

INFILTRATING CARCINOMA OF THE BLADDER: RELATION OF DEPTH OF PENETRATION OF THE BLADDER WALL TO INCIDENCE OF LOCAL EXTENSION AND METASTASES¹

HUGH J. JEWETT AND GEORGE H. STRONG

From the James Buchanan Brady Urological Institute, Johns Hopkins Hospital, Baltimore

During the last 25 years a variety of procedures for the treatment of infiltrating carcinoma of the bladder have been reported, and in general the results have been disappointing. There has been much diversity of opinion in regard to the best method of treatment, and this may be expected to continue until the efficacy of these different procedures can be accurately measured and compared. This, however, will never be possible unless metastasis and local, extravesical extension of the tumor can be excluded at the time treatment is commenced.

In order to determine the conditions under which local extension and metastasis occur, we found it necessary to make an exhaustive survey of autopsy material. We collected 127 cases of infiltrating tumor of the bladder upon which autopsies had been performed at the Johns Hopkins Hospital from October 1919 to March 1944, but were obliged to eliminate twenty because the pathological material was not suitable for our particular study.

We then undertook to determine, in these 107 autopsy cases, the relation of depth of penetration of the bladder wall to the incidence of (1) metastases, (2) lymphatic capillary invasion (incipient metastases), and (3) perivesical fixation.

First, we separated the cases into three groups according to depth of penetration of the bladder wall. Group A comprised those in which tumor cells were confined to the submucosa (fig. 1). Group B consisted of those in which infiltration had extended into, but not through the muscularis (fig. 2). Group C included all cases in which tumor cells had extended completely through the muscle coat (fig. 3). In all cases we satisfied ourselves that the sections had been taken through the bladder wall at the site of deepest penetration by the tumor. Occasionally we had to cut new blocks, and all questionable cases were discarded.

We then determined, in each group, the number of cases with regional or distant metastases, the number showing perivesical lymphatic or vascular invasion only, and the number with perivesical fixation of the mass. In each group the percentage of cases without these evidences of tumor spread gives us our figure for potential curability (fig. 4):

Group A, submucosal infiltration, 100 per cent

Group B, muscular infiltration, 86.6 per cent

Group C, perivesical infiltration, 26 per cent

The small number of cases in Groups A and B probably is due to the fact that

¹ Read at annual meeting, American Association of Genito-Urinary Surgeons, Stockbridge, Mass., June 8, 1944.

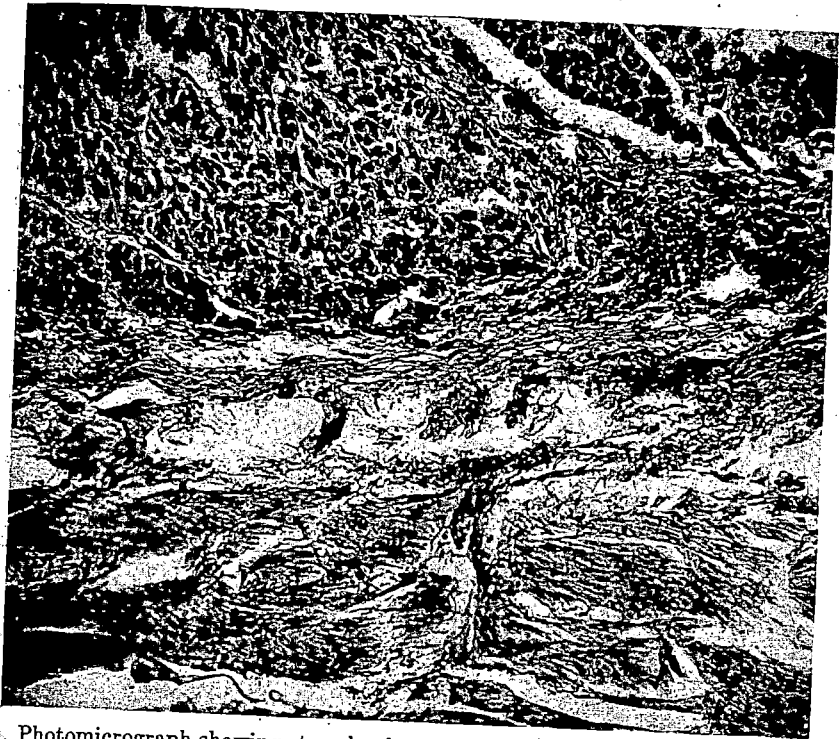


FIG. 1. Photomicrograph showing strands of carcinoma cells in submucosa of bladder. At no point has muscularis been invaded

