BLADDER CANCER

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Center for Urologic Cancer
Celebration, Florida
What percentage of the human population have an “innie” belly button?

A. 90%
B. 65%
C. 40%
D. 75%
90%!!
Demographics

2010 – est >70,000 new Dx and >12,500 bladder cancer related death

Second most common GU malignancy

Male female ratio slightly less that 3:1

**Men** 4th most common, 7th death, **Women** 8th most common, 10th death

One half as common in African-Americans

2/3 over the age of 65, rare under age 30
Bladder Cancer

Risk Factors

Overwhelmingly an underserved disease-difficult to diagnose and has a high recurrence rate

Environment and occupational exposure

- Analine dyes (rubber processing, herbicides, pigmentation)
- Cyclophosphamide (cytoxan- common chemo drug)
- Ionizing radiation (x-ray nuclear)
- Physical trauma (chronic infections, stones, indwelling catheter)
- Phenacetin ingestion (old analgesic/used to cut cocaine)

Smiths General Urology, 2004, Emil Tanagho et al., page 324
Bladder Cancer

Tobacco Abuse

Cigarette smoking strongly associated with bladder cancer

Relative risk is 2-4 fold above non-smokers

Risk climbs above 2 for >2 pack per day habit

Smoking cessation helps decrease risk yet it never fully returns to baseline
Risk Factors

**Blackfoot Disease**: Southern Taiwan high level of *Arsenic* in the drinking water.

**Tristolochia Fangchi**: Chinese herb used in weight reduction programs. Associated with upper and lower tract TCC.

**Decreased fluid intake**- (HPFS 22yr study- 47,909pts, >2000ml qd => 24% risk reduction*)

**Transplant status** – (especially after kidney transplants- worse prognosis. Imunosuppressed status makes treatment difficult)

* http://www.clinicaltrials.gov/ct2/show/NCT00005182
Risk Factors

Occupations at increased risk:

- Dry cleaners
- Painters
- Autoworkers
- Truck drivers
- Metal workers
- Paper manufacturers
- Plumbers
Molecular Pathology- any deviation => CANCER

**Cell Cycle Control Elements** – deregulation leads to genomic instability, neoplastic transformations and tumor progression.

P53, Rb – associated with increased risk and decreased survivability

**Signal Transduction Components** - “communication process’

- sustained angiogenesis
- apoptosis inhibition
- tissue invasion-> mets

**Cell Adhesion Molecules (CAMS)** – loss of adhesion

- desquamation of cells from lamina propria
- allowing for escape of cells->mets

E-Cadherin, Integrins
Molecular Pathology

Field defect theory

Urothelium a continuous organ with multifocal sites of cancer secondary to toxic exposure => INDEPENDENT transformation of cells => oncogenetically unrelated tumors

Clonal Theory

Bladder has 200 progenitor cells. A tumor is clonal and spreads to different areas to appear multifocal
Bladder cancer does not progress in an orderly, step-wise pattern from urothelium to papillary lesions or from fat-nodular lesions to muscle invasive tumor!

Only 10%-20% of superficial lesions progress to muscle invasion.

Majority of muscle invasive lesions present initially as muscle invasive tumors.
How much saliva do you produce in one day?

A. 2 quarts
B. 10 tablespoons
C. 1 gallon
D. 2 teaspoons
Up to TWO Quarts!

“Watch what I can make Pavlov do. As soon as I drool, he'll smile and write in his little book.”
Pathology

**Transitional Cell Carcinoma (TCC):** Urothelial carcinoma, 90%

**Squamous Cell Carcinoma:** 5%-7%, associated with chronic irritation (stones, Foley catheter, Schistosomiasis)

**Adenocarcinoma:** 1%-2%, urachal carcinoma, cystitis glandularis. Rule out metastatic source.

**Metaplastic Elements:** mixed containing squamous or adenocarcinoma in TCC.
Bladder Cancer

Pathology Report

Tumor histology
Tumor size
Layers of wall represented (smooth muscle identified or not)
Denuded/ulcerated
Papillary / nodular / flat
Grade
Depth
Angiymphatic invasion
Type of invasion - broad spread or tentacular (like tentacles)
Changes in benign appearing mucosa (carcinoma in situ, dysplasia, hyperplasia, normal)
# Bladder Cancer

