

## SMOOTH-MUSCLE TUMOURS OF THE OESOPHAGUS\*

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As is the case with hollow organs elsewhere in the body, the mucous membrane of the oesophagus has a much greater propensity for neoplastic change than the muscular coat. Thus in the Division of Surgical Pathology at the Mayo Clinic, in the 30-year period from 1920 to 1949 inclusive, the diagnosis of leiomyoma and leiomyosarcoma of the oesophagus was made on 18 occasions, whereas the diagnosis of carcinoma of the oesophagus was made in 2,312 cases.

The incidence of leiomyoma compared with other benign tumours of the oesophagus is variously reported. Thus Patterson, in 1932, found six leiomyomas in a total of 62 cases of benign oesophageal tumours reported in the literature; she also noted one lipomyoma and eight myomas of unspecified type. The total number of leiomyomas reported in the literature is not great. Rose, in a very exhaustive review of the world's literature from 1797 to 1936, was able to find 49 cases of leiomyoma, to which he added his own case. A careful review of the literature from that time reveals a further 66 cases, making a total of 116. It is of interest to note that, whereas up to 1947 almost all reports were of necropsy cases in which there usually had been few or no symptoms, yet from then onward almost all the reports have been of surgical cases in which the lesion has frequently caused dysphagia. The literature also contains reports of six cases of leiomyoma involving both the stomach and the oesophagus.

Surgical experience with this type of tumour is even more restricted. Indeed, after a careful review of the literature, we have found reports on only 32 patients operated on for leiomyoma of the oesophagus, and in four of these patients the leiomyoma was partly in the stomach. Details of these cases are presented in Table I.

The malignant variety of this tumour of the oesophagus is even more rare. Thorek and Neiman (1950) found that leiomyosarcoma comprised 14% of sarcomas of the oesophagus. Excluding two cases reported by Harrington which are included in the present study, there are reports of nine cases available in the literature (Howard, 1902; von Hacker, 1909; Bauer, 1917; Massachusetts General Hospital case records, 1935; Menne and Birge, 1937; French and Garland, 1941; Pennes, 1942; Ovens and Russell, 1951; and Lyons and Garlock, 1951). Only two of these patients had definitive surgical treatment. The patient of Lyons and Garlock had a polypoid tumour and they were able to perform an oesophagogastrectomy. The patient of Ovens and Russell had a double lesion: a well-differentiated squamous cell epithelioma in the middle third, and a polypoid leiomyosarcoma in the lower third, of the oesophagus. These authors were also able to perform an oesophagogastrectomy.

Because the reported surgical experience with these tumours is small, it was felt to be worth while to review the Mayo Clinic cases of smooth-muscle tumours of the oesophagus in which surgical treatment had been given. By so doing we hoped in some measure to clarify the natural history of these tumours, with a particular view to differentiating the benign from the malignant variety. We were also interested in studying the pathological aspects with particular reference to criteria of malignancy. Finally it was our aim to evaluate different methods of treatment.

On this basis we were able to study 21 cases of leiomyoma and five cases of leiomyosarcoma of the oesophagus. In four of the cases of leiomyoma, the lesion had extended to involve the stomach. Pathological material was available in all these cases, and after the gross specimens were studied, sections were cut and stained with haematoxylin and eosin, by the van Gieson technique to distinguish between muscle and connective

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TABLE I  
LEIOMYOMAS OF THE OESOPHAGUS TREATED SURGICALLY

Author	Age, Sex	Symptoms	Position	Treatment	Tumour (cm.)	Remarks	Recovery
Ohsawa, 1933 ..	43 F	Dysphagia	Lower third	Transpleural enucleation			Yes
Sauerbruch and O'Shaughnessy, 1937	33 M	Retrosternal pain, dysphagia	" "	Left thoracotomy, resection, oesophagogastrostomy	Encircling		"
Harper and Tiscenco, 1945	41 M	Post-prandial distension, vomiting	Middle third	Thoracotomy, enucleation	6 × 3		No
Bradford <i>et al.</i> , 1947	23 M	Substernal pain on swallowing	Scattered	Thoracotomy, enucleation	14 tumours 1 to 4		Yes
Schafer and Kittle, 1947	46 M	Epigastric pain, weight loss	Lower third	Left thoracotomy, resection with part of oesophageal wall	7 × 7 × 10, U-shaped	Accompanying diaphragmatic hernia	"
M. G. H. case 33252, 1947	49 F	Dysphagia, pain	Middle third	Thoracotomy, enucleation	5, oval	Biopsy had been done	Not stated
Nissen, 1949 ..	56 M	Dysphagia	" "	Left thoracotomy, resection with mucosa intact	Encircling	Lung graft used to cover muscle defect	Yes
Hurwitz, 1949 ..	31 M	Asymptomatic	" "	Right thoracotomy, enucleation	3 lobes: 5.2 × 2.0 × 2.8 3.5 × 2.6 × 1.6 3.0 × 2.5 × 1.1		"
Biasini, 1949 ..	49 F	Dysphagia	Lower third	Left thoraco-abdominal resection, oesophagogastrostomy	Size of hen's egg		"
Cornell <i>et al.</i> , 1950 ..	54 F	Epigastric distress	" "	Left thoracotomy, enucleation	7 × 4 × 4		"
Bigger <i>et al.</i> , 1950 ..	24 M	Dysphagia	Middle third	Thoracotomy, enucleation	6 × 2		"
Goldman and Masters, 1950	63 F	Dysphagia, vomiting	Lower third	Right thoracotomy, enucleation	5 × 4	Biopsy done	"
Dugan and Meagher, 1950	27 M	Substernal pain	Middle third	" "	2.5 × 6.5		"
Fulton, 1950 ..	36 M	Epigastric pain	" "	Thoracotomy, enucleation	3 × 2 × 2		"
Thomeret, 1950 ..	23 M	Retrosternal pain, weight loss, vomiting	Lower third	Right thoracotomy, enucleation	Fist-shaped mass		"
Lortat-Jacob, 1950 ..	26 M	Dysphagia intermittent	" "	Left thoracotomy, enucleation	U-shaped, encircling		"
" " " "	46 M	" "	" "	" "	Trilobed, encircling		"
Madden and Olmstead, 1950	28 M	Pain, cough	Upper third	Right thoracotomy, enucleation			"
Stojanovic and Jelisevic, 1950		Dyspnoea	" "	" "			"
Shaw, 1950 ..	24 M		Extensive	Oesophageal resection, cutaneous oesophageal gastrostomy	Extensive		"
Chi and Adams, 1950	25 M	None	Upper third	Right then left thoracotomy, resection, oesophagogastrostomy	7.5 × 3.5 × 8	Unable to remove through (right) biopsy	"
Daniel and Williams, 1950	38 F	"	Lower third	Thoracotomy, enucleation	7 × 6	Para-oesophageal hernia	"
Myers and Bradshaw, 1951	40 M	Regurgitation	" "	Left thoracotomy, enucleation	7 × 4 × 4		"
" " "	15 M	Dysphagia	Middle third	Thoracotomy, enucleation			"
Garlick and Stegmaier, 1951	48 M	Substernal pain with vomiting	" "	Left thoracotomy, enucleation	2.5 × 1.5	Biopsy (ulcerated)	"
Chalnot <i>et al.</i> , 1951 ..	26 M	Dysphagia intermittent	" "	Right thoracotomy, enucleation	15 × 8	Compressing trachea	"
" " " "	25 M	Dysphagia, pain	" "	" "	6 × 3, oval		"
Hoyne and Rogers, 1951	44 F	Asymptomatic	Lower third	Left thoracotomy, resected with diverticulum	12 × 3 × 3	Diverticulum	"
Brock, 1942 ..	47 M	Intermittent indigestion, vomiting	Lower third and cardia of stomach	Thoraco-abdominal resection, oesophagogastrostomy	10 × 7, lobulated	Ulcerated on gastric aspect	"
Kenworthy and Welch, 1948	56 F	Anorexia, weight loss	Lower third, large polypoid mass in cardia	Transpleural resection, oesophagogastrostomy	10 × 3, nodular	Ulcerated on gastric aspect	"
Goldman and Masters, 1950	51 F	Dysphagia, vomiting	Lower third, mainly in stomach	" "	10.5 encircling oesophagus	Large diaphragmatic hernia	"
Lortat-Jacob, 1951 ..	34 M	Dysphagia, pain	From pulmonary root into stomach	" "	Very large	Ulcerations on gastric aspect	Yes (already has oesophageal ulceration)

tissue, and by the Mallory phosphotungstic acid method to demonstrate myofibrils.

