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OBSERVATIONS ON BLADDER INVASION BY CERVICAL CANCER

DERK CRICHTON, D.PHIL., F.R.C.S. (EDIN.), F.R.C.O.G.* and TERENCE ROCKEY, M.B., B.S., D.OBST. R.C.O.G.
Department of Gynaecology, University of Natal

Bladder invasion by cervical cancer has received little attention in the recent British literature. Indeed only Dearing's[1] analysis of Stanley Way's results, and publications by Todd,[2] Strachan,[3] and Gemmell[4] deserve mention during the past 32 years.

Our experience in the treatment of more than 100 patients with cervical cancer a year** has impressed us sufficiently to submit a preliminary communication on this important subject.

RESUMÉ OF THE RELEVANT LITERATURE

Credit for first drawing attention to this subject is due to Williams[5] whose necropsy study of 78 cases of cervical cancer revealed bladder invasion in 56 with fistula formation in 29. More recent necropsy studies by Behney[6] and by Austen and Sala[7] have confirmed these findings — in their 2 series vesical fistulae were found in 22·3% and 30% of cases respectively.

From a clinical standpoint Ewing[8] stressed that the later stages of cervical cancer are typified by secondary invasion of neighbouring organs — particularly the bladder — with consequent ulceration, necrosis and fistula formation. There followed a masterly description of the typical cystoscopic findings in cervical cancer by Gemmell in 1928,[4] and subsequent publications by Graves, Kickham and Nathanson,[9] Todd,[2] and Dearing[1] have underlined the diagnostic and prognostic importance of cystoscopy.

Apart from carcinomatous invasion, however, surgery and, particularly, radiotherapy can produce serious bladder sequelae, and as late as 1929 the American College of Surgeons made the following statement after investigating 688 cases of cervical cancer: 'The danger of fistula formation is apparently increased by any method of treatment'.[10] Strachan,[3] however, came to the conclusion that in only a small proportion of cases could correctly applied radiotherapy be responsible for the formation of vesico-vaginal fistulae.

These radiation changes in the bladder were first described in detail by Dean in 1933,[11] and Colby[12] and Everett[13] subsequently found the incidence of severe bladder reactions to be 34·3% and 18% respectively among cured cases of cervical cancer. Everett *et al.*[14] and Kottmeier[15] agreed that there was a direct correlation between increasing dosage and severe post-radiation reaction; Everett *et al.*[14] found evidence of bladder disturbance in no less than 55% of their patients after radiotherapy.

* Professor and Head of the Division of Gynaecology at King Edward VIII Hospital, Durban.

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THE PRESENT STUDY

The case records of 150 patients with histologically proved carcinoma of the cervix who were admitted to the Department of Gynaecology of King Edward VIII Hospital (University of Natal), Durban, between August 1956 and August 1958, were examined.

Almost all these patients had had a full cystoscopic examination and had been 'staged' under anaesthesia by us, and the rest were examined by other senior members of the department. Radiotherapy, where used, followed the standard Manchester technique.

Every attempt was made to follow-up every patient at 1 month, at 3 months, and at 6-monthly intervals afterwards, but even so the follow-up rate has not been sufficiently high to assess the results of treatment with accuracy. This is true more especially of the earlier patients in this study. In any case, the period of follow-up is too short. It has been our experience, however, that the presence of a vesico-vaginal fistula is a potent factor in causing the return of treated patients, and we therefore believe that, unless moribund, the vast majority of patients with this complication have returned for treatment.

The cystoscopic appearances on the initial examination were graded into 4 main groups, based on the 6 types of change reported by Gemmell:[4]

Group O: In this group no significant abnormality was detected and the bladder was passed as normal.

Group A: In this group there were mainly circulatory changes such as hyperaemia or petechiae, which may be either local (trigonal) or general (cystitis), specific (bilharzia) or non-specific. Also in this group are included alterations in bladder shape due to extra-vesical pressure, usually resembling an accentuated uterine eminence. Both changes may exist together.

Group B: In this group were placed all cases where the bladder mucosa showed signs of oedema, either local (the transverse ridging of Gemmell), generalized, or diffuse. These changes were sometimes described as pseudo-trabeculation or cellule formation.

Group C: In this group were placed all cases where there was considered to be definite bladder-wall involvement by the growth.