## Pathological Staging

### Primary tumor (T)

<table>
<thead>
<tr>
<th>UICC/AJCC</th>
<th>Strong-Jewett</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>TX</td>
<td></td>
<td>Primary tumor cannot be assessed</td>
</tr>
<tr>
<td>T0</td>
<td></td>
<td>No evidence of primary tumor</td>
</tr>
<tr>
<td>Ta</td>
<td>0</td>
<td>Noninvasive papillary; i.e. confined to urothelium</td>
</tr>
<tr>
<td>Tis</td>
<td>CIS</td>
<td>Noninvasive flat (CIS, carcinoma in situ)</td>
</tr>
<tr>
<td>T1</td>
<td>A</td>
<td>Invasive, lamina propria</td>
</tr>
<tr>
<td>pT2a</td>
<td>B1</td>
<td>Invasive, into inner 1/2 of muscularis propria</td>
</tr>
<tr>
<td>pT2b</td>
<td>B2</td>
<td>Invasive, into outer 1/2 of muscularis propria</td>
</tr>
<tr>
<td>T3</td>
<td>C</td>
<td>Invasive, into perivesical fat</td>
</tr>
<tr>
<td>pT3a</td>
<td>C</td>
<td>Microscopic</td>
</tr>
<tr>
<td>pT3b</td>
<td>C</td>
<td>Macroscopic</td>
</tr>
<tr>
<td>T4</td>
<td>D</td>
<td>Invasive, into adjacent bladder structures (in situ invasion of prostatic ducts does not count)</td>
</tr>
<tr>
<td>pT4a</td>
<td>D</td>
<td>Prostate, uterus, vagina</td>
</tr>
<tr>
<td>pT4b</td>
<td>D</td>
<td>Pelvic wall or abdominal wall</td>
</tr>
</tbody>
</table>
BLADDER CANCER STAGING (TNM)

- Ureters
- Muscularis Propria
- Perivesical Fat
- Adjacent organs
- Urethra
- Lamina Propria
- Urothelial layer (mucosa)
Bladder Cancer

Pathological Staging

Regional lymph nodes (N)

Note: regional lymph nodes are those within the true pelvis

NX  Regional lymph nodes cannot be assessed
N0  No regional lymph node metastases
N1  Metastasis in single lymph node, 2 cm or less in greatest dimension
N2  Metastasis in single or multiple lymph nodes, 2-5 cm in greatest dimension
N3  Metastasis in any lymph node, > 5 cm in greatest dimension
Pathological Staging

Distant metastasis (M)

- **MX**: Distant metastasis cannot be assessed
- **M0**: No distant metastasis
- **M1**: Distant metastasis
Normal urothelium consists of a flat mucosa lined by urothelial cells covered by an umbrella cell layer.
Papillary hyperplasia where urothelium is thicker and thrown into undulating folds. Note prominent capillaries in papillary folds.
Papillary urothelial tumor of low malignant potential. Even at low magnification the cell thickness is much greater than what one would see within a benign urothelial papilloma.
Flat Urothelial carcinoma in situ
CIS characterized by enlarged nuclei, which are very hyperchromatic. Note urothelial nuclei with CIS are four to five times the size of lymphocytes within lamina propria. Often CIS cells show marked hyperchromasia such that nuclear chromatin detail is not evident.
Diagnosis

**Gross hematuria:** the most common presenting symptom

Microscopic hematuria: second

Irritative voiding symptoms

Incidental finding

The role of hematuria screening in general populations is uncertain
Diagnostic tools

**Urine Cytology:** A high specificity for a true cancer diagnosis. 20% false negative, 1-12% false positive rate (inflammation, prior chemotherapy of XRT)

**Flow Cytometry:** Automated measurement of cellular DNA. Ploidy (abnl amt of DNA) associated with recurrence, progression and survival. S phase (increased replication) correlated to tumor progression.

