Section of Proctology

President—ALAN H. HUNT, M.Ch.

Meeting
February 10, 1960

DISCUSSION ON SQUAMOUS CELL CARCINOMA OF THE ANUS AND ANAL CANAL

Mr. W. B. Gabriel (London):

When I previously addressed the Section on this subject (Gabriel, 1941), my analysis was based on 55 cases admitted to St. Mark's Hospital during the nineteen-year period 1922 to 1940 (Table I). I have now, with my colleagues' permission, studied the 96 cases of squamous carcinoma admitted to St. Mark's during the next fifteen-year period, 1941–55. In addition I have brought in 21 other cases under my care elsewhere during this period, making a total of 117 cases, as follows:

Carcinoma of the anus: 30 cases (25 males, 5 females).

Carcinoma of the anal canal: 87 cases (46 males, 41 females).

On comparing the two sets of figures shown in Table I it seems fair to make the following

TABLE I.—SQUAMOUS CELL CARCINOMA OF THE ANUS AND ANAL CANAL

	1922–1940			1941–1955		
	Males	Females	Total	Males	Females	Total
Squamous carcinoma of anus	24	5	29	25	5	30
Squamous carcinoma of anal canal ..	3	23	26	46	41	87
Total	27	28	55	71	46	117

comments: (1) The incidence and sex distribution of squamous carcinoma of the anus has remained constant in the periods studied, the disease being five times more common in men than in women. (2) There has been a threefold increase in the incidence of squamous cell carcinoma of the anal canal. (3) In the earlier period, females with squamous carcinoma of the anal canal greatly outnumbered the males, whereas in the 1941–55 period males outnumbered the females (46 to 41).

Later I will indicate the improved results of treatment by local excision for carcinoma of the anus instead of interstitial radium needling and radical combined excision for squamous carcinoma of the anal canal instead of perineal excision.

Although they arise in adjacent parts squamous cell or epidermoid carcinoma of the anus and squamous cell carcinoma of the anal canal are extremely different and, except that they are both malignant in varying degrees, they have little in common whether considered from the clinical, surgical or histological aspects.

Predisposing Conditions

It is difficult to explain the 5 to 1 preponderance of males over females in squamous carcinoma of the anus; although the following conditions may be considered they do not seem to provide an adequate answer to this question.

Pruritus ani.—Severe degrees of chronic anal pruritus are more common in men than in women and habitual rubbing and scratching might, one would think, initiate a localized carcinoma of the anus. But of the dozens of cases of pruritus ani seen in out-patient clinics few develop squamous carcinoma of the anus. Fig. 1 illustrates what

FIG. 1.—Squamous cell carcinoma of the anus with secondary pruritus ani.

appears to be a chronic pruritus ani with a localized carcinoma of the anus in the left anterior quadrant in a man aged 63. Yet the history is a complaint of bleeding and pain of one month's duration, with no mention of anal pruritus, so it would seem likely that the skin changes in this case were secondary to the discharge from the anal carcinoma and not the cause of it.

Leukoplakia of the anus (Fig. 2) occurs exclusively in men over the age of 60 and, however unpleasant some of the indolent traumatic ulcers may appear, with raised somewhat indurated margins, my experience is that these patients do not develop carcinoma of the anus. I have records of 10 of these cases who have been under observation for periods up to twelve years and in no case was there any malignant development.

FIG. 2.—Male aged 69 with chronic leukoplakia of the anus. There was an indolent chronic ulcer on the left side and the condition remained essentially unchanged during the ensuing nine years with no malignant change.

Simple papilloma.—The common anal wart or condyloma acuminatum shows no tendency to become malignant and it is only rarely that a massive papilloma in the anal region may in part undergo malignant change. For example (Fig. 3), a man aged 67 had anal warts for eight years

and finally developed a keratinizing squamous cell carcinoma in the right posterior quadrant. This was excised locally in January 1956 and there was no recurrence up to December 1959.

Long-standing fistula.—It is a commonplace that a long-standing fistula may undergo malignant change and in the St. Mark's series 1941–55 there were 2 such cases (1 male, 1 female) where fistulæ had been present for fourteen and fifteen years respectively.

Squamous cell replacement (Figs. 4 and 5).—The acquired squamous cell overgrowth or replacement over the original columnar epithelium of prolapsing hæmorrhoids might provide the starting point for a squamous cell carcinoma and some of the sections I have examined show evidence of superficial ulceration at the junction of the two types of epithelium with some inflammatory changes beneath. In the St. Mark's series just mentioned there were 2 cases where small squamous carcinomas developed over the lower pole of the right anterior hæmorrhoid. Both were excised locally: one was ¾ in. in diameter and proved to be of low malignancy; no recurrence followed and the patient survived for seven years. The other was 1 in. in diameter and
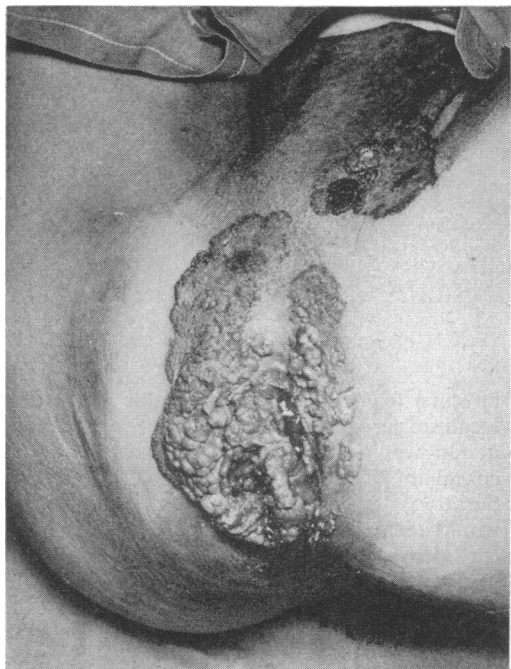

FIG. 3.—Extensive papilloma of the anus of eight years' duration with a localized squamous carcinoma in the right posterior anal quadrant. This was excised locally with cutting diathermy and the patient has been free from recurrence for four years. The right posterior hæmorrhoid which is seen presenting was ligated and excised in the course of operation.
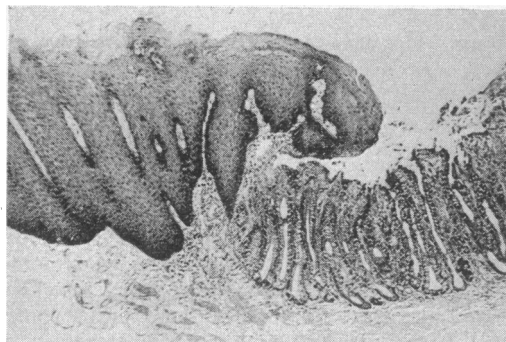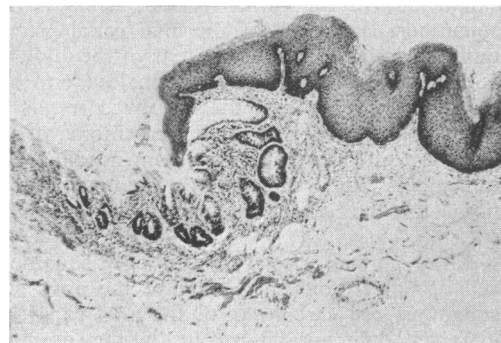

FIG. 4.

FIG. 5.

FIGS. 4 and 5.—Squamous cell replacement over the columnar epithelium of prolapsing hæmorrhoids. (Low power.)

was of a high grade of malignancy; on this account a synchronous combined excision of the rectum was carried out a month later. After an interval of two years metastases developed in both groins and a block dissection left and right was required (1 positive gland on each side). The patient died of recurrence fourteen months later.

Diagnosis

A typical localized squamous carcinoma of the anus, with its sharply defined raised indurated and everted edge, is generally sufficiently obvious to warrant local excision without a previous biopsy (Fig. 6).

When the lesion is more diffuse, as in Fig. 7, it may at first be difficult to say if we are dealing with a carcinoma of the anus or of the anal canal, or indeed it might be a carcinoma of the rectum extending downwards. A finger should be passed into the anal canal and if it feels rough and ulcerated then clearly the case is not one of carcinoma of the anus and a biopsy will show if the growth is squamous or columnar cell. This particular case, a woman of 56, had a differentiated squamous cell carcinoma of the anal canal and was treated by a perineo-abdominal excision together with a wide removal of the buttocks and posterior vaginal wall, B case. She has remained well for more than nine years and no spread has taken place to the groins.

When we meet an ulcerating neoplasm in the anal canal a biopsy is required for a precise diagnosis and examination under anæsthesia is often a useful if not an essential preliminary procedure, not only to get satisfactory fragments for biopsy but to assess operability. This applies particularly in the male when the ulcerated growth is situated anteriorly and one likes to form an estimate whether the growth is likely to come off the urethra and prostate kindly or not.

If the growth, as commonly happens, is of the anaplastic variety it may be a problem for the pathologist to say if it should be considered to be a squamous cell or columnar cell lesion. But from a practical point of view it makes little difference and the treatment will be the same, namely by a radical combined excision. In 7 cases in this series a growth in the anal canal has proved to be squamous cell in its lower part and adenocarcinoma in the upper part; this is a reasonable and not unexpected finding and metastases of both varieties of growth can occur in the hæmorrhoidal lymph nodes.

I should here offer a warning about primary chancres of the anus because there appears to be an increased incidence of this condition. Between November 1958 and February 1959 I saw 3 cases and the last one in a man aged 44 was the most deceptive. He presented an ulcerated anal lesion posteriorly (Fig. 8) and in addition there was a small hard gland in the left groin which was not tender. I thought that this fact together with the patient's age contraindicated a venereal lesion. Fortunately, however, I decided to have the tests done before submitting him to surgery and within twenty-four hours the dark ground search for spirochætes proved to be positive, and both W.R. and Kahn tests were strongly positive.

