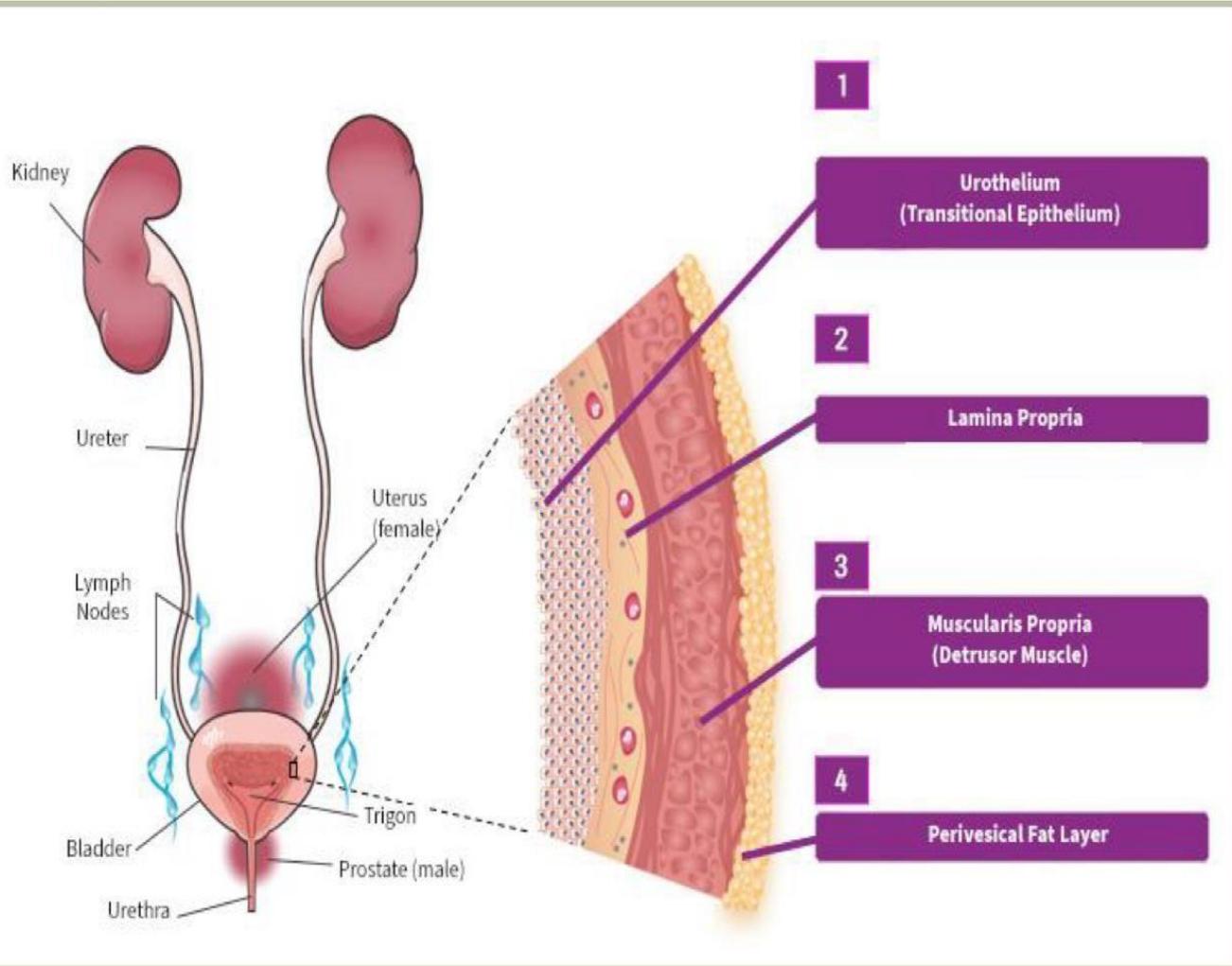


Bladder Cancer

Supervised by: Dr Samer Al Rawashdeh

Done by :
Rama Jehad
Asia Almasri
Heba Amaira

Normal bladder



Bladder is a hollow muscular organ in the lower abdomen

The wall of the bladder has four main layers:

1The inner layer is called the lining. This lining is made up of cells called urothelial or transitional cells. This layer is called the urothelium or transitional epithelium.

2Under the urothelium is a thin layer of connective tissue, blood vessels , and nerves, which is called the laminapropria.

