

# Contemporary Management of Clinically Localized Bladder Cancer

Vladimir A. Valera Romero MD PhD  
Staff Clinician/Assistant Research Physician  
Urologic Oncology Branch  
Center for Cancer Research  
National Cancer Institute

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## Contemporary Management of Clinically Localized Bladder Cancer

### Talk overview

- Review of anatomy and histology
- Introduction to Bladder Cancer
- Epidemiology, Risk Factors
- Classification
- Pathogenesis
- Diagnosis
- Risk Stratification

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## Contemporary Management of Clinically Localized Bladder Cancer

- Treatment
  - ✓ Intravesical therapy
    - Chemotherapy
    - Immunotherapy
    - Directed therapy (molecular targets)
    - Combinations/modifiers
    - Device-assisted intravesical chemotherapy
  - ✓ Surgical therapy
    - Radical Cystectomy and urinary diversion
  - ✓ Bladder sparing treatments

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## Contemporary Management of Clinically Localized Bladder Cancer

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### The Urothelium

The epithelium that lines the urinary tract and extends from the tip of the renal papillae to the urethra.

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### The Urothelium

- 3-6 layers of cells that are comprised of (from basement membrane to lumen)
  - ✓ basal cells
  - ✓ intermediate cells
  - ✓ umbrella cells

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### The Urothelium

• It is the **most impermeable of all human epithelia** and is also very inert (does not react with substances), a characteristic that arises due to three distinct factors:

- ✓ (i) a **glycosaminoglycan (GAG)** layer on top of umbrella cells
- ✓ (ii) **tight junctions** between umbrella cells
- ✓ (iii) **uropod** proteins in the apical umbrella cell membrane that form plaques and hinges

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### The Urothelium

• **Bladder cancer is thought to arise from:**

- **Basal cells:** CIS, muscle-invasive urothelial carcinoma, and squamous cell carcinoma
- **Intermediate cells:** non-invasive urothelial carcinoma

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### Bladder Anatomy

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### Microscopic Anatomy

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### Bladder Cancer

- Spectrum of tumors with origin in the urothelium
- Three main histologic types:
  - ✓ Urothelial carcinoma
  - ✓ Squamous cell carcinoma
  - ✓ Adenocarcinoma
- **90% Urothelial carcinoma**
  - ✓ Pure urothelial
  - ✓ urothelial carcinoma with divergent differentiation
  - ✓ Nested, Micropapillary, Lymphoepithelioma like, Plasmacytoid, Sarcomatoid

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### Epidemiology

- Bladder cancer is the **fourth** most common cancer in men and the fifth most common malignancy overall.
- In the United States in **2021, 83,730 new cases and 17,200 deaths from bladder cancer** were expected to occur.
- **The male to female ratio is 4:1**, with an age standardized incidence rate of 10/100,000 for males and 2.5/100,000 for females.
- Approximately **1 in 27 males** and **1 in 89 females** will develop bladder cancer over the course of their life.
- **Median age of diagnosis is 73.** Men over 70 have a 3.7% probability of developing bladder cancer compared with 0.38% for men 40 to 59.
- Caucasians are more likely to develop bladder cancer than other ethnic groups.


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### Etiology


#### Acquired/Environmental Risk Factors




Male sex  
Advanced age




Cigarette smoking




Occupational exposure to aromatic amines



Cyclophosphamide exposure



Genetics  
(*TP53*, *RB*)



Balkan endemic nephropathy

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### Etiology

#### Acquired/Environmental Risk Factors

Risk Factor	Comment
Tobacco Smoke	Attributable risk = 50-60% Important susceptibility gene: <i>NAT2</i> Pack-years exposure increases: <ul style="list-style-type: none"> <li>Risk of bladder cancer</li> <li>Risk of high stage and grade</li> <li>Recurrence and progression rates</li> <li>Mortality rate</li> </ul>
Occupational Exposures	
Aromatic hydrocarbons	Examples: benzo(a)pyrene, benzene, coal tar, bitumens, diesel exhaust Uses: industrial chemical, asphalt Occupations: metal processing, truck drivers, oil and coal production
Aromatic amines	Examples: 2-toluidine, 2-naphthylamine, 4-aminobiphenyl, aniline Uses: dyes Occupations: textiles, painter, hairdresser, chemical plant
N-nitrosamines	Examples: N-nitrosomethylamine, 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone Uses: rubber, tobacco curing, preservative Occupations: smokers, rubber and latex manufacturing
Metals and inorganics	Examples: chromium, cadmium, beryllium, cobalt, nickel Uses: numerous Occupations: metal smelting
Other	Arsenic in drinking water, risk is compounded by smoking and nutritional status Blackfoot disease: seen in Taiwan – urothelial tumors, cardiovascular problems, hyperkeratosis

