papillotubular adenoma, terminal rectum (4-year-old mongrel dog). *London*.

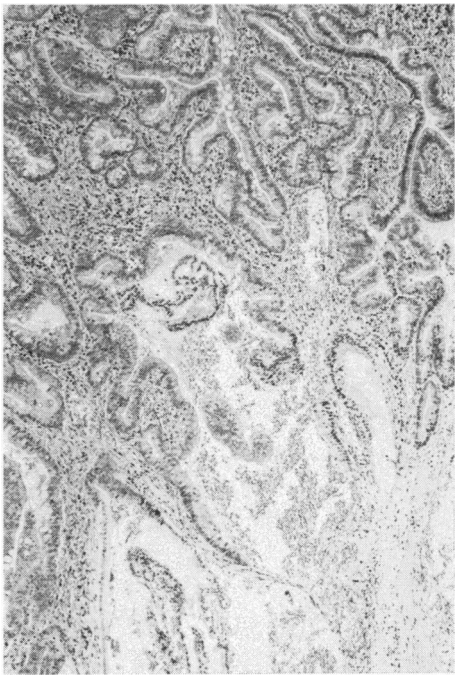

Fig. 6. Papillotubular adenoma. High power of centre of Fig. 5. Pseudocarcinomatous invasion due to haemorrhage into glands.

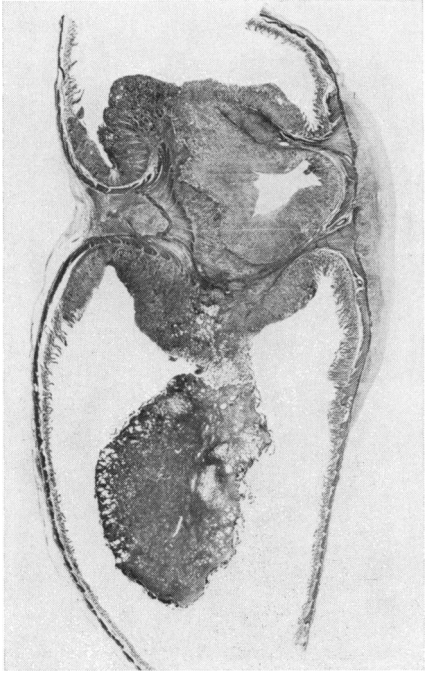

Fig. 7. Adenocarcinoma, longitudinal section of annular stenosing tubular tumour of upper jejunum (5-year-old ewe). Note polyp. *Edinburgh*.

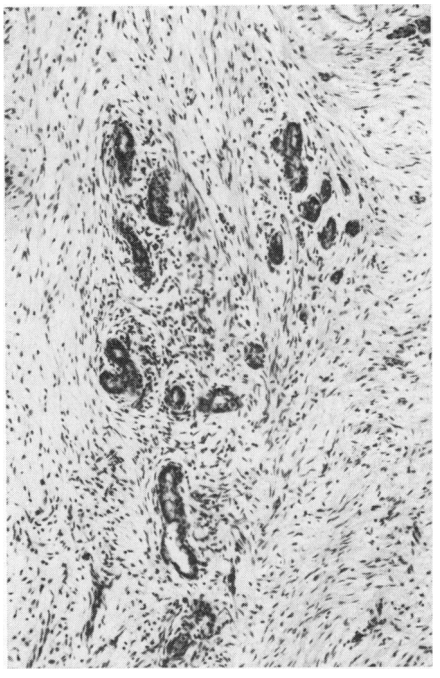

Fig. 8. Adenocarcinoma. High power of serosa in Fig. 7. Excessive fibrosis (scirrhous carcinoma).

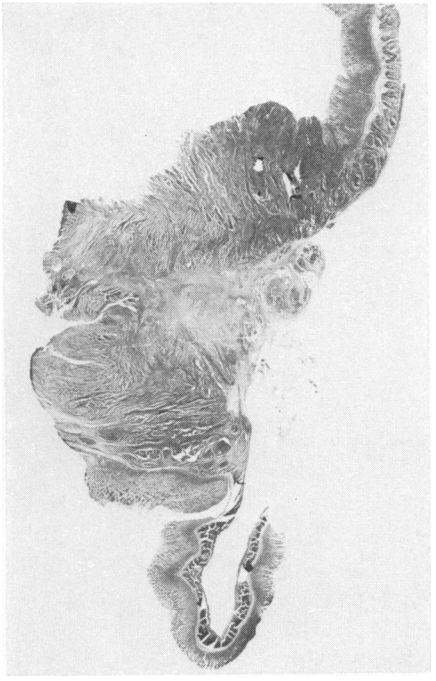

Fig. 9. Adenocarcinoma, longitudinal section of annular stenosing tubular tumour of lower jejunum (10-year-old Cairn terrier dog). Invasion of submucosa and muscle and also tumour plugs in mesenteric vessels. *Edinburgh*.

Fig. 10. Adenocarcinoma. High power of Fig. 9. Normal proximal intestine at top, tumour at bottom.

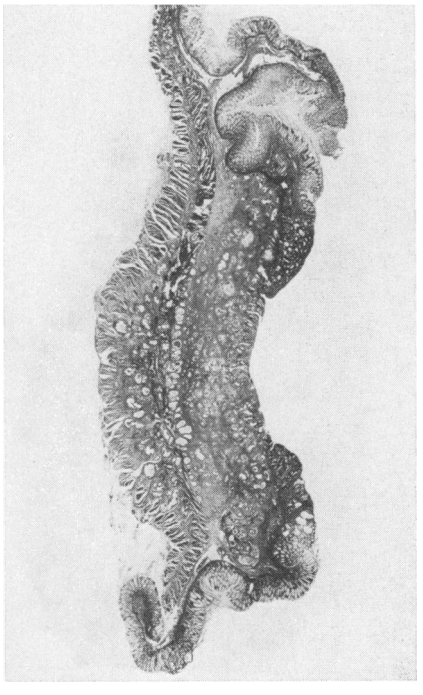

Fig. 11. Adenocarcinoma, oval plaque-like tubular tumour of terminal rectum (12-year-old fox terrier dog). *Edinburgh*.

