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**STAGING AND GRADING OF BLADDER CANCER**

**INTRODUCTION**

When a patient is found to have bladder cancer, his physician must learn many things about the patient and the cancer. Three important pieces of information about that individual's cancer are the TYPE, STAGE and GRADE. No decisions about treatment can be made until this information is estimated.

**TYPES OF BLADDER CANCER**

Bladder cancers are classified according to the type of cell that has become cancerous. About 90% of cancers of the bladder involve transitional cells. Transitional cells are merely the name of the usual cell that lines the bladder wall. Transitional cells are unique to the urinary tract and line the kidneys and ureters as well. Other types of cells that are found less frequently in bladder cancer include squamous cell cancers or adenocarcinomas. Transitional-cell cancers of the bladder can be further divided into 'papillary', 'solid' tumors and 'carcinoma-in-situ' (CIS).

Papillary, which means 'finger-like', are usually low grade. This means that they grow slowly. Papillary tumors also usually grow towards the inside of the bladder, not towards the muscle lining. Sometimes, particularly if untreated, papillary tumors will invade into the bladder muscle and then spread into the body. Papillary tumors occur more than twice as often as solid tumors. There may be one papillary tumor or several. Patients with tumors in multiple areas are more likely to have the cancer come back, or recur, after treatment. In general, papillary cancers of the bladder have a recurrence rate of up to 70%, meaning that even if all the cancer is removed, new cancers will develop in other parts of the bladder in 7 of 10 patients at a later time. These recurrences can occur at any time, but usually within two years.

Solid tumors are rarer but tend to be more aggressive, recur more often, and have a tendency to invade deeply into the bladder wall at an earlier stage.

Carcinoma in situ (CIS) is a unique situation. CIS is a very aggressive looking cancer, but involves only the inner lining of the bladder. It may occur diffusely throughout the bladder or in small areas. CIS does not look like a tumor, but more like a flat red area on the bladder wall. It is often associated with symptoms similar to a bladder infection, such as pain and or burning with urination and urinary frequency. CIS is associated with a high rate (more than 50%) of developing invasive, usually solid, bladder cancers within 5 years if not treated.

**STAGING BLADDER CANCER**

The STAGE is defined as the estimation of extent (size and location) of the cancer at the current time. More specifically, how extensive is the cancer within the bladder and if it has spread to tissues around the bladder, or to other parts of the body. The studies vary from patient to patient depending on various factors. The usual initial staging studies include the pathology report from the initial biopsy, the general physical examination and digital rectal examination, and, often, a CT scan of the pelvic area. On occasion, a CAT scan (computerized axial tomography) of the upper abdomen or MRI (magnetic resonance imaging) will be done of the pelvic and abdominal areas, and a chest X-ray. The stage of the cancer is the most important deciding factor in which treatment will be used.

### **Clinical Stage versus Pathological Stage?**

In some instances, physicians will discuss 'clinical stage' and 'pathologic stage'. The clinical stage is the stage estimated by the physician before any surgery is done. The pathologic stage is the true extent of the cancer as found by the pathologist in the bladder specimen after removal of the bladder and lymph nodes (if that option is performed). One obvious dilemma is the fact that clinical stage and pathological stage do not always agree. That is, the cancer can be more or less extensive than estimated by the pre-operative examinations and tests. If no surgery is done on the bladder or lymph nodes, the clinical stage is the only stage that is obtained.

### **What Staging systems are used?**

Two commonly used staging systems exist--ABCD and TNM.

The ABCD is older and is a broad description of the cancer. The TNM system describes the bladder (**T**), the lymph nodes (**N**), and evidence of metastatic disease (distant spread) (**M**) separately.

With the ABCD system the cancer is denoted by one letter followed by one number A1, B2 etc.

With the TNM system, the bladder is described by the T, the lymph nodes by the N and distant spread by the M. Each letter is followed by a describing number, T2aN0M0. This may be confusing but ask if you have questions.

