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THE TREATMENT OF TUMORS OF THE BLADDER, PAST AND PRESENT*

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I can well remember my first recollection of studying bladder tumors. It was early in the 1930's and I was reviewing a small series of cases which had been operated on 5 years or longer by various methods in vogue at that time. To my consternation, I found that none of the infiltrating cancers of the bladder had survived more than 24 months. Time has appreciably changed this picture. At the present time, a fair number of infiltrating cancers of the bladder can be given a fairly good prognosis if diagnosis and treatment has not been delayed too long. I believe this improvement in survival statistics is due, first, to a better understanding of all of the remifications of the disease and, second, of course, to better surgical therapy.

As long as 5 years ago I predicted that segmental resection and simple cystectomy might fall into the discard as methods of treating cancer of the bladder. Jewett,[1] in 1956, seems to have arrived at very nearly this same conclusion. Our follow-up of radical surgery as presented in 1954[2] seems also to bear out these conclusions.

We stage tumors according to Marshall's modification of Jewett's original classification[3] (Fig. 1):

Stage O, confined to mucosa. Stage A, not below the submucosa. Stage B_1, not deeper than the superficial half of

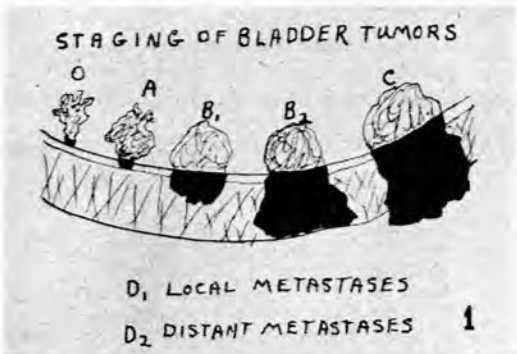

Fig. 1. Schematic drawing showing staging of tumors by depth of extension (see text).

the muscularis. Stage B_2, involving all of the muscularis. Stage C, extension to the perivesical fat. Stage D_1, local metastases. Stage D_2, distant metastases.

Accurate staging and grading of tumors both clinically and histologically is possible by our present methods.

* Paper read by Dr. Milner at 2nd Congress of Urological Association of South Africa (M.A.S.A.), Cape Town, July 1958.

Bimanual examinations under anesthesia are always carried out and great care is exercised in selecting the proper pieces

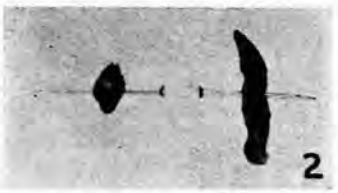

Fig. 2. Method of marking tissue to ensure sections cut in proper plane.

of tissue for study. They must be pieces taken from deep in the bladder wall and will invariably show bladder muscle. These special pieces are pinned with an ordinary pin so that they may be mounted in the paraffin block in such a way that perpendicular sections may be made through the tumor

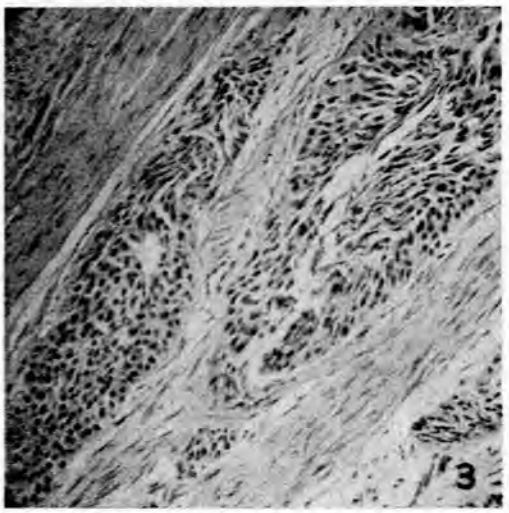

Fig. 3. Microscopic section of biopsy showing infiltration of muscle wall with bladder tumor.