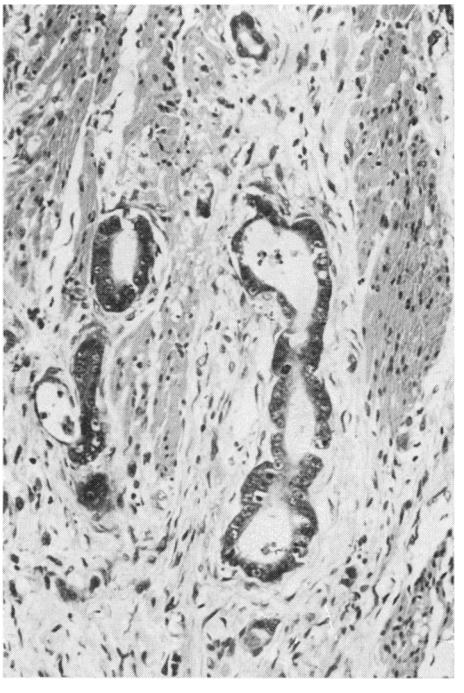

Fig. 12. Adenocarcinoma. High power of Fig. 11. Tumour penetrating between muscle bundles.

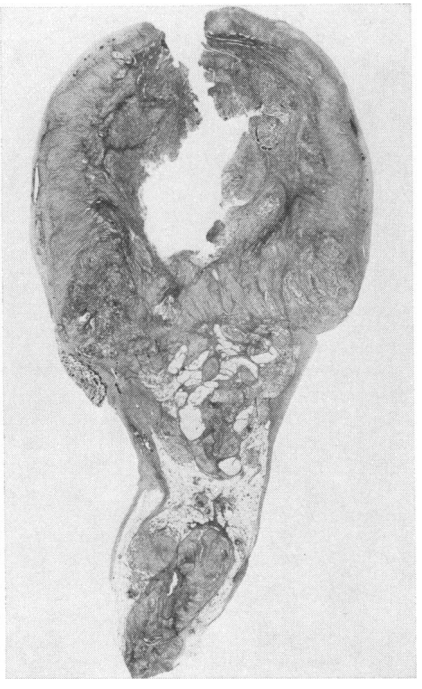

Fig. 13. Adenocarcinoma, transverse section of annular tubular tumour of lower jejunum (9-year-old Cairn terrier dog). Most of intestine and mesentery replaced by tumour. *Edinburgh*.

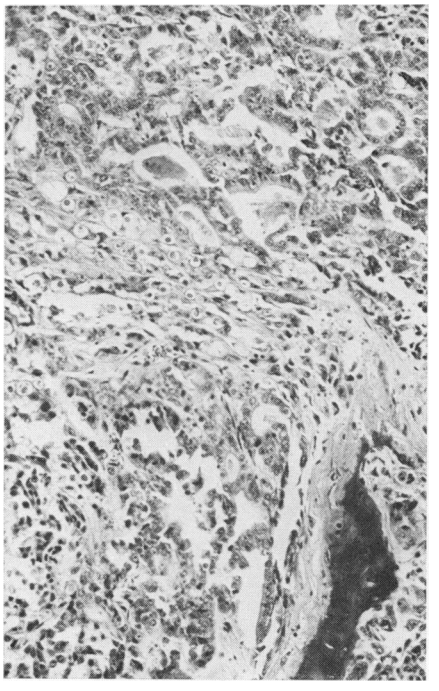

Fig. 14. Adenocarcinoma. High power of mucosa in Fig. 13. Poorly differentiated tumour and bone formation in stroma.

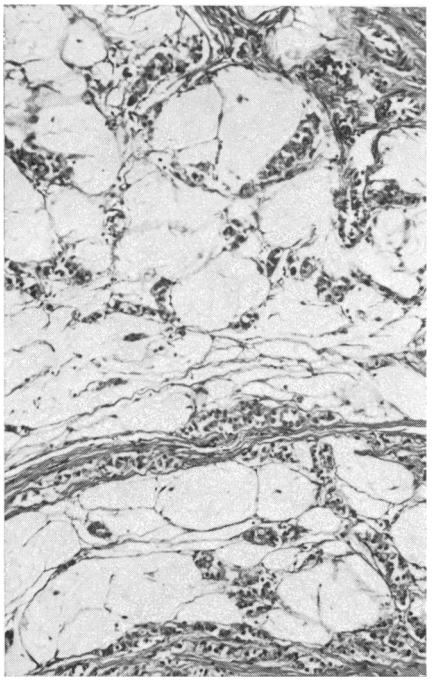

Fig. 15. Adenocarcinoma. High power of mesentery in Fig. 13. Area of mucinous adenocarcinoma pattern.

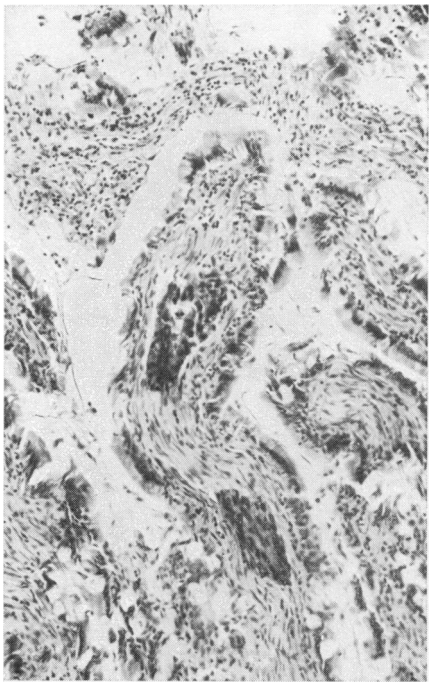

Fig. 16. Adenocarcinoma. Secondary lymphatic deposit in a villus near primary tumour shown in Fig. 13.