If a lesion in the anal canal appears to be dusky in colour and there is a possibility of it being a malignant melanoma, biopsy should be deferred until the patient has been hospitalized. Then no doubt a frozen section in the theatre can be organized and if positive a radical operation can

Fig. 6.—Differentiated squamous cell carcinoma of left lateral anal margin. This was excised with cutting diathermy (June 1951) without previous biopsy. Patient alive and well for the ensuing eight and a half years without indication at any time for a block dissection of the groin.
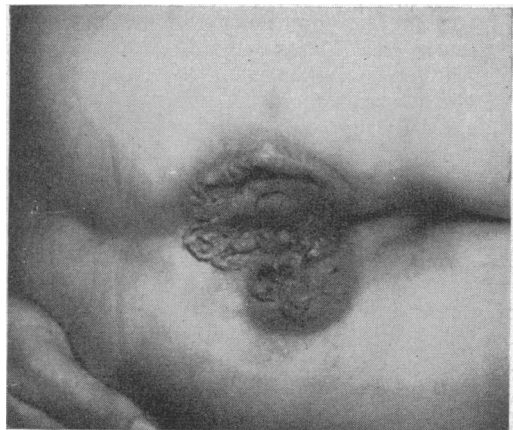

Fig. 7.—Female aged 56 with extensive squamous cell carcinoma of the anal canal extending down to the anus and perianal region. Perineo-abdominal excision (March 1950) and patient has survived for nine and a half years. There has been no indication during this period for a block dissection of either groin.
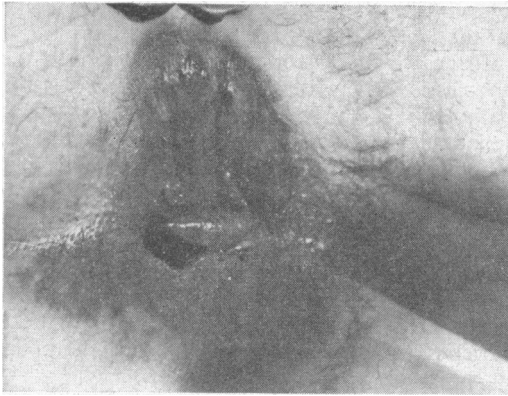
FIG. 8.—Primary chancre of the anus in a male aged 44. There was a hard gland in the left groin and the resemblance to a squamous carcinoma was very close.

FIG. 9.—Tuberculous ulcer of the anus in a male aged 33.

be proceeded with at once. This opinion is based on an unfortunate case I had ten years ago when a delay occurred after a biopsy on a melanoma and it seemed likely that rapid metastasis might have been initiated by the biopsy.

There is not, as a rule, any difficulty in diagnosing tuberculous ulceration of the anus (Fig. 9) and except for those due to a milk-borne bovine infection the condition is secondary to active pulmonary tuberculosis so that all we have to do is to X-ray the chest and examine the sputum. In this case the patient had bilateral active pulmonary tuberculosis with cavitation in the right apex. In addition I snipped off a small projecting nodule of granulation tissue and the section confirmed a tuberculous lesion.

Prognosis

In my experience carcinoma of the anal canal is a much more dangerous and serious disease than carcinoma of the anus.

Some five years ago Dr. Cuthbert Dukes and I examined the histology of this series and on a histological basis we classified them into two main groups—squamous cell and basal cell, each group being divided into (1) differentiated, (2) anaplastic. These groups are discussed together because so far as the anal canal is concerned it seems likely that the degree of differentiation is of greater importance from the surgical aspect than slight differences in the histological picture depending on the level of origin of the growth.

Of the 87 carcinomas of the anal canal 66 or rather more than two-thirds were anaplastic, whereas of the 30 carcinomas of the anus only 10 or one-third were of the anaplastic variety. This difference is reflected when we examine operability and the results of treatment.

Of the carcinomas of the anal canal 21 or approximately one-quarter were advanced locally
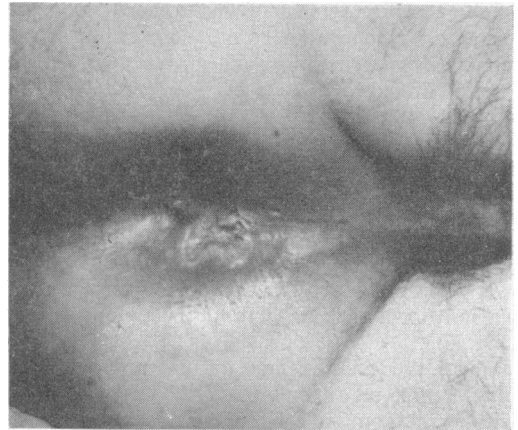
and were inoperable either owing to the local state or on account of metastases in the lungs or liver. Table II shows that 19 out of 21 were anaplastic.

TABLE II

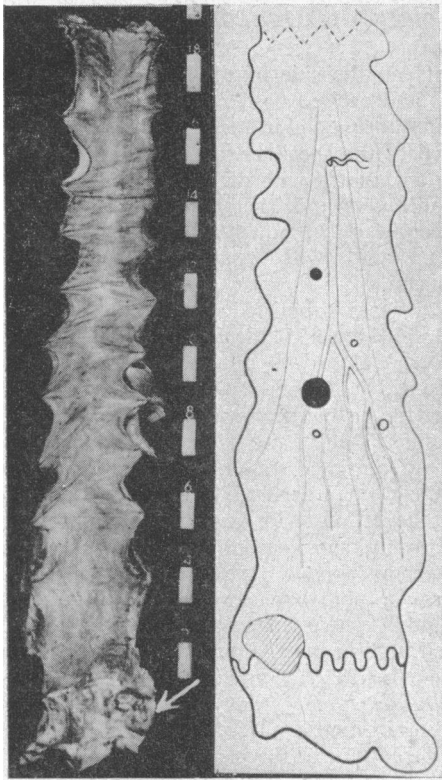|	Operable		Inoperable		
	Differentiated	Anaplastic	Differentiated	Anaplastic	Total
Carcinoma of anal canal	19	47	2	19	87
Carcinoma of anus ..	19	9	1	1	30

On the other hand 28 out of 30 carcinomas of the anus were operable and were resected mostly by local excision and only 2 were inoperable. The one inoperable differentiated carcinoma of the anus was a case arising in a fistula of fifteen years' duration which had extensively invaded the buttocks (Table II).
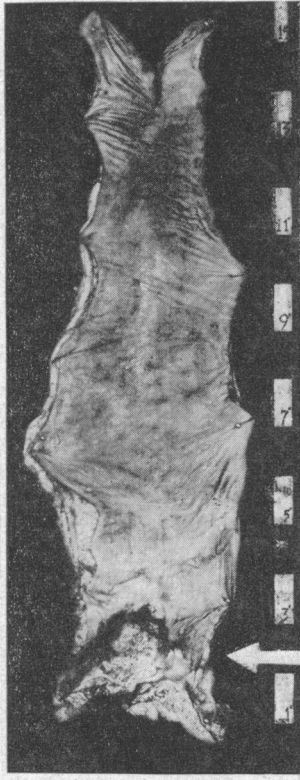
Treatment

Carcinoma of the anal canal.—During the first five years (1941–45) of the fifteen-year period reviewed most of the operable cases were treated by colostomy and perineal excision, but since 1946 radical combined excision (synchronous or perineo-abdominal) has been the method of choice.

Of 67 cases treated by radical operation there were only 5 A cases (7·5%) which is exactly half the usual expectancy of A cases in adenocarcinoma of the rectum. The remaining 62 cases were almost equally divided between the B and C groups. In view of the frequency of spread to the superior hæmorrhoidal lymph nodes (Fig. 10),
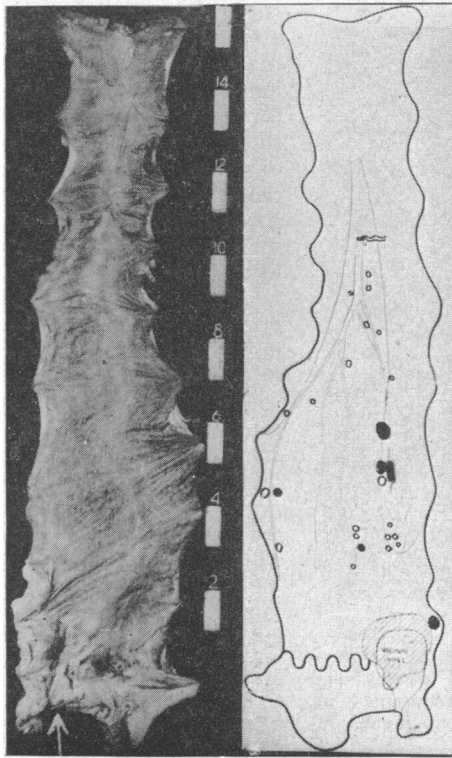
FIG. 10.—Four examples of anaplastic squamous cell carcinomas of the anal canal removed by radical combined excision. These were all C cases with lymph node involvement. Discontinuous lymphatic spread and also venous involvement are evident in D. The patient (A) had previously received deep X-ray therapy.   →
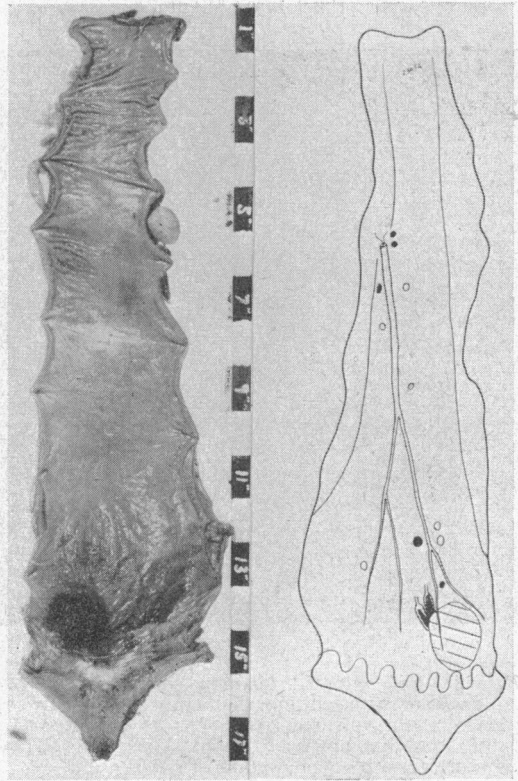
FIG. 10.

often by interrupted spread, a combined excision is clearly the best treatment when the primary growth is judged to be operable, but in poor-risk cases a colostomy and perineal excision has still a field of usefulness and may give equally good results. In women if the growth is anterior it is essential to remove the posterior half of the vaginal wall in continuity and not attempt to define a plane of cleavage.

