

Medications Instilled into the Bladder to Treat Cancer

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Intravesical Chemotherapy for Urothelial Carcinoma

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Presenter Disclosure

- **Faculty/Speaker: Jeff Saranchuk**

- **Relationships with financial sponsors:**

- **Grants/Research Support:** CCMB Foundation, industry funding for trials at the Manitoba Prostate Centre

- **Speakers Bureau/Honoraria:** none

- **Consulting Fees:** none

- **Other:** none

Mitigating Potential Bias

- Not Applicable

Equity Commitment

- In preparing for this presentation, I have considered the Health Equity Resource for Presenters provided by the conference planning committee.
- This was provided to help presenters reflect on how these topics and content can have good effects or bad effects on people or populations that are underserved.

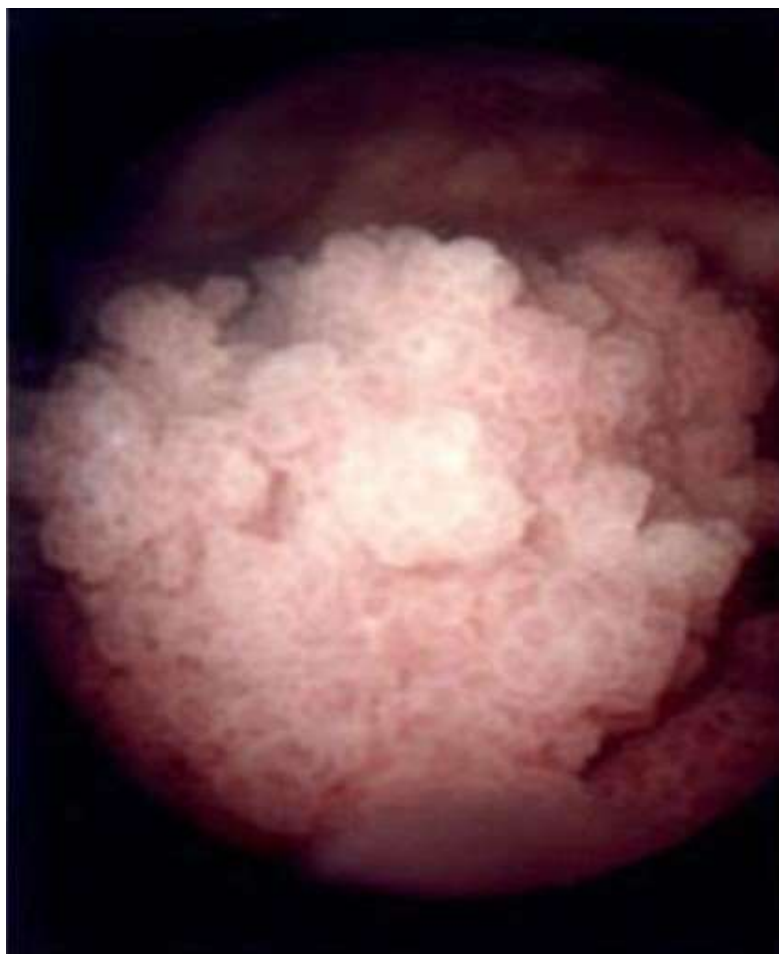
Learning Objectives

- Describe intravesical therapy
- List common side effects of intravesical therapy with BCG
- List the contraindications to BCG intravesical therapy