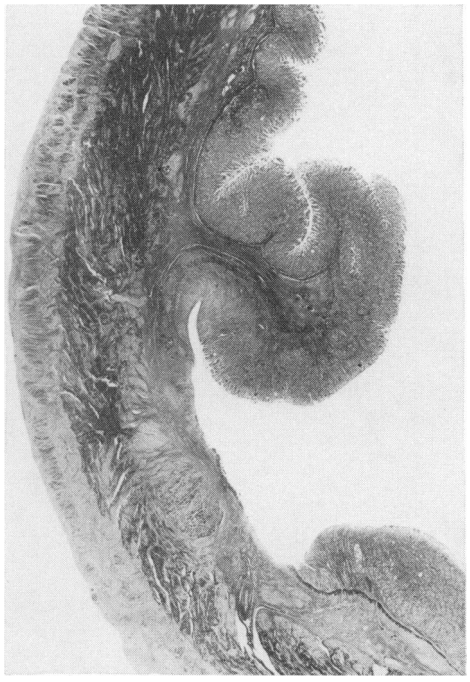

Fig. 17. Signet-ring cell carcinoma (ulcerated), fundus of stomach (5-year-old West Highland White terrier bitch). *Edinburgh.*

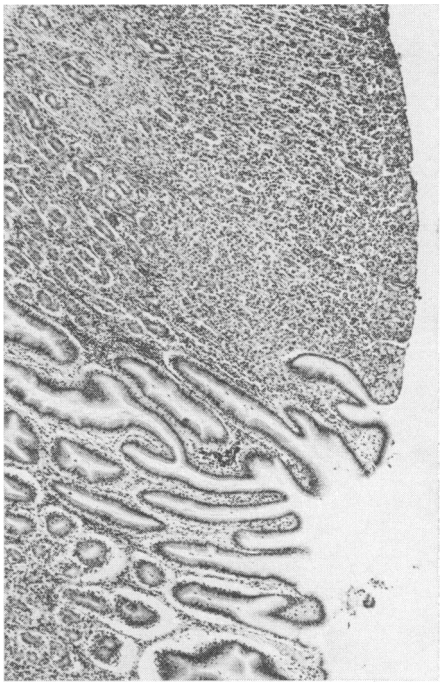

Fig. 18. Signet-ring cell carcinoma. High power of edge of ulcer in centre of Fig. 17.

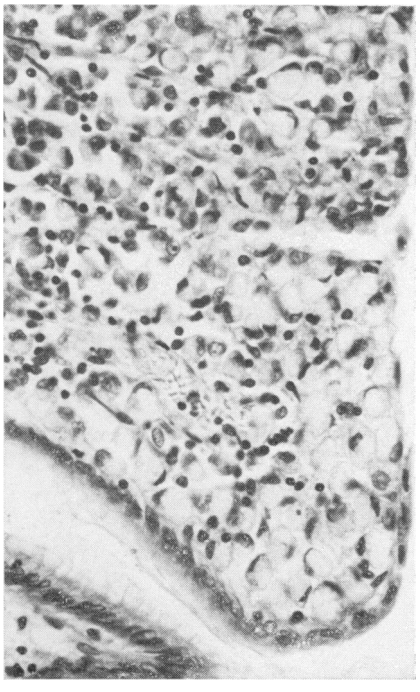

Fig. 19. Signet-ring cell carcinoma. High power of surface of edge of tumour in centre of Fig. 18.

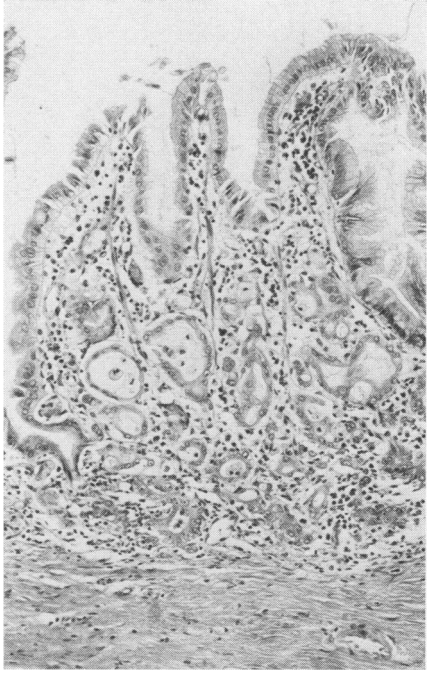

Fig. 20. Carcinoma, intramucosal, stomach (dog). *Tokyo.*

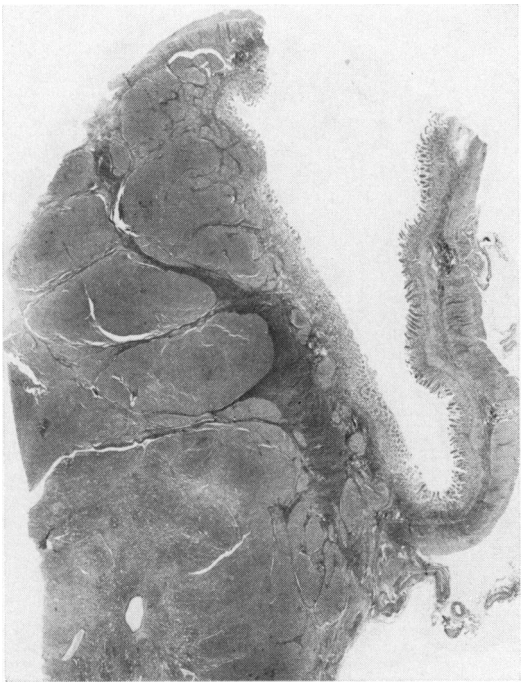

Fig. 21. Carcinoid tumour, terminal ileum (9-year-old English sheep dog). Small mucosal involvement at top left. *Washington, DC.*