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### Etiology

#### Acquired/Environmental Risk Factors

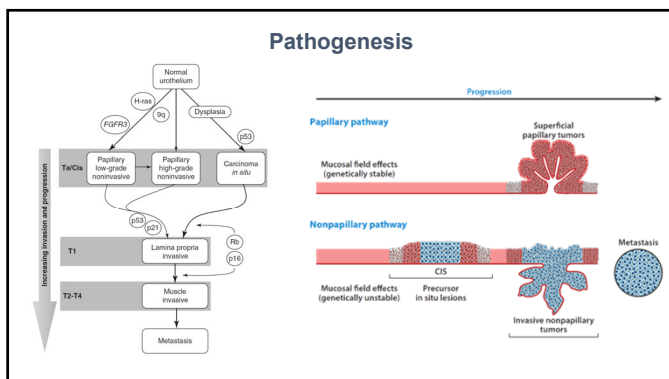
Risk Factor	Comment
Dietary <ul style="list-style-type: none"> <li>Low fluid intake</li> <li>Meat</li> </ul>	Urgent contact hypothesis: more water = less contact time for carcinogens Meat consumption (in general) is associated with higher risk Worse culprits: barbecued meat and processed meat
Infectious Organisms <ul style="list-style-type: none"> <li>Schistosomiasis</li> <li>Chronic UTIs</li> <li>Polyma viruses</li> </ul>	<i>S. Hematobium</i> Chronic Foley catheters in paraplegic patients BK virus
Botanicals <ul style="list-style-type: none"> <li>Aristolochia plants</li> </ul>	Product: Aristolochic Acid, known carcinogen Aristolochia fangchi: Chinese Herb nephropathy Aristolochia clematica: Balkan nephropathy
Drugs <ul style="list-style-type: none"> <li>Phenacetin</li> <li>Cyclophosphamide</li> </ul>	Similar to Acetaminophen. Analgesic nephropathy Metabolized to Acrolein (carcinogen). Neutralized by MESNA
Radiation	Pelvic radiation for Cervical/Colorectal/Prostate cancers

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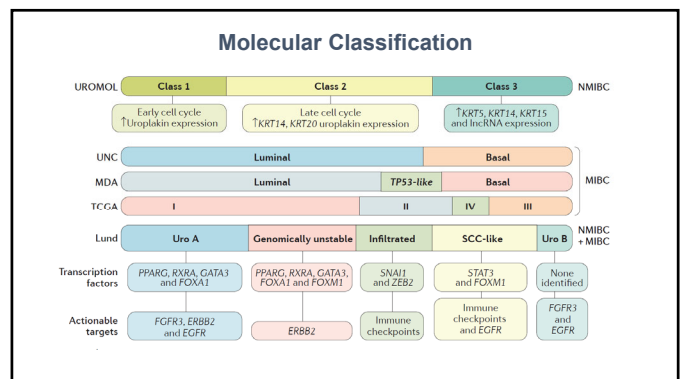
### Genetic Factors Associated with Bladder Cancer

- Syndromes associated with Bladder cancer**
  - ✓ Lynch and Muir-Torre syndrome (MSH)
  - ✓ Peutz-Jeghers syndrome
  - ✓ Cowden syndrome
  - ✓ Li-Fraumeni syndrome (p53)
  - ✓ Costello syndrome
  - ✓ Neurofibromatosis (NF1)
- Susceptibility genes associated with bladder cancer**
  - ✓ N-acetyltransferases (*NAT1* and *NAT2* genes)
  - ✓ Glutathione S-transferases (*GST* genes)
  - ✓ Mismatch repair genes (*MSH* and *MLH* genes)

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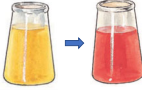
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
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### Signs and Symptoms

- **Hematuria** is the most common presenting symptom in patients with bladder cancer.
- Cancer Rates:
  - ✓ **Gross Hematuria: 13-34.5%**



- ✓ **Microscopic hematuria: 0.5-10.5%**





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### Signs and Symptoms


- **Irritative voiding symptoms**
  - ✓ Can manifest with primary symptoms: urgency, dysuria, frequency and nocturia
  - ✓ Can lead to delayed diagnosis especially in females

**Hematuria and voiding symptoms** are seen commonly with other urologic conditions such as enlarged prostates, urinary tract infection and urolithiasis







Hematuria, either gross or microscopic (predominant symptom)



Urinary frequency  
Urinary urgency  
Dysuria



Flank pain (rare, suggests an advanced mass)



Lower extremity edema (rare, suggests an advanced mass)

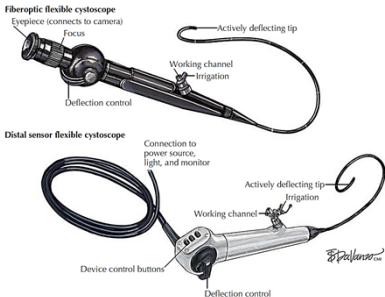
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### Diagnostic Tests (Cystoscopy, Urine tests)

- Patients suspected of having bladder cancer due to hematuria or symptoms should first undergo office **cystoscopy**
- Not all tumors are readily visible on conventional white light (WL) cystoscopy, and CIS is notorious for being indistinguishable from normal urothelium or inflamed mucosa
- **Biopsy or resection in the operating room** is the next typical diagnostic and therapeutic step
- Cytology:
  - ✓ Most commonly used adjunct for identification of bladder cancer
  - ✓ Detect neoplastic cells in the urine
  - ✓ **low sensitivity** for identification of **low-grade tumors**
  - ✓ can be difficult to interpret in patients with inflammation
  - ✓ operator dependent variability