#### LEIOMYOMAS

SEX.—Of 17 patients with leiomyomas limited to the oesophagus, 15 were men and two were women. If these data are combined with the reports in the literature it is found that where the sex is indicated leiomyoma of the oesophagus has been reported in 65 men and 23 women, a ratio of approximately 3:1. Forty-five of these patients (28 men and 17 women) have had the lesion removed surgically. The sex and age were not available in Stojanovic's case, but in the other cases 35 were men and nine were women, a ratio of approximately 4:1. Interestingly enough, the four patients in our series who had a leiomyoma involving the lower end of the oesophagus and extending on to the cardia of the stomach were all women. There are also four such surgical cases in the literature, two being men and two women.

AGE.—The age of the patients in our series varied from 31 to 58 years, eight being in the fourth, four in the fifth, and five in the sixth decade of life. When these cases are combined with the surgical cases in the literature, the age distribution is found to be that seen in Table II. Thus the

TABLE II  
AGE DISTRIBUTION OF ALL PATIENTS WITH LEIOMYOMA OF THE OESOPHAGUS TREATED SURGICALLY

Age (Years)	Patients	Percentage
11-20	1	2.3
21-30	10	22.7
31-40	13	29.5
41-50	12	27.3
51-60	7	15.9
61-70	1	2.3
	44	100

majority of patients with leiomyoma of the oesophagus treated surgically are between 20 and 50 years of age.

Of the four additional patients with a combined lesion of the oesophagus and stomach, two were in the second decade of life, one was 30 years old, and the other was 56.

SYMPTOMS.—It has been noted elsewhere that many patients with a leiomyoma of the oesophagus are asymptomatic. This was found to be the case in seven of the 17 patients in our series. The lesion was discovered on radiological examination of the chest either during a routine examination or during the investigation of some unrelated complaint. Dysphagia was the presenting symptom in six patients; one patient presented with

excessive salivation at night, and an inability to swallow the saliva; another had post-prandial epigastric distress which may have been related to the tumour; one patient presented with melaena, but this was more probably related to a concomitant duodenal ulcer; and one patient presented with a history of chills and fever which were probably due to a pneumonic condition. This patient incidentally had slight burning in the throat. It is a fair conclusion then that at least half of the patients were without symptoms directly referable to the leiomyoma.

Dysphagia as a symptom was mild in at least half of the cases studied; occasionally solid food would seem to stick, or on eating rapidly the patient would have a little difficulty. It was more severe in the others. The symptom was usually periodic, and although progressive was not rapidly so: in one patient there had been no great change over a period of 10 years, and in another the tumour had been discovered 10 years before the onset of mild dysphagia. The average period between the onset of dysphagia and discovery of the tumour was less than one year. Although several patients complained of a peculiar retrosternal sensation, only one had definite pain on swallowing. In this instance it extended to the back. Three patients complained of vomiting infrequently, and five had epigastric distress, usually bloating, after a meal. This may not have been related to the presence of the leiomyoma. Some loss of weight was noted in three patients, but in no instance did this exceed 20 lb. (9.1 kg.).

This mildness of symptoms is in keeping with the findings in surgical cases in the literature. It will be recalled that only 13 of 27 patients had dysphagia, and in four the leiomyoma was asymptomatic.

Of the four patients with a combined lesion of the oesophagus and stomach in our series, in one the lesion was picked up by radiological examination of the chest, while the patient was being investigated for the complaint of menometrorrhagia. The remaining three patients had dysphagia; in two this was associated with retrosternal pain, and in the third the complaint took the form of regurgitation of every meal, so that eventually only a liquid diet would stay down. In these patients with a combined lesion the process is more extensive, and the symptoms would be expected to be more severe.

The almost complete absence of bleeding as a symptom, and of ulceration of the mucosa as a finding, is of very considerable interest. In none of our 21 cases was there a clear-cut history of

bleeding as a direct sequel to the presence of a leiomyoma in the oesophagus. One patient had a history of melaena, but in addition an active duodenal ulcer. Another had had an episode of haematemesis. However, this lesion straddled the oesophago-cardiac junction, and the specimen contained a small ulcer of the mucosa overlying the gastric extension of the tumour. There were two small ulcers of the oesophageal mucosa in another patient, but the lesion here extended to the stomach, and there may well have been regurgitation of gastric juice through an incompetent sphincteric mechanism.

It is interesting to contrast this state of affairs with that found where a leiomyoma is present elsewhere in the alimentary tract. In the past few years, leiomyomas of the alimentary tract have been studied by a group of investigators at the Mayo Clinic. Hoppes (1947) found that of 76 patients who had had leiomyomas of the stomach removed, 34 had bleeding as a symptom—frequently the presenting symptom—and a similar number had ulceration of the gastric mucosa over the lesion. Starr (personal communication) was able to collect data on 45 patients who had had leiomyomas removed from the small intestine. Twenty-six of these patients had bled from an ulcer over the lesion. MacKenzie (personal communication) noted that three of eight patients with leiomyomas of the colon had ulceration and bleeding. Anderson, Dockerty, and Buie (1950) investigated leiomyomas of the rectum. Most of these lesions were small and were picked up on routine proctoscopic examination. Of 10 patients, only one had bled, and in no instance was an ulcer found overlying the lesion.

It is suggested that there are at least two reasons to account for bleeding and ulceration when they occur. The frequently cited cause, namely, thinning of the mucosa from stretching, with compromise of the blood supply, is common to leiomyomas in any segment of the alimentary tract, and since those in the oesophagus and rectum do not bleed, it cannot be the whole answer. The other factor, the effect of the nature of the contents of the particular segment of the alimentary tract, is probably of equal importance. The reaction of the contents of the oesophagus is comparatively neutral, whereas that of the stomach is strongly acid and that of the intestines alkaline. The pepto-acid factor, although not necessarily the fundamental cause of peptic ulceration, is without any doubt very important, as is witnessed by the comparatively good results following the empirical procedure of partial gastrectomy, which aims at

reducing the production of acid by the stomach. It is known that some segments of the alimentary tract are more susceptible to change in reaction than others. Ripley, Olsen, and Kirklin (1952) found an amazingly high incidence of peptic ulceration of the oesophagus following procedures which destroyed the cardio-oesophageal sphincteric mechanism. It would be interesting to observe the fate of the mucosa overlying a leiomyoma of the oesophagus in a patient with free regurgitation of gastric juice. Arroyave, Clatworthy, and Wangenstein (1951) demonstrated in dogs that ulceration of the oesophagus could be produced readily by implanting a portion of the gastric mucosa in the wall of the oesophagus.

It seems reasonable to believe that the normal contents of certain segments of the alimentary tract may cause ulceration of the mucosa in that segment when the blood supply is impaired.

**PHYSICAL EXAMINATION.**—This gave negative results in every case except two, in which findings were present on percussion and auscultation of the chest. In the one instance this was due to the size of the tumour, and in the other to the marked dilatation of the oesophagus produced by the tumour.

**OTHER EXAMINATIONS.**—Such factors as the concentration of haemoglobin, the erythrocyte and leucocyte counts, and the sedimentation rate were not significantly altered.