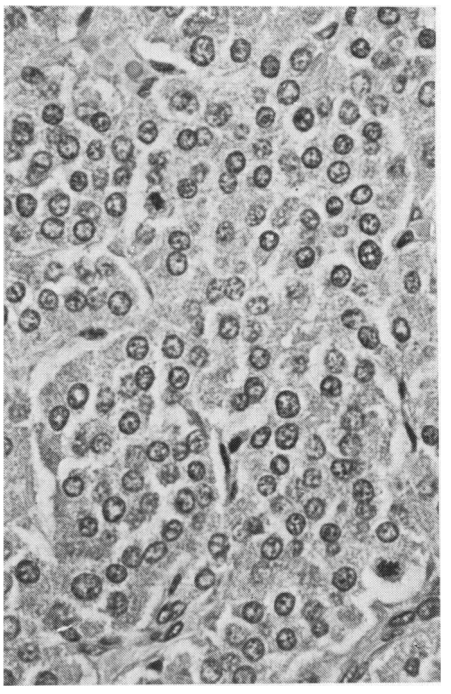

Fig. 22. Carcinoid tumour. High power of Fig. 21. Closely packed groups of cells with finely granular cytoplasm.

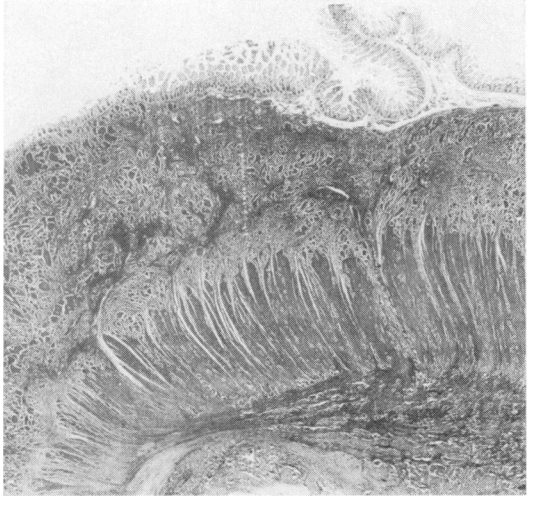

Fig. 23. Carcinoid tumour, terminal ileum (man). *H. Gilmour.*

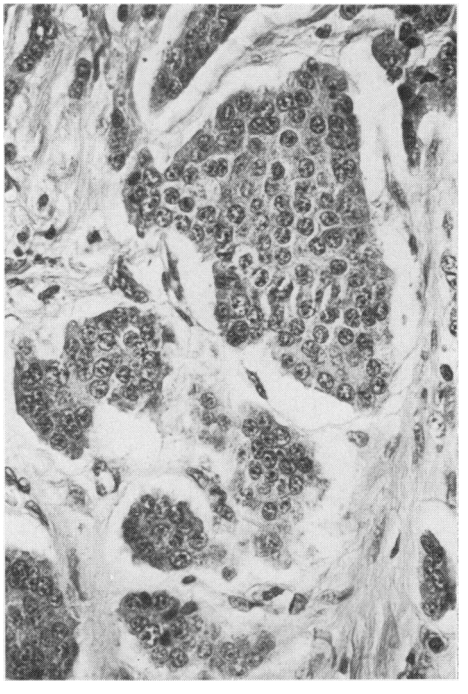

Fig. 24. Carcinoid tumour. High power of Fig. 23.

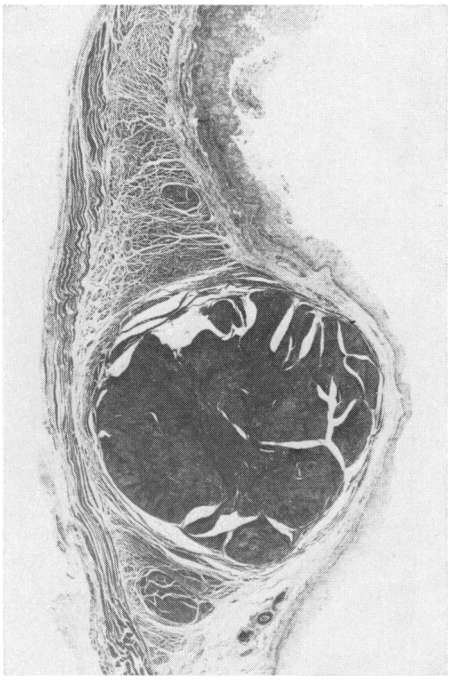

Fig. 25. Multiple leiomyomas, inner muscle coat, cardia of stomach (13-year-old boxer dog). *Edinburgh*.