**NMP22** highly sensitive- up to 91% with values > 10u/ml => with cysto up to 99%; neg predictive value up to 99%

**BTA** uses monoclonal antibodies to detect the presence of bladder tumor associated antigens in urine (qualitative)
- used to monitor patients with a history of bladder cancer in conjunction with cystoscopy
- 38%-72% sensitivity based on stage
## Natural History

<table>
<thead>
<tr>
<th>Pathology</th>
<th>%Recurrence</th>
<th>%Progression</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 1</td>
<td>63</td>
<td>2-10</td>
</tr>
<tr>
<td>Grade 2</td>
<td>67</td>
<td>11-19</td>
</tr>
<tr>
<td>Grade 3</td>
<td>71</td>
<td>33-45</td>
</tr>
<tr>
<td>Stage Ta</td>
<td>52</td>
<td>4</td>
</tr>
<tr>
<td>Stage T1</td>
<td>77</td>
<td>30</td>
</tr>
<tr>
<td>Diploid lesion</td>
<td>34</td>
<td>2</td>
</tr>
<tr>
<td>Aneuploid</td>
<td>87</td>
<td>60</td>
</tr>
</tbody>
</table>
Introduction

- The term *superficial bladder cancer*: Tis, Ta, and T1 lesions of any grade

- Approximately 70% of bladder tumors are superficial lesions. 10%-30% of these progress to muscle-invasive lesions.

- Approximately 70% of superficial lesions present as stage Ta, 20% as T1, and 10% as Tis.
Management of Superficial Bladder Cancer

Introduction

- Low-grade Ta lesions
  - recur at a rate of 50%-70% with a 5% chance of progression

- High-grade (grade III) T1 lesions and CIS
  - recur in more than 80% of cases
  - progress in 50% of patients within 3 years.
Groucho Marks
A man is only as old as the woman he feels
Management of Superficial Bladder Cancer

Outline

- Endoscopic Management of Superficial Bladder Cancer
- Cystectomy in Superficial Disease
- Intravesical Therapy
- Alternative Therapy
- Disease Surveillance
Management of Superficial Bladder Cancer

Endoscopic Management

- Cystoscopy is critical to the accurate diagnosis and treatment of superficial disease.

- Decompression of the bladder and suprapubic pressure can present the lesion in a more favorable orientation for resection when it is situated on the anterior wall.
Endoscopic Management

- In the case of bladder diverticula, it is generally better to resect at the neck of the diverticulum and avoid TUR in the deeper portions of the structure.

- Biopsies of the urethra or prostate may be useful when orthotopic bladder substitution is contemplated or in the case of carcinoma in situ.
Endoscopic Management

- In the evaluation of T1 tumors specifically, a repeat TUR can demonstrate worse prognostic findings in up to 25% of specimens.

- Given the borderline status of high-grade T1 lesions, repeat TUR is appropriate, especially if no muscle is identified on initial pathology.
Superficial Bladder Cancer
Endoscopic Management

Side Effects of Transurethral Resection

Clot retention may occur and necessitate repeat endoscopic fulguration.

Removal of residual clot, avoidance of anticoagulant agents for several weeks, and avoidance of Valsalva-like activity reduce the potential for a repeat occurrence.
Management of Superficial Bladder Cancer

Endoscopic Management

Side Effects of Transurethral Resection

Damage to the ureteral orifices:

If suspicion of damage to the orifice exists, an earlier repeat cystoscopy can be performed in conjunction with ultrasonic imaging of the upper tracts.
Management of Superficial Bladder Cancer

Endoscopic Management

Side Effects of Transurethral Resection

Bladder Perforation:

The principal distinction to make is whether the perforation is extraperitoneal, in which case it can be generally managed by catheter drainage, or intraperitoneal, which may not respond to drainage alone and could require open repair.
Endoscopic Management

Tissue Biopsy of Adjacent Urothelium

Select biopsies of suspicious areas are an important part of a complete evaluation.