The crude five-year survival rate after excision of the rectum for the period 1941–54 was 51% (29 out of 56 cases). In the differentiated carcinomas of the anal canal the five-year survival rate was 73% (11 out of 15 cases) and in the anaplastic carcinomas it was reduced to 44% (18 out of 41 cases).

Carcinoma of the anus.—There may be differences of opinion as to the best treatment for these cases and some of us will recall the good results obtained by Sir Charles Gordon-Watson by interstitial radium needling. In view of the risk of a radium proctitis developing I think diathermy excision is preferable. A one-quarter-inch margin should be taken on each side and the actual edge of the lesion should not be touched by toothed dissecting forceps for fear of causing implantation of cancer cells. Some of the sphincter muscle can be excised on the deep aspect, and a ∧ of tissue should be removed with the apex leading up into the anal canal (Fig. 11). If a hæmorrhoid

presents on the side of the lesion it should be ligated and excised or it may subsequently prolapse into the wound in a troublesome way. After removal of the specimen the resulting wound is lightly coagulated with diathermy and is dressed with tulle gras and Milton or Bradosol lotion. The wound is subsequently managed as for a fistula wound with routine irrigations and dressings.

Of 28 cases submitted to surgical treatment between 1941 and 1954 there have been 17 five-year survivors (60%). All but one were treated by local excision and it seems to make little difference whether the histological grade is differentiated or anaplastic. One of the worst cases I can recall was a differentiated squamous carcinoma of the anus in a woman aged 53. The growth was situated in the left posterior quadrant and at the time of operation there was no evidence of unusual subcutaneous spread. After local excision with diathermy a rapid extension took place to the left groin and in spite of a block dissection the growth recurred both in the anal region and in the groin and the patient died within a year of operation.

Metastases to the groin.—Each case must be treated on its merits. I do not believe in routine block dissections of the groin and the operation should only be done if a hard localized enlargement takes place on one or other side according to the site of the primary lesion. I submit that it is a bad practice to remove a solitary gland for biopsy; if there is a suspicion of inguinal metastases having formed a block dissection should be done. The pathologist should be asked to report on the number of lymph nodes present and the number occupied by metastases: if only one or two contain metastases the prognosis is often good and no further extension takes place subsequently. It would seem that if one gland acts as a filter and enlarges perhaps to a diameter of $\frac{1}{2}$–$\frac{3}{4}$ in. the prognosis is good provided the block dissection is done while the gland is still mobile and its capsule intact. The prognosis is extremely bad if a chain of 3 or more glands is proved to contain metastases and I do not know of any patients who did not develop recur-
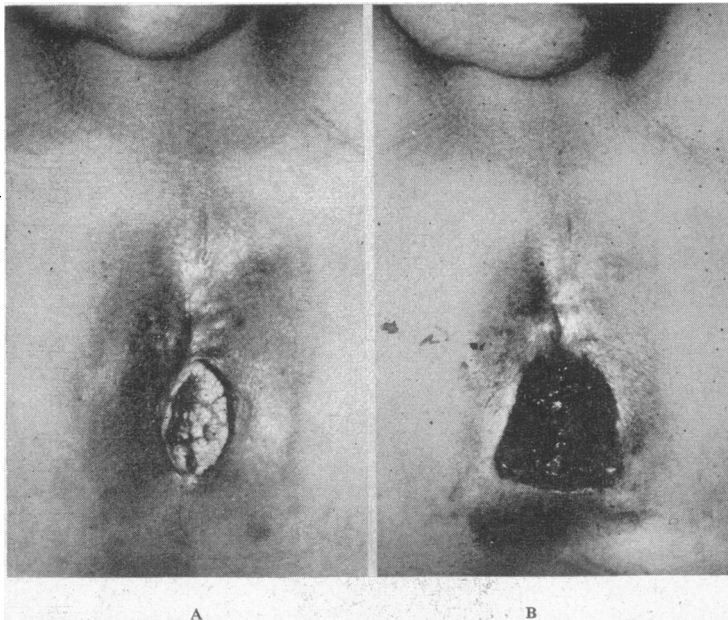

FIG. 11.—Differentiated squamous carcinoma of the anus before and after local excision with cutting diathermy (male, aged 60, July 1950). He remained free from recurrence for seven years when he emigrated to Australia and has not been traced since then. There was no indication at any time for a block dissection of either groin.

rence when a bilateral block dissection of the groins was positive.

I must emphasize the need for regular supervision of the groins after the primary operation whether it is for a carcinoma of the anal canal or the anus. The patient should be seen every month for the first six months after operation and then at two-monthly intervals for at least three years. Even when the five-year mark is reached the patient should not be dismissed and I should like to relate the details of the following remarkable case:

Case I.—Mrs. E. M., aged 65, presented a deeply ulcerated growth involving the anterior wall of the anal canal. Biopsy: squamous cell carcinoma. 29.1.42: left iliac colostomy; 19.2.42: perineal excision. The growth was a flat ulcerating one, 1½ in. in diameter and was an anaplastic squamous cell carcinoma spreading into the sphincter musculature. Six glands were free from metastases—B case. She made a good recovery and remained under regular supervision for ten years and no need arose for a gland dissection of the groins. In June 1952 a gynæcologist performed a vaginal hysterectomy and perineal repair. In March 1954 I repaired a sacral hernia from which she made a good recovery and there was no clinical evidence of recurrence. In July 1954 she was seen and was well. In November 1954 she returned after an interval of four months as instructed, and was found to have developed a hard mobile gland in the left groin. A block dissection of the left groin was done in December 1954 and the one large gland out of 4 examined was proved to contain anaplastic squamous cell carcinoma similar to the primary removed in 1942. This was nearly thirteen years after the original operation. Since then the patient has kept well with no evidence of recurrence to November 1959.

X-ray Therapy

At present X-ray therapy cannot be offered as an equal alternative to radical surgery in carcinoma of the anal canal, chiefly on account of the frequency with which the sphincter muscles are invaded by growth and the liability to early upward lymphatic spread along the superior hæmorrhoidal chain.

My impression is that patients with squamous carcinoma of the anal canal who are sent for deep X-ray therapy and fail to respond to treatment or recur after an initial regression of the growth usually do badly when referred back for radical operation. I have notes of 3 cases and only one patient survived for over five years: this was a female aged 54 who has lived for twelve years after colostomy and perineal excision of the rectum after X-ray therapy had failed; the other 2 patients developed early recurrence. In addition one patient with carcinoma of the anus who did not respond to X-ray therapy died of the disease in the same year after perineal excision.

I should like to record the following successful cases of inoperable squamous carcinoma of the anal canal after million volt therapy and this gives me the opportunity of recording the thanks we at St. Mark's Hospital owe to Mr. Ralph Phillips and to Mr. I. G. Williams at St. Bartholomew's Hospital for the invaluable help we have received from their department with many of our cases.

Case II.—A. I., male, aged 68 in May 1942. He presented a deeply ulcerated growth in the lower third of the rectum and anal canal anteriorly and laterally. He had hard enlarged glands in both groins, the right larger than the left. Biopsy showed it to be of the anaplastic basal cell type. A palliative left iliac loop colostomy was done on May 21, 1942. Two weeks later bilateral perianal abscesses anteriorly had to be drained. When these had cleared he was referred to St. Bartholomew's Hospital for X-ray therapy. Three months later the ulcer in the anal canal was small and by February 1943 the anal canal was smooth with no evidence of growth. In January 1944 I closed his colostomy and he was subsequently seen at intervals to August 1951, when his anal canal was normal and the groins clear. He finally died in October 1952 at the age of 78 from cardiac failure, hypertension and arteriosclerosis, i.e. ten years after the course of X-ray treatment.

Case III.—L. A., a Cypriot, aged 48, was referred to St. Mark's Hospital in November 1953 with an advanced carcinoma of the anal canal for which a left iliac loop colostomy had already been performed. The growth was deeply ulcerated anteriorly and of doubtful operability. Biopsy proved it to be anaplastic squamous. I attempted a perineal excision but it was quickly apparent that the growth was quite inoperable and the operation was terminated by cutting the rectum across through the growth below the peritoneal reflexion, chiefly in the hope that removal of the invaded sphincter apparatus would spare the patient subsequent pain to some extent. He was then referred to St. Bartholomew's Hospital for X-ray therapy to which he made a rapid response and when last seen in mid-February 1954 before his return to Cyprus he was excellent. Subsequent enquiry has established that he is still alive and well (March 1960).