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### Diagnostic Tests OFFICE CYSTOSCOPY (Flexible Cysto)

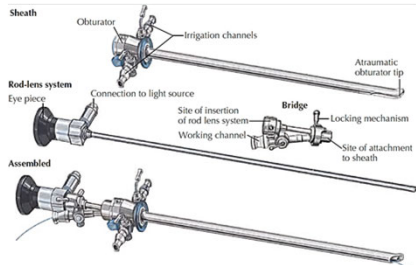


**Fiberoptic flexible cystoscope:** Eye piece (connects to camera), Focus, Actively deflecting tip, Working channel, Irrigation, Deflection control.

**Distal sensor flexible cystoscope:** Connection to power source, light and monitor, Actively deflecting tip, Irrigation, Working channel, Device control buttons, Deflection control.

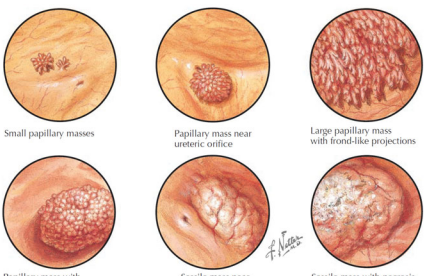
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### Diagnostic Tests OPERATING ROOM CYSTOSCOPY (Rigid Cysto)



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### Diagnostic Tests CYSTOSCOPY



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### Enhanced Cystoscopy

Hexaminolevulinate (HAL) and Narrow Band Imaging (NBI)

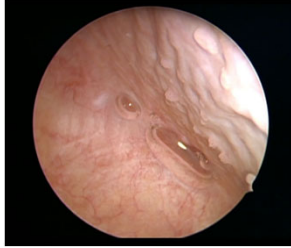
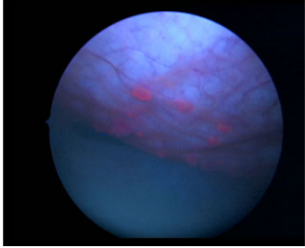
- Two technologies are currently available that may increase the effectiveness of TURBT, hexaminolevulinate blue light and narrow band imaging
- HAL cystoscopy requires the intravesical instillation of a photosensitizing agent (Cysview®) for 1-3 hours prior to cystoscopy.**
- HAL has preferential intracellular accumulation of photoactive porphyrins in **malignant vs non-malignant** cells
- Excitation with blue light illumination results in fluorescence of cancer cells resulting in better tumor visualization

HAL cystoscopy is associated with:
Increased detection of sub-clinical papillary tumors and CIS
Improved TURBT when done at time of TURBT
Reduction in bladder tumor recurrences of 25%

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### Enhanced Cystoscopy

Hexaminolevulinate (HAL) and Narrow Band Imaging (NBI)

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### Diagnostic Tests

CYTOLOGY

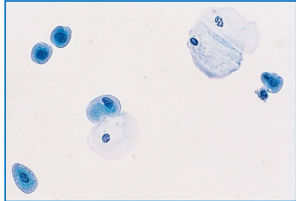
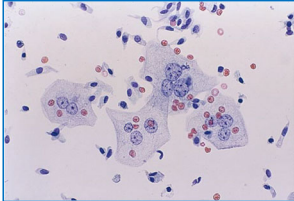
RELATIVE ADVANTAGES AND DISADVANTAGES OF URINE SPECIMEN TYPES

Specimen Type	Advantages	Disadvantages
Voided urine	Noninvasive No instrumentation artifact	Low cellularity Vaginal contamination Poor preservation
Catheterized	High cellularity	Invasive Instrumentation artifact Poor preservation
Bladder washing	High cellularity Good cell preservation	Invasive Instrumentation artifact
Upper tract washing	High cellularity Good preservation	Invasive Instrumentation artifact
Brush cytology	Selective sampling Selective sampling	Invasive
Ileal loop	Permits screening for recurrent bladder cancer	Air drying possible (if direct smear) Low cellularity Poor preservation

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### Diagnostic Tests

CYTOLOGY

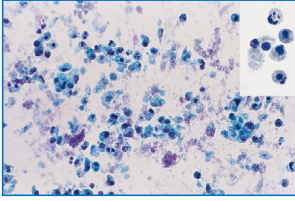
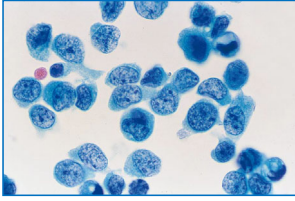
**Normal voided urine**  
Most benign voided urine samples show a mixture of urothelial cells and squamous cells. In voided urine, most of the urothelial cells are of "intermediate" type, with an oval or pyramidal shape.