Older studies suggest a useful prognostic role for random biopsies. More recent work suggests that the additional value provided by biopsies from random sites of normal-appearing tissue at the time of resection appears to be minimal, and, theoretically, the process may aid tumor implantation.

LASER THERAPY, PHOTODYNAMIC THERAPY
Management of Superficial Bladder Cancer

Cystectomy in Superficial Disease

Rationale

- Although the initial response rate to BCG therapy in tumor in situ patients can be above 80%, those patients who fail have a 50% chance of disease progression and potential for disease mortality.

- Disease progression in T1 patients can be 50%, with 30% experiencing bladder cancer–related death over 15 years.

- Ten-year survival after cystectomy for superficial disease can range from 67% to 92%.
Cystectomy in Superficial Disease

**Indications**

- In healthy patients with persistent or recurrent, high-risk, superficial disease who have failed intravesical therapy,

- Cystectomy for superficial disease is appropriate in those patients with low- to moderate-grade polychronotropic disease that renders the bladder nonfunctional or with high-risk superficial disease that has not responded to early intravesical therapy.

- Immediate cystectomy is an option in high-grade T1 disease, is multifocal, but it is generally considered as a treatment option after assessing the response to a course of intravesical therapy.
Management of Superficial Bladder Cancer

Intravesical Therapy

Bacille Calmette-Guérin (BCG)

- BCG is an attenuated mycobacterium that has been used as a vaccine for tuberculosis and that has also demonstrated antitumor activity.

- Established a standard for intravesical therapy for patients with high-risk superficial disease.
Management of Superficial Bladder Cancer

Intravesical Therapy

Bacille Calmette-Guérin (BCG)

- BCG remains the most effective form of intravesical therapy for prophylaxis and treatment of superficial bladder cancer.
- Carcinoma in situ
- Residual papillary disease
- Prophylactic agent in recurrent superficial disease
Intravesical Therapy (BCG)

Preparation

BCG is provided as a powder that is stored at 4°C until instillation.

(Connaught, Tice, Armand Frappier, Pasteur, Tokyo, and RIVM strains)

Therapeutic efficacy is associated with the ability to deliver approximately 10 million organisms per instillation.

Reconstituted with 50 mL of saline and should be administered soon thereafter because aggregation occurs with time and may affect its potency (Ratliff et al, 1994a, 1994b).
Intravesical Therapy (BCG)

**Administration**

Treatments are generally begun 2 to 4 weeks after tumor resection.

Catheterization should be atraumatic, and administration should be performed under gravity drainage.

In the event of a traumatic catheterization, the treatment should be delayed for several days.

Optimally, the patient should retain the solution for 2 hours.

**Gross hematuria and likely bacterial infection are contraindications for administration because toxicity is associated with intravascular inoculation**
Management of Superficial Bladder Cancer

Intravesical Therapy (BCG)

Contraindications

Immunosuppressed and Immunocompromised

Relative Contraindications:
- Poor overall performance status
- Advanced age
- Prior history of tuberculosis (tend to have a higher incidence of side effects)
- Persistent microscopic hematuria

Prosthetics or Valvular heart disease. Appropriate prophylactic antibiotic therapy for urinary tract instrumentation
Intravesical Therapy (BCG)

**Side Effects**

Well tolerated with only moderate side effects, yet the potential for serious illness and death exists.

- dysuria
- urinary urgency
- frequency
  
  may last for several days and can worsen

- microscopic hematuria (persistent -> relative contraindication)

**Treatments:** anticholinergics, acetaminophen, or phenazopyridine.
Management of Superficial Bladder Cancer

Intravesical Therapy (BCG)

Side Effects/Complications

Granulomatous prostatitis can be an asymptomatic finding in 20% to 30% of patients and may cause elevated serum PSA. This condition is symptomatic in approximately 1% of cases.

Testicular involvement is less common but may progress to orchiectomy if untreated.