As in the cases recorded in the literature, diagnosis in our series was usually arrived at by a combination of radiological and oesophagoscopy examination. It is not the purpose of this paper to establish the radiological characteristics of these tumours. This subject has been very adequately treated by Schatzki and Hawes (1942). However, it is of interest to note that routine radiographs of the chest showed the lesion as a circumscribed mass in three cases. In the four cases in which both the oesophagus and the stomach were involved, a shadow was present on routine radiological examination in every instance, although in one this was later established as being due to the widely dilated oesophagus caused by the tumour. Outlining the oesophagus with barium was very valuable (Fig. 1), and in all but three of the 17 cases a lesion was picked up which was felt to be definitely extramucosal. Of the three exceptions, the lesion was diagnosed as oesophageal varices in one case, the possibility of carcinoma was suggested as an alternative diagnosis in another, and the lesion was not detected in a third. However, in the last-mentioned case, the

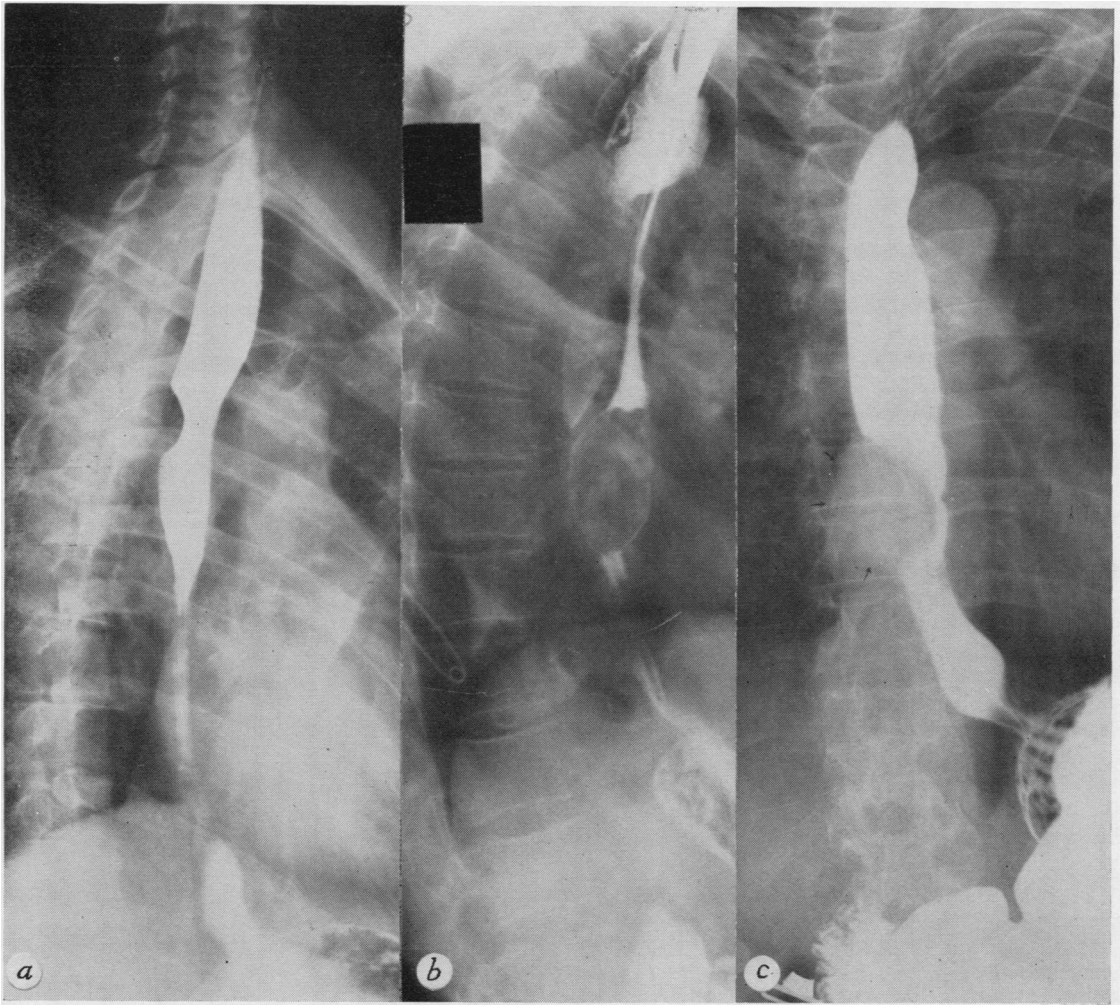


FIG. 1.—(a) Indentation of the oesophagus by a leiomyoma. The outline is smooth and the upper and lower borders are sharp. (b) A leiomyosarcoma causing a forked appearance of the stream of barium, with a mould effect over the surface of the tumour. There is minimal dilatation of the oesophagus above the tumour. (c) Same case as in *b*. Antero-posterior view demonstrating the smooth filling defect produced by the tumour. The soft-tissue mass would indicate that the tumour had expanded the wall of the oesophagus or had extended beyond it.

tumour was very small and purely incidental to the presence of a large benign gastric ulcer. In 14 of the 16 instances in which a deformity was found, the first vote was given to an extramucosal intramural lesion, and in the others it was felt that the defect was more likely due to extrinsic pressure. Radiological diagnosis was less accurate in the four cases of combined lesions. An intramural tumour, possibly leiomyoma, was diagnosed once, the other diagnoses being hiatal hernia, hiatal hernia with carcinoma of the cardia, and cardiospasm.

Oesophagoscopy was done in all but two of the 17 cases of leiomyoma of the oesophagus. The mucosa was intact in all the cases, although there was some degree of oesophagitis in three instances. The presence of intact mucosa was very helpful in ruling out carcinoma. The appearance of the mucosa was equivocal in one case, so that the examiner suspected an infiltrating malignant neoplasm, probably rhabdomyosarcoma, and performed the only biopsy done in the series. This merely showed inflammatory reaction. The lesion, while usually protruding into the lumen of the

oesophagus, was truly pedunculated in only two cases, leading the examiner to suggest fibrolipoma. In 13 of the other 15 cases the oesophagoscopist made the diagnosis of an intramural tumour, while in the remaining two he felt that the lesion was extrinsic. The firmness of the tumour led him to make the diagnosis of leiomyoma in the great majority of cases, and only once did he feel that the lesion was an enterogenous cyst rather than a leiomyoma. In the four cases in which both the oesophagus and the stomach were involved, leiomyoma was suspected twice by the oesophagoscopist. In the third, he felt that the lesion was a traumatic diaphragmatic hernia with compression of the wall of the oesophagus by a herniated viscus, and in the fourth it was felt that the condition was cardiospasm.

When the surgeon was asked to give an opinion, he therefore had a considerable amount of evidence on which to base this. If the case in which the leiomyoma was small and purely incidental be excluded, we find that he made the diagnosis of leiomyoma accurately before operation in 12 of 16 cases. In none of the other four cases did he feel that the lesion was malignant. Therefore, in leiomyoma of the oesophagus, the diagnosis can be made with a high degree of accuracy, and it is very unusual for such a tumour to be mistaken for a malignant lesion.

Where the lesion extended on to the cardia of the stomach, the surgeon was much less accurate in his appraisal, but in none of the four cases did he suspect malignancy.

**TREATMENT.**—In 15 of the 17 cases it was found possible to enucleate the leiomyoma from the wall of the oesophagus. In one case part of the oesophageal mucosa was removed with the lesion, but in all the others the mucosa was left intact. In one case it was necessary to resect the lower part of the oesophagus and perform an oesophago-gastrostomy, and in another the leiomyoma was removed incidentally during a gastro-oesophageal resection for high gastric ulcer. In every instance the approach was transthoracic, being on the left in 10 cases and on the right in the remainder.

In the four cases in which the lesion had extended on to the stomach the treatment was more difficult. In one instance the gastric segment of the tumour was removed through a left rectus incision, and the defect in the stomach repaired. Resection of the lower part of the oesophagus and the cardia of the stomach was performed in the other three cases.

**COMPLICATIONS.**—In the entire series there were two deaths. In one case, this was due to broncho-

pneumonia developing in the immediate post-operative period. In the other patient in whom resection was necessary, the anastomosis separated, and the child eventually died of bilateral empyema.

One patient developed empyema, which cleared up, and two patients had a temporary pleural effusion. In another patient oesophagoscopy was followed by the development of acute mediastinitis. This resolved completely following antibiotic therapy and surgical drainage.

**PATHOLOGY.**—The tumour was located in the lower third of the oesophagus in eight instances, in the middle third in five, and in the upper third in two. In one instance it extended from the middle into the upper third, and in one from the lower into the middle third. In addition, there were four tumours extending from the lower third on to the cardia of the stomach. Combining these with reports from the literature where this information has been given, there have been 53 in the lower, 35 in the middle, and 12 in the upper third. For the surgical cases the corresponding figures are 20 in the lower, 16 in the middle, and five in the upper third. When it is recalled that the musculature of the upper third of the oesophagus is of the striated variety, the presence of smooth-muscle tumours in this region is surprising. In 14 patients the lesion was single, being multiple in three. When this series of surgical cases is added to the corresponding series from the literature, it is found that 41 patients have had single lesions and four have had multiple lesions. The greatest number in any one case in our series was three tumours.