(Fig. 2). Figure 3 shows a microscopic section of a typical biopsy showing tumor invading the muscularis. I have conclusively proved that adequate and accurate biopsies can be made transurethrally.[4]

We grade tumors according to the method used by the Army Institute of Pathology, namely, grades I, II, III and IV. Grade I is not malignant except as it has a tendency to recur. It is very interesting to note that at present the operator and the pathologist are over 90% accurate in their staging and grading of tumor, although it is done individually in

each case without reference to each other until the decision has been made. This would seem to indicate that our methods, clinical on one hand and microscopic on the other, must be fairly accurate. I feel equally certain that only by accurate staging and grading of tumors can one predict what the patient's clinical course is going to be.

I feel that transurethral surgery is the treatment of choice for most bladder tumors. The tumors which have not gone beyond the bladder wall can usually be adequately controlled by this method, and those which have gone further do not respond well to more radical types of surgery, namely, simple cystectomy or segmental resection. No pre-operative medication is employed and a spinal anesthesia is used in almost every case. Pontocaine in glucose is the one used most commonly, 10 mg. of Pontocaine in 10% glucose solution.

The technique of operation consists of removing all of the tumor if possible. Muscle layer is readily recognized by its fibrous appearance. If the tumor extends more deeply than it is possible to resect, then radon seeds are implanted at 1 cm. intervals after careful mapping. Obviously stage O, A and B_1 tumors can be resected cleanly. Interstitial radiation can be carried out more accurately in the distended bladder cystoscopically than in the bladder which is open. Care must be exercised after radiation to keep the bladder distended with 1 oz. of water at all times until the catheter is removed. This prevents the painful bladder associated with radiation in a collapsed bladder where the good side of the bladder has been in contact with the radiated area. In our clinic, we rarely see a painful bladder following interstitial radiation.

ANALYSIS OF CASES

In this paper I shall present, largely for comparison, cases treated by all methods. This report is based upon 679 cases of bladder tumors all operated upon more than 5 years ago (Table I). 627 cases, or 92·4%, have been accurately

TABLE I. CASES OF BLADDER TUMORS REVIEWED

Alive	
Resection	86
Resection and Radon	10
Segmental Resection	2
Cystectomy	3
Papillomas, Resection	75
Dead	
Resection	224
Deep Therapy	6
Papillomas, Resection	56
Resection and Radon	107
Cystectomy	34
Suprapubic Fulguration	33
No Therapy	9
Cystoscopic Fulguration	8
Hemicystectomy	26
Total	679

52 cases (7·6%) not followed
627 cases (92·4%) followed

followed-up to the reporting period and 52 cases, or 7·6%, have not had complete follow-ups, though many of these have been followed for 2 or more years.

131 cases, or 19·2%, were grade-I carcinoma or papillomas. 548 cases or 80·8% were cancers. In the early 1930s suprapubic cystotomy and fulguration of the tumor was a common form of therapy. I do not believe any tumor measuring more than 0·5 cm. should be fulgurated. They should be resected cleanly.

Segmental resections and uretero-sigmoidal anastomosis with or without cystectomy are still being done where it is impossible to offer the patient any chance with conservative methods.

The morbidity of conservative surgery is low. The average patient who has resection with or without radon seed implantation stays in the hospital about 4 or 5 days. Segmental resections require about 14 days' hospitalization and cystectomies and transplants take about 3 weeks.

Operative mortality is lower in resection than in open surgery (Table II). The operative mortality in cystotomy and fulguration was 21%. This was years ago, of course,

TABLE II. OPERATIVE MORTALITY RATE

Procedure	*Number of Cases*	*Number of Deaths*	*Per cent*
Cystotomy and fulguration	33	7	21·2
Segmental resection	28	1	3·5
Uretero-intestinal anastomosis and cystectomy	37	7	18·9
Operative mortality for open surgery, 15·3%.			
Transurethral resection	441	2	·4
Transurethral resection and radon	117	1	·8
Cystoscopic fulguration	8	None	None
Operative mortality for conservative surgery, 0·5%.			

and probably not a fair figure in comparison with present-day statistics.

Segmental resection showed a 3·5% mortality and uretero-intestinal anastomosis and total cystectomy showed an operative mortality of 19%. Transurethral resection had an operative mortality of 0·4% and with radon seed implantantion only 0·8. Cystoscopic fulguration showed no mortality but the number of cases was statistically insignificant.