Bladder contracture is seen in fewer than 0.5% of patients treated with BCG.
Intravesical Therapy (BCG)

Side Effects/Complications

Fever
- > 38.5°C persists for longer than 24 hrs and does not resolve with antipyretic therapy or ;
- fever higher than 39.5°C -> treatment with isoniazid (300 mg daily for 3 months)

Systemic BCGosis is generally manifested as;
- pulmonary or hepatic disease and is a serious condition.
- isoniazid-rifampin for 6 months with addition of ethambutol in acutely ill patients (Pyridoxine is added to any long courses of isoniazid treatment to decrease peripheral neuropathy and CNS effects)

BCG sepsis is a rare (0% to 4%) yet life-threatening condition that should be treated with standard life support methods as well as triple drug therapy.
Management of Superficial Bladder Cancer

Intravesical Therapy (BCG)

Therapeutic Indications—CIS

BCG has an undisputed role as the principal form of therapy for treatment of carcinoma in situ and is approved for this indication by the U.S. Food and Drug Administration (FDA).

The data from several series demonstrate that 50% of patients experience a durable response for a median period of 4 years.

Over a 10-year period, approximately 30% of patients remain free of tumor progression or recurrence. The majority of these patients recur or progress within the first 5 years (Herr et al, 1992).
Intravesical Therapy (BCG)

Therapeutic Indications—CIS

Although BCG has replaced cystectomy as the initial form of therapy for this condition, failure to respond to two 6-week courses of therapy or early recurrence of high-risk disease indicates the need for more aggressive therapy if the patient is clinically fit.
Management of Superficial Bladder Cancer

Intravesical Therapy (BCG)

Therapeutic Indications—Residual tumors

- Should *not* be used as a substitute for surgical resection when that is possible, however;

- Several investigators have demonstrated a nearly 60 response by residual tumor with intravesical BCG alone.
Management of Superficial Bladder Cancer

Intravesical Therapy (BCG)

Therapeutic Indications—Tumor prophylaxis

- T1 lesions and recurrent high-grade Ta lesions are generally treated with BCG prophylactically after complete TUR.

- Multiple series have compared the effect of TUR alone with that of BCG and TUR
  - approximately decrease was 40%.
Intravesical Therapy—Chemotherapy

**Mitomycin**

Mitomycin C is a cross-linking agent that, in part, inhibits DNA synthesis

Instilled weekly for 6 to 8 weeks at dose ranges from 20 to 60 mg.

Average complete response rate is approximately 36%, and there is a decrease in recurrence ranging from 19% to 42% ([88] Kim & Lee, 1988).

In a review of several major series, the average benefit was 15%, with only two out of five of these studies demonstrating statistical significance.
Management of Superficial Bladder Cancer

Intravesical Therapy—Chemotherapy

**Mitomycin**

Several well-performed studies have failed to demonstrate a significant effect of mitomycin C over TUR alone (4% versus 7.3%) on decreasing tumor progression over 5 years.

**Side effects**
- chemical cystitis (up to 40% of patients)
- decreased bladder capacity
- palmar desquamation
- skin rash. Skin contact should be avoided
- leukopenia and bladder contraction (0.05%), are rare (Thrasher & Crawford, 1992).

Other agents: Doxorubicin, Epirubicin, Thiotepa, Valrubicin, Ethoglucid.
## Intravesical Chemotherapy

<table>
<thead>
<tr>
<th>Agent</th>
<th>Mechanism</th>
<th>Dose Range (Mg)</th>
<th>Common Toxicity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thiotepa</td>
<td>Alkylating Agent</td>
<td>30 - 90</td>
<td>Myelosuppression</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Mild cystitis</td>
</tr>
<tr>
<td>Doxorubicin</td>
<td>Intercalating Agent</td>
<td>30 - 90</td>
<td>Cystitis</td>
</tr>
<tr>
<td>Mitomycin C</td>
<td>Alkylating Agent</td>
<td>20 - 60</td>
<td>Cystitis dermatis</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Allergic reaction</td>
</tr>
<tr>
<td>Epirubicin</td>
<td>Intercalating Agent</td>
<td>50 - 80</td>
<td>Cystitis</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Allergic reaction</td>
</tr>
<tr>
<td>Ethogluclid</td>
<td>Alkylating Agent</td>
<td>1 - 2&lt;sup&gt;(4)&lt;/sup&gt;</td>
<td>Cystitis</td>
</tr>
<tr>
<td>Mitoxantrone</td>
<td>Intercalating Agent</td>
<td>5 - 10.5</td>
<td>Cystitis</td>
</tr>
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</table>
# SUPERFICIAL BLADDER CANCER