Both Stewart (1931) and Hoyne and Rogers (1951) noted the association of a leiomyoma of the lower part of the oesophagus with a hiatal hernia. This was observed in three instances in our series. Another patient had a coincident leiomyoma of the labium majus. Four patients had peptic ulceration—duodenal in three, and gastric in one. No logical reason apart from coincidence can be found to account for this association.

The weight of the tumours varied from 0.25 to 237 g., with an average of 29.4 g. The tumours which also involved the stomach were larger still, weighing 70, 175, 317, and 625 g. respectively. Morphologically the tumours fell into three groups. The smaller tumours were rounded or oval. Some of the larger tumours were U-shaped, consisting of two limbs linked by a narrow bridge, and tending to enclose the oesophagus (Fig. 2a). Finally there were several lesions which completely encircled the oesophagus (Fig. 2b). They were all confined to the lower part, and frequently

had extended on to the cardia of the stomach. The tumours were grey, pink, or white on the surface. Generally the smaller tumours had a smooth surface whereas the larger tumours were distinctly nodular. In some instances the surface was ragged where the tumour had been dissected free from the normal musculature of the oesophagus. In one case the presence of root-like processes which extended from the tumour and blended with the gastric musculature was of interest. A capsule was never very prominent on gross examination. When the tumour was cut across the multicentric nature was sometimes apparent, the various nodules

being separated by fibrous strands. The general appearance of the cut surface was of numerous interlacing strands of tissue. In between these the substance was grey and homogeneous. Occasional dark areas were seen, representing haemorrhage or degeneration. There was ulceration through the mucosa of the gastric portion in one case, and two small ulcers were present in the oesophageal portion in another.

The microscopic picture was fairly standard. The tumour was frequently multicentric in origin. It consisted of bundles of spindle-shaped cells which interlaced with one another (Fig. 3). The nuclei were rod-shaped, centrally located in the cell, had a distinct nucleolar membrane, contained finely granular nucleoplasm, and had an occasional nucleolus, but no mitotic figures. The nuclei were uniform in size. The amount of connective tissue was variable, and was arranged either around the lobule, or around the bundles of cells, or even around the individual cell. Mallory's phosphotungstic acid stain was useful in showing up the individual myofibrils in the cytoplasm. Blood vessels were not numerous, although occasionally many large sinusoidal blood vessels would be seen in the tumour, and not infrequently there was a collection of larger blood vessels at the periphery of the tumour. Several tumours contained foci of lymphocytic infiltration, and these lymphocytes were occasionally arranged around the blood vessels. Haemorrhagic necrosis, cloudy swelling, and hyaline degeneration were occasionally seen.

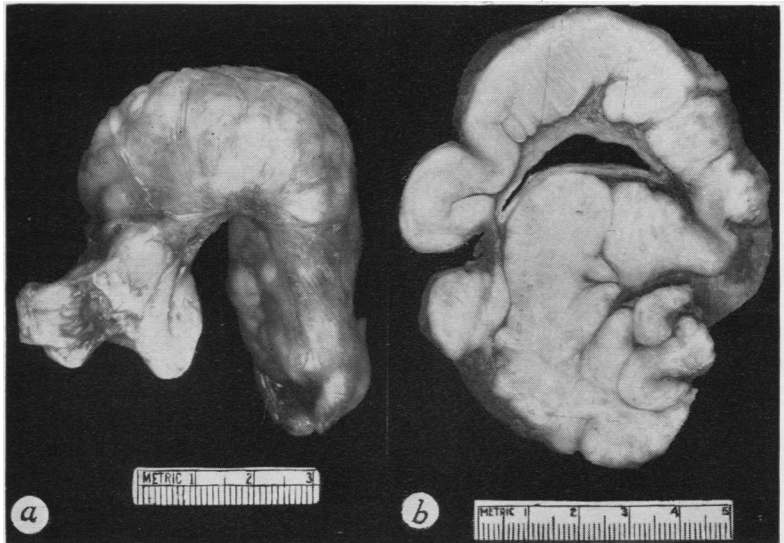


FIG. 2.—(a) U-shaped leiomyoma of the oesophagus. (b) Cross section showing the oesophagus completely encircled by a leiomyoma.

#### LEIOMYOSARCOMAS

The five cases of leiomyosarcoma in our series and the eight cases reported in the literature make a total of 13 available for study (one of the patients in our series was originally seen here, and subsequently operated on and reported by Lyons and Garlock).

**SEX.**—There were four women and one man in our series. This apparent preponderance in favour of women is offset by the figures from the literature. When the eight patients referred to in the literature are added to ours, it is found that eight have been men and five women.

**AGE.**—In our series the ages varied from 58 to 64, three patients being 60 years of age. The youngest patient in the series from the literature was 38 and the oldest 70 years. The average age of the 13 patients under consideration was 57.1 years. Leiomyosarcoma of the oesophagus occurs in an older age group than leiomyoma, and it is very unusual for the patient to be less than 50 years of age.

**SYMPTOMS.**—None of the 13 patients was asymptomatic. This is in contrast to many of the patients with leiomyoma of the oesophagus, where approximately 50% were without symptoms. All of the 13 had dysphagia in varying degree. In our series dysphagia was slight and intermittent in one, but usually it was much more severe, and several of the patients were able to swallow liquids



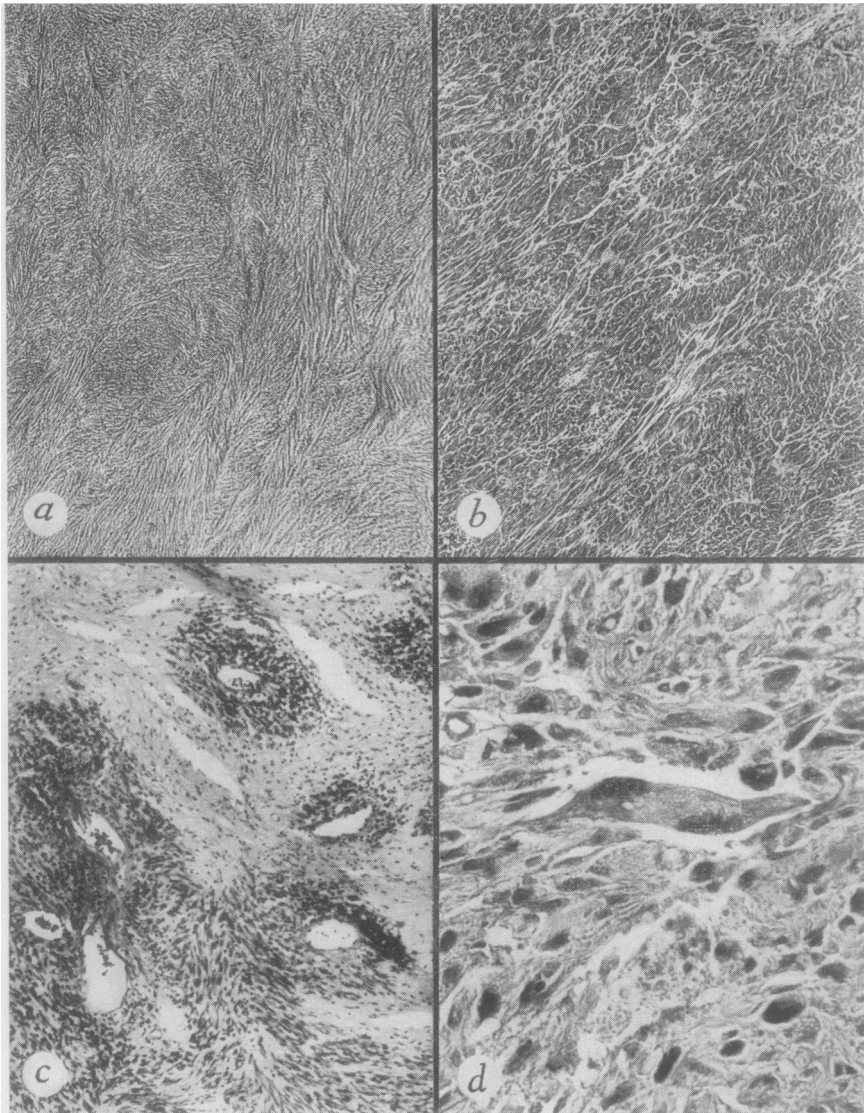


FIG. 3.—(a) Leiomyoma of the oesophagus showing the typical pattern of interlacing bundles of spindle-shaped cells (haematoxylin and eosin;  $\times 35$ ). (b) Leiomyosarcoma of the oesophagus showing the same pattern as in a, but the cells are larger and the tissue is much more cellular (haematoxylin and eosin;  $\times 35$ ). (c) Leiomyosarcoma of the oesophagus showing the perivascular arrangement of the cells (haematoxylin and eosin;  $\times 75$ ). (d) Leiomyosarcoma of the oesophagus showing large hyperchromatic nuclei and one cell with multiple nuclei (haematoxylin and eosin;  $\times 325$ ).

only, and even those with difficulty. The duration of dysphagia was short, varying from two months to two years, but the average was less than one year, which is in keeping with the reports from the literature. Frequently the dysphagia was accompanied by pain behind the sternum. Of the five patients, three were regurgitating their food, and the vomitus of one contained blood. All the patients except one had lost weight, varying from

10 to 50 lb. (4.5 to 22.7 kg.), and usually in a short space of time.