**Umbrella cells**  
These are the largest urothelial cells and cover the surface of the urothelium. Normal columnar urothelial cells are also present

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### Diagnostic Tests

CYTOLOGY

**Ileal conduit urine**  
Most cells in ileal loop specimens are degenerated intestinal cells that resemble macrophages.

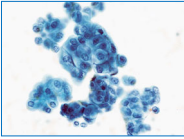
**High-grade urothelial carcinoma (UC)**  
Numerous isolated malignant cells have enlarged, dark nuclei and an increased nuclear-to-cytoplasmic ratio.

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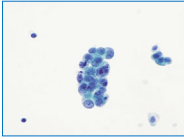
### Diagnostic Tests

CYTOLOGY

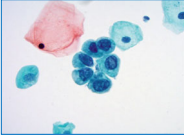
Normal



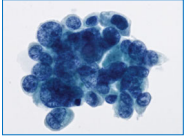
Atypia



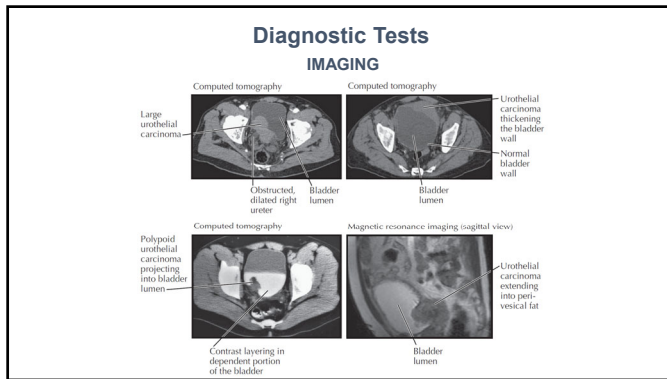
Suspicious



Positive



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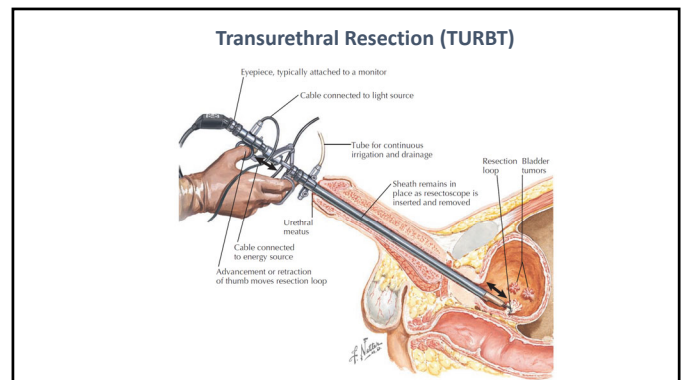
### New bladder-imaging technology

	Macroscopic		Microscopic	
	Photodynamic diagnosis (PDD)/ fluorescence cystoscopy	Narrow band imaging (NBI)	Optical coherence tomography (OCT)	Confocal laser endomicroscopy (CLE)
Field of view	Wide	Wide	Narrow	Narrow
Contrast agent	Yes – HAL	No	No	Yes – fluorescein
Scope/probe size	Scope: 5–7 mm	Scope: 5–7 mm	Probe: 2–7 mm	Probe: 1 to 2–6 mm
Depth	Mucosal	Mucosal	1–3 mm	120 µm
Resolution	mm	mm	10–20 µm	1–5 µm
Commercially available?	Yes	Yes	Yes	No

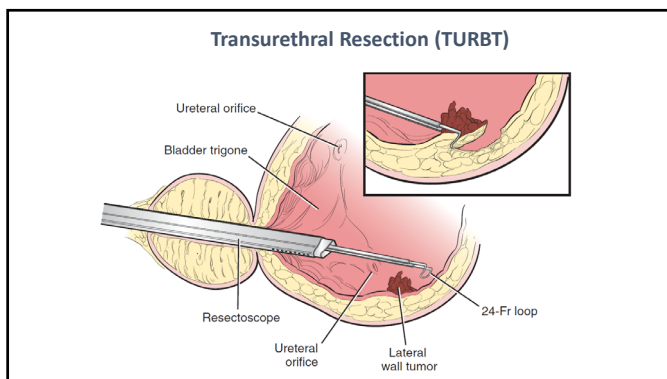
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- ### Transurethral Resection (TURBT)
- Primary way that bladder tumors are diagnosed and treated
    - General or spinal anesthesia = SURGICAL procedure, not a lab test!
  - Small tumors can be removed with cold cup biopsy forceps and the biopsy crater and surrounding urothelium (important due to field effect) can be fulgurated.
  - Larger tumors require the use of an endoscopic resectoscope.
  - Large or nodular tumors should be resected and submitted in steps.
    - The first step is to resect the endoluminal part of the tumor so that it is flush with the normal adjacent bladder wall.
    - Second step of resecting deeper into the bladder wall occurs.
    - Deeper chips are sent separately for pathology to aid in the identification of lamina propria or muscle invasion