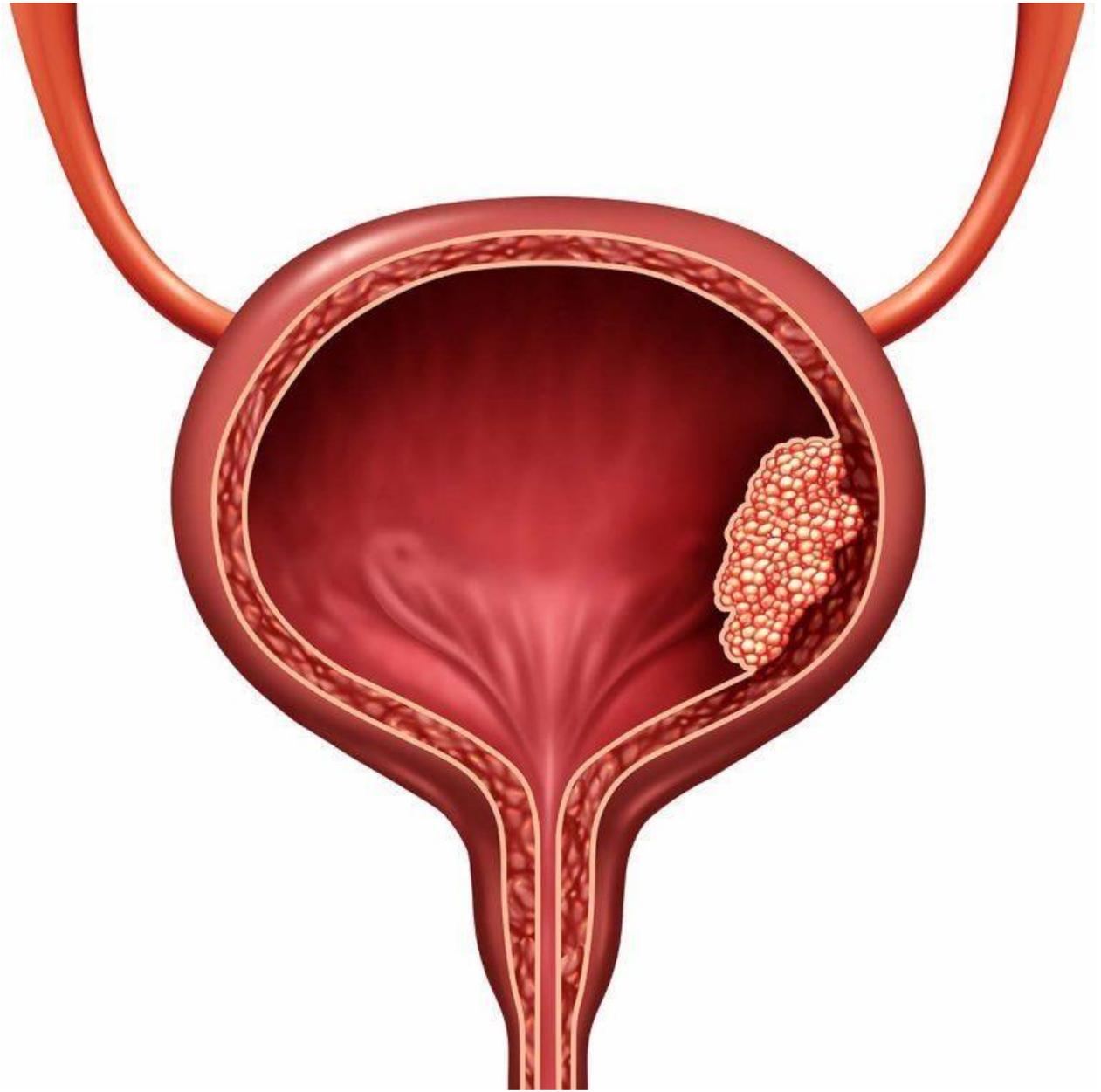
3Next is a thick layer of muscle called the muscularispropria (detrusor muscle).

4Outside of this muscle, a layer of fatty connective tissue

•Bladder cancer is the second most common urological malignancy.

(Renal cell carcinoma is first)

still majority of patients have curable or controllable disease.



Risk factors

Men are 2.5 times more likely to develop the disease than women, may be associated with greater urine residuals in the bladder.

Age increases risk , most commonly diagnosed in the 8th decade and rare <50 years.

Racially, Black people have a lower incidence than White people, but inexplicably they appear to carry a poorer prognosis.

Drugs: phenacetin and cyclophosphamide.

Pelvic radiotherapy.

Environmental carcinogens found in urine, are the major cause of bladder cancer.