The reports from the literature suggested, and our cases confirm, that the symptoms in leiomyosarcoma are much more severe in character, and tend to be of shorter duration than those exhibited by patients with leiomyoma of the oesophagus. Although undoubtedly leiomyosarcoma of the oesophagus in its early phase is asymp-



tomatic, up to the present no case has been diagnosed at this stage.

**PHYSICAL EXAMINATION.**—As with leiomyoma of the oesophagus, physical examination was not very helpful in patients suffering from leiomyosarcoma of the oesophagus.

**OTHER EXAMINATIONS.**—The concentration of haemoglobin of these patients tended to be below normal, the average being 11.6 g. per 100 ml. In two instances the sedimentation rate (Westergren method) was elevated, being 55 and 52 mm. in the first hour.

Ordinary radiographs of the chest revealed the tumour as a shadow in one patient. It has been suggested in the literature that the classical radiological appearance of a leiomyosarcoma of the oesophagus would be a defect in the wall of the oesophagus with the characteristics of an intramural tumour, in combination with an extrinsic mass. This combination was not met in our five patients. In two the obstructive lesion was considered to be intramural, probably a leiomyoma; in the third, the lesion was defined as a pedunculated polypoid mass; in the fourth, the radiologist felt that the lesion had all the characteristics of a carcinoma of the oesophagus; and in the fifth, the lesion was described as being tumefactive with some of the features of an intramural lesion, but it was difficult to differentiate from carcinoma.

Oesophagoscopy was more helpful in arriving at the diagnosis of the exact nature of the lesion. In only one instance did the examiner feel that he was not dealing with a malignant lesion. Here the mucosa was intact and the lesion was pulsating—presumably transmitted—so that he felt that he was dealing with an abnormal vascular arrangement, and thus he did not perform a biopsy. In the other cases, the lesion was large and polypoid although in one patient it was infiltrating the wall. In two instances, the surface was ulcerated and the examiner felt that he was dealing with a carcinoma. Biopsy was performed in four of the five cases, with the following diagnoses: grade four squamous cell epithelioma imitating a fibrosarcoma, grade 4 malignant neoplasm possibly rhabdomyosarcoma, grade 3 leiomyosarcoma, and grade 1 leiomyosarcoma. These results are in agreement with what was found in the literature, namely, that, although biopsy will usually reveal the malignant nature of the lesion, yet the exact diagnosis is frequently missed.

In only one instance therefore was the diagnosis completely missed, but even here the radiological appearance was that of a leiomyoma, and although

the oesophagoscopist felt that the obstruction was due to an abnormal vascular arrangement, yet the patient's symptoms were sufficiently severe and exploration would undoubtedly have been advised. The disadvantage would have been that the tumour would probably have been entered before the diagnosis was made. Unfortunately, however, this patient suffered a perforation at the time of oesophagoscopy and subsequently died from the effects of mediastinitis. In the other four cases the surgeon had no doubt that he was dealing with a malignant growth, and in two of these he knew that this was a leiomyosarcoma.

**TREATMENT.**—In two instances, the segment of oesophagus involved was resected and an oesophago-gastric anastomosis was performed. In the one instance the tumour was well circumscribed by mucosa on the one side and by musculature on the other, while in the second case the lesion was pedunculated. These patients were both alive, the one seven years and the other six years post-operatively. Although the first patient was having symptoms suggestive of oesophageal obstruction, this may have been due to stenosis at the oesophago-gastric junction caused by fibrosis. In the third case, it was unfortunate that the patient died of mediastinitis before radical surgical treatment could be attempted, as this lesion was well circumscribed in the wall of the oesophagus and had not penetrated the outer coat, so that resection might well have been successful. In the fourth case thoracotomy was performed, but because of the infiltration of the surrounding structures the lesion was deemed inoperable. In the fifth case, in which the lesion was in the uppermost portion of the oesophagus, the procedure would have had to be very extensive, and the patient was not prepared to accept the risk.

Leiomyosarcoma of the oesophagus does not offer a hopeless outlook, and there are now three cases on record in which a radical approach has been successful (two cases in our series, and the case reported by Ovens and Russell (1951), in which the patient was alive and well 25 months post-operatively).

**PATHOLOGICAL CHARACTERISTICS.**—The lesion involved the upper third of the oesophagus in one instance, and the lower third in four instances. If this series is combined with those in the literature, it is found that the lesion has been in the lower third of the oesophagus in eight cases, in the middle in three, and in the upper third in two. This lesion is therefore located in the various segments of the oesophagus in much the same way as leiomyoma. Various reports in the literature emphasize that

the lesions grossly are of two types: polypoid and infiltrating. The lesion was described as being polypoid in four instances in our series, but in two it had, in addition, infiltrated the wall of the oesophagus. In the fifth, the lesion was entirely within the wall, having no polypoid features. In one instance, the tumour was attached to the oesophageal wall by a narrow pedicle which was infiltrated with tumour tissue. In the two instances in which the whole lesion was available for study, the appearance was remarkably similar. The tumour was rounded and was contained within a capsule,

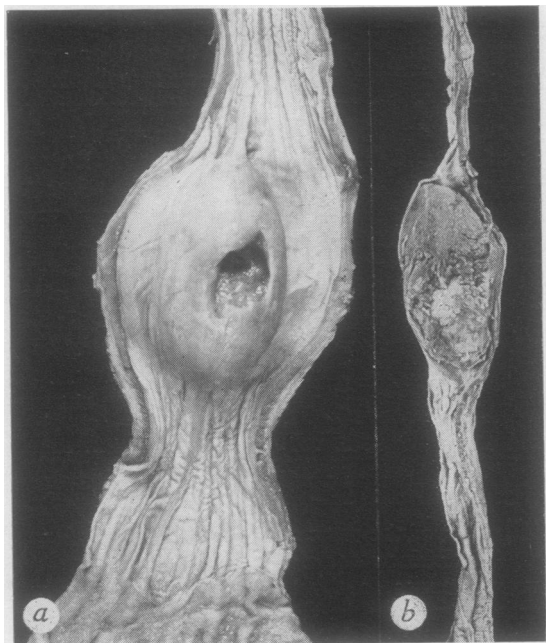


FIG. 4.—Leiomyosarcoma of the oesophagus. (a) Appearance of the tumour as viewed from the mucosal side. There is ulceration at one point. (b) A sagittal section of the tumour discloses that it is contained between the mucosa and the muscularis of the oesophagus.

formed on the one side by mucosa, and on the other by attenuated but otherwise normal oesophageal musculature (Fig. 4b). Ulceration of the mucosa was mentioned in the oesophagoscopy report in two instances, and was noted in the necropsy specimen in a third (Fig. 4a). Grossly the tumour was homogeneous, yellowish brown, and soft, so that it could be shelled out from its capsule.

Although the suggestion is made in the literature that only the polypoid type is amenable to surgical treatment, this has not entirely agreed with our experience. In two instances in which resection would have been possible, the lesion was largely

intramural, infiltrating within but not through the wall of the oesophagus.