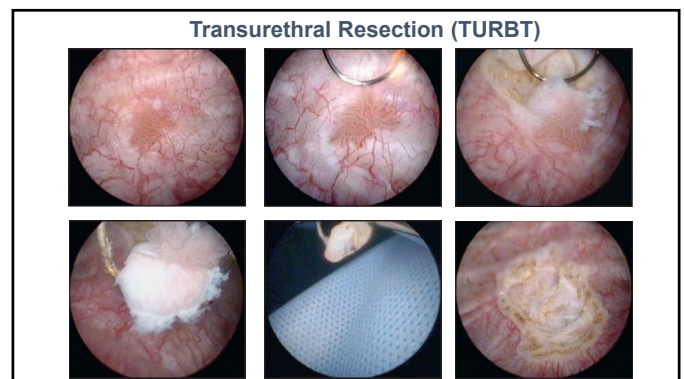
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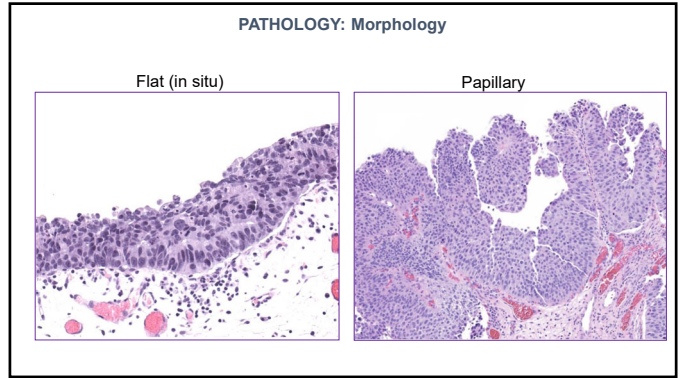


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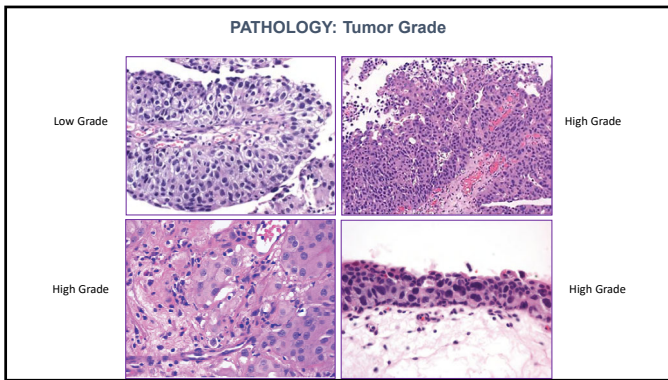
### Complications of TURBT)

Complication	Rate	Management
UTI	3%	Urinalysis and culture Antibiotics
Bleeding requiring intervention or transfusion	2%	IV fluids +/- blood transfusion Reverse systemic blood thinners Manual bedside clot evacuation 3-way Foley + continuous bladder irrigation Clot evacuation and fulguration in operating room Prothrombotic bladder irrigants Consider systemic agents like aminocaproic acid (Amicar®) Angioembolization of bladder Cystectomy
Bladder perforation		Stop resection
Any	2%	Place large (>20 F) Foley catheter
Intraperitoneal	0.4%	Do not perform continuous bladder irrigation
Extraperitoneal	1.6%	Do not administer postoperative chemotherapy
		Start empiric antibiotics
		Observe in hospital overnight and possibly longer
		Laparotomy and bladder repair if (open repair may increase the risk of tumor seeding):
		Very large intra-peritoneal rupture
		Large amount of iatrogenic ascites
		Pending intra-abdominal sepsis
		Periodic imaging to rule out extra-vesical seeding
TUR syndrome	<1%	Extremely rare with saline TURBT
Mortality	<1%	

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### PATHOLOGY: Tumor Grade

		Grading of papillary urothelial neoplasia			
		Papilloma	Papillary neoplasia of low malignant potential	Low grade papillary carcinoma	High grade papillary carcinoma
<b>Architecture</b>	Papillae	Delicate, occasionally fused	Delicate, occasionally fused	Fused or branching, delicate	Fused or branching, delicate
	Organization of cells	Identical to normal	Polarly identical to normal, often thickened, cohesive	Predominantly ordered, minimal crowding and minimal loss of polarity, any thickness, cohesive	Predominantly disordered with frequent loss of polarity, any thickness, often discohesive
	Nuclear size	Identical to normal	Uniform, may show minimal enlargement	Enlarged with variation in size, usually <8x size of lymphocyte	Enlarged with variation in size, often >8x size of lymphocyte
<b>Cytology</b>	Nuclear shape	Identical to normal	Elongated, round to oval, uniform	Round to oval, slight variation in shape and contour	Moderate to marked pleomorphism
	Nuclear chromatin	Fine	Fine	Mild variation between cells, occasional hyperchromasia	Hyperchromasia, moderate to marked variation between cells
	Nucleoli	Absent	Absent or inconspicuous	Usually inconspicuous	Multiple prominent nucleoli may be present
	Mitoses	Absent	Rare, basally located	Occasional, present at any level	Usually frequent, present at any level, may be atypical