For the purpose of this grouping (*i*) severe oedema in association with extra-vesical pressure in the bladder base and/or (*ii*) bullous oedema of the trigone, associated with impairment of mobility of the underlying tissues, were considered to be presumptive evidence of carcinomatous invasion. This impairment of mobility was assessed with the cystoscope in the bladder exploring against counter-pressure exerted by a finger in the anterior vaginal fornix.

Where doubt existed, the case was classified under group B.

Desquamation of the mucosa or actual malignant invasion by tumour tissue, or finally, the presence of a malignant fistula, were classed under group C.

RESULTS

One hundred and fifty patients with carcinoma of the cervix had cystoscopies performed before any form of treatment.

The cystoscopic findings were graded into the 4 groups described, and are recorded in Table I.

TABLE I. CYSTOSCOPIC FINDINGS IN 150 PATIENTS WITH CARCINOMA OF THE CERVIX

	Group O	*Group A*	*Group B*	*Group C*	*Total*
Number of patients	27	42	19	62	150
Percentage	18	28	12·7	41·3	100

A comparison between the clinical staging of the extent of the growths recorded before cystoscopy and the revised diagnoses after cystoscopy are recorded in Table II.

TABLE II. STAGING OF CASES BEFORE AND AFTER CYSTOSCOPY

	Stage I	*Stage II*	*Stage III*	*Stage IV*
Before cystoscopy ..	6	38	68	38
After cystoscopy ..	6	34	44	66
Error in diagnosis ..	0	4	24	0
Percentage error ..	0	10·5	35·3	0

Only 4 of the 66 stage IV carcinomas (6·1%) had no definite evidence of bladder involvement on cystoscopy.

Vesico-vaginal Fistulae

There were 22 vesico-vaginal fistulae in the series of 150 cases, an incidence of 14·7%. Of these, 16 had developed before admission or treatment, and 6 had

TABLE III. VESICO-VAGINAL FISTULA—22 CASES (14·7% OF TOTAL)

Mode of treatment	*No.*
Fistulae present before treatment:	
Palliative irradiation only	3
Deviation of urinary stream followed by radiotherapy	2
Deviation of urinary stream only	1
Beyond any form of treatment	10
Total	16
Fistula present after treatment:	
Radiotherapy alone	3
Radiotherapy followed by Wertheim hysterectomy ..	2
Wertheim hysterectomy only	1
Total	6

received some form of therapy. The findings are summarized in Table III.

In the 6 cases in which a vesico-vaginal fistula developed after treatment, this was shown at necropsy to be due to a persistence of the growth, and in no case could radiotherapy be shown to be responsible for the fistula.

All patients with a vesico-vaginal fistula were dead within a year of developing this complication except for 2 treated by deviation of the urinary stream (uretero-colic anastomosis), followed by radiotherapy. One patient was last heard of 2 years after completion of treatment and 1 was apparently well 6 months after treatment, after which contact with her was lost.

Twenty-nine of the 62 patients (48·4%) in group C (stage IV cervical cancer with definite bladder involvement) had a full course of radium and deep-X-ray therapy without a single case of radio-necrosis of the bladder being recorded.

Type of Growth and Bladder Involvement

In the 150 cases, there were 100 in which the growth was described as endophytic or ulcerative in type, and 50 in which the growth was exophytic. Of the 62 cases in

TABLE IV. INVOLVEMENT OF BLADDER WALL ACCORDING TO TYPE OF TUMOUR

Type of tumour	*Bladder wall*		*Total*
	Involved	*Not involved*	
Exophytic ..	13 (26%)	37	50 (100%)
Endophytic ..	49 (49%)	51	100 (100%)
Total ..	62	88	

group C, there were 13 with exophytic growths. This gives an incidence of exophytic growths of 33% in the whole series but only 20·9% in group C.

These findings have been recorded in Table IV.

On chi-square analysis, P is less than ·02, thus the frequency of bladder involvement was significantly higher with endophytic growths.

DISCUSSION

In this series the cystoscopic findings were abnormal in 82%. This emphasizes the importance of a full cystoscopic examination in every case of carcinoma of the cervix. We agree with the statement of Graves *et al.*[9] that 'cystoscopic examination may be just as important as pelvic and pathological examination'.

Its importance in diagnosis is shown in this series where 10·5% of stage II, and 35·3% of stage III carcinomas were placed in the wrong stage before cystoscopy, and it shows how local spread may be anterior towards the bladder before extensive parametrial involvement has occurred. On the other hand, extensive infiltration may occur without obvious bladder involvement — 6·1% of the stage IV carcinomas did not have definite bladder involvement on cystoscopy.