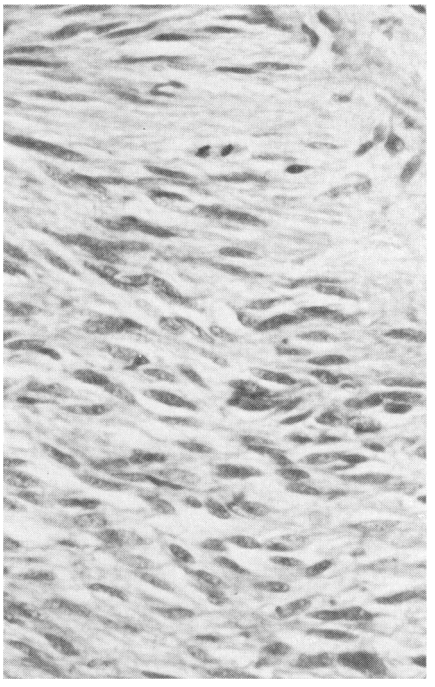

Fig. 26. Leiomyosarcoma, well differentiated, duodenum (12-year-old neutered collie bitch). *Edinburgh*.

Fig. 27. Leiomyosarcoma, poorly differentiated, rectum (12-year-old collie bitch). Note normal muscle coat at top left and presumed origin of tumour at top right under normal mucosa. *Edinburgh*.

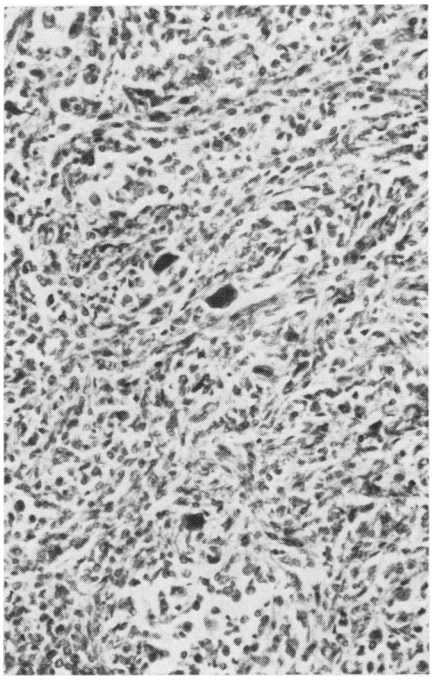

Fig. 28. Leiomyosarcoma. High power of Fig. 27. Note cell pleomorphism and giant cells.

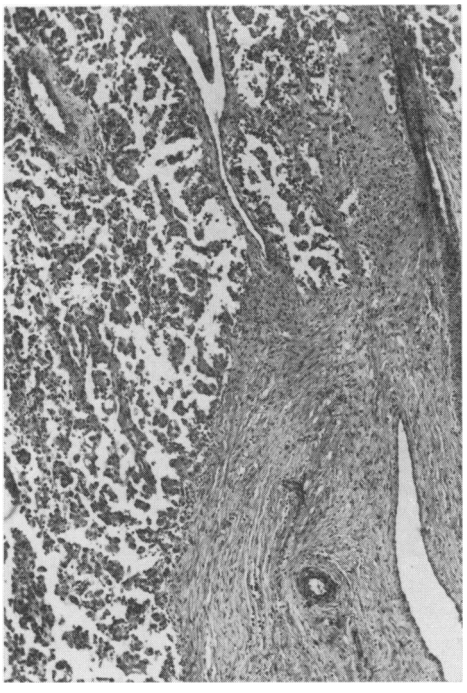

Fig. 29. Mesothelioma, epithelioid pattern, peritoneum (ox fetus). *Amsterdam*.

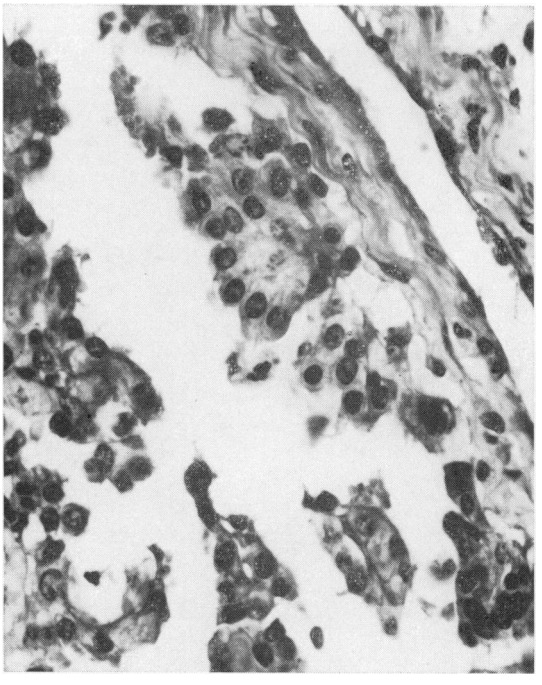

Fig. 30. Mesothelioma. High power of Fig. 29.

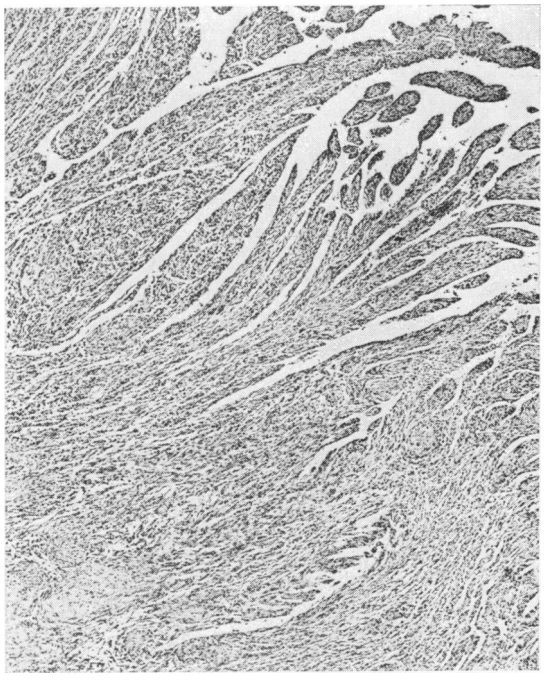

Fig. 31. Mesothelioma, sarcomatous pattern, pleura (13-year-old Alsatian dog). *Amsterdam*.