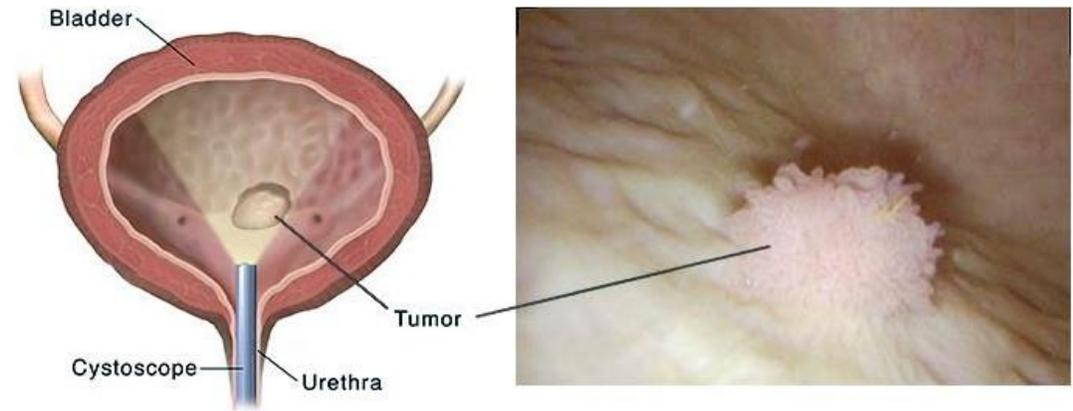
Chronic inflammation of bladder mucosa: bladder stones, long-term catheters

Smoking is the major cause of bladder cancer in the developed world .

Occupational exposure to carcinogens, in particular aromatic hydrocarbons like aniline



Tumors of urinary bladder :



Benign tumors of the bladder, including inverted papilloma and nephrogenic adenoma, are uncommon.

The vast majority of primary bladder tumors are malignant and epithelial in origin.

Types of Bladder Cancer :

- 1 Transitional cell (urothelial) carcinoma
- 2 Squamous cell carcinoma
- 3 Adenocarcinoma

Secondary bladder cancers are mostly metastatic adenocarcinoma from gut, prostate, kidney, or ovary

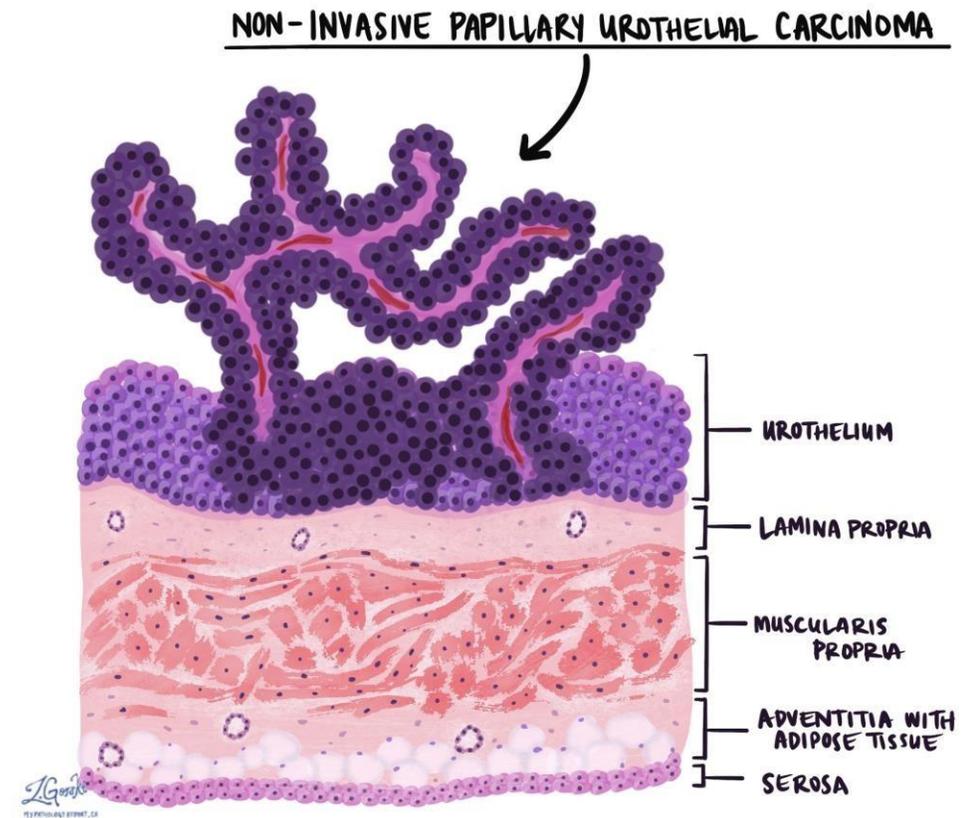
Rarities include pheochromocytoma, melanoma, lymphoma, and sarcoma arising within the bladder muscle

1- Urothelial carcinoma (transitional cell carcinoma)

This is the most common form of bladder cancer. It represents roughly 95% of bladder cancers

Bladder cancer can be described as superficial or non-muscle invasive

Urothelial carcinoma (transitional cell carcinoma) UC may be single or multifocal. Because 5% of patients will have a synchronous upper tract UC and metachronous recurrences may develop after several years, the urothelial field-change theory of polyclonality is favored over the theory of tumor monoclonality with implantation (seeding).