## Analysis of Recurrence in 18 Controlled Trials

<table>
<thead>
<tr>
<th>Agent</th>
<th>No. Trials</th>
<th>No. Pts</th>
<th>No. Con.</th>
<th>No. with Recurrence (%)</th>
<th>No. RX.</th>
<th>No. with Recurrence (%)</th>
<th>Ave. Benefit (%)</th>
<th>Pos Trials</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thiotepa</td>
<td>9</td>
<td>1,130</td>
<td>505</td>
<td>309 (61)</td>
<td>625</td>
<td>288 (49)</td>
<td>12</td>
<td>5/9</td>
</tr>
<tr>
<td>Mitomycin C</td>
<td>6</td>
<td>1,157</td>
<td>509</td>
<td>270 (53)</td>
<td>648</td>
<td>286 (44)</td>
<td>9</td>
<td>2/6</td>
</tr>
<tr>
<td>Dixorubicin</td>
<td>5</td>
<td>1,389</td>
<td>467</td>
<td>246 (53)</td>
<td>922</td>
<td>351 (38)</td>
<td>15</td>
<td>3/5</td>
</tr>
<tr>
<td>Epirubicin</td>
<td>1</td>
<td>399</td>
<td>205</td>
<td>84 (41)</td>
<td>194</td>
<td>56 (29)</td>
<td>12</td>
<td>1/1</td>
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<tr>
<td>Ethoglucid</td>
<td>1</td>
<td>209</td>
<td>70</td>
<td>41 (59)</td>
<td>139</td>
<td>39 (28)</td>
<td>31</td>
<td>1/1</td>
</tr>
</tbody>
</table>

## INTRAVESICAL CHEMOTHERAPY

Analysis of Progression in 10 Controlled Trials

<table>
<thead>
<tr>
<th>Agent</th>
<th>No.</th>
<th>Control</th>
<th>No. with Progression(%)</th>
<th>Chemotherapy</th>
<th>No.</th>
<th>No. with Progression (%)</th>
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</thead>
<tbody>
<tr>
<td>Thiotepa</td>
<td>3</td>
<td>199</td>
<td>12 (6)</td>
<td>314</td>
<td>14</td>
<td>14 (4.5)</td>
</tr>
<tr>
<td>Mitomycin</td>
<td>3</td>
<td>191</td>
<td>14 (7.3)</td>
<td>336</td>
<td>13</td>
<td>13 (3.9)</td>
</tr>
<tr>
<td>Dixorubicin</td>
<td>3</td>
<td>183</td>
<td>23 (12.8)</td>
<td>389</td>
<td>59</td>
<td>59 (15.2)</td>
</tr>
<tr>
<td>Epirubicin</td>
<td>1</td>
<td>205</td>
<td>5 (2.4)</td>
<td>194</td>
<td>7</td>
<td>7 (3.6)</td>
</tr>
<tr>
<td><strong>Cumulative</strong></td>
<td><strong>10</strong></td>
<td><strong>778</strong></td>
<td><strong>54 (6.9)</strong></td>
<td><strong>1,233</strong></td>
<td><strong>93</strong></td>
<td><strong>93 (7.5)</strong></td>
</tr>
</tbody>
</table>

(Sylvester et al: J Urol 2002 – Follow-up, risk factors varied between studies)
The original story from "Tales of 1001 Arabian Nights" begins, "Aladdin was a little Chinese boy."
The role for radiation therapy in the treatment of superficial bladder cancer is limited and generally restricted to those individuals who refuse cystectomy after the failure of intravesical therapy or who are unsuitable for major surgery.