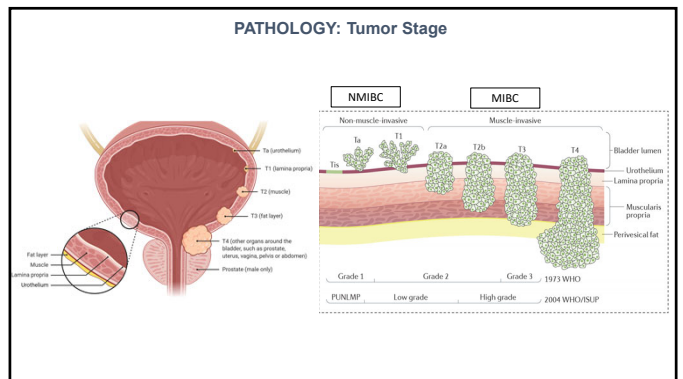
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### PATHOLOGY: Tumor Grade

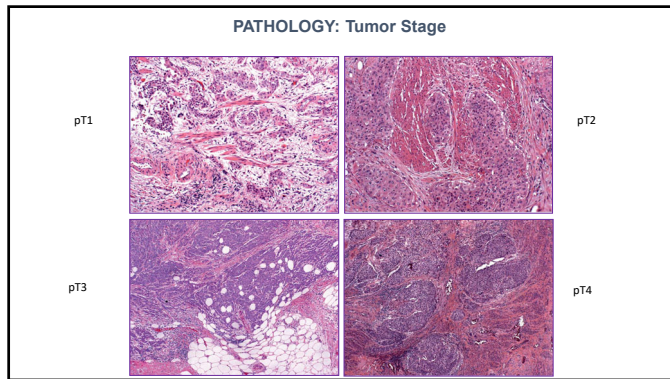
Normal Urothelium      Urothelial dysplasia      Carcinoma in situ

	Reactive atypia	Hyperplasia	Dysplasia	Carcinoma in situ
Cell layers	Variable	>7 cells	Variable	Variable
Polarization	Slightly abnormal	Normal	Slightly abnormal	Abnormal
Cytology	Vacuolated	Homogeneous	Slightly increased	Increased
N:C ratio	Normal or slightly increased	Normal or slightly increased	Slightly increased	Increased
Nuclei	Normal	Normal	Mild	Moderate to severe
Arrangement	Regular/smooth	Regular/smooth	Irregular/irregular	Pleomorphic
Borders	Regular/smooth	Regular/smooth	Slight hyperchromasia	Coarse/hyperchromatic
Chromatin	Fine/dusty	Fine	Even	Uneven
Chromatin distribution	Even	Even	Small/absent	Large/prominent
Nucleoli	Large	Small/absent	None	Often
Mitotic figures	Variable	Absent	Rare	Often
Denudation	Variable	No	No	Variable
Cytokeratin 20	Surface	Surface	Variable	Variable
Stromal microvascular proliferation	Variable	Variable	Less prominent	Often prominent

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**Risk Stratification**

Low Risk	Intermediate Risk	High Risk
LG <sup>a</sup> solitary Ta ≤ 3cm	Recurrence within 1 year, LG Ta	HG T1
PUNLMP <sup>b</sup>	Solitary LG Ta > 3cm	Any recurrent, HG Ta
	Multifocal LG Ta	HG Ta, >3cm (or multifocal)
	HG <sup>c</sup> Ta, ≤ 3cm	Any CIS <sup>d</sup>
	LG T1	Any BCG failure in HG patient
		Any variant histology
		Any LVI <sup>e</sup>
		Any HG prostatic urethral involvement

<sup>a</sup>LG = low grade; <sup>b</sup>PUNLMP = papillary urothelial neoplasm of low malignant potential; <sup>c</sup>HG = high grade; <sup>d</sup>CIS=carcinoma in situ; <sup>e</sup>LVI = lymphovascular invasion

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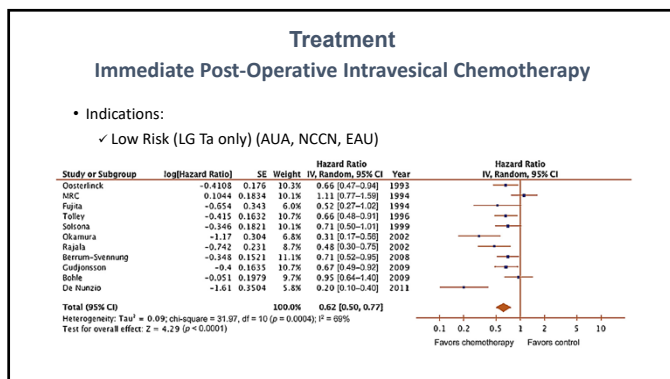
**Risk Stratification**

Risk group	Recurrence(%)		Progression(%)	
	1yr	5yr	1yr	5yr
Low	15	31	0.2	0.8
Intermediate	24-38	46-62	1-5	6-17
High	61	78	17	45