1- Urothelial carcinoma (transitional cell carcinoma)

70% of tumors are papillary, usually G1 or G2, exhibiting at least 7 transitional cell layers covering a fibro-vascular core (normal transitional epithelium has ~5 cell layers). Papillary TCC is usually superficial, confined to the bladder mucosa (Ta) or submucosa (T1).

10% of patients subsequently develop muscle-invasive or metastatic disease. However, a subset of superficial TCC, G3T1 tumors, are more aggressive, with 40% subsequently upstaging.

10% of TCC have mixed papillary and solid morphology and 10% are solid. These are usually G3, half of which are muscle-invasive at presentation.

Carcinoma in situ (Flat carcinomas) :

10% of TCC is flat carcinoma in situ (CIS). This is poorly differentiated carcinoma, but confined to the epithelium and associated with an intact basement membrane. 50% of CIS lesions occur in isolation; the remainder occur in association with muscle-invasive TCC.

Do not grow toward the hollow part of the bladder. It is a flat tumor. The cells are poorly cohesive, up to 100% of patients with CIS exhibiting positive urine cytology

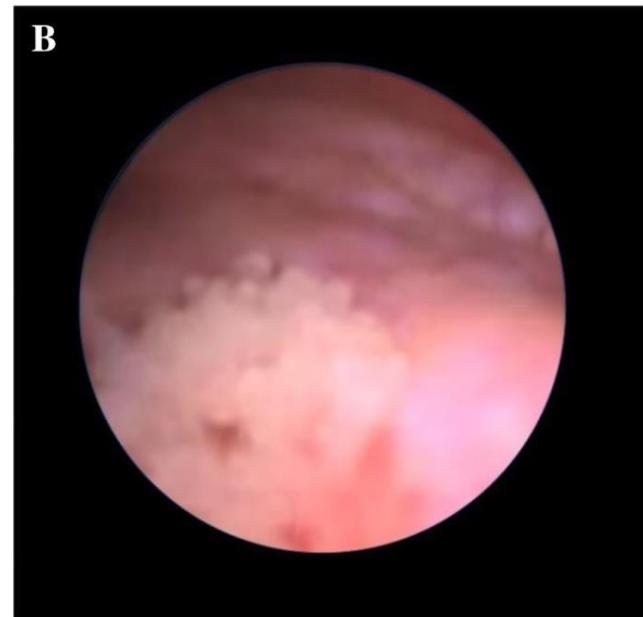
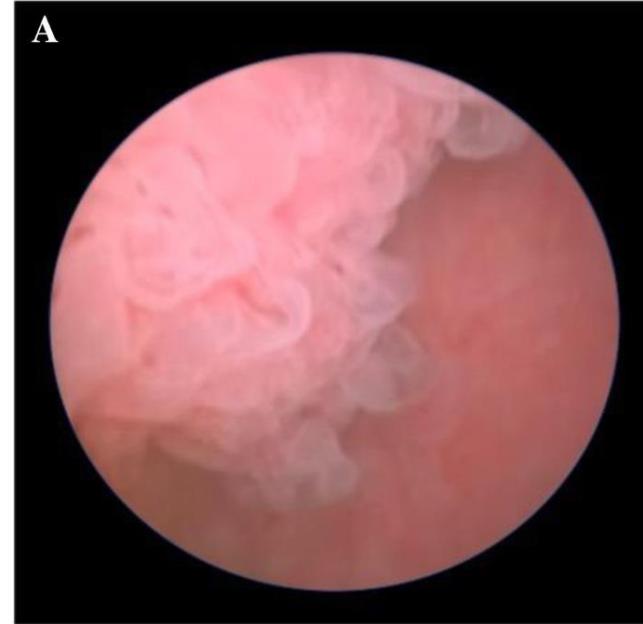
From 40% to 83% of untreated CIS lesions will progress to muscle invasive UC, making CIS the most aggressive form of superficial UC.