These 2 cases suggest, as might be expected, that the high grade anaplastic variety of anal canal growth is the more likely to respond to deep X-ray therapy.

REFERENCE

GABRIEL, W. B. (1941) *Proc. R. Soc. Med.*, **34**, 139.

Mr. T. McW. Millar (Edinburgh):

My personal experience of carcinoma of the anus and anal canal is small. Only 2–3 cases of this serious disease are admitted to the 250–300 surgical beds in the Royal Infirmary, Edinburgh, each year. By the courtesy of my surgical colleagues I have been able to review the records of 22 cases admitted during the last ten to twelve years. Though these cases are not complete I have extracted what information I could, and I offer some observations based on that information, on my study of the literature and on my experience.

I found the sex incidence rather more than 2 to 1 in favour of the male sex. The age of the patients varied from 30–83 years, with an average about 60. I found it difficult from case notes to decide in many cases whether the tumour had begun as an anal tumour and had invaded the anal canal or whether it had begun primarily in the latter, but after deciding in each case what I thought had been the primary site I found the number beginning in each site approximately equal.

Inguinal lymph node involvement had occurred in 5 cases, approximately one-quarter. Figures from the literature vary from 8%–30%. Stearns (1955), reviewing 69 cases, found 23% had involvement when first seen and a further 19% developed metastases later.

While a pathological report was available for all cases studied, no grading of the tumours on a histological basis had been done. Various descriptions were used by the pathologists: well-differentiated, 6 cases; well-differentiated but "actively growing" or "with many mitoses", 4 cases; moderately differentiated, 5 cases; poorly differentiated, 4 cases; basi-squamous, 3 cases. There is thus a widespread and an almost equal proportion of the total to each of the main types. I was unable to find any definite correlation between the histological type and the subsequent fate of the patient, except perhaps that undifferentiated tumours of the anal canal carry a bad prognosis. I think Wittoesch *et al.* (1957) refer to the same tumour as basaloid small cell carcinoma, which, they find, occurs near the dentate line, is highly malignant and gives poor results after treatment.

Treatment employed in this series has been on the usual lines. About three-quarters were treated surgically and the remainder by surgery and radiotherapy, or by radiotherapy alone, usually as a palliative measure.

Of the 22 patients studied 3 survived for at least eight, five, and four years. 9 are dead or presumed dead because it was known that the disease was not controlled. In 2 cases there is no record of the patient having reported to hospital after the primary treatment. Of the remaining 8, 3 are recent and the other 5 were known to be alive and well for periods round about one year after treatment when follow up ceased.

Lymphatic Spread

This disease presents several problems, not the least of which is how to deal with the regional lymph nodes, whether these are involved clinically or whether they are apparently uninvolved. It is generally agreed that tumours of the anus metastasize to the superficial inguinal nodes via lymphatics which pass forward between the perineum and the upper medial thigh. The further spread is along the external and common iliac vessels to the pre-aortic nodes, but I would call attention to the possibility of involvement of what are called the obturator nodes which lie over the entrance to the obturator canal and which apparently can become involved by spread from the inguinal nodes even in the absence of involvement of nodes along the iliac vessels. Several authors refer to this involvement, and I have seen these nodes heavily invaded by carcinoma in a patient who had massive involvement of the inguinal group but no involvement of the iliac group. These obturator nodes lay proximal to the point at which the obturator artery and nerve entered the obturator canal and were lightly adherent to these structures.

When the tumour originates in the anal canal the lymphatic drainage is both more complicated and more difficult to deal with surgically. There may be a spread upwards with involvement of the pararectal, superior rectal and inferior mesenteric nodes. Such a spread is satisfactorily dealt with by the abdominoperineal operation. The lateral spread along the inferior rectal (hæmorrhoidal) and middle rectal vessels leads to involvement of nodes along the levator muscles and the internal iliac nodes on the side wall of the pelvis. These nodes are not dealt with in the classical abdominoperineal operation and a deep pelvic node dissection has been suggested and practised in an attempt to deal with them. I cannot say much about this from personal experience but I have, on occasion, attempted such a dissection when operating for a low carcinoma of the rectum in which I thought there was evidence of lateral spread and I found the procedure difficult and unsatisfactory.

Treatment of the Primary Lesion

It is generally agreed that small superficial lesions of the anus, involving only a sector of the circumference (perhaps not more than a third) and not extending far up the anal canal should be treated by *wide* local diathermy excision, even if some of the outer layers of the external sphincter

muscle have to be sacrificed. The resulting wound may be covered with an immediate skin graft. For larger anal lesions, and for all tumours originating in or extensively involving the anal canal the abdominoperineal excision is the correct treatment. In carrying out the perineal part of the operation wide removal of the ischiorectal fat and levator muscles should be performed. Whether such an excision should be combined with an attempt at deep pelvic node dissection is a moot point.

Treatment of the Lymph Nodes

With regard to the treatment of the inguinal and iliac lymph nodes I would agree that, if one is satisfied on clinical examination there is no suspicion of inguinal involvement, no removal of these nodes should be carried out. I do not favour prophylactic groin dissection.

I would, however, emphasize strongly the necessity for careful post-operative review of patients who have had the primary lesion dealt with by one means or another, but who have not had groin dissection carried out. Recurrence in the inguinal nodes may appear early or late, and I have been impressed with the rapidity with which such a recurrence may grow. An elderly patient, who had had a local removal of the tumour, had no clinical evidence of inguinal involvement before operation nor up to three months after operation, at which time he defaulted. Five months later he had an almost inoperable mass in one groin.

Operation for groin metastases at an early stage, with perhaps only one node palpably enlarged, is well worth while, and by careful follow up after treatment of the primary such metastases should be found at an early stage. I have referred to the review by Stearns (1955) of 69 cases of epidermoid carcinoma in the anal region in which he found inguinal metastases in 29: in 16 cases the nodes were obviously involved at the first admission, and in 13 they appeared subsequently, nearly all within two years; 9 of the 16 were submitted to groin dissection and 8 of the 13 follow-up cases were operated on—a total of 17. All those with involved nodes when first seen had died, but 5 of the 8 whose metastases were discovered on follow-up examination were well from two to six years later. Careful follow up and operation as soon as inguinal involvement is discovered may be rewarding.

Our practice in dealing with regional lymph nodes in the groin has not been quite logical and not in line with our practice elsewhere, e.g. the radical dissection of the axilla or the block dissection of the neck where we do not hesitate to do an extensive operation with wide removal of the deep fascia, the sternomastoid muscle and the

internal jugular vein. The reason for this is not far to seek. Lee (1955) has described removal of the inguinal lymph nodes in the past as a bugbear, vexatious to the surgeon and a sore affliction to the patient. As commonly performed it carries a considerable morbidity from necrosis of the skin flaps with delayed healing by granulation, lymph fistula, infection and consequent œdema of the limb. Furthermore a true ilio-inguinal block dissection cannot be done if it is agreed that the inguinal ligament should not be divided. But can most of these difficulties not be overcome? I would agree that a superficial inguinal node dissection might be considered adequate for early involvement, but if we are going to operate at all for more serious involvement surely we should carry out the most radical operation possible. In this connexion I would draw attention to the ilio-inguinal block dissection described by Lee (1955). By this method a truly radical operation is done, primary healing of the wound can be obtained without drainage and without the leakage of lymph, and, in my own experience, lymphœdema of the leg is not marked and occurs chiefly in the thigh.

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   R. J. (1957) *Surg. Gynec. Obstet.*, **104,** 75.

Mr. W. H. Bond (Birmingham):

True squamous cell carcinoma of the anus is rare; between 1936 and 1956 the United Birmingham Hospitals registered only ninety-six cases—about 0·1% of all malignancy. To provide five-year figures the initial study was done on the 73 cases treated up to 1954, but in common with squamous cancer at most other sites, three-year figures give determinate results, for only one death from growth occurred between the third and the fifth year. Histological proof was not obtained in all, but all tumours in which the rectum was involved were proven as were all but two of those treated in an attempt to cure (Table I).

TABLE I

			3-year survivors
1936–1954	Palliative or no treatment—	24	0%
	Radical surgery or radiation—	49	36·7%
1936–1956	Palliative or no treatment—	34	0%
	Radical surgery or radiation—	62	38·8%
	Histological proof 73 cases		
	Overall five-year survival rate 1936–1954—24·6%		

The classification adopted depends on the anatomical extent of the tumour and its site. Anal: In this group the tumour lay mainly

externally. Anal canal: Here, though the skin may have been involved, the greater extent lay in the canal. Anorectal: The tumour arose in the upper part of the anal canal and extended within the internal sphincter to involve the rectum.

The age incidence (Table II) and symptoma-

TABLE II.—AGE INCIDENCE (1936–1954)

Age in years

	M	F	40	45	50	55	60	65	70	75	80	85
Anus ..	14	4	—	1	2	2	3	3	3	4	—	—
Anal canal	31	4	—	3	3	4	5	8	7	5	—	—
Anorectal	9	11	3	1	2	1	3	2	5	—	1	2
Total			3	5	7	7	11	13	15	9	1	2

tology did not differ in the three groups, save that the 3 youngest and the 3 oldest were all anorectal tumours; the maximum incidence was between 60 and 70. There are differences in the sex incidence for whereas 55% of the anorectal series are female, this sex is affected in only 15% of the anal and anal canal series. Inguinal node involvement when first seen is similar in all groups, no case surviving into a third year (Table III). 6 cases developed nodes after an

TABLE III

	Percentage presenting with clinical node involvement	Percentage treated palliatively or not treated	
Anus ..	28%	3/18	17%
Anal canal ..	34%	11/35	31%
Anorectal ..	30%	10/20	50%
All cases ..	30%	24/73	31%

attempt at radical treatment, in spite of radiation or lymphadenectomy and died before the third anniversary. In common with malignancy at other sites distal metastasis was commoner in those with nodes at any stage, and I have little support for attempts at curing those with involved inguinal nodes. This is a sad conclusion for 10% of the deaths are attributable to catastrophic hæmorrhage from an eroded femoral artery.