The age incidence of these cases was rather interesting. Four cases were less than 30 years of age. The majority of the cases fell in the decades from 50 to 80 (Table III). There were

TABLE III. AGE INCIDENCE . 679 CASES OF BLADDER TUMOR

Age in Years	*Number of Cases*
20 to 30	4
30 to 40	8
40 to 50	52
50 to 60	165
60 to 70	249
70 to 80	139
80 and over	39
No age given	23

TABLE IV. SEX INCIDENCE. 679 CASES OF BLADDER TUMOR TREATED BY ALL METHODS

Type of Treatment	*Males*	*Females*
Not operated on	4	2
Cystoscopic fulguration	4	4
Transurethral resection	327	114
Transurethral resection and radon seed implantation	78	39
Cystotomy and fulguration	30	3
Cystectomy and transplantation of ureters	28	9
Segmental resection	10	18
Total	481	189

Sex not stated—9.

39 cases over 80 years of age. Nine cases were not operated upon; they either refused operation or were moribund on admission. 481 of the cases were males and 189 females; in 9 the sex was not recorded (Table IV).

Deep therapy was employed in 6 cases. Of these, 4 died within the first year. One survived 5 years and died without bladder disease but this was a case of multiple papillomatosis treated to reduce the frequency of recurrences. In most of these cases transurethral biopsies were performed, but they were old cases and none were graded or staged.

Most of the cases treated by cystotomy and fulguration

TABLE V. 33 CASES TREATED BY CYSTOTOMY AND FULGURATION

Years	Alive		Dead		Not followed	
	Without Tumor	With Tumor	Without Tumor	With Tumor	Without Tumor	With Tumor
1	...	...	...	25	...	...
2	...	...	...	1	...	...
3	...	...	...	1	...	...
8	...	...	1	1	...	...
9	...	...	...	1	...	...
12	...	...	1	...	...	...
17	...	...	1	...	...	...
27	1	...	...	...	...	...
Total ..	1	...	3	29	...	...

Depth of extension classification—B_1,2; B_2,3; C,2;D_1, 3; D_2,1; not classified, 21.
Grade—II,1; III,2; IV,1; not graded, 28.

(Table V) died of their tumors in the first year. Hence my pessimistic attitude concerning this type of therapy.

Of the 31 cases (Table VI) treated by segmental resection

TABLE VI. 31 CASES OF INFILTRATING CANCER TREATED BY SEGMENTAL RESECTION

Years	Alive		Dead		Not followed	
	Without Tumor	With Tumor	Without Tumor	With Tumor	Without Tumor	With Tumor
1	...	...	...	8	...	2
2	...	...	...	2	...	...
3	...	...	...	3	...	...
4	...	...	...	2	...	...
5	...	...	...	1*	...	...
6	...	...	...	3	...	...
10	...	...	2	...	...	...
11	...	...	...	1*	...	...
13	...	...	1	...	...	...
14	...	...	1	...	...	...
16	...	...	...	1*	...	...
17	1†	...	...	...	...	...
Total ..	1	...	4	21	...	2

*Multiple recurrences.
† Cured by resection, no tumor found at resection.
Operative mortality 1.
Depth of extension classification—A,2; B_1,12; B_2,11; C,1; D_1,2; D_2,2.
Grade—II,4; III,15; IV,8; not graded, 1.

(all infiltrating cancers, of high grade for the most part) 5, or 16·1%, have apparently been cured. One of these, however, was cured by resection (no tumor was found by serial sections in the bladder removed). 83·9% of these patients have died of their disease although 6 of this group survived 5 years or longer, the 5-year survival being roughly 35%.

Uretero-sigmoidal anastomosis and cystectomy was used in 37 cases of this group (Table VII). These cases were

TABLE VII. 37 CASES TREATED BY CYSTECTOMY WITH OR WITHOUT TRANSPLANTATION OF URETERS

Years	Alive		Dead		Not followed	
	Without Tumor	With Tumor	Without Tumor	With Tumor	Without Tumor	With Tumor
1	...	...	1	22	...	...
2	...	...	...	6	...	...
3	...	...	...	1	...	...
4	...	...	1	1	...	...
5	...	...	...	1*	...	...
6	...	...	...	...	...	...
7	...	...	...	...	...	...
8	1	...	...	...	...	...
10	...	...	1	...	...	...
11	1	...	...	...	...	...
13	1	...	...	...	...	...
Total ..	3	...	3	31	...	...