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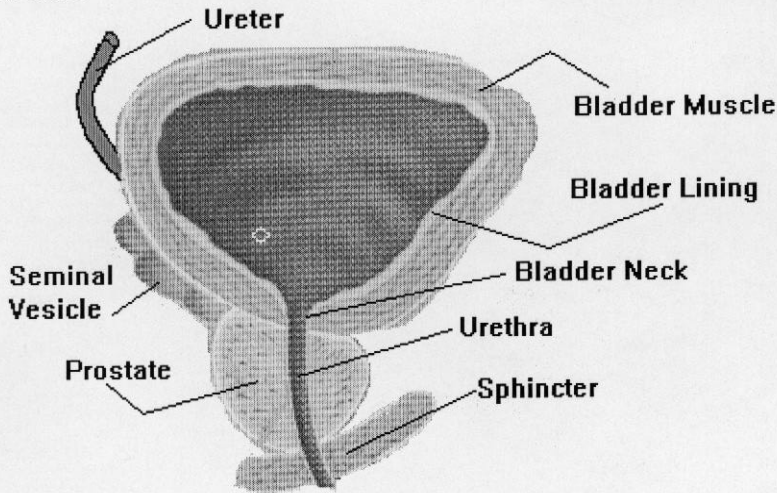
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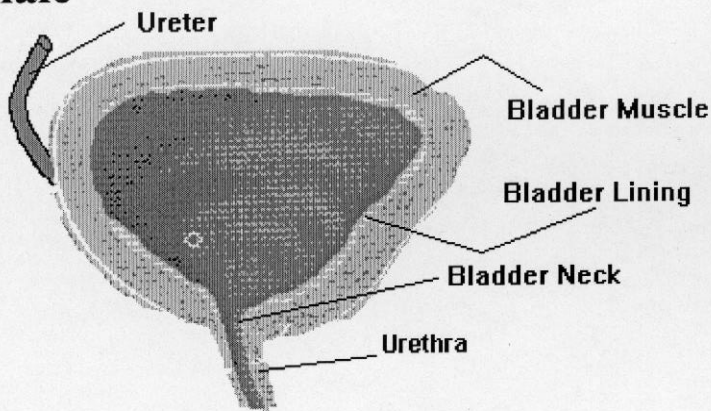
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Normal Anatomy

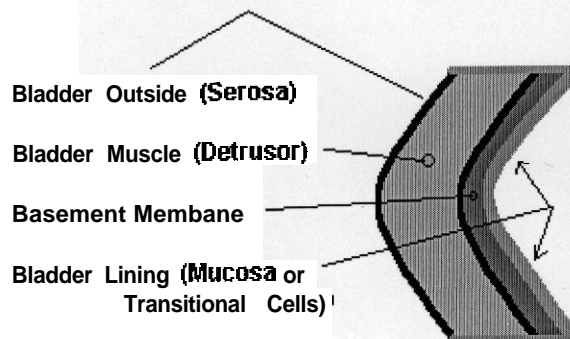
**Male**



**Female**



**Magnification of Bladder Lining!**



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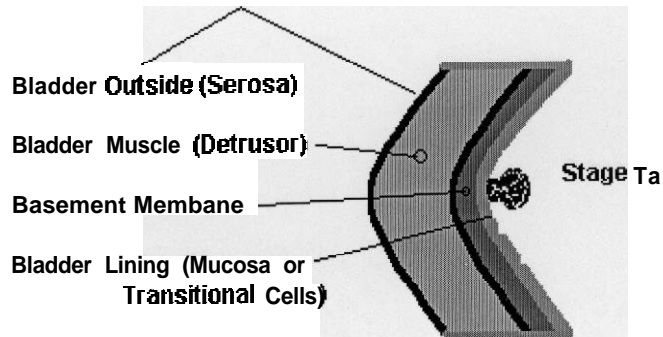
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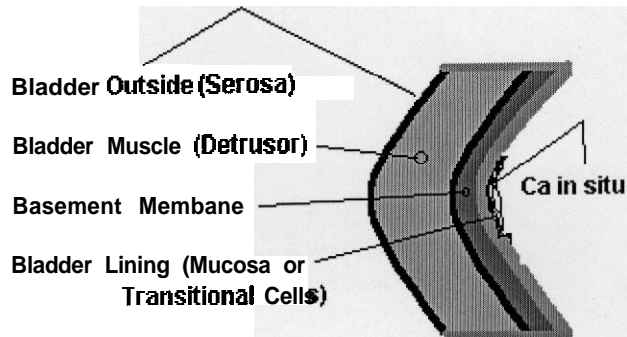
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**Primary Tumor**