Treatment of the primary tumour.—There were 24 patients for whom no curative procedure was undertaken. Half died within six months of first attendance and all died within two years.

By modern standards undoubtedly perineal or abdominoperineal excision would be done in some and there is a definite place for a short course of X-ray therapy to simplify nursing care. 49 cases received curative treatment, 28 by radiation and 21 by surgery, successful in 18, giving a five-year cure rate of 36·7%, the overall rate being 24·6%.

The tumours treated by radical radiation (Table IV) were nearly all anal or anal canal,

TABLE IV.—CASES TREATED BY RADICAL RADIATION METHODS (1936–1954)

Anus	10	} 28	
Anal canal	16		
Anorectal	2		
Primary site healed	..	12	(43%)
Uncontrolled tumour	..	5	} 16 (57%)
Local recurrence	..	4	
Radiation necrosis	..	7	
Spread to inguinal nodes ..	..	3	
Distal metastases	..	2	
Average age	..	65 years	
Five-year survivors	..	9 (32%)	

only 2 being anorectal. Local control of disease during the lifetime of the patient was obtained in 12, 16 failed from recurrence, radioresistance or necrosis. The average age was 65 and the five-year survival rate 32%.

The techniques of radium implant require no special description, planar implants being used for the smaller lesions, a volume implant with or without a central source in the canal for the larger. Radium needle implant is technically difficult and commonly geometrically unsatisfactory; even so, the study of dose levels is useful. Overdosage not only gives a high incidence of radiation damage, but local recurrence and failure to control the tumour increase in frequency. This possibly arises from a biological effect, but errors in the needle implant are merely magnified by the higher dosages. In this series local complications arose in 13 of 16 given 6,000 r or over, but in only 3 of the 11 treated to lower dose levels (Table V). A fair

TABLE V.—CASES TREATED BY RADICAL RADIUM IMPLANT (1936–1956)

Tumour dosage

	4,500 r and under	5,000 to 5,500 r	6,000 r and over
Primary site healed ..	3	8	3
Uncontrolled tumour ..	0	1	4
Local recurrence ..	0	0 } 3/11	4 } 13/16
Radiation necrosis ..	0	2	5
Spread to inguinal nodes	1	1	1
Distal metastases ..	0	4	1
Total	3	11	16
Three-year survivors ..	2	5	6 (43%)

conclusion is that the dose level at 0·5 cm from the radium should not exceed 5,500 r in five to seven days, and the use of simpler and more controllable implants to a lower dosage level in recent years may account for the 43% three-year survival rate when the more recently treated cases are included.

The picture presented by the 21 cases treated surgically (Table VI) is happier, local control

TABLE VI.—CASES TREATED BY RADICAL SURGICAL METHODS (1936–1954)

Anus	5	} 21	
Anal canal	8		
Anorectal	8		
Primary site healed ..	..	13	(61%)
Uncontrolled tumour ..	..	1	} 7 (33%)
Local recurrence ..	..	6	
Spread to inguinal nodes	..	3	
Distal metastases ..	..	5	
Average age	..	58 years	
Five-year survivors ..	..	9 (43%)	

being obtained in 13; only 7 had persistent or recurrent disease. There was one post-operative death. The average age was somewhat lower at 58, and the three- and five-year survival rate 43%. In the whole series of 27 (Table VII), 9 were

TABLE VII.—CASES TREATED BY RADICAL SURGICAL METHODS (1936–1956)

	Local excision	Perineal excision	Total
Primary site healed ..	4	12	16
Uncontrolled	1	—	1 } 8 (30%)
Local recurrence ..	2	5	7
Spread to inguinal nodes	1	3	4
Distal metastases ..	2	5	7
Total	9	18	27
Three-year survivors ..	4	9	13 (48%)

treated by local excision, three recurred locally and 4 survived three years. The result of the 18 perineal or abdominoperineal excisions was better, with a 50% three-year survival rate, only 5 in 18 recurring locally.

These results may be due to selection, save that some surgeons consistently excised the tumours and others always referred them for radiation. On this basis one may presume fairly random selection, although the difference in average ages suggests that this is not the case.

In presenting the case for radiotherapy I know that the figures given show a slight bias in favour of surgery, preferably radical as opposed to local excision. Consideration shows that at modest dosage levels the local cure by radiation is as good as that achieved by surgery, and only in the incidence of necrosis does radiation fall behind, distal metastases and node recurrence being equally common with either method. In the larger tumours and those extending into the rectum surgery offers greater benefit, but successful surgery depends on the patient's willingness to sacrifice the anus, and one-third of the patients are over 65, when major surgery for a seemingly minor lesion may be undesirable.

Any treatment scheme for anal carcinoma must include radiation, as a palliative for the incurable and as a method of choice for selected cases.

In *anorectal* lesions external methods of radiation and radium needling have little part to play. Whilst a tumour lying mainly on the anterior wall of the rectum can be implanted, posterior and laterally sited lesions above the internal sphincter cannot be adequately covered by needle implant. Fig. 1 illustrates the difficulty, for the tumour lies on the double curve at the junction of rectum and anal canal, and it is virtually impossible to design an implant which fully treats the tumour and avoids necrosis. A possible solution is the use of radioactive gold grains, but this group are unquestionably best treated by abdominoperineal excision. Tumours of the *anal canal* may be treated by a curved single plane implant using 42 mm or 58 mm needles, and with care a parallel implant can be achieved (Fig. 2). It has, however, one weakness in that it is impossible to close the top of the implant by a crossing needle, and this considerably reduces the fully treated area. Even using differentially loaded needles this objection remains and recurrence appears from underdosage. A possible solution is a gold grain implant, for the tissues can be drawn over the needle, the additional top loading provided by two or three grains placed in one spot, the rest of the chain inserted as the needle is withdrawn. The pattern of a radium needle implant can be readily reproduced, with the additional advantages that no needles have to be removed, neither will they slip out of place, and finally nursing is easier for bowel movements take place normally.

Somewhat similar considerations apply to tumours of the *anus*. These tumours can be effectively treated by a single plane radium im-
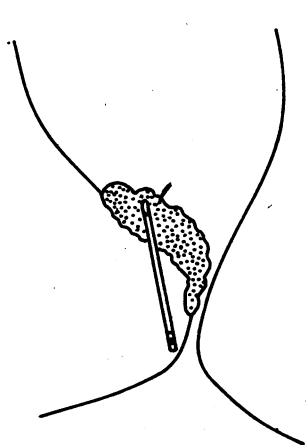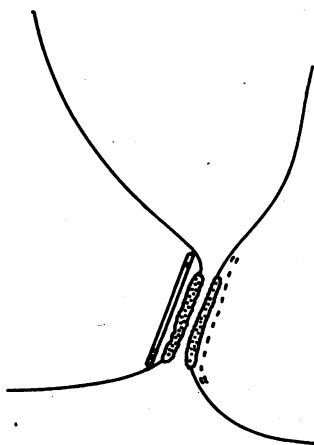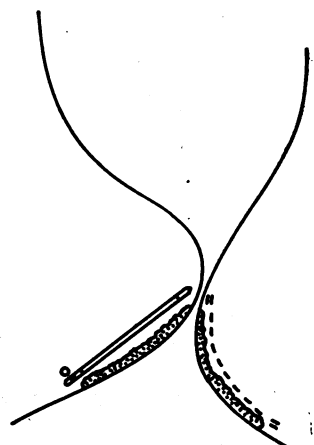

FIG. 1.　　FIG. 2.　　FIG. 3.

plant, but as with anorectal tumours one has to deal with a double curve at the junction of the anus and canal (Fig. 3). Here, since these tumours are fairly superficial, one can deal with the problem by threading the needle just deep to the skin so that the curves are obliterated. This distortion of the tissues, however, stretches the external sphincter which on contracting distorts the implant and extrudes the needles. Again this implant is weak at the uncrossed end, and the solution is probably a gold grain implant which, accurately performed, avoids the difficulties of a rigid radium needle insertion.

Selection of cases.—All anorectal tumours are best treated surgically; failing this, gold grain implant has much to commend it for full dosage can be given in safety to the whole of the tumour. Lesions of the anus and anal canal involving less than half the circumference, of superficial character and less than 1·0 cm thick are fully treatable by radiation. The smallest are best excised for healing is quicker than after implant, and the larger, where the growth is still local, should be removed by abdominoperineal excision.

Mr. Gordon S. Ramsay (London):

Treatment

I have based my remarks, mainly, upon an analysis of cases seen at the Royal Marsden Hospital from 1940 to 1959, and at the Gordon Hospital from 1947 to 1959.

I excluded 5 cases that were recorded as having squamous cell carcinoma of the anus, but in whom the diagnosis was either wrong or doubtful. One was a large papillomatous lesion of the buttock which was histologically benign and which was cured by local excision. Two were straightforward basal cell tumours which require no comment and the remaining 2 patients each had anaplastic growths. The first was in a woman of 81; it extended 5 cm up the anal canal and also involved the perianal skin and was so anaplastic that it was impossible to determine its ætiology; she died nine months after treatment with high voltage therapy (H.V.T.) and radium needles, having developed metastases in the buttock and groin. The second was diagnosed originally as being a double primary, adeno and squamous, but on review belongs to the rare group of muco-epidermoid tumours arising from the ducts of the anal glands—it certainly bears no resemblance to either squamous or adeno-carcinoma.