Microscopically the diagnosis of a malignant smooth-muscle tumour was based on the association of several factors. Low-power view consistently revealed a highly cellular pattern with relatively a much greater proportion of nuclear material to cytoplasm than in benign leiomyomas. As with leiomyomas, the pattern of interlacing bundles of cells was always evident in some area of the section (Fig. 3b). Unlike leiomyomas the cells showed a varying degree of differentiation, some being to all intents and purposes normal smooth-muscle cells, whereas others consisted almost entirely of nuclear material with little or no cytoplasm. Although the cell was usually spindle-shaped, there was considerable variation in shape. The nuclei also varied greatly in size and shape, some being small, rod-shaped, and contained in the centre of the cell as in normal smooth-muscle cells, whereas others were very large and very densely staining. Nucleoli were occasionally present in benign cells, but in leiomyosarcomas these were always present, were very large, and usually there was more than one per cell. Mitotic figures were present and numerous in all except one case. In this instance, the diagnosis was substantiated by the fact that the tumour had infiltrated the mucosa, and also in between the bundles of normal muscle, together with the fact that there was a definite perivascular arrangement of the cells (Fig. 3c). Giant cells with multiple nuclei were also seen in every case except this one (Fig. 3d). The van Gieson stain showed an almost complete absence of connective tissue within the tumour, although frequently connective tissue was disposed as a capsule around the tumour. Infiltration of the tumour through the walls of the oesophagus was never seen in leiomyomas. Mallory's phosphotungstic acid stain was found useful, as in the more differentiated cells a definite longitudinal fibrillar pattern was distinguishable in the cytoplasm. In one instance, tumour cells were found within a blood vessel. No lymph node was found involved by the tumour, and this is consistent with the reports in the literature.

#### REPORT OF ILLUSTRATIVE CASES

CASE 1.—A 52-year-old man was seen at the Mayo Clinic on September 10, 1945. For the past 10 years, once or twice a year for one to two days at a time, he had had distress behind the middle of the sternum, and food would occasionally stick there. For five years he had had occasional bouts of epigastric distress not related chronologically to the above. He

had lost no weight, and the results of physical examination were negative.

Laboratory tests revealed a haemoglobin level of 14.4 g. per 100 ml. X-ray examination of the chest gave negative results, but radiographs of the oesophagus showed a large intramural tumour in the posterior wall of the lower third of the oesophagus with a smaller defect of a similar character just above this. Oesophagoscopy disclosed two tumours. The upper was at the junction of the upper and middle thirds, arising from the left wall. Below this, arising from the left anterior wall of the middle third, was a large tumour projecting into the lumen. The mucosa was intact. The appearance suggested a fibrolipoma.

The surgeon felt that the tumours were leiomyomas, and on September 17, 1945, a left thoracotomy was performed through the bed of the fifth rib. Two masses presented from the oesophagus just below the aortic arch, being hard and cartilaginous in character. They were enucleated, without damaging the mucosa. The chest was closed, and closed intercostal drainage was used.

Convalescence was uninterrupted, and the patient was dismissed on the eighth post-operative day. A letter from the patient on November 23, 1946, indicated that he was well.

*Pathological Aspects.*—The lower tumour measured 8 by 3 by 3 cm. and weighed 40 g. It was oval, elongated, nodular, hard, and pinkish brown. It was prolonged as a nodule at the lower end. The cut surface showed the usual white interlacing bands. The upper tumour measured 2 by 1 by 0.5 cm., weighed 2 g., and was round, smooth, pink, and hard.

Microscopically the picture of interlacing bundles of spindle-shaped cells with centrally placed nuclei was present in both. In the larger tumour there were several small areas where the spindle cells were broken up, the nuclei being pyknotic, and the individual myofibrils could be seen separating from one another. In the smaller tumour there were several circumscribing strands of smooth muscle around the periphery. It had practically no connective tissue, but in the larger tumour there was a fair amount of infiltration around the cells. Fibrils could be detected by use of the Mallory phosphotungstic acid stain. Blood vessels were very sparse. The diagnosis was leiomyomas of the oesophagus.

CASE 2.—A 53-year-old man came to the clinic on June 8, 1948, stating that, in 1939, a shadow measuring 4 cm. in diameter had been discovered in a radiograph of the chest. This did not change in size until 1948, when it was noted to measure 10 to 12 cm. in diameter. The complaints were minimal, although he did experience a slight sense of pressure behind the sternum for a few minutes after hurrying a meal. He had occasional sharp, electric-like pains in the lower thoracic region. For two or three years he had had mild bloating. He had lost no weight.

The results of physical examination were negative. Laboratory tests showed a haemoglobin level of

14.1 g. and an erythrocyte count of 4,580,000. Radiological examination of the chest disclosed a rounded mass in the right posterior mediastinum. When barium was swallowed, this mass seemed to indent the lower part of the oesophagus, distorting it and retracting it to the right. There was a small associated hiatal hernia. It was felt that this was an intramural tumour or a tumour attached to the oesophageal wall. Oesophagoscopy revealed anterior angulation of the oesophagus 16 in. from the incisor teeth. One inch farther on the oesophagus was obstructed by an extraoesophageal mass which appeared to arise posteriorly. There was no ulceration.

The surgeon's diagnosis was leiomyoma or a tumour displacing the oesophagus. On June 28, 1948, a right thoracotomy performed through the bed of the seventh rib revealed a lobulated tumour infiltrating through two-thirds of the circumference of the lower 5 in. of the oesophagus. The tumour was removed along with 3 cm. of the mucosa. The oesophagus was closed with interrupted sutures.

Convalescence was uneventful, and the patient was dismissed on the twentieth post-operative day. Nine months later he had only mild post-prandial epigastric pain, and the x-ray appearance of the oesophagus was normal.

*Pathological Aspects.*—The tumour weighed 237 g., and consisted of two main masses, the one measuring 10 by 8 by 4 cm., and the other 8 by 7 by 3 cm.; they were connected by a thin bridge of tissue. The larger mass had a lobule measuring 4 by 2.5 by 2 cm. attached to its lower border. The two masses had encircled about two-thirds of the oesophageal wall. The tumour was hard, brownish white, and very irregularly lobulated. The cut surface was composed of white strands with very little intervening material.

Microscopically the pattern was multilobular, and the spindle-shaped cells were arranged in interlacing strands. The nuclei were rod-shaped, with fine granular nucleoplasm. There were several areas of hyaline degeneration, and there was marked oedema between the cells. The blood vessels were fairly numerous, had thick walls, and were small. Van Gieson's stain showed little connective tissue apart from some around the blood vessels. Each lobule had a capsule with numerous blood vessels contained therein. The Mallory phosphotungstic acid stain showed longitudinal fibrils in the cytoplasm. The diagnosis was leiomyoma of the oesophagus.

CASE 3.—An 18-year-old girl came to the clinic on May 7, 1947, with the predominant complaint of dysphagia. Three years previously she had started having bouts of epigastric burning, accompanied by choking and an inability to swallow or breathe. By 1947 this had progressed so that every time she ate solid food rapidly she would get a choking spell. She seemed to fill up very easily, the food apparently stopping in the middle of her chest. She had no actual pain apart from mild substernal discomfort on eating. She had

a non-productive cough in the mornings and after meals. She had lost no weight. Her past history was of interest in that she had had nephritis at the of 9 years. Four years before coming to the clinic she was involved in an accident in which she sustained a head injury and a fracture of the pelvis and right tibia. Two months after this accident she had had haematemesis, for which she required transfusion of 11 pints of blood.

Physical examination revealed rales and diminished breath sounds over the lower half of the right side of the chest in the anterior portion. There was a soft irreducible, non-compressible tumour, measuring 1.5 by 5 cm., beneath the left labium majus, and a firm mass, measuring 2 by 6 cm., in the left anterior part of the vagina; the latter mass extended up beneath the bladder, and it was not connected with the labial mass.

Laboratory examination revealed a haemoglobin level of 11.7 g. and an erythrocyte count of 4,760,000. Analysis of urine disclosed albuminuria, grade 3, erythuria grade 1 to 2, and leucocyturia grade 1 to 2 (on a grading basis of 1 to 4). The blood urea measured 38 mg. per 100 ml. Excretory urography and cystoscopic examination gave negative results, and a diagnosis of chronic nephritis with good renal function was made. Radiographs of the chest showed a mass in the right lower pulmonary field near the midline; this mass extended laterally just above the diaphragm and contained a portion of the alimentary tract. On swallowing barium the patient was seen to have an oesophageal hernia with pronounced displacement of the oesophagus to the right. The hernia contained about one-quarter of the stomach, together with a large sac which extended to the right and contained the lower half of the oesophagus. The colon was in its normal position. Oesophagoscopy disclosed marked angulation of the oesophagus, which extended almost to the right chest wall; the angulation occurred at the junction of the upper and middle thirds, and then the oesophagus passed downward. The instrument could not be passed farther. Beneath the medial wall of the displaced portion there seemed to be a hard, firm mass. The impression was that a solid viscus had perforated through the ruptured diaphragm and was displacing the oesophagus. The surgeon concurred in the diagnosis of traumatic diaphragmatic hernia, but admitted considerable doubt in coming to an opinion.