* Treated 9 years for carcinoma of bladder.
Operative mortality 7 cases.
Depth of extension classification—B_1,7; B_2,14; C,8; D_1,8.
Grade—II,2; III,20; IV,14; not graded, 1.

all bad tumors in which nothing else could be offered and this undoubtedly colors the statistics. Only 6 cases have apparently had their disease eradicated, a percentage of 16·2. Only 5 patients, or 13·5%, survived 5 years or longer. Of the 37 patients 31 died of their disease.

Transurethral resection with or without radon-seed implantation was used in 558 cases. Of this group, 131 cases

TABLE VIII. 131 CASES PAPILLOMAS OF BLADDER TREATED BY TRANSURETHRAL RESECTION ALONE

Years	Alive		Dead		Not followed	
	Without Tumor	With Tumor	Without Tumor	With Tumor	Without Tumor	With Tumor
1	...	...	12	3	10	...
2	...	...	10	...	4	...
3	...	...	2	...	...	...
4	...	...	4	...	1	...
5	5	...	9	...	1	...
6	12	...	2	...	2	...
7	4	...	6	...	1	...
8	3	...	2	...	...	...
9	1	...	2	...	...	...
10	3	...	1	...	4	...
11	5	...	...	...	3	...
12	6	...	3	...	...	...
13	2	...	...	...	...	...
14	1	...	...	...	...	...
15	4	...	...	...	...	...
16	2	...	...	...	...	...
18	1	...	...	...	...	...
Total ..	49	...	53	3	26	...

Depth of extension classification—O,81; A,50. Grade—I,131.

were papillomas (Table VIII) and will not be discussed further except to say that the poorest follow-up was in this group, which would indicate the necessity of telling these people the nature of their disease. The 5-year survival rate is 64% in this group and the probable cure rate approximately 100%, and the only problem is that of recurrence in new areas. Deep X-ray has proved effective in controlling recurrences where they are too frequent and multiple in character.

310 cases of cancer of the bladder were treated by transurethral resection alone (Table IX). This group included not only cases which were thought to be curable by this method but

TABLE IX. 310 CASES OF CANCER OF THE BLADDER TREATED BY TRANSURETHRAL RESECTION ALONE

Years	Alive		Dead		Not followed	
	Without Tumor	With Tumor	Without Tumor	With Tumor	Without Tumor	With Tumor
1	...	...	8	112	1	4
2	...	...	6	16	5	...
3	...	...	6	6	2	...
4	...	...	8	6	1	...
5	3	...	8	3*	...	...
6	7	...	8	1*	1	...
7	8	...	7	...	4	...
8	5	...	3	1	3	...
9	7	...	4	1	...	...
10	12	1	2	2	1	...
11	5	...	3	...	...	...
12	2	...	3	2	...	...
13	3	...	2	1	1	...
14	2	1	3	...	...	...
15	1	...	...	...	...	...
16	3	...	1	...	...	...
17	...	...	...	...	...	...
18	1	...	...	...	...	...
19	...	...	...	...	...	...
20	1	...	...	...	...	...
21	1	...	...	...	...	...
22	...	...	1	...	...	...
Total	61	2	73	151	19	4

* 2 cases died of metastases with normal bladders.

Depth of extension classification—O,6; A_1,93; B_1,102; B_2,72; C,9; D_1,24; D_2,2; not staged, 2.

Grade—II,161; III,114; IV,27; not graded, 8.

also some which were treated largely for palliation without hope of cure at the time of operation. Of this group, 154 cases, or roughly 50%, would seem to have had their disease eradicated. 128 cases, or 41·2% survived 5 years or longer. It will be noted that 209 of these tumors were B_1 or greater and almost half of them were Grade III or greater.

