THE SURGICAL TREATMENT OF CARCINOMA OF THE BLADDER

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It would seem reasonable to assume that more patients with vesical cancer would be permanently cured of their disease today if each bladder containing a tumor were completely removed as soon as the diagnosis is made. The sacrifice of the bladder however is an exorbitant price to pay in the case in which cure can also be obtained without cystectomy. But an accurate discrimination between suitability for conservative treatment and unsuitability demands a thorough working knowledge of the gross and microscopic pathology of vesical cancer and its protean clinical manifestations. At the two ends of the spectrum of this disease the choice of treatment may be simple, but towards the center, it becomes increasingly difficult to steer a course between what may prove excessively radical on the one hand and ineffectually conservative on the other.

At the outset it is important to know whether the complete removal or destruction of the primary local growth can be reasonably expected to result in cure. The extent to which it can is called the potential curability of the tumor. If potential curability is high, the aim should be to rid the patient of his disease and salvage the bladder if possible; if low, it should be primarily concerned with keeping him comfortable.

Potential curability, however, is not always easy to establish, although it has been the object of intensive search for more than 40 years. Geraghty (1915) demonstrated that infiltration of the bladder wall impaired the prognosis, and Broders (1922) showed that the prognosis was worse when the grade of malignancy was high. This, however, was found subsequently not to be consistently true, and, in 1936, the Carcinoma Registry of the American Urological Association reported, after a study of 1224 specimens, that it was impracticable to segregate bladder tumors into definite groups corresponding to their cell types. By combining the best features of Geraghty's and of Broders' classifications, in 1940 the Armed Forces Institute of Pathology (Dean and associates, 1954) developed a microscopic classification that has proved reliable for predicting the collective prognosis for each group of tumors.

Between 1944 and 1951 an exhaustive pathological and clinical study was undertaken at the Johns Hopkins Hospital to determine whether it is possible to classify each individual case in such a way as to establish potential curability and therefore the outlook for that particular patient. This study, based on a series of 206 cases, showed that classification according to the degree of cellular differentiation (or grade of malignancy) alone was accurate in only 50 per cent of the group. Moreover, in 97 autopsy cases papillary and epidermoid carcinoma were almost equally represented (table 1). When poorly differentiated the papillary tumors had metastasized in 33 per cent, the epidermoid in 67 per cent, and the undifferentiated tumors in 83 per cent of the cases. As in the case of other

classifications, this segregation roughly demonstrated only the potential curability of the group but not of the individual case. It did not reveal which tumors in each group had, and which had not, metastasized.

In 107 autopsy cases the depth of infiltration of the bladder wall was correlated with the presence of metastasis and local extension (table 2). From this study one may conclude that the incidence of metastasis is greatest when the penetration is deepest. Although the ability of the tumor to invade vascular channels depends on its malignancy, the presence or absence of such invasion in the case of a tumor of known malignancy is governed largely by accident.

TABLE 1

	Primary Tumor		Metastases	
Papillary carcinoma......................	40		12	
Poorly differentiated.....:..........		18		6	33%
Epidermoid carcinoma..................	39		22	
Poorly differentiated...........:........		24		16	67%
Undifferentiated carcinoma...............	18		15		83%
Total...............................	97		49	

Jewett, H. J., in chapter on Tumors of Bladder, Meredith Campbell's Urology; Philadelphia, W. B. Saunders Company, 1955.

TABLE 2. *Relation of curability to depth of infiltration in 107 autopsy cases*

	Infiltrating Carcinoma of Bladder		
	Group A (Submucosa)	Group B (Musculature)	Group C (Perivesical fat)
Number of cases.................................	3	15	89
Metastases..	0	1	52
Perivesical lymphatic invasion only...............	0	1	6
Perivesical fixation only..........................	0	0	8
Potentially curable...............................	3	13	23

TABLE 3. *Histologic classification of fourteen tumors in group B*

	Primary Tumor	Metastases
Papillary carcinoma............................	10	1
Epidermoid carcinoma..........................	4	0
Undifferentiated carcinoma......................	0	0

TABLE 4. *Histologic classification of eighty-one tumors in group C*

	Primary Tumor	Metastases
Papillary carcinoma............................	28	11
Epidermoid carcinoma..........................	35	22
Undifferentiated carcinoma......................	18	15

Since tumors deep in the bladder wall are larger, and the vascular channels in the deeper layers are larger and more numerous, the opportunity for vascular invasion and metastasis is greater in this group.

The correlation of the histopathology of these infiltrating tumors with the depth to which they had penetrated the bladder wall showed that, with the exception of undifferentiated carcinoma, tumors of similar types were present in both the superficially infiltrating and the deeply infiltrating groups. Yet only one tumor in group B, a papillary carcinoma, had metastasized (table 3), as compared with 48 of 81 classified tumors in group C (table 4). Although undifferentiated carcinoma did not occur in group B in this small series of autopsy cases, it has been found in both group A and group B in a larger clinical series.