CIS usually appears as a flat, red, velvety patch on the bladder mucosa



Papillary urothelial neoplasm of low malignant potential (PUNLMP)

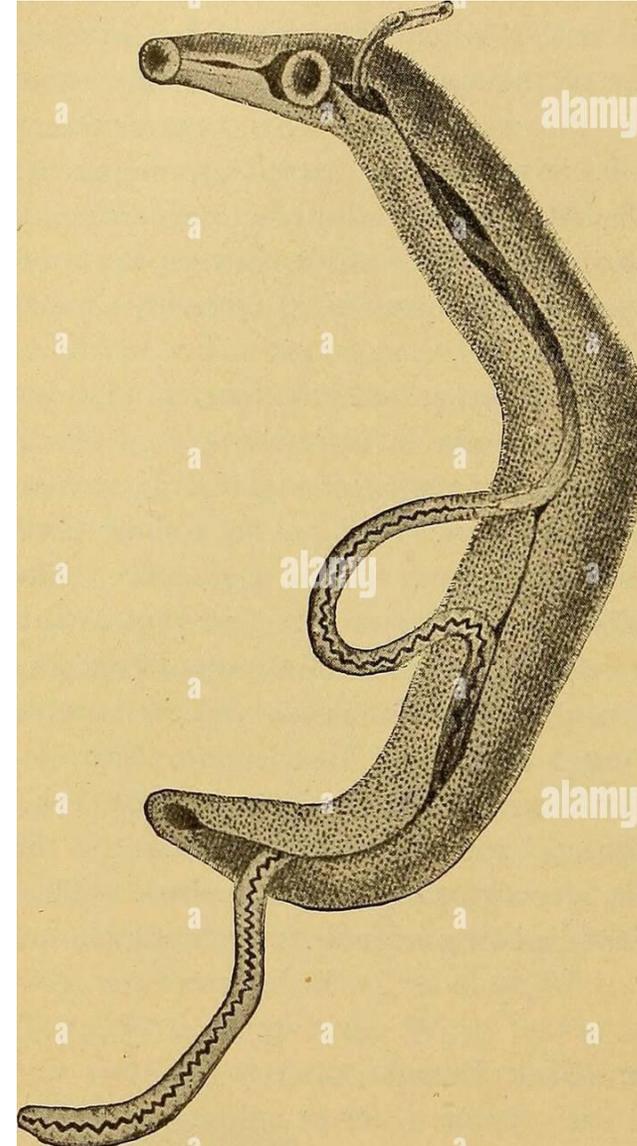
Papillary urothelial neoplasm of low malignant potential (PUNLMP) The World Health Organization (WHO) defines PUNLMP as a papillary urothelial tumor that resembles an exophytic urothelial papilloma but shows increased cellular proliferation exceeding the thickness of normal urothelium. They are typically small (1-2 cm) and have little, if any, cytological atypia. Treatment and follow-up are the same as for low-grade noninvasive urothelial carcinoma.



2-Squamous cell carcinoma

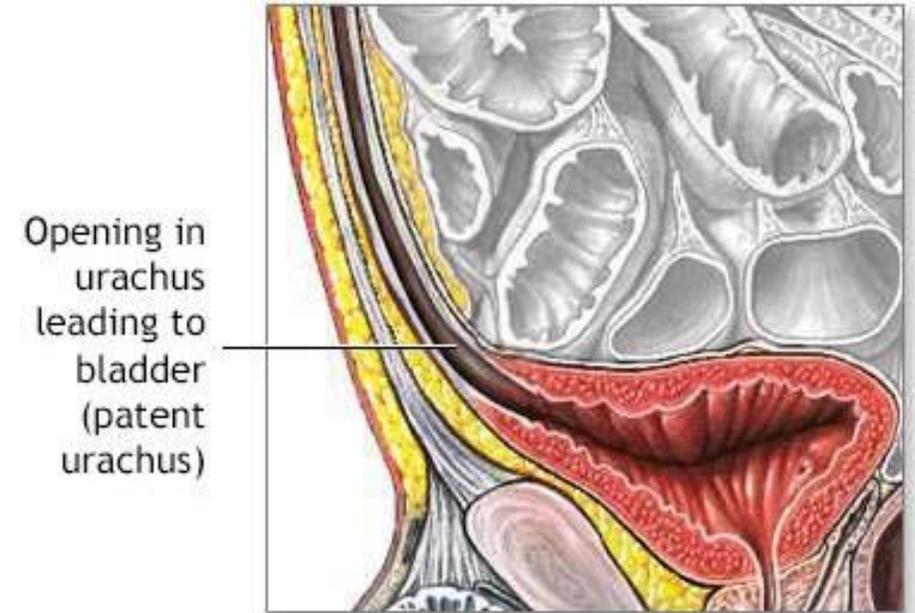
SCC is usually solid or ulcerative and muscle-invasive at presentation. SCC accounts for only 1% of UK bladder cancers. SCC in the bladder is associated with chronic inflammation and urothelial squamous metaplasia, rather than CIS. In Egypt, 80% of SCC is induced by the ova of *Schistosoma haematobium*. 5% of paraplegics with long-term catheters develop SCC. Smoking is also a risk factor for SCC.