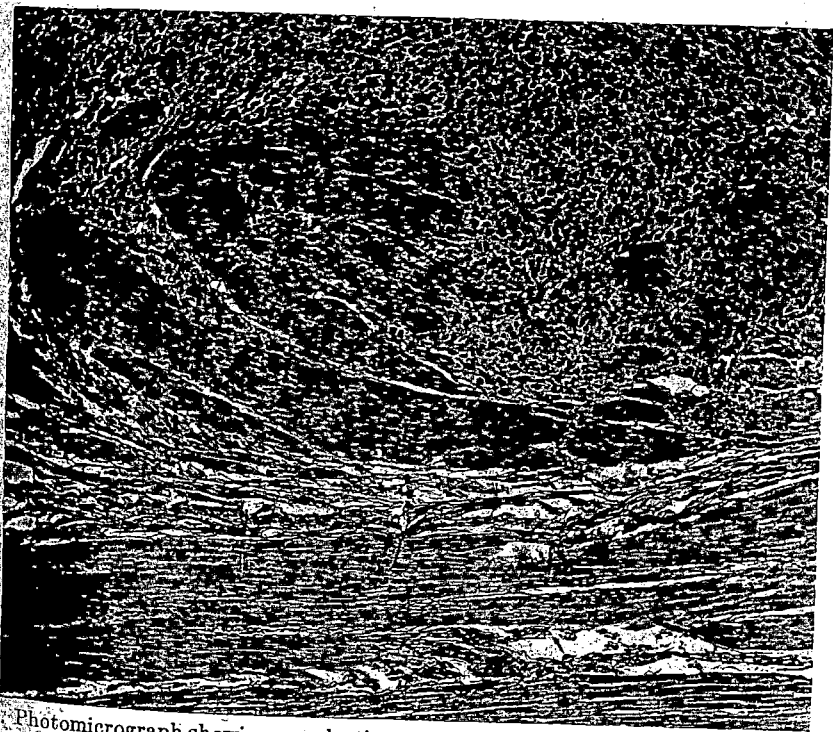


FIG. 2. Photomicrograph showing anaplastic carcinoma invading muscularis of bladder. It has not yet passed all the way through muscle coat



FIG. 3. Photomicrograph showing carcinoma extending all the way through muscularis, which it has largely replaced. Long, elliptical structure in center is last visible external muscle bundle. At right end of this, carcinoma cells can be seen swirling around its edge. External to this there is only perivesical connective tissue.




Group A	Group B	Group C
		
Submucosal infiltration	Muscular infiltration	Perivesical infiltration
No. of cases 3	No. of cases 15	No. of cases 89
Metastases 0	Metastases 1	Metastases 52
Perivesical lymph. only 0	Perivesical lymph. only 1	Perivesical lymph. only 6
Perivesical fixation only 0	Perivesical fixation only 0	Perivesical fixation only 8
Potentially curable 100%	Potentially curable 86.6%	Potentially curable 21%

FIG. 4. Infiltrating carcinoma of bladder. Relation of curability to depth of infiltration in 107 autopsy cases. Schematic drawing showing relation of potential curability to depth of infiltration. Figure for potential curability in each group represents exclusively percentage of cases without evidence of tumor spread.

autopsy cases for the most part represent late stages of the disease. By the term potential curability we mean to imply only a theoretical possibility based upon the gross and microscopic exclusion of all evidence of tumor spread, actual on

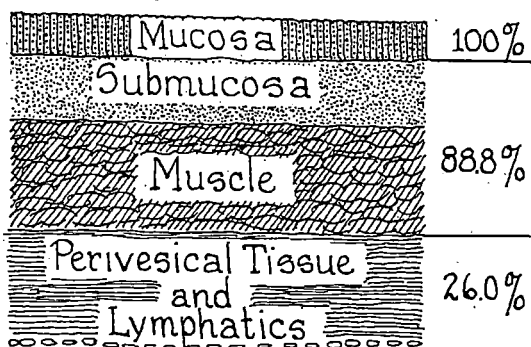


Fig. 5. Potential curability in carcinoma of bladder. Schematic drawing of layers of bladder wall. When basement membrane upon which mucosa rests is penetrated, tumor becomes infiltrating. It then proceeds through submucosa and muscularis. While it is still confined to these two layers, potential curability is high. When the perivesical (subfacial) layer is reached, curability drops sharply.