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- Treatment**  
**Risk Adapted Treatment**
- **Low Risk** –peri-operative intravesical chemotherapy only
  - **Intermediate Risk** – peri-op intravesical chemo OR induction chemotherapy ± maintenance
  - **High risk** – Immunotherapy (i.e intravesical BCG): induction BCG plus maintenance
  - **Very high** – consider primary cystectomy

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- Treatment**  
**Immediate Post-Operative Intravesical Chemotherapy**
- A single instillation of chemotherapy administered within 24 hours of surgery (ideally within 6 hours)
  - Gemcitabine (preferred) and mitomycin C are the most commonly used agents
  - Immediate postoperative intravesical chemotherapy **reduces** the 5-year recurrence rate by approximately 35% and has a number needed to treat to prevent a recurrence of 7. However, it **does not reduce** the risk of progression or the risk of cancer mortality
  - It is not effective in patients with an elevated EORTC recurrence risk score (>=5). This includes patients with >=8 tumors and those with >= 1 recurrence/year
  - Contraindications include: bladder perforation, known drug allergy

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### Treatment

#### Induction and Maintenance Intravesical Chemotherapy

- Indications:
  - Intermediate risk patients
  - Weekly instillation, 6-week induction course (Gemcitabine, MMC), 2-6 weeks after TURBT
  - Patients must retain the drug for two hours for peak efficacy
  - Since urine production during treatment will dilute the drug and fill the bladder (making it hard for the patient to hold the drug in), patients should not drink for 4-6 hours prior to treatment.
  - Cystoscopy is done 6 weeks later to assess for response
  - The most common maintenance schedule for chemotherapy is once monthly for 1 year.

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### Treatment

#### Common Intravesical Chemotherapy Agents

Drug	Dose	Volume	Mechanism of action	Side-effects
<b>Anthracyclines</b>			Cross-links DNA/RNA	Chemical cystitis (15-20%)
Doxorubicin	50 mg	50 mL	Inhibits topoisomerase II	Severe (3-5%)
Epirubicin	50 mg	50 mL	Creates iron-mediated free radicals	Cardiotoxicity (<1%)
Valrubicin	800 mg	75 mL	Histone removal from chromatin	Myelotoxicity (<1%)
<b>Antitumor antibiotics</b>			Cross-links DNA	Chemical cystitis (15-20%)
<b>Mitomycin C</b>	40 mg	20 mL		Severe (3-5%) Myelotoxicity (<1%) Skin desquamation (if spillage onto skin)
<b>Alkylating Agents</b>			Cross-links DNA	Chemical cystitis (10-15%)
ThioTEPA	60 mg	30 mL		Severe (1-3%) Myelosuppression (5%) (very small molecule)
<b>Toxanes</b>			Inhibits microtubules and spindle	Chemical cystitis (10-15%)
Paclitaxel	500 mg	100 mL	Blocks metaphase progression	Myelosuppression (<1%)
Docetaxel	75 mg	100 mL		
<b>Antimetabolites</b>			Pyrimidine analog (fake nucleotide)	-chemical cystitis (5-10%)
<b>Gemcitabine</b>	2 g	100 mL	G1/S cell cycle arrest	-myelosuppression (<1%)

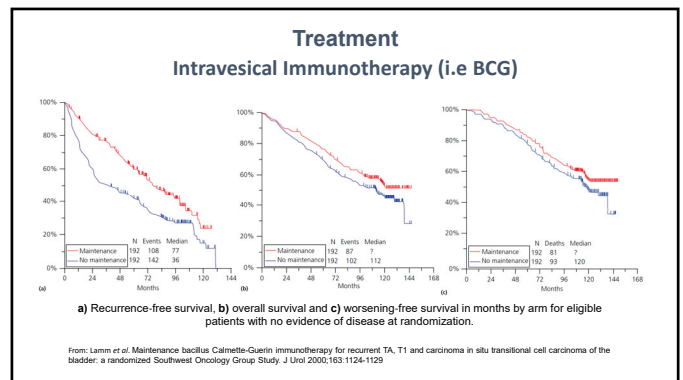
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### Treatment

#### Intravesical Immunotherapy (i.e BCG)

- Indications:
  - All high risk patients (Induction BCG + maintenance 3 yr )
  - Once weekly instillations for 6 weeks (induction course)
  - Maintenance: 3 weekly instillations at 3, 6, 12, 18, 24, 30 and 36 months
  - Can be dose reduced (worldwide BCG shortage!) to 1/2 or 1/3 dose
  - Withhold if: traumatic catheterization, bacteriuria, persistent gross hematuria, persistent severe local symptoms, systemic symptoms
  - Data suggest the benefit of maintenance BCG through a decreased recurrence for NMIBC

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### Treatment

#### Radical Cystectomy

- Treatment of choice for MIBC
- With or without Neoadjuvant chemotherapy (NAC)
- Not commonly performed for NMIBC. Several situations where it is justifiable:
  - BCG-Unresponsive High-Risk Bladder Cancer
    - Bladder tumors recur despite prior BCG are at very high risk of recurrence (60-80%) and progression (10-20%).
    - Cystectomy is the most effective cancer therapy in this situation but comes with the morbidity of urinary diversion and the morbidity and mortality risks of the operation.
  - Very Large (> 10 cm) Bladder Tumors
    - Occasionally patients will present with enormous bladder masses that occupy the majority of the bladder and that appear potentially NMIBC