Interstitial and external-beam therapies have been employed with moderate success in select cases (van der Werf-Messin, 1984).

Five-year response rates are 44% to 60% with external-beam therapy. Recurrence is generally associated with progression and disease-related death.
In patients treated with radiation therapy, distant recurrence occurs in 10% to 25% of patients. Series suggest lower morbidity rates with modern techniques, with radiation cystitis or bladder contracture in the 5% range.

Presently, there is a minimal role for radiation therapy in the treatment of superficial bladder cancer!!
Management of Superficial Bladder Cancer

Disease Surveillance

Standard:

- History and Physical (U/A)
- Cystoscopy q 3 months (can miss CIS and sm lesions)
- Cytology q 3 months
- Upper tract imaging
Management of Superficial Bladder Cancer

Disease Surveillance

Urine Cytology

Urine cytology - excellent specificity (98% to 100%) and reasonable sensitivity in high-grade lesions.

The poor sensitivity of cytology (approximately 25%) in low-grade lesions reduces its overall value as a surveillance marker.

The presence of a positive cytology result should elicit evaluation of the entire urothelium, including the prostatic fossa.
Management of Superficial Bladder Cancer

Disease Surveillance

Upper Tract Recurrence

The rate of developing upper tract TCC after the diagnosis and treatment of **superficial disease** has classically been reported as 0.002% to 2.4% over surveillance intervals of 5 to 13 years (Shinka et al, 1988; Oldbring et al, 1989; Holmang et al, 1995; Sadek et al, 1999).

Most occurrences present within the first 5 years. Even in populations reporting low recurrence rates, the appearance of upper tract disease is often lethal, with mortality of 40% to 70%.
Disease Surveillance

Upper Tract Recurrence

Contemporary series describing high-risk superficial disease (multiple recurrent papillary lesions and tumor in situ) treated with BCG demonstrate a significantly increased hazard for upper tract recurrence, with rates of 13% to 18% (Miller et al, 1993; Herr et al, 1997).

Additionally, such patients are at risk for extravesical recurrence in the prostatic fossa. This occurs at a median time of 11 months with a cumulative incidence of 37% at 15 years. The prostatic relapses are lethal in 44% of cases (Herr et al, 1988).
Management of Superficial Bladder Cancer

Disease Surveillance

Upper Tract Recurrence

Evidence suggests:

**High-risk** superficial disease successfully treated with BCG require close, lifelong observation of their upper tracts with routine intravenous urograms on a **yearly basis or at the detection of positive urine cytology.**

**Low-risk** patients evaluation of the upper tracts on a 3- to 4-year schedule is reasonable.
Management of Superficial Bladder Cancer

Algorithm

Figure 77-2. Algorithm for diagnosis of superficial transitional cell carcinoma.
Who is Barbara Millicent Roberts?
Management of Invasive Bladder Cancer

Outline

- Clinical Presentation, Diagnosis, and Evaluation
- Radical Cystectomy
- Adjuncts to Standard Surgical Therapy
- Alternatives to Standard Therapy
Management of Invasive Bladder Cancer

Transurethral Resection

- Essential to establish pathological diagnosis.

- For patients in whom an invasive lesion is suspected before TUR, imaging studies should be accomplished before TUR to avoid confounding artifact produced by TUR.

- Restaging TUR is recommended for some cases.
Management of Invasive Bladder Cancer

Clinical Presentation

- Hematuria, gross or microscopic
- Irritative voiding symptoms
- Upper urinary obstruction
- Constitutional symptoms
Management of Invasive Bladder Cancer

Bimanual Examination

- Usually performed before and after TUR under anesthesia.
- The presence of a palpable mass after TUR correlates significantly with stage T3 cancer and poorer prognosis after treatment.
Management of Invasive Bladder Cancer

Imaging Studies

- **CT, MRI:** Understaging and overstaging remain persistent problems. CT findings correlate with pathology of the cystectomy specimens in 65%-80% of cases. CT detects metastatic disease in regional LN in 50%-85% of cases.