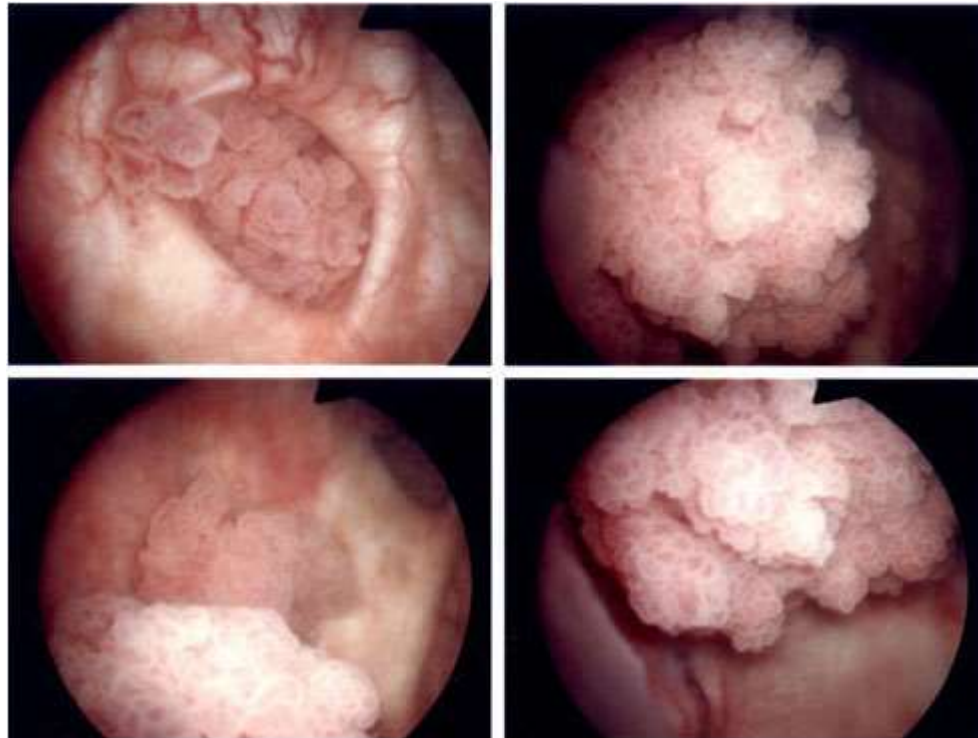
Bladder Cancer

- Transitional cell carcinoma (TCC) or urothelial carcinoma
- Can arise from the lining of the renal pelvis, ureters, or bladder
- Hematuria most common symptom
- Cystoscopy indicated, followed by resection (TUR)

Papillary Bladder Tumours



More examples



Bladder Tumour on CT



Bladder Tumour on MRI



Bladder Cancer Treatment

- Transurethral resection for superficial disease
 - 70% recurrence rate
 - Surveillance cystoscopies (q3 mo X 1 yr, q6 mo X 1yr, then annually)
 - Intravesical therapies as appropriate
 - Primarily BCG
- Radical therapy for muscle invasive disease
 - Cystectomy with creation of ileal conduit/neobladder
 - Radiotherapy +/- chemotherapy

BCG Therapy

- Bacille Calmette-Guerin, attenuated strain of *Mycobacterium bovis*
- Stimulates inflammatory/immune response which destroys the tumour (not anti-bladder ca immunity)
- Medication administered once a week for six weeks (induction course)
- Then given in a maintenance capacity (three doses every six months) for three years

Intravesical Treatment

Advantages of intravesical route

- Little or no systemic uptake
- Optimal contact between drug and tumour/tissue at risk

Disadvantages

- Local effects
- Need for urethral manipulation

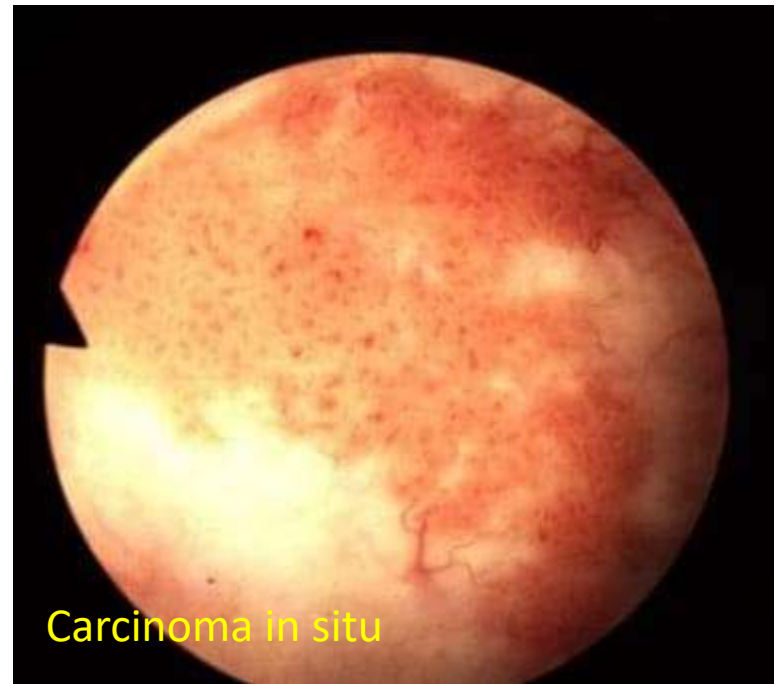
Technique

- Catheter inserted aseptically
- Drain bladder
- Instill agent
- Remove catheter and leave indwelling for 1-2 hours