There remain 50 cases for study, 28 men and 22 women. Their age and sex distribution is shown in Fig. 1 which emphasizes the fact that this disease usually affects elderly people. The division of the cases into three grades of malignancy (Table I) using the criteria of Mr. Gabriel (1941),
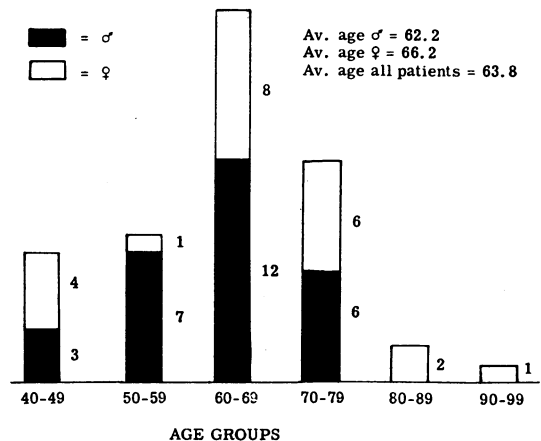

FIG. 1.—Squamous cell carcinoma of anus, Royal Marsden and Gordon Hospitals series. Age and sex on entry (50 patients).

illustrates the tendency for low-grade tumours to occur more commonly in men and for high-grade tumours to affect women. The 6 cases not graded had had biopsies taken at other hospitals and, although there is no doubt about the diagnosis, the reports made no mention of the degree of differentiation of the tumour and I have been unable to obtain the slides for review. The site of origin is also different in the two sexes; of 22 patients with anal canal tumours 10 were male and 12 female, whilst of the 28 patients with anal margin tumours, 18 were male and only 10 female.

TABLE I.—SQUAMOUS CELL CARCINOMA OF ANUS
50 CASES GRADED HISTOLOGICALLY

	Males	Females	Total
Low grade ..	9	5	14
Medium grade	9	3	12
High grade ..	8	10	18
Not graded ..	2	4	6
Total	28	22	50

It is extraordinary how advanced many of the cases are when they reach hospital and simple clinical staging based upon the size of the growth (up to 3 cm—early, more than 3 cm—late) shows that almost two-thirds of this series were late cases (Table II).

41 cases are available for assessment of five-year survival (Table III). (I have avoided the use of percentages in this small series.)

The fate of the patients in the various groups was as follows: Of the 14 patients with well-differentiated growths, 6 are alive for periods of from three to nine years and 3 others died from unrelated causes: 1 in the fourteenth year, cause unknown, 1 in the fifth year from carcinoma of the bronchus and 1 from peritonitis twelve days after an abdominoperineal (A.P.) excision of the rectum. The remaining 5 patients all died from recurrence of their disease in less than two years.

TABLE II.—SQUAMOUS CELL CARCINOMA OF ANUS
CLINICAL STAGING AND HISTOLOGICAL GRADE

	Early	Late	Total
Low grade ..	8	6	14
Medium grade	4	8	12
High grade ..	6	12	18
Not graded ..	1	5	6
Total	19	31	50

TABLE III.—SQUAMOUS CELL CARCINOMA OF ANUS
FIVE-YEAR SURVIVAL

	All cases	Five-year survivals
Low grade	13	6
Medium grade ..	7	3
High grade	15	2
Not graded	6	1
Total	41	12

All 6 patients with early anal margin lesions were cured by local excision. One patient with an early anal canal growth is alive three years without recurrence after an A.P. excision. The other patient who had an A.P. died from peritonitis and one died from recurrence after perineal resection. The remaining 5 were treated with radiotherapy; 3 had a preliminary colostomy. 4 received high voltage therapy and the only success was achieved in the fifth patient, a man of 63. His primary was treated with about 5,000 r at 60 kV in sixteen days and both inguinal regions were then treated with H.V.T. He died four years eleven months later from carcinoma of bronchus.

Of the 12 medium-grade cases, 7 are alive. 1 was treated only 4 months ago and the remaining 6 survived from three to six years; 2 died without recurrence, 1 in the ninth year from pneumonia and 1 in the fifth year from coronary thrombosis.

Of the 6 who survive more than three years, 3 had A.P. excisions, 2 had local excisions and one, a woman of 68, received 2,900 r skin dose in twenty-three days at 220 kV. Two months later radium needles were implanted and she received a further 5,000 r. She remains well six years after treatment apart from a small area of radio-necrosis which she steadfastly refuses to have excised.

The other 2 successes were treated by surgery. One, an early case, was treated by diathermy excision, and the other, more advanced, had a perineal excision of the rectum.

3 died of their disease, 1 from recurrence following perineal excision of the rectum, another, advanced, was untreated and the third was a woman of 75 with a late anal canal growth which was treated by a combination of H.V.T., low voltage therapy and the interstitial implant of radioactive gold grains. The tumour failed to respond and a palliative abdominoperineal excision of the rectum was carried out. At operation, extensive spread in the pelvis was found and post-mortem examination shortly afterwards revealed multiple metastases in the lungs and in the bladder.

The high-grade group of 18 patients presents a gloomy picture. Only 3 survive, all treated by abdominoperineal excision of the rectum and are free from recurrence ten, nine and three years after operation.

The remainder died of their disease with the exception of one patient who succumbed to a pulmonary embolus fifteen days after A.P. excision of the rectum but at autopsy was found to have multiple metastases in the liver and pelvic lymph nodes.

3 were early cases and were treated by local excision and all recurred rapidly. The remaining 12, all late cases, were treated as follows: 6 had radical surgery and 6 radiotherapy. The longest survival was two years ten months.

The ungraded group is also depressing. 1 man is alive nine years nine months after radium needle implant. 1 woman aged 65 received approx. 6,000 r at 60 kV to the anus in twelve days. She developed marked stenosis, but when she died three years later from cardiac failure there was no sign of recurrence. The remaining 4 patients died of their disease. 1, a man aged 77 with advanced disease and poor general condition, was not treated and the rest, all women with late anal canal lesions, were treated with radiotherapy with no success.

The treatment of carcinoma of the anus is still controversial and it is impossible to lay down hard and fast rules for every case, but there are a few lessons to be learned even from this small series.

During the past twenty years there has been a tendency to use surgery in preference to radiotherapy in the treatment of the operable case. This change has occurred because of the disappointing results of radiotherapy; the unpredictable response of the primary, the necessity for a colostomy in some cases and the frequent production of pain and tenesmus. It is now generally agreed that radiotherapy is incapable of controlling lymph-node metastases in most cases. In this series there were 4 successes from radiotherapy alone, but in a further 9 patients, in whom there appeared to be some hope of cure, it failed. Surgery appears to offer a little more hope; it may be local or radical (as in this series), or super-radical as advocated by some American surgeons. Local surgery should be reserved for really small lesions at the anal margin, proved by biopsy to be of low-grade malignancy, and all other operable cases should be treated by abdominoperineal excision of the rectum. There is not enough evidence yet to show whether or not radical abdominopelvic and inguinal node dissections are of value, but it is interesting to note that, of 12

patients who had an A.P. excision and in whom the pararectal lymph nodes were found to be tumour free, 4 died from local recurrences and another, who died of a pulmonary embolus, was found to have involvement of the pelvic nodes although the pararectal nodes were free. It is in the treatment of such cases as these that the super-radical operation may have a place.

Management of the inguinal nodes.—Few patients who develop inguinal node metastases live five years. In this series there is one man who has no sign of recurrence four years ten months after an A.P. excision followed six months later by a right inguinal block dissection; both the pararectal and the inguinal nodes were involved. Inguinal node dissections were done in 11 other cases, in 7 the nodes were involved and these patients died in less than six months, in the remaining 4 cases the nodes showed evidence of chronic inflammation only. Stearns (1955) has demonstrated convincingly the futility of doing prophylactic inguinal node dissections and, since the operation is one associated with considerable morbidity, it should, in my opinion, be reserved for use if and when the nodes become involved. The difficulty is in deciding when this is so as clinical judgment is often wrong. There were no prophylactic dissections in this series and the 4 patients whose nodes were found on histological examination to be unaffected suffered an unnecessary operation. This error could be avoided by the use of the frozen section technique, one of the most satisfactory applications of which is the detection of squamous cell carcinoma in lymph nodes, and I advocate strongly its use in this type of case.

The plan of treatment may be summarized as follows: (1) Biopsy in all cases, however small the lesion. (2) Local excision reserved for lesions that are small, at the anal margin and of low-grade malignancy. (3) All other operable cases to be treated by abdominoperineal excision of the rectum. (4) Inguinal nodes should be observed and if suspicious, frozen section followed by block dissection if section is positive. (5) Radiotherapy as palliative treatment in the advanced case.

Acknowledgments.—I wish to thank the surgical staffs of the Royal Marsden and Gordon Hospitals for permission to use the case records. I am grateful to Dr. I. P. M. Dawson and Dr. N. F. C. Gowing for reviewing some of the histology.

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Dr. Basil C. Morson (London):
The Pathology and Results of Treatment of Squamous Cell Carcinoma of the Anal Canal and Anal Margin

In his Presidential Address to the Section of Proctology of this Society Mr. W. B. Gabriel (1941) emphasized the differences between squamous cell carcinoma of the anal canal and squamous cell carcinoma of the anal margin. I shall describe the differences in the pathology of these anal cancers together with some comments on their diagnosis, treatment and prognosis from the point of view of a pathologist.