The prognosis is better for bilharzial SCC than for non-bilharzial disease, probably because it tends to be lower grade and metastases are less common in these patients.



3- Adenocarcinoma

Adenocarcinoma is rare, usually solid/ulcerative and carries a poor prognosis. One third originate in the urachus, the remnant of the allantois, located deep to the bladder mucosa in the dome of the bladder. Adenocarcinoma is a long-term (10 years) complication of bladder exstrophy and bowel implantation into the urinary tract, particularly bladder substitutions and ileal conduits after cystectomy. There is association with cystitis glandularis, rather than CIS.



ADAM.

The urachus is a remnant of a channel between the bladder and the umbilicus (belly button) where urine initially drains in the fetus during the 1st trimester of pregnancy .

Bladder cancer: presentation

Symptoms

The most common presenting symptom (85% of cases) is **painless haematuria**. This may be initial or terminal if the lesion is at the bladder neck or in the prostatic urethra. 35% of patients >50 years and 10% <50 years with macroscopic haematuria have bladder cancer. **History of smoking or occupational exposure is relevant.**

Asymptomatic microscopic haematuria, found on routine urine stick-testing. Up to 16% of females and 4% of males have stick-test haematuria: less than 5% of those <50 years, while 7-13% of those >50 years will have a malignancy.

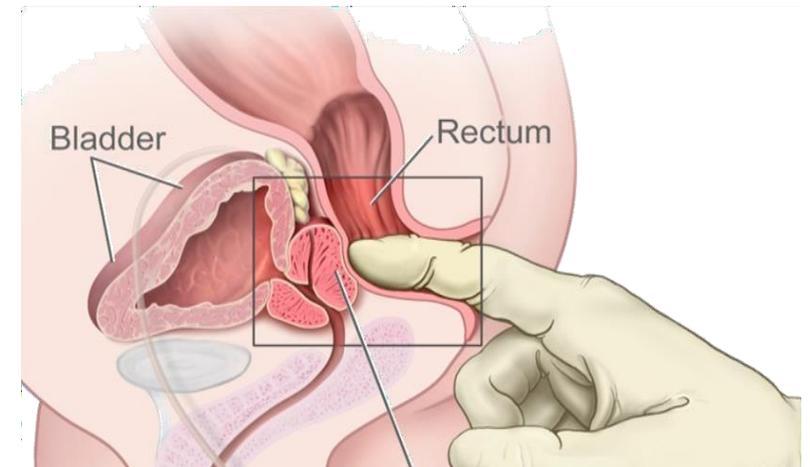
Pain is unusual, even if the patient has obstructed upper tracts, since the obstruction and renal deterioration arise gradually, Pain may be caused by locally advanced (T4 disease).



- **Filling-type lower urinary tract symptoms**, such as urgency or suprapubic pain. There is almost always microscopic or macroscopic haematuria. This so-called malignant cystitis is typical in patients with CIS.
- Recurrent urinary tract infections and pneumaturia due to malignant colovesical fistula, though less common than benign causes (diverticular and Crohn's disease).
- More advanced cases may present with **lower-limb swelling** due to lymphatic/venous obstruction, bone pain, weight loss, anorexia, confusion, and anuria (renal failure due to bilateral ureteric obstruction).
- Urachal adenocarcinomas may present with a **blood or mucus umbilical discharge or a deep subumbilical mass** (rare).

▶ **Signs**

- ▶ General examination may reveal pallor, indicating anaemia due to chronic renal impairment or blood loss.
- ▶ Abdominal examination may reveal a suprapubic mass in the case of locally advanced disease.
- ▶ Digital rectal examination may reveal a mass above or involving the prostate.



Tumor spread :

Direct tumor growth to involve the detrusor muscle, the ureteric orifices, prostate, urethra, uterus, vagina, perivesical fat, bowel, or pelvic side walls.

Implantation into wounds/percutaneous catheter tracts.

It's contraindicated to do suprapubic catheterization for any pt suspected to have bladder cancer

Lymphatic infiltration of the iliac and para-aortic nodes.

Haematogenous most commonly to **liver** (38%), lung (36%), adrenal gland (21%), and bone (27%). Any other organ may be involved.

Bladder cancer grading and staging

- **Histological grading**

- is divided into: well, moderately, poorly differentiate and undifferentiated

(abbreviated to G1, G2, G3 and G4 respectively).