A right thoracotomy was performed through the bed of the eighth rib on May 19, 1947. This revealed a large mass, apparently coming from the abdomen through the hiatus and displacing and partially obstructing the oesophagus. It was felt that it could be approached more successfully through the abdomen, and so, on June 20, 1947, a laparotomy through a left rectus incision was performed. This revealed a gall-bladder filled with stones, and the tumour was found to involve the cardia of the stomach. It was not possible to mobilize the thoracic portion into the abdomen, and the chest was again opened through the bed of the ninth right rib. The

tumour could now be seen involving the lower half of the oesophagus and the upper third of the stomach. The entire circumference of the oesophagus and stomach was involved. The lower half of the oesophagus and the upper third of the stomach were resected and a direct oesophago-gastric anastomosis was performed. The oesophagus was greatly thickened above the tumour. Both the abdominal and chest wounds were closed, and the chest was drained.

Convalescence was interrupted by the development of fluid in the right side of the chest with some collapse of the right lower lobe. This cleared up and the patient was dismissed on the thirty-sixth post-operative day.

A year later the patient felt well, the only complaint being that she filled up easily on eating. She had gained 17 lb. (7.7 kg.). Oesophagoscopy at this time revealed a fair degree of oesophagitis involving the lower end of the oesophagus. There was a stricture at the oesophago-gastric junction with free regurgitation of gastric juice. Dilatation was advised, but the patient refused. Radiographs showed that all the remaining part of the stomach was above the diaphragm, the pylorus being just below the hiatus. At this time the labial tumour was removed. It measured 8 by 5 by 3 cm. and was identified as a leiomyoma.

*Pathological Aspects.*—The oesophageal tumour weighed 625 g. and was firm and brownish white. It completely encircled the lower end of the oesophagus and extended for 6 cm. along the lesser curvature of the stomach, and over the anterior and posterior walls almost to the greater curvature. The lumen of the oesophagus was considerably narrowed. The surface of the tumour was smooth and moderately nodular. No evidence of degeneration could be found on the cut surface, which was composed of thick white strands with little homogeneous material in between. There was a small mucosal ulcer over the gastric aspect of the tumour.

Microscopically the tumour consisted of many lobules separated from one another by a small amount of connective tissue. The tumour extended over the cardio-oesophageal junction. There were numerous collections of lymphocytes in the subepithelial connective tissue. There were several fairly large blood vessels between the tumour and the submucosa. The cells were spindle-shaped and arranged in interlacing bundles. The cell outline in many instances was indistinct. The nuclei were rod-shaped and centrally located, and many showed pyknosis. There was little connective tissue present. Longitudinal fibrils were seen when Mallory's phosphotungstic acid stain was used. The diagnosis was leiomyoma of the lower part of the oesophagus and the upper part of the stomach, with associated hiatal hernia.

CASE 4.—A 64-year-old man came to the clinic on November 4, 1942, with a complaint that for two years solid food had been sticking in his throat. The trouble was intermittent, but occasionally he had diffi-

culty with liquids. He had lost 20 lb. (9.1 kg.) in the last three months. His doctor at home had found an ovoid mass in the oesophagus. In addition the patient had had mild hoarseness in the last 10 years, with definite huskiness in the last two years.

Physical examination gave negative results apart from a hydrocele of the left testis and mild prostatic hypertrophy.

Laboratory examination revealed a haemoglobin level of 12.5 g. and grade 1 pyuria. Radiological examination of the chest gave negative results, but when barium was swallowed a mass measuring 5.5 by 3 cm. was seen in the right postero-lateral wall at the junction of the middle and lower thirds of the oesophagus (Fig. 1*b* and *c*). Oesophagoscopy disclosed much narrowing of the lumen of the oesophagus at a point 10½ in. from the incisor teeth, and the instrument could not be introduced beyond this point. There was mild oesophagitis, and at the obstruction the wall of the oesophagus pulsated synchronously with the heart beat, raising the question of an abnormal vascular arrangement causing compression. The picture was not that of malignancy. No biopsy specimen was taken, and the whole procedure was done with ease.

Four hours later, however, the patient experienced retrosternal pain that extended to the back and into the neck. Subcutaneous cervical emphysema also developed, and he was admitted to the hospital, where radiographs disclosed widening of the superior mediastinum and congestion of the right base. His temperature was 103° F., and the leucocyte count was 17,900. He apparently had acute mediastinitis. Oral feeding was stopped, and he was given sulphadiazine intravenously, with the aim of maintaining a blood level of 10 to 14 mg. per 100 ml. He gradually improved, and two days later his temperature was 101° F., but radiological examination showed more widening of the mediastinum, with gas at the level of the aortic arch on the right, pneumonia of the right lung, and some fluid at the right base. Conservative treatment with sulphadiazine was continued for three more days, but then stridor developed and there was more widening of the mediastinum. It was decided to drain the mediastinum, and eight days after the original oesophagoscopy drainage was performed through an incision alongside the right sternocleidomastoid muscle. Several ounces of foul-smelling pus and gas were evacuated. Drains were inserted, and breathing improved immediately. Culture revealed *Streptococcus viridans*.

In spite of this treatment his condition gradually deteriorated. Bilateral empyema developed, and drainage was of no avail. Before death he had evidence of septicaemia.

Necropsy confirmed the presence of bilateral pneumonia and empyema. Examination of the oesophagus revealed that at 4 cm. from the cardio-oesophageal junction on the posterior wall of the oesophagus there was a smooth tumour that measured 4.5 by 2.5 by 3 cm. and was not pedunculated. An ulcer 1 cm. in diameter overlay the centre of the tumour (Fig. 4*a*).

On cut section the tumour was yellowish brown, homogeneous and soft, and appeared to arise in the submucosa. It was completely encapsulated by the mucosa and the submucosa on one side, and by the muscle coat of the oesophagus on the other (Fig. 4*b*). There was no gross penetration of the latter. There was no evidence of degeneration. In addition, there was a diverticulum of the upper part of the oesophagus with a 2 mm. opening. No perforation of the oesophagus was apparent.

Microscopically, staining with haematoxylin and eosin revealed a highly cellular tumour composed of bundles of spindle cells, the bundles interlacing. There was an area of necrosis in the centre of the section. Some areas showed pyknosis of the nuclei. In the active tumour, high-power magnification disclosed a preponderance of nucleoplasm to cytoplasm. The cells were larger than in a benign leiomyoma. The nuclei were very irregular in size and shape, but mitotic figures and giant cells could not be seen. Nucleoli were large and frequently multiple. However, there was a pronounced degree of infiltration of the tumour around the blood vessels, giving a cuffing effect (Fig. 3*c*). The van Gieson stain showed that the tumour was well encapsulated by connective tissue, but there was no connective tissue in the tumour itself. In one area the squamous epithelium was ulcerated, and the tumour had penetrated through the capsule at this point. On the outer surface, the tumour was covered by the normal muscle layers of the oesophagus, but it had penetrated into the surrounding fat in one place. The tumour did not appear to arise directly from either the longitudinal or circular muscle coats. Staining with Mallory's phosphotungstic acid disclosed the same fibrillary character of the cytoplasm as seen in smooth-muscle cells. Four lymph nodes were examined and found to contain no tumour tissue.

A diagnosis of leiomyosarcoma of the oesophagus was made, and death was due to septicaemia secondary to bilateral empyema which presumably followed perforation of the oesophagus at oesophagoscopy.

CASE 5.—A 60-year-old woman came to the clinic on May 25, 1945, complaining of substernal pain with dysphagia and regurgitation of food shortly after eating. This had been going on for one year. She had recently noticed a little hoarseness, but had lost no weight.