It is necessary first to attempt an anatomical definition of what we mean by anal canal carcinoma and anal margin carcinoma. At St. Mark's Hospital we have chosen to classify all anal cancers by their relationship to the dentate line or line of the anal valves, as judged by the examination of operation specimens or, in the absence of such a specimen, by reference to the clinical notes (Table I). The

TABLE I.—POSITION OF PRIMARY TUMOUR IN 157 CASES

Anal Canal:			
Entirely above the dentate line..	..	38 ⎱ 85 ⎱	
Mainly above the dentate line ..	..	47 ⎰ ⎰ 103	
Exactly astride the dentate line..	..	18 ⎰	
Anal Margin:			
Mainly below the dentate line ..	..	13 ⎱	38
Entirely below the dentate line	..	25 ⎰	
Unclassified ..	..	.. ..	16
			157

position of the primary tumour in 157 cases of squamous cell carcinoma of the anal region seen at St. Mark's Hospital from 1928 to 1956 has been so defined. All squamous cell cancers lying entirely above, mainly above or exactly astride the line of the anal valves have been defined as anal canal tumours, whereas those lying mainly below or entirely below the line of the anal valves are regarded as anal margin tumours. This is an arbitrary classification, but in practice it works well from both the clinical and pathological points of view.

By the above criteria it has been possible to classify all but 16 of these 157 tumours. Either these were large growths or records were inadequate for an accurate estimate of the site of origin. Of the remaining 141 cases, 103 were anal canal tumours and 38 anal margin tumours. Thus anal canal cancer is about two and a half times as common as anal margin cancer. However, it is of interest that of the 103 anal canal cancers 85 arose above or mainly above the line of the anal valves and 38 of these lay entirely above this line. It is not sufficiently known that such a high proportion of squamous cell carcinomas of the anal canal arise from epithelium entirely above the line of the anal valves (Fig. 1).

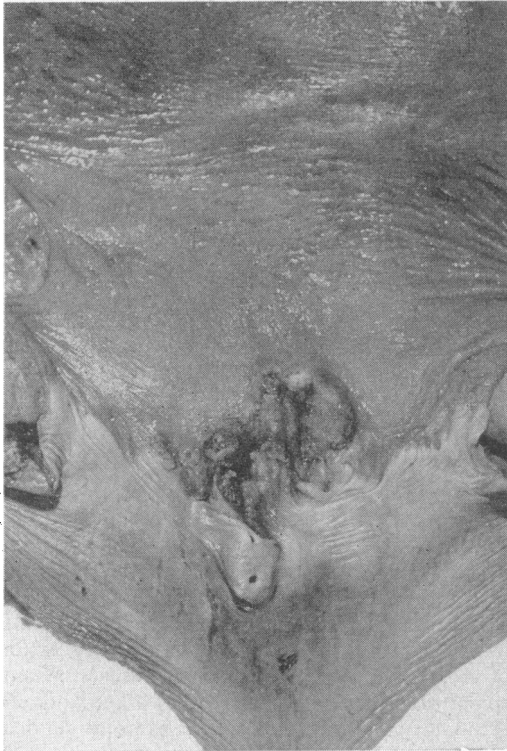The normal epithelial lining of the anal canal

FIG. 1.—Squamous cell carcinoma of anal canal. The tumour is arising from epithelium entirely above the level of the anal valves.

Rectal mucosa

} Transitional zone.
} Squamous mucous membrane.
} True skin —
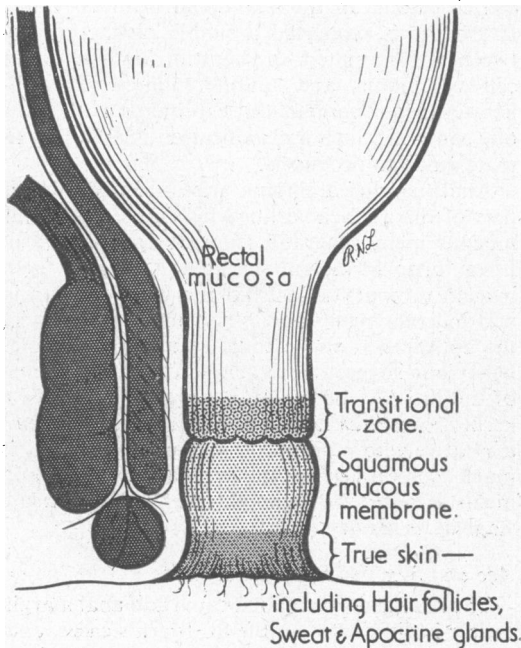— including Hair follicles, Sweat & Apocrine glands.

FIG. 2.

and perianal region is illustrated in Fig. 2. The anal canal above the anal valves is lined by rectal mucosa except for a narrow zone, seldom more than half an inch wide, immediately above the valves and covering the lower part of the internal hæmorrhoidal plexus, which may be called the "transitional" or "junctional" zone, as the structure of its epithelium is a compromise between the glandular rectal mucosa above and the squamous mucous membrane or modified skin below the level of the valves which merges with the true skin of the perianal region. The transitional or junctional zone, as pointed out by Walls (1958), is an area of considerable epithelial instability which contains a number of different varieties of epithelium. Here we may see a transitional type of mucosa (Fig. 3) resembling urinary tract epithelium, stratified columnar epithelium and squamous mucous membrane (Fig. 4) as well as "mixed" epithelium which may show features of all these varieties and also contains scattered
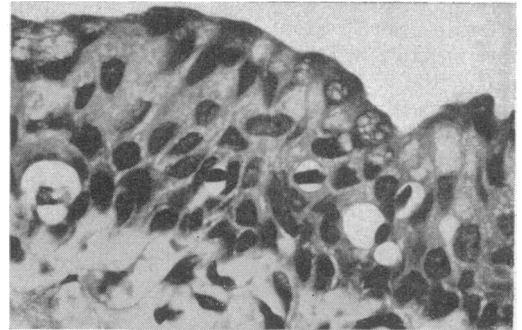

FIG. 3.—Transitional epithelium from the transitional or junctional zone above the line of the anal valves. The appearances resemble urinary tract epithelium but some of the cells in the superficial part of the mucous membrane are secreting mucus and can be seen in the photograph as goblet cells.   × 400.
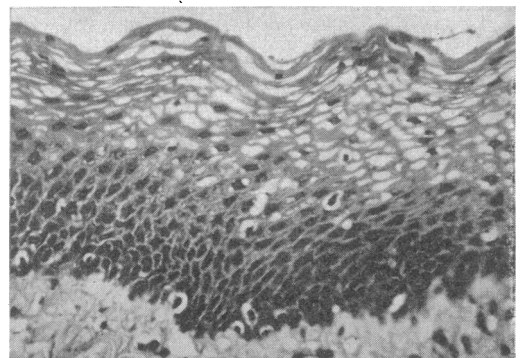

FIG. 4.—Simple squamous epithelium. This is the lining of the anal canal below the level of the anal valves but in many cases is also found in the transitional zone above the valves.   × 400.
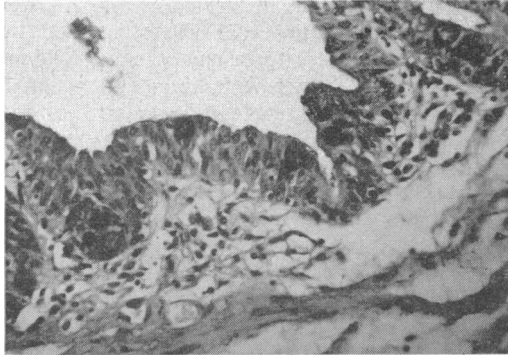
FIG. 5.—"Mixed" epithelium from the transitional zone above the anal valves which is stratified columnar but also contains mucus-secreting goblet cells. × 350.
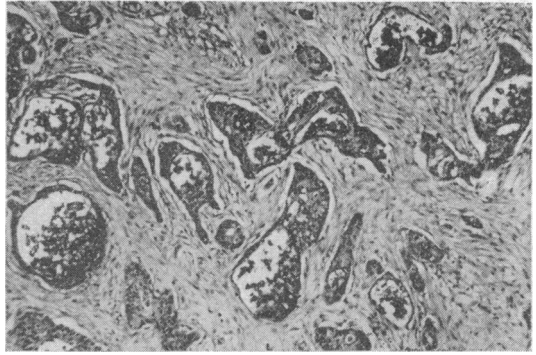

FIG. 6.—Muco-epidermoid carcinoma of anal canal. Typically this arises from the transitional zone and tumours of this type are only found in the upper part of the anal canal. × 80.

droplets of mucous secretion (Fig. 5). The structure of the epithelium in this junctional zone varies with age and with pathological changes, such as hæmorrhoids.

Most anal canal cancers arise from the unstable transitional zone of epithelium above the anal valves. It is not surprising, therefore, that anal canal carcinomas have a variable histology. Many of them resemble bladder carcinoma, and indeed the diagnosis of transitional cell carcinoma of the anal canal is commonly made by pathologists. The term basal cell carcinoma of the anal canal or basi-squamous carcinoma is also used because of the resemblance of some anal canal cancers to rodent ulcer. However, true rodent ulcer or basal cell carcinoma of the anus is a non-metastasizing tumour of the perianal skin and is rare. The tumours of the anal canal, called "basal cell" by some, are metastasizing tumours and should be treated as for squamous cell carcinoma. To avoid confusion I call all these anal canal cancers "non-keratinizing squamous cell carcinoma", because most of them produce little keratin. On the other hand squamous cell tumours of the anal margin are mostly of the keratinizing type (Table II).

TABLE II.—RELATIONSHIP OF SITE TO KERATIN PRODUCTION IN SQUAMOUS CELL CARCINOMA

	Proportion of cases forming keratin
Anal canal	45·1%
Anal margin..	84·2%

For many years it has been customary to regard keratin production as a rough guide to the degree of malignancy of squamous cell carcinoma. The greater the amount of keratin the lower the grade of malignancy. This is the main reason why the prognosis of anal margin disease after surgical treatment is better than anal canal carcinoma.