Fig. 6. Diagram of bladder wall showing size and distribution of lymphatics after injection. In superficial areas of bladder lymphatic collectors begin in submucosa as tiny cylinders. In this area they are much smaller and fewer than in deeper portions of bladder wall. (See Powell, Tracy O.: Studies in the Lymphatics of the Female Urinary Bladder. Surg. Gynec. & Obst., 78: 605-609, 1944.)

occupant beyond the confines of the bladder wall. The figures for each group may not represent an accurate absolute value, but the wide discrepancy between

the potential curability in Group B and that in Group C is statistically significant.²

In the majority of cases it would seem that the tumor does not metastasize until it has passed through the muscle layer (fig. 5). When the basement membrane has not been invaded the tumor is not infiltrating, and 100 per cent of these cases are theoretically curable. When invasion is limited to the area between basement membrane and external muscle fibers, 88.8 per cent are theoretically curable. But as soon as the tumor has reached the prevesical tissue, the incidence of curability drops sharply. Apparently, after breaking through the basement membrane, these tumors proceed through the bladder wall with varying rapidity, depending upon their different characteristics, and eventually reach the perivesical tissue. In many cases, before this perivesical layer is invaded a latent period exists during which potential curability is high. This is not surprising when one considers the variation in size and distribution of the lymphatics of the bladder wall, so beautifully demonstrated by Powell. As can be seen in his illustration (fig. 6), the lymphatics are larger and more numerous in the depths of the bladder wall, which may explain the higher incidence of metastases in Group C tumors.

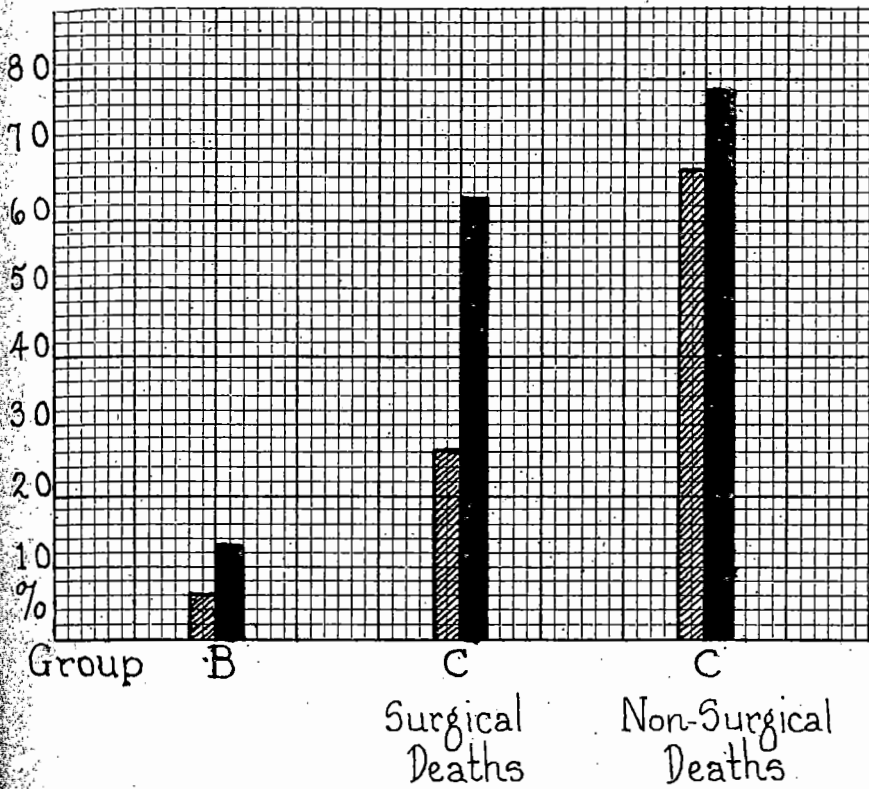
Of the 89 cases comprising Group C, regional or distant metastases were present in fifty-two. The regional lymph nodes were the site of metastases in 33 instances, the liver in twenty-six, the lungs in eighteen, and the vertebral column, including the sacrum and pelvis, in eleven. Other tissues were involved 20 times, but in only 7.7 per cent of the cases without involvement of lymph nodes, liver, lungs, or bones. In 36.5 per cent of the cases in which metastases were found, the regional lymph nodes were not involved.

In 26 per cent of 89 cases in which tumor cells were present in the perivesical tissue, metastases, lymphatic invasion, and fixation had not occurred. It, therefore, is evident that infiltration of the perivesical tissue and invasion of lymphatics are not necessarily simultaneous. Further evidence to support this was obtained by dividing Group C into one group of nineteen relatively early cases in which death occurred after operation undertaken as a means of cure, and into another group of 70 late cases in which death occurred after palliative treatment or no treatment at all.³ In the 19 cases of surgical deaths, metastases were present in only 26 per cent, whereas in the group of late cases, metastases were present in 67 per cent (fig. 7). Lymphatic invasion and fixation to neighboring structures, however, brought the theoretical incurability in the first group to 63 per cent, and in the second, to 78.5 per cent, which is very high when compared with the low figure of 13 per cent for Group B.