Indications for BCG Intravesical Treatment

- Therapy for carcinoma in situ
- Preventing or delaying tumour recurrence post TUR (prophylaxis)
- Unresectable disease

- Reduces recurrence rate from 70% to 20%



Side Effects of BCG

- Bladder irritability
 - Dysuria, frequency, urgency
- Fever
- UTI
- Hematuria

- Disseminated infection
- Granulomatous prostatitis

Contraindications to BCG

- Traumatic catheterization
- Active UTI
- Immunocompromised patient

Miscellaneous

- Second induction course can be given if first course fails
- Pts who can't tolerate BCG (prior sepsis or severe side effects) or BCG refractory disease, refuse or can't undergo cystectomy could be candidates for other intravesical agents

Alternative Medications

- Mitomycin C
- Gemcitabine
- Valrubicin/Doxorubicin/epirubicin
- Thiotepa (triethylenethiophosphoramidate)
- Taxanes

Mitomycin C

- Alkylating agent inhibiting DNA synthesis
- 20 to 60 ml per weekly instillation for 6 weeks
- Minimally absorbed, myelosuppression is rare
- Chemical cystitis, allergic reaction (skin symptoms)
- Currently given post TUR bladder tumour in post op, done for many years now
- 7.7% vs 9.4% progression vs BCG in a meta-analysis
- 38% reduction in tumour recurrence

Gemcitabine

- novel deoxycytidine analog with a broad spectrum of antitumor activity
- small phase 1 and 2 studies demonstrated 39 – 70% reduction in recurrence
- Cochrane review showed conflicting results in 3 trials vs BCG
- Well tolerated with less frequency and dysuria

Valrubicin

- Semisynthetic analogue of doxorubicin, an anthracycline antibiotic which binds DNA base pairs, inhibiting topoisomerase II and protein synthesis
- Currently indicated in cases of BCG refractory CIS
- 6 weekly instillations of 800 mg
- 21% of 90 patients with BCG refractory disease showed complete response at median 30 months
- main side effects were reversible local bladder symptoms

Doxorubicin

- anthracycline antibiotic which binds DNA base pairs, inhibiting topoisomerase II and protein synthesis
- Main side effect chemical cystitis which can occur in 25 -50% patients – reduced bladder capacity
- Almost no systemic effects
- 13 to 17% improvement over TUR in preventing recurrence but no improvement in preventing progression

Thiotepa (Triethylenethiophosphoramidate)

- Alkylating agent inhibiting nucleic acid synthesis thus interfering with protein synthesis
- Decrease tumour recurrence in 6 of 11 studies by up to 41% (mean decrease 16%)
- Low molecular weight leads to absorption
- 30mg in 30ml sterile water weekly for 6 weeks then monthly for one year
- Myelosuppression – must follow CBC
- Acute nonlymphocytic leukemia-myelodysplastic syndrome late complication a mean of 57 months (27 to 84) in 6 cases all fatal

Comparison of Agents

AGENT	MW	PERIOPERATIVE USE	RISK GROUP	CYSTITIS (%)	OTHER TOXICITY	DROPOUT (%)	CONCENTRATION/DO SAGE
Doxorubicin (Adriamycin)	580	Yes	Low-Intermediate	20-40	Fever, allergy, contracted bladder, 5%	2-16	50 mg/50 mL
Epirubicin	580	Yes	Low-Intermediate	10-30	Contracted bladder rare	3-6	50 mg/50 mL
Thiotepa	189	Yes	Low-Intermediate	10-30	Myelosuppression 8%-19%	2-11	30 mg/30 mL
Mitomycin	334	Yes	Low-Intermediate	30-40	Rash 8%-19%, contracted bladder 5%	2-14	40 mg/20-40 mL
BCG	N/A	No	Intermediate-High	60-80	Serious infection, 5%	5-10	1 vial/50 mL
Interferon	23,000	No	Salvage	<5	Flulike symptoms 20%	Rare	50-100 MU/50 mL
Gemcitabine	300	Yes	Salvage	Mild	Occasional nausea	<10	1-2 g/50-100 mL

Thank you

Go Blue!



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