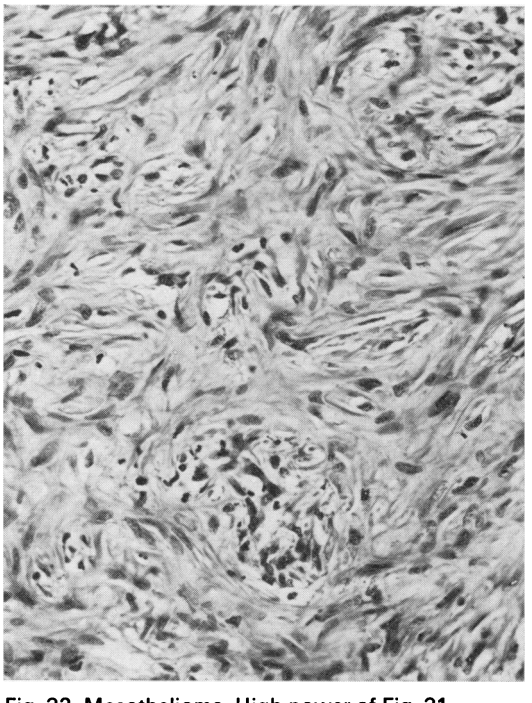

Fig. 32. Mesothelioma. High power of Fig. 31.

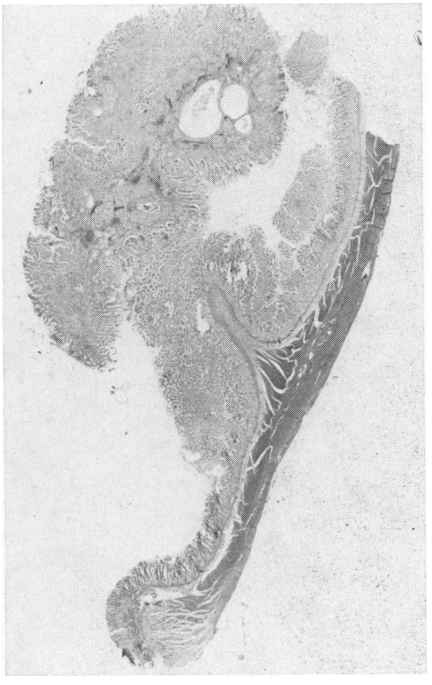

Fig. 33. Hyperplastic polyp, pyloric region of stomach (14-year-old West Highland White terrier bitch). *Edinburgh*.

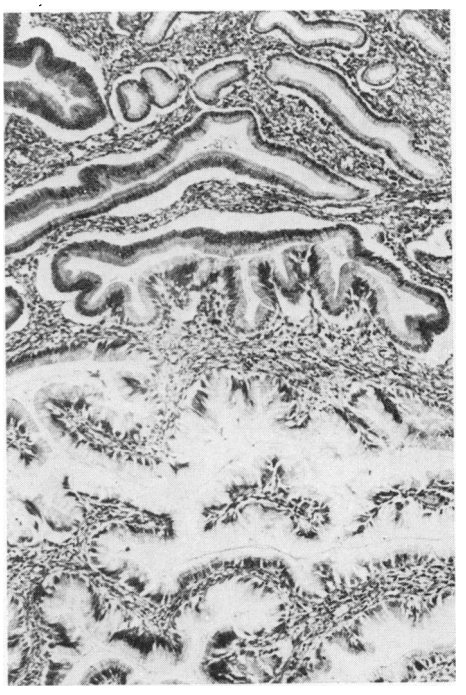

Fig. 34. Hyperplastic polyp. High power of Fig. 33 showing different degrees of mucin formation in the non-neoplastic glands.

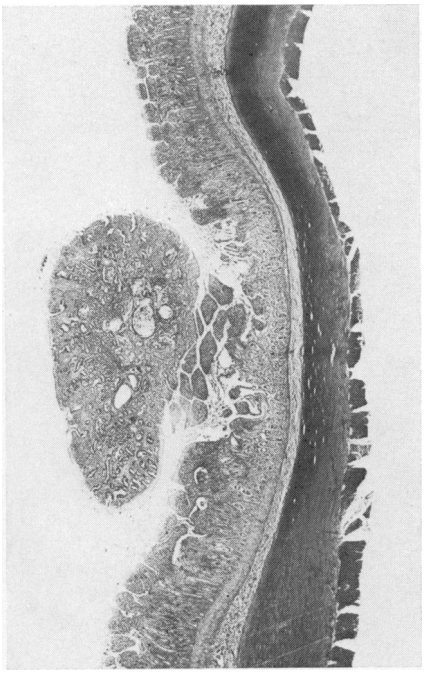

Fig. 35. Hyperplastic polyp, duodenum (12-year-old Dalmatian bitch). *Edinburgh*.

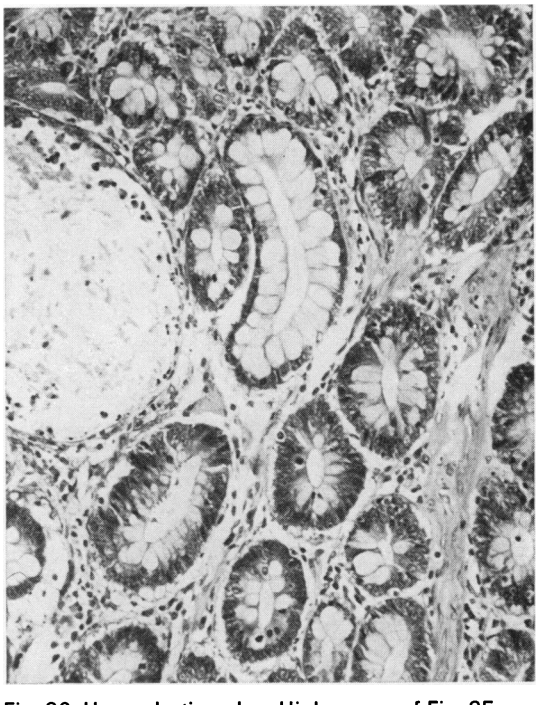

Fig. 36. Hyperplastic polyp. High power of Fig. 35.