From this comparison one may conclude that cellular appearance alone indicates neither the presence nor the absence of metastasis or local extension, but only, in a general way, the "speed" of the tumor. Nevertheless its grade of malignancy, as a measure of its "speed," aids us in assessing its lethal potential. The depth of infiltration, however, governs to a great extent potential curability.

TABLE 5. *Relation of depth of infiltration of carcinoma of bladder to five-year survival rate after complete extirpation*

Depth of Infiltration	No. of Patients	No. Living 5–14 Yr. Without Tumor
Submucosal (group A)	14	10
Superficial muscular (group B₁)*	5	4
Total superficial infiltration	19	14
Deep muscular (group B₂)†	13	1
Perivesical (group C)	48	1
Total deep infiltration	61	2

* Group B₁ represents infiltration less than halfway through the muscularis.

† Group B₂ represents infiltration halfway or more through the muscularis.

TABLE 6

Bimanual Examination	Depth of Infiltration	Prospect for Cure
No thickening; no mass	Submucosal or superficial muscular (see biopsy)	Good
Thickening; no mass	Submucosal or superficial muscular (see biopsy)	Good
Mass, rubbery consistency, movable. Lateral ligaments negative	Deep muscular or perivesical (if not large papilloma; see biopsy)	Poor
Mass, stony consistency, movable. Lateral ligaments negative	Perivesical	Poor
Mass, stony consistency, movable. Ligament thickened and indurated	Perivesical	Very poor
Mass, stony consistency, fixed	Perivesical	Very poor

Jewett, H. J., in chapter on Neoplasms of Bladder, The Cyclopedia of Medicine, Surgery, Specialties; Philadelphia, F. A. Davis Company, 1950.

TABLE 7. *Classification of primary tumors of the urinary bladder*

Level of Bladder Wall	Maximum Depth of Infiltration (Stage)	Histologic Pattern							
		Grade of malignancy						Adeno-carcinoma	Miscel-laneous
		Low grade (1–2)		High grade (3–4)					
		Trans. cell (pap-illary)	Epidermoid (squamous)	Trans. cell	Epiderm.	Undiff. (ana-plastic)			
Mucosa	O								
Submucosa	A								
Superficial muscle	B₁								
Deep muscle	B₂								
Perivesical fat	C								

In general, the higher the grade of malignancy the faster the tumor penetrates the bladder wall, but at any given moment one cannot predict from grade alone just how far penetration has progressed.

Since the first observation in 1944[1] that the incidence of metastasis was highest when the depth of penetration was greatest, it was soon suspected, in 1947,[2] from an analysis of cystectomy cases, that the halfway level within the muscularis was the approximate point in the course of infiltration at which curability abruptly diminished. This suspicion was confirmed in 1951[3] by an analysis of 80 clinical cases (table 5), and subsequently by a number of independent observers.

This conclusion, based on a statistical analysis of pathological and clinical material, was never intended to imply that intramural or even extravesical metastasis cannot occur until infiltration is well along. Such a concept would be naive since it is well known that metastasis can occur at any stage of infiltration, and from the implication of 1 reported case, before infiltration has even begun.[4] Nevertheless the likelihood of metastasis is much less and the outlook much better when the infiltration has not reached the halfway level within the muscularis. Otherwise not nearly so many cases would be cured by conservative procedures.

To disregard any ascertainable characteristics of the primary tumor that might help one to predict the existence or non-existence of extravesical dissemination will needlessly reduce one's ability to estimate potential curability. Unless potential curability, or lack of it, can be fairly accurately established, the report of survival rates following treatment will not bear critical analysis. It is largely the disregard of comparable stages of infiltration that has made it impossible to evaluate and compare in so many instances the reported results of different methods of treatment.

At this juncture it should be emphasized that the preoperative segregation

[1] Jewett, H. J. and Strong, G. H.: J. Urol., 55: 366–372, 1946.
[2] Jewett, H. J. and Lewis, E. L.: J. Urol., 48: 107–112, 1948.
[3] Jewett, H. J.: J. Urol., 67: 672–676, 1952.
[4] Dean, A. L.: In Textbook of Surgery, edited by Frederick Christopher, 5th ed., p. 1281. Philadelphia: W. B. Saunders Co., 1949.

TABLE 8. *Results of surgical treatment for infiltrating carcinoma at Brady Urological Institute, Johns Hopkins Hospital, to October 1951*

(Among the cases showing deep infiltration, stage C was reached by 68 per cent of those treated by segmental resection, and by 88 per cent of those subjected to cystectomy.)