² It is possible that if serial sections had been cut through the bladder wall at the site of the tumor, a higher incidence of lymphatic invasion would have been observed. Similarly, if at autopsy a meticulous search for tumor cells had been made through all normal appearing regional lymph nodes, and elsewhere, a higher incidence of metastasis might have been found.

³ Urosepsis was said to have been the cause of death in 44 per cent of the 89 cases comprising Group C.

The lymphatics which drain the posterior bladder wall probably run a longer course before leaving the bladder than those which drain the other walls, as emphasized by Dr. George Gilbert Smith. It therefore seemed advisable to



← Metastases
 ← Metastases + Lymph invasion + Fixation.

FIG. 7. Showing incidence of metastases in Group B, in early Group C cases, and in late Group C cases. Chart also shows that incidence of microscopic invasion of perivesical lymphatics in early and late Group C cases is nearly the same.

Correlate the incidence of metastases with the location of the tumor among the cases of surgical and non-surgical deaths comprising Group C (fig. 8). In the Group consisting of surgical deaths, only 16 per cent of posterior wall tumors were associated with metastases, whereas 36 per cent of the tumors confined to one or

more of the other walls had metastasized. In the group comprising non-surgical deaths, location of the tumor was of no significance. Regardless of position, 67 per cent had metastasized.

These observations show the importance of the time factor in the development of metastases after infiltration has commenced, and the generally more favorable outlook enjoyed by patients with posterior wall tumors, possibly because a longer course may be pursued by the lymphatics of the posterior bladder wall.

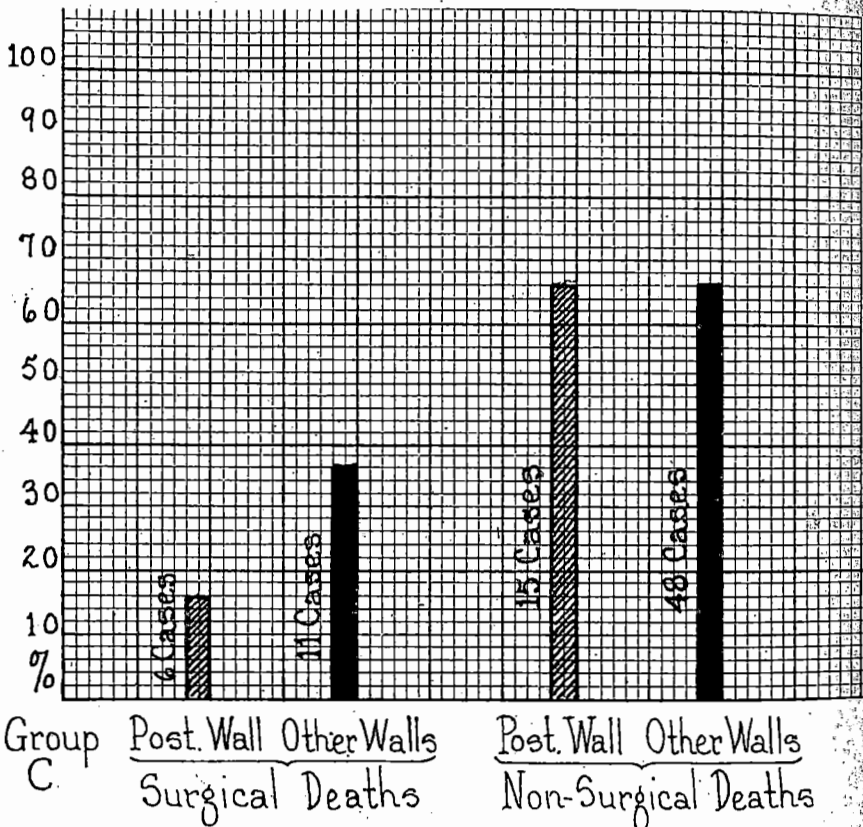


FIG. 8. Showing relatively low incidence of metastases in early Group C tumors of posterior wall, as compared with other walls. In late cases, location was of no significance.

SUMMARY AND CONCLUSIONS

The incidence of local extravescical extension and metastasis increases with the degree of penetration of the bladder wall, being low in the case of superficially infiltrating tumors, and high in the case of deeply infiltrating tumors.

The cardinal sites of metastasis are (1) regional lymph nodes, (2) liver, (3) lungs, and (4) vertebral column, including sacrum and pelvis.

The clinical determination of the depth of penetration of the bladder wall may provide the index of potential curability.