117 cases (Table X) were treated by transurethral resection and radon-seed implantation. These were cases which involved the muscularis with only one exception, that of a Stage A. Most of these tumors were of high-grade malignancy. These are the tumors in which the expected salvage rate is poor at the time the patient first visits the office. 26 cases or 22·2% have survived 5 years or longer. According to Marshall's statistics, 47 of these patients probably had metastases when first seen.

TABLE X. 117 CASES OF INFILTRATING CANCER TREATED BY TRANSURETHRAL RESECTION AND RADON SEED IMPLANTATION

Years	Alive		Dead		Not followed	
	Without Tumor	With Tumor	Without Tumor	With Tumor	Without Tumor	With Tumor
1	...	...	...	55	...	1
2	...	...	1	10	...	...
3	...	...	3	13*	...	...
4	...	...	2	6†	...	...
5	1	...	1	7‡	...	...
6	1	...	...	1	...	...
7	...	...	2	1¶	...	...
8	...	...	1	1	...	...
9	1	...	1	...	...	...
10	...	1	...	...	...	...
11	...	...	1	1	...	...
13	1	...	...	...	1	...
14	1	...	...	...	...	...
16	1	...	...	...	...	...
21	...	1	...	...	...	...
Total	6	2	12	95	1	1

* 1 case malignant melanoma. † 1 case metastases but negative bladder.

‡ 1 case cystectomy after 5 years. ¶ 1 case spindle-cell carcinoma following radon.

Depth of extension classification—A,1; B_1,41; B_2,51; C,9; D_1,10; D_2,2; not staged, 3.

Grade—II,24; III,60; IV,17; not graded, 16.

Table XI shows a previous study of 280 cases of bladder cancer treated by conservative methods. This chart showing the percentage of possible eradication of disease would indicate that transurethral surgery more closely approximates the possible cure rate as set up by Jewett when he first discussed the staging of bladder cancer.

TABLE XI. SURVIVAL RATE IN CONSERVATIVE SURGERY ON 280 CASES GRADED AS TO DEPTH OF EXTENSION

Years	A		B_1		B_2		C		D_1		D_2	
	O	X	O	X	O	X	O	X	O	X	O	X
1	5	4	10	18	5	50	...	10	...	28	...	1
2	4	...	3	5	2	9	...	3	...	2	...	...
3	2	...	5	4	...	2	...	...	...	...	...	...
4	3	4	4	2	...	3	...	...	...	...	...	...
5	1	...	1	3	...	1	...	...	...	1	...	1
6	7	...	8	1	3	...	...	...	...	...	...	...
7	4	...	12	2	3	...	...	...	...	...	...	...
8	4	8	3	...	1	...	...	...	...	...	...	...
9	1	1	1	1	1	...	...	...	...	...	...	...
10	4	...	1	...	3	...	...	...	...	1	...	...
11	...	...	1	...	...	1	...	...	...	...	...	...
12	2	...	2	...	1	...	...	...	...	...	...	...
13	1	...	...	1	...	...	...	...	...	...	...	...
14	...	...	...	...	1	...	...	...	...	...	...	...
15	...	...	...	1	...	...	...	...	...	...	...	...
16	2	...	...	...	...	...	...	...	...	...	...	...
17	...	...	...	...	...	...	1	...	...	...	...	...
Total	40	17	51	38	20	66	1	13	...	32	...	2
Possible eradication of disease	70%		57·3%		23·2%		7·1%					

X—With Tumor. O—Without Tumor.

All cases classified as to extension.

Operative mortality nil.

All cases treated by transurethral resection with or without radon seed implantation.

SUMMARY AND CONCLUSIONS

1. 679 cases of bladder tumors have been studied and analyzed. These cases are all 5 years or more post-operative.

2. Great difficulty was encountered in obtaining a 92·4% accurate follow-up. It would seem that a more accurate follow-up is possible if the patient is truly appraised of his condition.

3. A careful study of the foregoing statistics would strongly suggest that transurethral resection with or without radon-seed implantation offers a better chance of 5-year survival than other more radical types of surgery in tumors which have not penetrated the bladder wall.

4. Stage C and D tumors should be treated by the method which will give the patient his greatest palliation.

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