The anal canal is one site where muco-epidermoid carcinoma may be found (Fig. 6). This tumour is a type of squamous cell carcinoma which produces mucus as well as differentiating towards keratin production. It is found exclusively above the anal valves, arising from the transitional zone of epithelium, and is a reflection of the epithelial instability of this area. Muco-epidermoid carcinoma is found at other squamo-glandular junctional zones, such as in the cervical canal, but it has no pathological properties which suggest any special form of treatment.

Because of the great histological variability I have not found histological grading of squamous cell carcinoma of the anal canal of much value. If grading is requested a simple distinction between differentiated or keratinizing squamous cell carcinoma and undifferentiated or non-keratinizing squamous cell carcinoma is the best one can do. Such a classification is an approximate guide to prognosis.

Anal margin carcinoma arises from the lower part of the anal canal lined by simple squamous mucous membrane and from the perianal skin. I would go farther and suggest that most anal margin tumours arise from the junction of skin and mucous membrane. This junctional origin, the appearance of the tumour, its histology and behaviour suggest a comparison with carcinoma of the lip. At both sites we are dealing with a keratinizing squamous cell carcinoma, usually of a relatively low grade of malignancy, which is much commoner in males than females and metastasizes to the regional lymph nodes at a late stage in its history.

Age and Sex Incidence (Table III)

The sex incidence of anal canal and anal margin cancer is different. In the St. Mark's cases, anal canal tumours are commoner in women, in a proportion of about 4 : 3, whereas anal margin

TABLE III.—SQUAMOUS CELL CARCINOMA OF ANAL
CANAL AND ANAL MARGIN
St. Mark's Hospital, 1928–1956

Sex ratio	Males	Females	Ratio of males to females
Anal canal ..	44	59	3 : 4
Anal margin	31	7	4·4 : 1
Average age			
Anal canal ..	57·5 years		
Anal margin	57·9 years		

cancer is about 4 : 1 in favour of men. The age incidence shows no difference between the two sites, or any significant difference when compared with adenocarcinoma of the rectum.

Spread (Figs. 7, 8, 9 and 10; Table IV)

(1) *Direct.*—Squamous cell carcinoma of the anal canal shows preferential direct spread upwards into the lower third of the rectum and this explains why many squamous cell carcinomas of the anal canal present clinically as tumours of the lower rectum. Direct spread occurs by permeation of malignant cells along lines of least resistance such as tissue spaces and natural anatomical clefts. In anal canal cancer the line of least resistance appears to be upwards in the submucous layer, often with secondary ulceration through the rectal mucosa. Downward spread is held up by the arrangement of the anal musculature and in particular by the mucosal suspensory ligament of Parks, which partly obliterates the submucosal layer at its attachment to the squamous mucous membrane in the region of the anal valves.

(2) *Lymphatic* (Table IV).—Anal canal cancer spreads to the superior hæmorrhoidal lymphatic glands, the glands on the lateral walls of the pelvis as well as to the inguinal glands. There is hæmorrhoidal gland involvement in 42·9% of
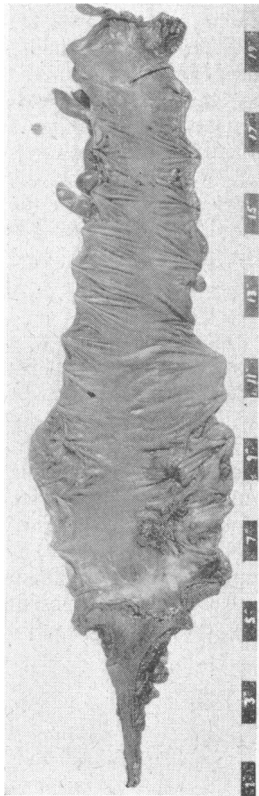
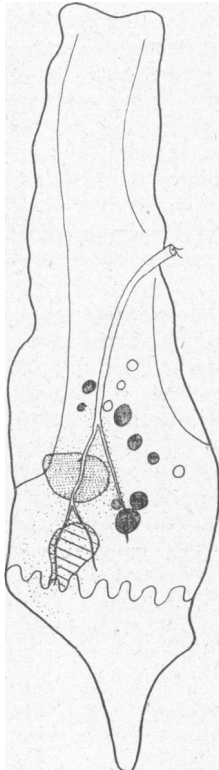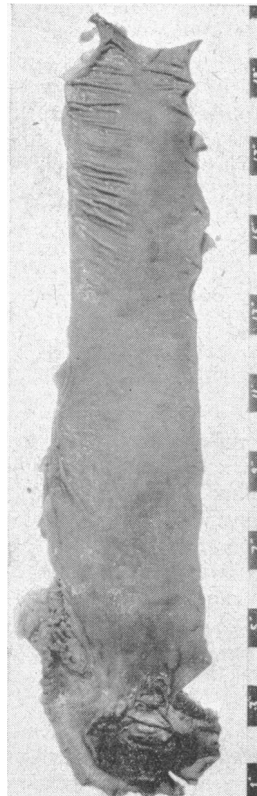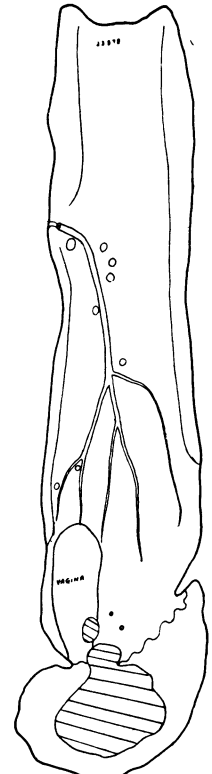

FIG. 7.   FIG. 8.   FIG. 9.   FIG. 10.

FIG. 7.—Squamous cell carcinoma arising from epithelium above the line of the anal valves with preferential spread upwards into the rectum.

FIG. 8.—Line drawing of specimen illustrated in Fig. 7 showing deposits of growth in hæmorrhoidal lymphatic glands.

FIG. 9.—Large squamous cell carcinoma of anal margin with involvement of the anal sphincters and early spread into the lower third of the rectum.

FIG. 10.—Line drawing of Fig. 9. There are no lymphatic metastases in the hæmorrhoidal glands.

Figs. 1, 7, 8, 9 and 10 are reproduced from Morson (1960) by kind permission.

major operation cases of anal canal cancer seen at St. Mark's Hospital, and clinical and pathological evidence of inguinal gland metastases in 35·9% of cases. However, there is clinical evidence that in anal canal carcinoma the inguinal glands are involved at a later stage than the hæmorrhoidal glands.

TABLE IV.—LYMPHATIC SPREAD IN SQUAMOUS CELL
CARCINOMA OF ANUS
St. Mark's Hospital, 1928–1956

Hæmorrhoidal glands (major operation cases only)	=42·9%
Inguinal glands (all cases)	..=35·0%
Inguinal glands: Anal canal	...=35·9%
Anal margin	..=39·5%
Hæmorrhoidal glands involved in anal margin cases treated by excision of rectum ..	..= 0·0%

In anal margin disease, inguinal gland metastasis has been found in 39·5% of cases. Most of these patients were treated by local excision of the primary tumour, but of the 9 cases of anal margin cancer which were so extensive as to require a radical operation none showed involvement of the hæmorrhoidal group of lymphatic glands (Figs. 9 and 10). It would appear that hæmorrhoidal gland involvement is extremely rare in anal margin cancer, if it ever occurs, and this justifies the current practice of local excision of these tumours where possible.

Treatment (Table V)

TABLE V.—COMPARISON OF OPERATIVE TREATMENT OF
SQUAMOUS CELL CARCINOMA OF THE ANAL CANAL AND
ANAL MARGIN
St. Mark's Hospital, 1928–1956

Treatment	Anal canal		Anal margin	
Major excision	79	93·0%	9	31·0%
Local excision	6	7·0%	20	69·0%

There is no significant difference between the operability rates for the two sites, the figures being 85·9% for cancers of the anal canal and 78·4% for those of the anal margin. The method of removing the growth in operable cases, however, differs considerably in the two groups. Whereas only 6 of the 85 anal canal tumours (7·0%) were removed by local excision, no fewer than 69% of the 29 anal margin growths received a limited excision.

Prognosis (Table VI)

The crude five-year survival rate of all 157 cases of squamous cell carcinoma of the anal region seen at St. Mark's Hospital from 1928 to 1956 is 42·6%, which is slightly better than the crude five-year survival of all cases of adenocarcinoma of the rectum. Reports from the United States (Grinnell, 1954; Stearns, 1958) agree that the

TABLE VI.—SURVIVAL RATE OF SQUAMOUS CELL CARCINOMA OF
ANUS
St. Mark's Hospital, 1928–1956

Five-year survival rate:	Crude	=42·6% (rectal cancer=34·7%)
	Corrected	=50·1% (rectal cancer=41·8%)

	Anal canal	Anal margin
Five-year survival rate:		
Crude	42·4%	51·4%
Corrected	48·7%	60·8%

prognosis in anal canal and anal margin disease taken together is slightly better than rectal cancer. Unfortunately I cannot find any figures in the literature on the prognosis of the two sites taken separately.

If the five-year survival rate is broken down for site, that is into anal canal and anal margin tumours, the figures show that the prognosis of anal margin disease is more favourable than in anal canal cancer, the crude five-year survival rate for anal margin cancer being 51·4% and for anal canal cancer 42·4%. Moreover, this better five-year survival occurs despite the fact that most anal margin tumours were treated by local excision whereas the majority of anal canal cancers had a radical operation, with complete removal of the hæmorrhoidal lymphatic glands. In at least 75% of our cases of anal margin and anal canal cancer there was no treatment directed towards the inguinal gland method of spread either by surgery or radiotherapy. It is probable that the prognosis of anal cancer could be improved if a more radical approach to the inguinal gland spread could be devised.

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