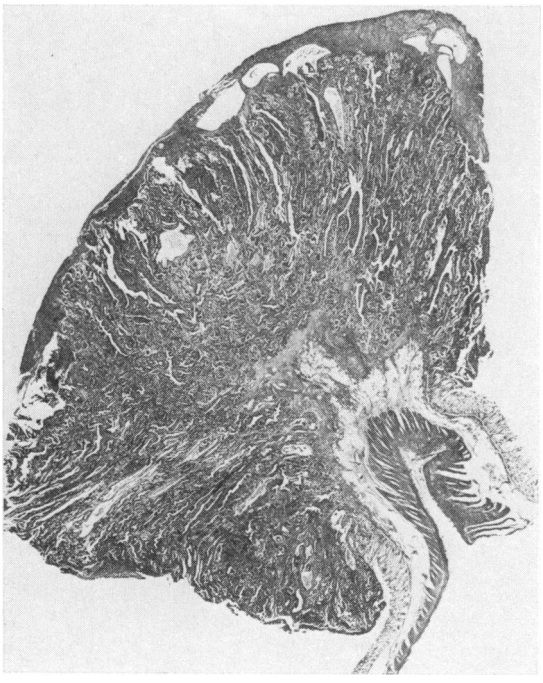

Fig. 37. Porcine intestinal adenomatosis, polypoid form. *Edinburgh*.

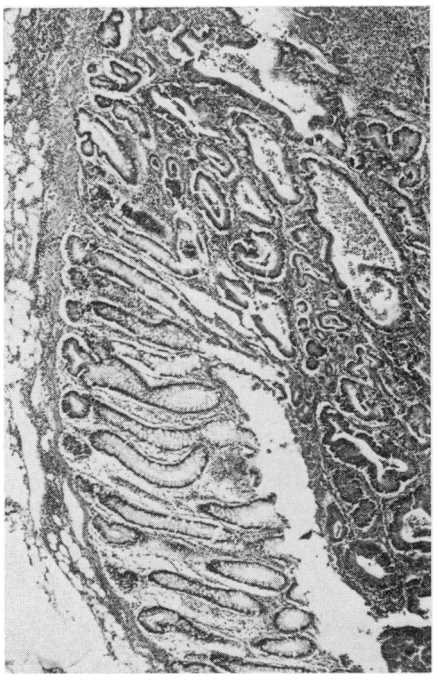

Fig. 38. Porcine intestinal adenomatosis. High power of Fig. 37 showing transition from normal to abnormal mucosa.

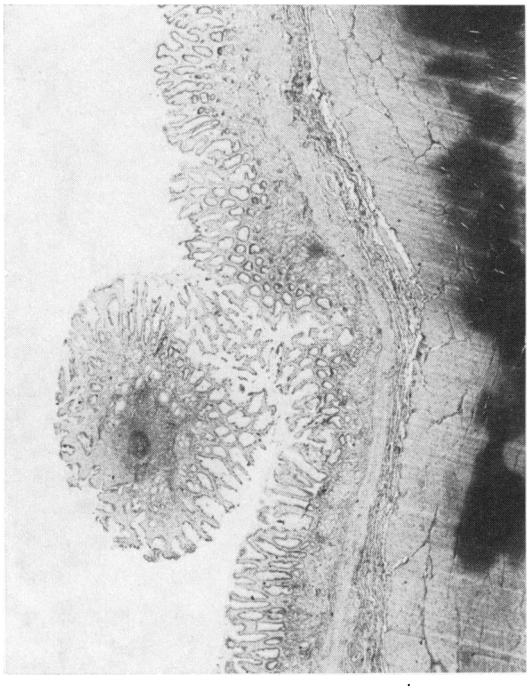

Fig. 39. Benign lymphoid polyp, pyloric region of stomach (12-year-old neutered boxer bitch). *Edinburgh*.

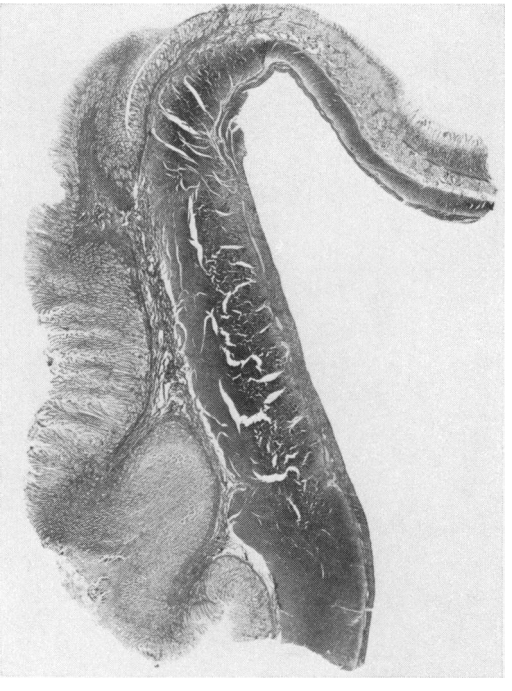

Fig. 40. Annular hypertrophy of muscle coats, pyloric region of stomach (11-year-old terrier bitch). *Edinburgh*.