- Also can be divided into low grade or high grade:

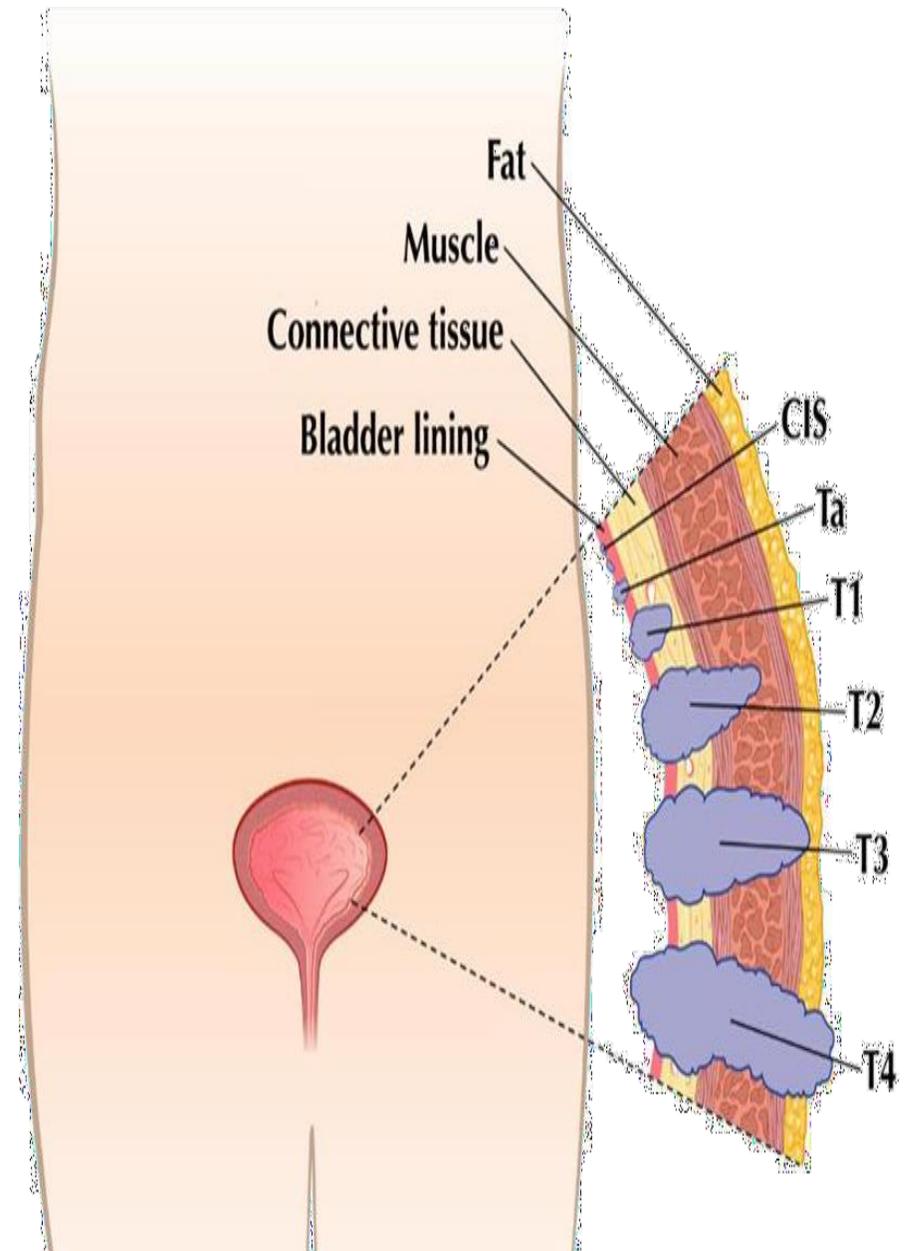
low-grade - the cancer cells are slow-growing and are less likely to spread

high-grade - the cancer cells grow more quickly and are more likely to spread. **Carcinoma in situ (CIS) is always classed as high-grade.**