Depth of Infiltration	Segmental Resection			Simple Cystectomy		
	Lived 5 years or more without tumor	Died with tumor	Died without tumor in less than 5 years	Lived 5 years or more without tumor	Died with tumor	Died without tumor in less than 5 years
Superficial...	16/23, 70%	6/23, 26%	1/23, 4%	5/10, 50%	3/10, 30%	2/10, 20%
Deep........	4/48, 8.3%	41/48, 85.4%	3/48, 6.2%	4/44, 9%	32/44, 73%	8/44, 18% (6/44, 14% died of kidney complications)

TABLE 9. *Five-year survival rates after surgical treatment of infiltrating carcinoma*

(Milner's cases, presumed cured, were not all followed 5 years. Whitmore's and Marshall's cases of radical cystectomy were followed 4 years.)

Depth of Infiltration	Electro-excision	Segmental Resection	Simple Cystectomy	Radical Cystectomy
Superficial (stage O, A, B_1)	82.6% (low grade) (A), Nichols 76.5% (high grade) (A), Nichols 70% (A), Milner 57% (B_1), Milner 56% (B_1), Flocks	62.5%, Marshall 70%, B.U.I.	36.8%, Brice ('56) 50%, B.U.I.	39% (4 years), Whitmore and Marshall
Deep (stage B_2, C, D)	15% (includes B_1), Nichols 23% (B_2), Milner 3% (B_2), Flocks 7% (C), Milner	22%, Marshall 8.3%, B.U.I.	10.9%, Brice 9%, B.U.I.	11% (4 years), Whitmore and Marshall

of tumors into those that are superficial and those that are deep is not only highly desirable but is actually possible in a high percentage of cases. Deep biopsy of the bladder wall beneath the presenting tumor is correlated with the findings on bimanual pelvic examination under completely relaxing anesthesia (table 6). Absence of palpable induration, in an area ordinarily accessible, together with a sprinkling of carcinoma cells only in the submucosa, or superficial muscle layer, means superficial invasion. Palpable induration remaining after deep electroexcision, with sections showing massive invasion of the muscle bundles, means deep infiltration.

Table 7 represents a classification that has been found useful in indicating the potential curability of an individual tumor, as well as its lethal capacity, since it combines stage of infiltration, histologic pattern, and degree of cellular

differentiation or grade of malignancy. Some authors add stage D to indicate the presence of known metastasis.

A conscientious attempt to use this classification will prove rewarding. It will enable one to avoid radical and mutilating surgery when it is unnecessary, to employ more effective instead of less effective measures when the tumor is deeper, and to compare intelligently the results of different kinds of treatment for tumors having roughly the same degree of potential curability.

In the consideration of treatment it is well to bear in mind three significant factors that may stand in the way of cure: 1) the limitations imposed by the tumor itself, 2) the limitations inherent in the particular procedure selected, and 3) the limitations resulting from one's method of application of the procedure.

Standardized therapy today is of three varieties: surgical excision, surgical diathermy, and radiation. This discussion is concerned with a comparison of the end results following all types of surgical treatment in the case of tumors in comparable stages of infiltration.

Table 8 represents the results of segmental resection in 71 cases and of simple cystectomy in 54 cases at the Johns Hopkins Hospital up to October 1951.[5] Seventy per cent of patients with tumors infiltrating up to the halfway level of the muscularis lived 5 to 14 years after partial cystectomy, as compared with 50 per cent after total cystectomy. In the deeply infiltrating group, 8.3 per cent of the patients survived 5 or more years after partial cystectomy, and 9 per cent after total cystectomy.

It has been suggested that improved methods of urinary diversion might increase to a considerable degree the survival rate after cystectomy. Since six of the 44 patients (14 per cent) with deep tumors in this series died of renal complications within five years, but without evidence of cancer, one might assume that if renal damage could have been prevented in these six patients, a total of 23 per cent instead of nine per cent might have been enabled to survive five years. Such an assumption, however, is purely conjectural and does not envisage the possibility that most if not all of these six patients, if spared early death from renal failure, might have died within five years of carcinoma.

Table 9 illustrates the survival rates reported by different authors using different excisional techniques for tumors classified in respect to depth of infiltration. The followup period was five years, with two exceptions. Some of Milner's cases were presumed cured in less than five years (1954), and the radical cystectomy cases of Whitmore and Marshall were followed only four years (1956). All of these figures are recent, having been submitted between 1952 and 1956. Some of Nichols' cases were treated through the opened bladder with the cutting loop (1956); the rest, along with those reported by Milner and by Flocks (1952), were subjected to transurethral resection.

A comparison of these figures suggests that the best results follow the simpler procedures, and in many situations this is true. It is not always true, however,

[5] Jewett, H. J.: Pennsylvania Med. J., **60**: 473–477, 1957.

since the extensive operations are more often used for cases that, because of total tumor mass, are obviously unsuitable for conservative treatment.

SUMMARY AND CONCLUSIONS

Carcinoma characteristically invades the bladder wall, and curability by any method of treatment decreases as infiltration increases. The extent of the infiltration should first be estimated as accurately as possible, so that the magnitude of the problem will be fully appreciated.

After careful preoperative classification it becomes much easier to select the procedure that is most ideally suited to the individual case.

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