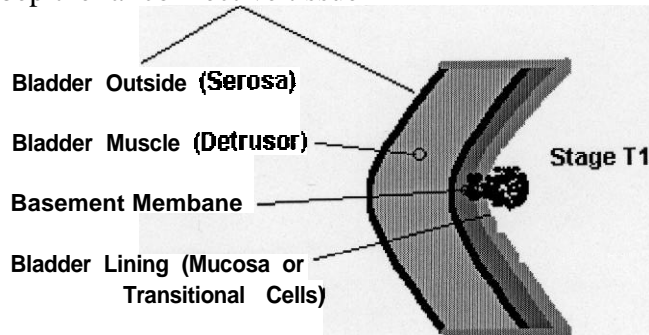
- TX Primary tumor cannot be assessed
- TO No evidence of primary tumor
- Ta Non-invasive papillary carcinoma



- TIS Carcinoma in situ: "flat tumor"



- T1 Tumor invades subepithelial connective tissue



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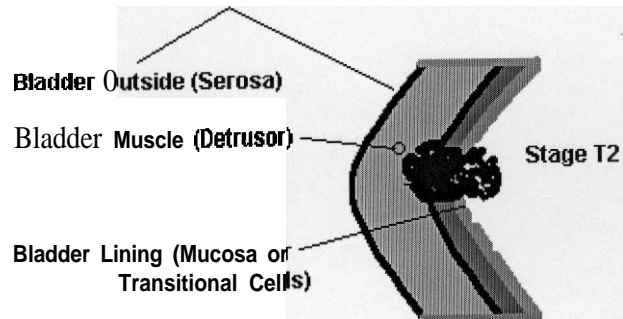
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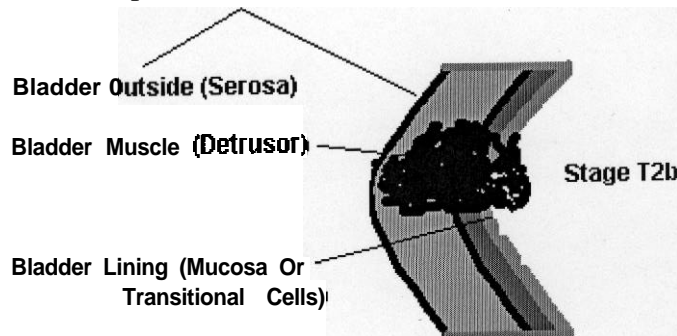
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**T2** Tumor invades bladder muscle