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### Treatment

#### Radical Cystectomy

- Divergent histology (urothelial cancer with variant histology)
  - Prognosis and overall outcome likely inferior to urothelial bladder cancer

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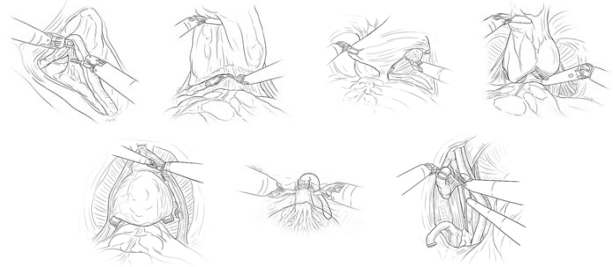
### Treatment Radical Cystectomy

- *Small Capacity Contracted Bladder or Neurogenic Bladder*
  - ✓ Very **small capacity contracted bladders** (from repeated TURBT or intravesical therapy) or who have **neurogenic bladders** with NMIBC
  - ✓ Intravesical therapy is impossible to do effectively in these patients and often makes their bladder symptoms worse.
  - ✓ Cystectomy cures the vast majority of these patients and results in improved quality of life for most



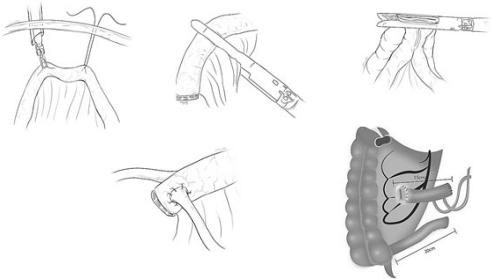
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### Treatment Radical Cystectomy



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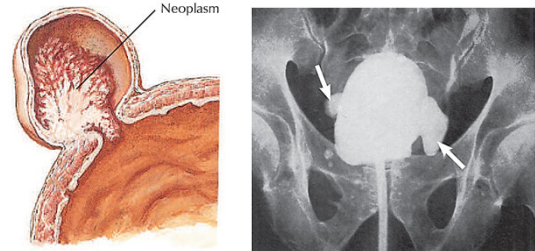
### Treatment Radical Cystectomy



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### Treatment Partial Cystectomy

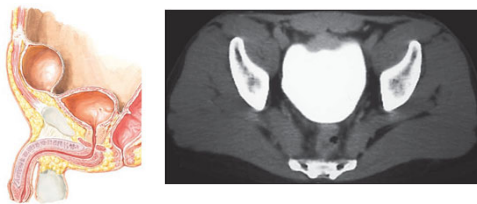
- Indications
  - ✓ Tumors occurring in a **bladder diverticulum**



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### Treatment Partial Cystectomy

- Indications
  - ✓ Tumors occurring at the **dome of the bladder**
    - **partial cystectomy** with *en bloc* urachectomy is the treatment of choice for urachal tumors



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### Treatment Radiation, ChemoRT, Trimodality (TMT)

- The role of radiation or combined chemoradiation in NMIBC is evolving.
- One trial in high-grade T1 patients demonstrated that **radiotherapy alone** did not improve recurrence or progression-free survival vs. **intravesical therapy** and was associated with 5% incidence of long-term complications.
- Few data exist for combined ChemoRT therapy in NMIBC
- TMT (Maximal TURBT+Chemotherapy+Radiotherapy) for MIBC
- Immunotherapy+RT+/-Surgery Trials

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### Surveillance

- Bladder cancer has a high risk of **recurrence** and **progression** requiring life-time surveillance.
- The main modality used is **cystoscopic** evaluation of the bladder accompanied frequently by **cytologic** evaluation of the urine.
- No consensus on optimal follow up regimen
- Most guidelines recommend that the first cystoscopy following TURBT should take place at three months, since recurrence at this time is recognized as an important prognosticator for both recurrence and progression
- The National Comprehensive Cancer Network (NCCN) guidelines recommend **cystoscopic evaluation every 3-6 months** and then at increasing intervals as appropriate
- Urine based tumor markers are optional adjunctive tests

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### Surveillance

- **Higher risk** patients are usually assessed cystoscopically at **3-month** intervals for the first two years, and then at **6-month** intervals for the next 2-3 years, and then **annually** thereafter.
- For **low-risk** tumors
  - ✓ AUA guidelines recommend that if first surveillance cystoscopy is negative for tumor, a clinician should perform subsequent surveillance cystoscopy **six to nine months** later, and then **annually** thereafter.
  - ✓ EAU guidelines recommend cystoscopy at **3 months** and if negative then another cystoscopy at **12 months** and **annually thereafter** for the next five years.
- The surveillance cycle restarts every time a tumor is identified.
- If a tumor is identified on surveillance cystoscopy, the patient will require another TURBT to reassess the stage and grade

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**Thank You!**

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