The importance of cystoscopy is appreciated all the more in view of the unreliability of other urological methods of investigation. Frequently, bladder involvement is asymptomatic and both examination of the urine and pyelography may reveal no significant abnormality.

Bladder biopsy was performed in a small number of these patients. The difficulty was to obtain an adequate specimen where there was no frank ulceration of the mucosa, and we were awaiting the arrival of a suitable type of biopsy forceps. A further method which is at present undergoing trial in this unit is the cytological examination of the centrifuged urinary deposit.

Thus, the diagnosis of bladder-wall involvement on cystoscopy is essentially a matter of experience in which correlation of the cystoscopic findings with the operative findings, the subsequent progress of the disease, and the

necropsy findings can best be made by the gynaecologist in charge of the case.

Our follow-up has not been long enough to make any firm statements regarding prognosis, but our initial impressions agree with those of Dearing,[1] Todd,[2] Graves *et al.*[9] and others who have all shown the grave prognosis of abnormal cystoscopic findings in association with cervical cancer. For instance, Dearing[1] found that 51% of patients with abnormal cystoscopic findings and a normal intravenous pyelogram had died within the first year.

The high percentage (14·7%) of vesico-vaginal fistulae found upon initial examination of our patients reflects the late stage at which our African patients seek treatment. By comparison, Graves *et al.*[9] found a 12·9% fistula rate in 425 cases, and Howes and Strauss[16] a 4% fistula rate, whereas Brack *et al.*[17] and Kottmeier[15] found a 5·4% and a 0·25% fistula rate, respectively, following irradiation.

Our results show that the complications of vesical involvement and vesical necrosis are more common with endophytic as opposed to exophytic cervical growths.

Most authorities agree with Strachan[3] and Todd[2] that, though radium necrosis does occur, persistent or recurrent carcinoma causes the majority of fistulae. This would appear to have been borne out by our figures, which also indicate that fistulae are more common among untreated as opposed to treated cases. From experience, even palliative radiotherapy offers the patient some measure of immunity from, or defers the development of, vesical fistula in the normal course of cervical cancer.

Differentiation of malignant from radiation fistulae is often difficult and may even be impossible without awaiting developments with the passage of time. True, radiation fistulae tend to occur in the mid-line just above the trigone, as stated by Graves *et al.*[9] and Dean,[11] whereas malignant fistula nearly always originates in the trigone, associated with more induration of the bladder base. The universally accepted method of distinguishing these fistulae by bladder biopsy is not infrequently misleading, in our experience.

The most effective method of palliation of our fistulae was diversion of the urinary stream followed by irradiation. Schewe and Sala[18] suggest that in this type of case 'the opportunity to render treatment is dictated by the status of the urinary tract rather than the status of the neoplasm'. They report 2 cases of skin ureterostomies with encouraging results.

Uretero-colic anastomosis in the presence of a damaged renal tract is a hazardous procedure and carries with it an appreciable mortality (1 of the 3 patients on which this operation was performed died shortly afterwards from a suppurative pyelonephritis), but the majority of our African patients refuse ileal bladders or skin ureterostomies, leaving only this alternative.

More recently, however, we have met with a greater measure of success with deviation of the urinary stream into ileal bladders or by performing skin ureterostomies, especially upon selected late cases.

CONCLUSION AND SUMMARY

1. Urethro-cystoscopy is of the utmost importance in the assessment, selection for treatment, and prognosis of all patients with cervical cancer, and this investigation is best done by a competent gynaecologist in charge of the case.

2. Endophytic growths are more likely to cause early bladder involvement than exophytic growths, and radium treatment to these is more likely to be followed by a fistula.

3. On the other hand, vesico-vaginal fistulae are seldom the result of radiation ; therefore this form of treatment is not contra-indicated by bladder involvement. Indeed, radio-therapy to carcinomatous extension from cervical cancer offers some measure of immunity from subsequent fistula formation — even if radiation is merely palliative.

4. In cases of malignant vesico-vaginal fistulae or severe urinary-tract involvement, diversion of the urinary stream by uretero-colic anastomosis, skin ureterostomy or ileal conduit, followed by a full course of irradiation, may offer the best palliative advantages in those cases which are not ideally suited to anterior exenteration.

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