**T2a** Tumor invades superficial muscle (inner half)



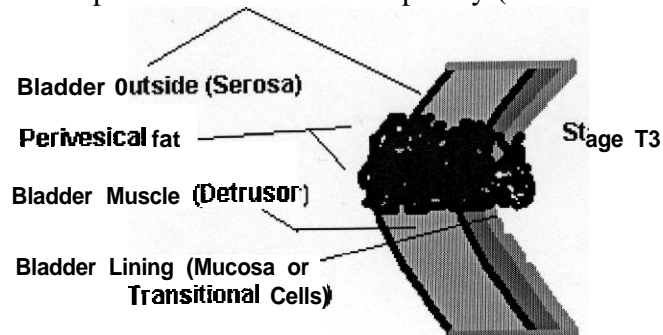
**T2b** Tumor invades deep muscle



**T3** Tumor invades perivesical fat

**T3a** Tumor invades perivesical fat microscopically (pathologist's interpretation)

**T3b** Tumor invades perivesical fat macroscopically (can be seen or felt)



**T4** Tumor invades prostate, uterus, vagina, pelvic wall or abdominal wall

**T4a** Tumor invades prostate, uterus, vagina

**T4b** Tumor invades pelvic wall or abdominal wall

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**Lymph Node (N)**

- NX** Regional lymph nodes cannot be assessed
- NO** No regional lymph node metastasis
- N1** Metastasis in a single lymph node, 2 cm or less in greatest dimension
- N2** Metastasis in a single lymph node, more than 2 cm but not more than 5 cm in greatest dimension, or multiple lymph nodes, none more than 5 cm in greatest dimension
- N3** Metastasis in a lymph node more than 5 cm in greatest dimension

**Distant Metastasis (M)**

- MX** Presence of distant metastasis cannot be assessed
- MO** No distant metastasis
- M1** Distant metastasis

**Stage Grouping**

Oa	Ta	NO	MO
Ois	Tis	NO	MO
I	T1	NO	MO
II	T2	NO	MO
	T3a	NO	MO
III	T3b	NO	MO
	T4a	NO	MO
IV	T4b	NO	MO
	AnyT	N1	MO
	AnyT	N 2	MO
	AnyT	N 3	MO
	AnyT	AnyN	M1

**Other Staging Criteria....**

**--Recurrent Cancer --**

Recurrent disease means that the cancer has come back (recurred) after it has been treated. It may come back in the bladder or in another part of the body.

**GRADING BLADDER CANCER**

The GRADE is defined by the pathologist from the bladder biopsy. The grade gives us an idea of how fast the cancer might be growing or how aggressive it might be. High grade cancers grow faster and spread earlier than low grade cancers. The current system of grading uses only three different grades: well-differentiated, moderately differentiated, and poorly differentiated (or Grade I, II or III). It is still used in general discussions about cancer. Some pathologists will use a 4-level grading system, I, II, III and IV. Either system is acceptable, and the pathologist will always note how many levels they use by declaring the cancer as a II/III or II/IV. The denominator or second number states what system they use.

Well-differentiated means the cancer has more **resemblance** to normal bladder tissue and therefore usually does not grow or spread quickly. Poorly differentiated tumors do not resemble normal bladder

and usually grow quickly and spread to other tissues earlier. Moderately differentiated are in the middle.

Grade, while important, has less bearing on the treatment decisions than does the Stage. After the grade and stage are known, other factors also come into play before making any decision about future treatment.

### **Other tests to help GRADE bladder cancer**

Another less commonly used grading test looks at the number of chromosomes in the cancer cells or 'ploidy' (poy-dee). The test is called 'flow cytometry'. Normal human cells have 46 chromosomes. This is referred to as 'diploid' (dip-ployed), meaning 23 pairs. When flow cytometry is used to count the chromosomes, we discover that some cancers have an extra chromosome and are called 'aneuploid' (an-u-ployed). Aneuploid cancers tend to spread more quickly and have a worse prognosis-- but not always!

Much of the research on bladder cancer is aimed at DNA, the genetic information inside the cancer cells. Many cancer cells have DNA abnormalities these may be able to identify more cancers that need to be treated more aggressively. In addition, some of these DNA tests may help identify pre-cancerous conditions that cannot be identified with current techniques. The most common of the DNA markers include **p53**, **Ki 67**, **Cyclin D1**, **G-actin**.

While 'ploidy' and other chromosome tests do give us some information, the STAGE of one's cancer is still more important in determining treatment options. However, just as important are each individual's health, life expectancy and current medical conditions.