- **PET Scan:** Based on the uptake of fluorodeoxyglucose (FDG) by tumor cells.

- **Bone Scan:** In general, preoperative bone scan is not necessary for patients with clinically organ-confined, muscle-invasive bladder cancer, unless patients have signs or symptoms suggestive of bone involvement.

- **Laparoscopic Staging:** (PLND) pelvic lymph node dissection
Radical Cystectomy

- Radical cystoprostatectomy in the male patient and anterior exenteration in the female patient, coupled with en bloc pelvic lymphadenectomy

- Patients with local symptoms, such as refractory hemorrhage, may be candidates for palliative surgical intervention even if evidence of locoregional or distant metastases exists.
Management of Invasive Bladder Cancer

Radical Cystectomy

Standard Technical Points

- In the male patient, bilateral pelvic lymphadenectomy and subsequent removal of the prostate and bladder en bloc.

- In the female patient, bilateral pelvic lymphadenectomy and removal of the uterus, fallopian tubes, ovaries, bladder, urethra, and a segment of the anterior vaginal wall.

- Nerve-sparing techniques.
Management of Invasive Bladder Cancer

Radical Cystectomy

Urinary tract diversion

- **continent urinary reservoir** – colon used, cath stoma

- **ileal conduit** - intestinal “urethra” with ureters to stoma

- **neobladder** - intestinal pouch, no catheter

*Analysis of the ureteral margin at the time of cystectomy before urinary tract reconstruction is standard practice.*
Management of Invasive Bladder Cancer

Adjuncts to Standard Surgical Therapy

- Preoperative radiation therapy.
- Neoadjuvant chemotherapy.
- Perioperative chemotherapy.
- Adjuvant chemotherapy.
Management of Invasive Bladder Cancer

Alternatives to Standard Therapy

- Conventional external beam therapy (30%-50%).
- Transurethral resection and partial cystectomy (Well-defined, small, superficially invasive bladder T2).
- Transurethral resection and partial cystectomy with systemic chemotherapy.
- Bladder-preservation protocols (TUR, neoadjuvant chemotherapy and subsequent radiation).
- Interstitial radiation therapy.
- Intra-arterial chemotherapy.
- Hyperthermia and chemotherapy.
Management of Metastatic Bladder Cancer

Outline

- Systemic Chemotherapy
- Local Salvage and Palliative Therapy
Management of Metastatic Bladder Cancer

Systemic Chemotherapy

- MVAC: methotrexate, vinblastine, doxorubicin, and cisplatin.

- Complete response (CR) can be achieved in approximately 20% of patients, although long-term disease-free survival is rare.

- Death from sepsis has been reported in 4% of patients receiving MVAC.
Systemic Chemotherapy

NEW AGENTS

- Gemcitabine (Gemzar), an analogue of cytosine arabinoside, has been used as a single agent (>25% CR) and in combination with cisplatin (~40% PR and CR) in patients with metastatic disease.

- Taxoids, including paclitaxel (Taxol) and docetaxel (Taxotere), are microtubule disassembly inhibitors and produce response rates ranging from 25%-83%.

- Second line treatments-(no stnd has been set and median survival is 6 months
  - pemetrexed
  - Vinflunine
Management of Metastatic Bladder Cancer

Salvage Cystectomy

- Definitive surgical intervention may be considered when systemic chemotherapy has produced a PR and residual disease remains clinically confined to the bladder.

- Orthotopic reconstruction is safe and effective in selected patients undergoing salvage surgery.

- Surgery for residual extravesical disease confers no long-term survival advantage and should generally be discouraged.
I don't think of all the misery but of the beauty that still remains. ~Anne Frank

Attitude is a little thing that makes a big difference. ~Winston Churchill

Once you choose hope, anything's possible ~Christopher Reeve