Physical examination revealed a blood pressure of 170 mm. of mercury systolic, and 110 mm. diastolic. There was a diffuse swelling on the right side of the neck, and a moderate degree of cervicitis.

Laboratory examination disclosed a haemoglobin level of 12.7 g., an erythrocyte count of 4,450,000, a leucocyte count of 8,500, grade 2 erythruia, grade 1 leukocyturia, and negative findings on excretory urography. Radiological examination revealed a tumour that involved the lower part of the oesophagus and displaced it to the left and anteriorly, rather like an intramural leiomyoma. On oesophagoscopy, at 11½ in. from the incisor teeth, a large lesion was

found arising from the right wall and occluding the oesophagus. Beyond this, at 14 in., there was a large ulcerating polypoid lesion that looked like a carcinoma. It was friable and necrotic. On biopsy it was interpreted as a high-grade squamous epithelioma, simulating a fibrosarcoma.

With this diagnosis in mind, a left thoracotomy was performed through the bed of the eighth rib. A large spherical tumour involving the lower two-thirds of the oesophagus and having the appearance of a leiomyoma was found. The diaphragm was opened, and the oesophagus and the upper part of the stomach were mobilized. The oesophagus was resected at the cardia. The latter was inverted, and, after removal of the lower third of the oesophagus, anastomosis was carried out between the anterior surface of the stomach and the distal end of the oesophagus. The stomach was stitched to the diaphragm, and after the phrenic nerve had been divided the chest was closed, the closed type of intercostal drainage being employed.

Convalescence was fairly smooth, apart from the development of a left pleural effusion, some atelectasis of the left lung, and a temperature of 101° F. The chest was repeatedly aspirated, and the patient was dismissed on the forty-fifth post-operative day. Radiological examination at this time showed the chest to be clear, and when barium was swallowed the anastomosis was seen to be free. Since then radiographs taken elsewhere have been seen. In 1950 these showed an adequate passage, with no evidence of recurrence. The patient wrote in 1952 complaining of retrosternal pain, vomiting, and loss of 15 lb. (6.8 kg.). Fluoroscopy elsewhere revealed stricture of the oesophago-gastric junction. This may have been due to recurrence, but could certainly have been due to stricture following fibrosis.

*Pathological Aspects.*—The tumour weighed 64 g., and was circular, measuring 5 by 5 by 3.5 cm. On the mucosal surface there was an ulcer measuring 3 by 3 by 0.5 cm. On cut section the tumour was seen to be encapsulated on one side by mucosa, and on the other by attenuated muscle of the oesophageal wall. Grossly there was no penetration posteriorly through the muscle. The tumour was soft, homogeneous, and light brown, although there were several darker areas probably denoting degeneration, and there was one yellow spot 0.5 cm. in diameter, near the mucosal surface. The whorled appearance of leiomyosarcoma was absent on cross section.

Microscopically, the tumour was highly cellular with a pattern of bundles of spindle-shaped cells which interlaced (Fig. 3*b*). The tumour was located between the squamous epithelium and the inner muscle coat. In areas it had penetrated through the submucosa to the squamous epithelium. There was some infiltration between the layers of the inner muscle coat. These layers passed into the tumour and then lost their identity. The predominant cell was spindle-shaped with proportionately much less nucleoplasm than in leiomyomas. Some of the more active cells were angulated, resembling squamous epithelium to

a slight degree. The nuclei were very large and irregular in size and shape. The nuclear membrane was usually distinct, and the nucleoplasm was coarsely granular. Nucleoli were of giant proportions, and usually there was more than one per cell. Some of the larger cells had multiple nuclei. Mitotic figures varied in frequency, but some areas had as many as 10 per high-power field. One vein in the periphery of the tumour had a few tumour cells in its lumen. There was an area of hyaline necrosis. The van Gieson stain revealed almost complete absence of connective tissue in the tumour. Mallory's phosphotungstic acid stain showed fibrils in the spindle-shaped cells very distinctly. The diagnosis was leiomyosarcoma of the oesophagus.

#### SUMMARY AND CONCLUSIONS

A thorough review of the world's literature on the subject of smooth-muscle tumours of the oesophagus has been carried out, and all the surgical cases seen at the Mayo Clinic before July, 1952, have been studied. Twenty-one cases of leiomyoma (including four in which the stomach also was involved), and five cases of leiomyosarcoma have been carefully analysed from the standpoint of clinical features, laboratory diagnosis, treatment, and prognosis. Throughout the study, emphasis has been placed on the features of contrast between the benign and malignant smooth-muscle tumours of the oesophagus. On the basis of this study, the following statements are made.

(1) Smooth-muscle tumours of the oesophagus of rare occurrence as is witnessed by the fact that there are available for study only 133 cases of leiomyoma and 13 cases of leiomyosarcoma.

(2) Smooth-muscle tumours of the oesophagus are seen more often in males than in females, in the ratio of 2.8:1 for leiomyomas, and 1.6:1 for leiomyosarcomas. The great majority of patients with leiomyomas are rather evenly distributed among the third, fourth, and fifth decades of life. In contrast the patient with leiomyosarcoma is older, and the average age of patients in this series and those from the literature was 57.1 years. Only one patient with leiomyosarcoma was less than 40 years old.

(3) The symptoms produced by leiomyoma of the oesophagus are usually slight. Indeed, almost half of the present series of patients were asymptomatic. When the lesion is more widespread and has extended on to the stomach, dysphagia is much more prominent. In contrast, none of the patients with leiomyosarcoma was asymptomatic. Dysphagia was usually severe in this group, and frequently accompanied by pain and loss of weight. Leiomyomas occurring in the intestines and

stomach frequently ulcerate and bleed. Those in the oesophagus apparently do not.

(4) Physical examination of the patient gives little information, but a combination of radiological examination of the oesophagus and oesophagoscopy achieves a high degree of accuracy in the diagnosis of leiomyoma. In only one instance in the 17 studied in the present series did the clinician feel that the lesion might be malignant. Although this high degree of accuracy was not attained with leiomyosarcoma in the series studied, yet in only one instance did the clinician feel that the lesion was not malignant. An important point in differentiation is the appearance of the mucosa as seen through the oesophagoscope. In leiomyomas the mucosa is rarely, if ever, not intact, whereas in leiomyosarcomas it is usually ulcerated.

(5) Leiomyomas of the oesophagus may be round, oval, or U-shaped, or they may completely encircle the oesophagus, particularly when the lesion is in the lower part of this structure. Leiomyosarcomas may be pedunculated, or may be contained within the layers of the oesophageal wall, and may extend to involve the surrounding structures. Leiomyomas differ grossly from leiomyosarcomas in being white or pink whereas leiomyosarcomas are yellowish. Leiomyomas are firm, whereas leiomyosarcomas are soft and crumble. The whorled appearance on the cut surface of a leiomyoma is not usually seen with leiomyosarcomas.

(6) Under the microscope both tumours have the pattern of interlacing bundles of spindle-shaped cells. The malignant tumours differ in being more cellular, with a higher proportion of nucleoplasm, the cells vary in their degree of differentiation, the nuclei may be large, with prominent nucleoli, and they may have mitotic figures. Leiomyosarcomas frequently have giant cells with multiple nuclei. In leiomyosarcomas, in contrast to leiomyomas, the tumour cells infiltrate through the mucosa and the normal musculature, and may have a perivascular arrangement. Tumour cells may be seen within blood vessels. Leiomyosarcomas have very little connective tissue within their substance, while this is usually abundant in benign tumours.

(7) In this series of patients studied, it was not possible to demonstrate malignant transformation of a previously benign smooth-muscle tumour of the oesophagus.

(8) The majority of leiomyomas can be treated simply by enucleation without damaging the mucosa. In the cases in which this was done in the present series, there were no post-operative

deaths. When the lesion is more extensive, and particularly when it has extended on to the stomach, it is usually necessary to perform resection with anastomosis. In view of the high degree of the accuracy of the diagnosis of leiomyoma of the oesophagus, and because the tumour is relatively slow-growing, it seems reasonable to conclude that when a patient is having no symptoms there is no great urgency for surgical treatment. Leiomyosarcoma of the oesophagus is not a hopeless disease, and if the tumour is pedunculated or encapsulated, and has not spread extensively into the surrounding tissues, it is amenable to resection. The number of cases reported so far is very small, but in three instances in which radical operation has been performed the result has apparently been satisfactory.

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