Since the epithelial cells are not neoplastic, they are regular in size and shape and are not stratified. Between the basal glands there is usually an easily identifiable amount of smooth muscle branching from the muscularis mucosa. The surface of the polyp is often ulcerated and the stroma shows a variable number of inflammatory cells. The glands, especially in the deeper portions, often show cystic dilatation.

B. *Porcine intestinal adenomatosis* (Fig. 37, 38)

This disease, which affects pigs between six and sixteen weeks of age, is associated with the presence of *Campylobacter sputorum* subsp. *mucosalis* within the epithelial cells of the terminal ileum, the caecum, and the first third of the spiral colon. The lesions vary from slight changes visible only on histological examination, through exaggeration of the normal folds, to small sessile or, more rarely, pedunculated polyps. The altered mucosa may be diffusely or focally involved; it may have a sharp border with normal epithelium and any or all of the regions of the intestine mentioned above can be affected. In the affected mucosa, the nuclei may be hyperchromatic, stratification may be seen, and there are numerous mitoses. Mucus secretion is reduced so that goblet cells are rare even in lesions in the large intestine. There is a loss of villi in the small intestine so that the thickened mucosa has an exaggerated tubular rather than a villous pattern. Sometimes only the upper two-thirds of the mucosa is involved. Occasionally, the glands penetrate the submucosa, even in regions distant from the lymphoid nodules where the muscularis mucosa is normally discontinuous. Such invasion is never extensive and does not reach the muscle coat; on very rare occasions, however, acini of epithelial cells have been found in the " subcapsular sinus " in the centre of the drainage lymph nodes (in the pig, the cortex is in the centre of the lymph node). These lesions resolve spontaneously by the age of six months if the pig does not die because of intestinal dysfunction.

The lesion is histologically more similar to adenoma in man than to hyperplastic polyp, adenomatous polyposis coli, or juvenile polyposis. It seems to have no premalignant significance since adenocarcinoma of the intestine of pigs is a rare, and possibly nonexistent, condition. This fact, together with the apparent need for the presence of the organism within the affected cell and the spontaneous regression in surviving pigs, argue against it being classified as a true benign neoplasm.

C. *Benign lymphoid polyp* (Fig. 39)

These are solitary or multiple polyps having a central mass of lymphoreticular cells. They often take the form of lymphoid nodules with reaction centres covered by epithelium that may be normal or regenerating. Neither the epithelium nor the lymphoreticular cells show cellular atypia.

D. *Annular hypertrophy of muscle coats* (Fig. 40)

This condition may be seen in the pylorus of dogs and in the ileum of pigs with regional ileitis. In the pyloric region, the overlying mucosa is thickened by enlarged hyperplastic glands showing branching in their lower third, as recorded in giant rugal hypertrophy of the stomach in man. In the regional ileitis lesion the mucosa, if present, resembles that seen in porcine intestinal adenomatosis. Although macroscopically this lesion resembles annular stenosing adenocarcinoma, histologically there is no doubt that the epithelium is not malignant and that the hyperplastic muscle coat is not a leiomyoma.

Tumours of the anal canal and anal margin

I. EPITHELIAL TUMOURS

A. *Tumours of the hepatoid (perianal) glands* [a]

These tumours are very common in old male dogs, accounting for 90% of the tumours of the anal canal and anal margin in this series. Only about 20% of tumours encountered are malignant.

B. *Squamous cell carcinoma* [a]

C. *Adenocarcinoma of rectal type*

This tumour resembles adenocarcinoma of the large intestine but occurs at the mucocutaneous junction. The malignant glandular acini are therefore in direct contact with stratified squamous epithelium.

D. *Mucoepidermoid (adenosquamous) carcinoma*

Mucoepidermoid carcinoma shows columns and tubules composed of mucus-secreting and squamous cells; the term " adenosquamous carcinoma " should be used where these two cell types appear separately in different parts of the tumour. These tumours, as well as simple squamous cell carcinomas, have occasionally been seen in the dog.

[a] For a detailed description of these tumour types see WEISS, E. & FRESE, K. *Bulletin of the World Health Organization*, **50**: 79-100 (1974).

E. *Tumours of the anal sac glands*

These resemble sweat gland tumours. In the benign form they usually appear as cystadenomas, whereas in the malignant form papillary, tubular, or solid carcinoma subdivisions are seen. These tumours occur in old dogs but there is no sex predisposition as there is for hepatoid gland tumours.

The tumour at first fills the anal sac before showing extensive peripheral invasion and metastasis to the drainage (iliac) lymph nodes; ulceration of the overlying mucocutaneous junction is therefore not often seen. Very rarely, tumours with this morphology arise in the anal region from glands opening on to the mucocutaneous surface and this form may be ulcerated and macroscopically resemble adenocarcinoma of the rectal type.

F. *Undifferentiated carcinoma*

II. TUMOURS OF THE MELANOGENIC SYSTEM [a]

Old grey horses often show multiple benign and malignant melanotic tumours. These usually occur in the skin of the anal margin rather than under the mucous membrane.

III. TUMOURS OF HAEMATOPOIETIC AND RELATED TISSUES [b]

Lymphoid and mast cell tumours are sometimes found in dogs. The latter are more common than the former and take the form of ill-defined, plaque-like ulcers that are usually poorly differentiated histologically.

IV. TUMOURS OF SOFT (MESENCHYMAL) TISSUES [c]

V. UNCLASSIFIED TUMOURS

These are tumours that cannot be placed in any of the above categories.

[a] See WEISS, E. & FRESE, K. *Bulletin of the World Health Organization*, **50**: 79-100 (1974).

[b] See JARRETT, W. F. & MACKEY, L. J. *Bulletin of the World Health Organization*, **50**: 21-34 (1974).

[c] See WEISS, E. *Bulletin of the World Health Organization*, **50**: 101-110 (1974).