Table 6.8 2002 TNM staging of bladder carcinoma

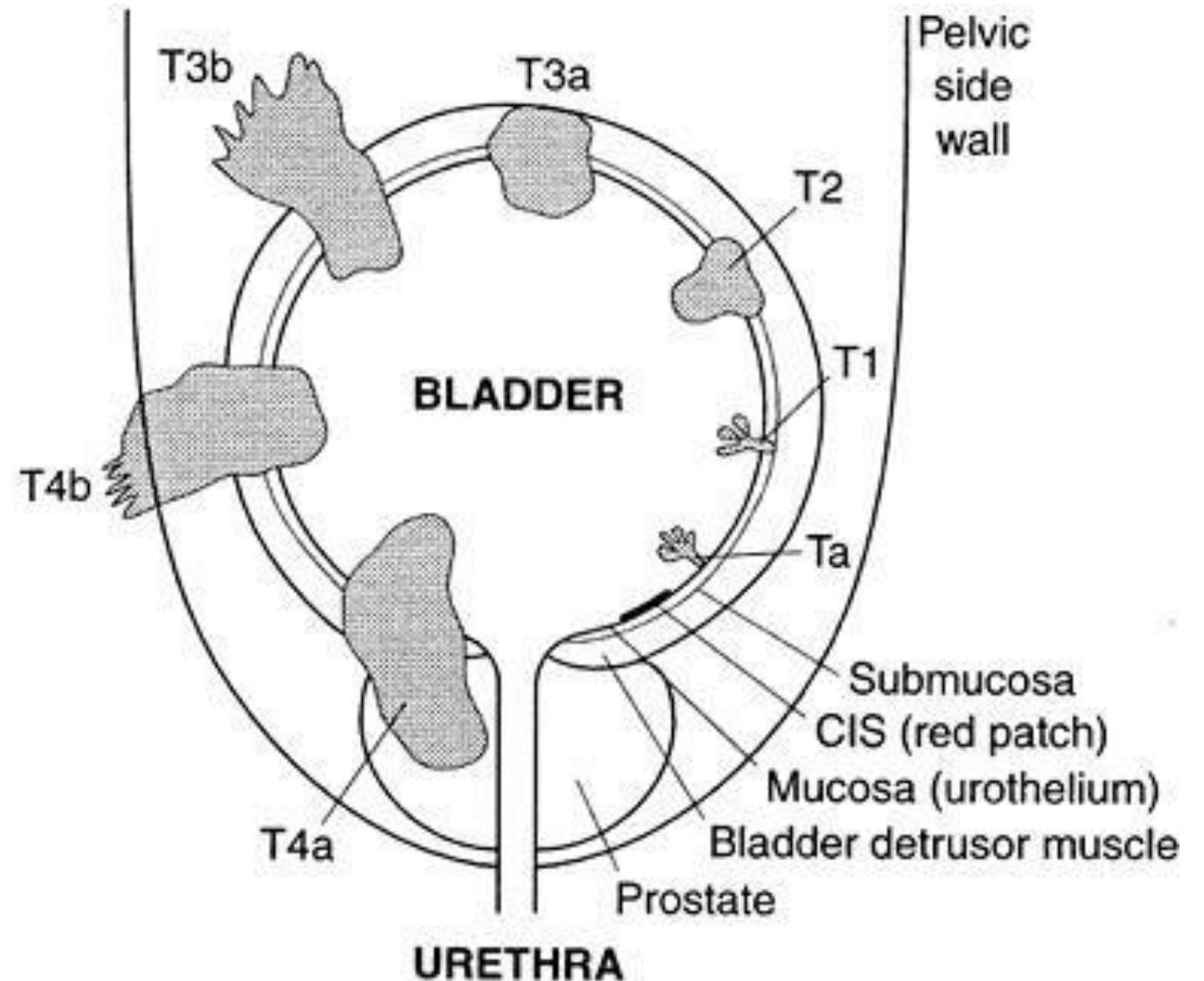
Tx	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Ta	Noninvasive papillary carcinoma
Tis	Carcinoma in situ
T1	Tumor invades subepithelial connective tissue
T2	Tumor invades muscularis propria (detrusor): T2a inner half; T2b outer half
T3	Tumor invades beyond muscularis propria into perivesical fat: T3a = microscopic; T3b = macroscopic (extravesical mass)
T4a	Tumor invades any of prostate, uterus, vagina, bowel
T4b	Tumor invades pelvic or abdominal wall
Nx	Regional (iliac and para-aortic) lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis in a single lymph node <2 cm in greatest dimension
N2	Metastasis in a single lymph node 2–5 cm or multiple nodes <5 cm
N3	Metastasis in a single lymph node or multiple nodes >5 cm in greatest dimension
Mx	Distant metastasis cannot be assessed
M0	No distant metastasis
M1	Distant metastasis present

Bladder cancer staging



Staging

- is by the TNM (1997) classification. All rely upon physical examination and imaging.



Keep in mind :

Non muscle invasive

means the cancer cells are only in the inner lining of the bladder

Muscle invasive

The cancer is in the muscle layer of the bladder or has spread into the fat layer. But it has not spread outside the bladder.

Locally advanced

This is when the cancer has spread outside the bladder into nearby tissues, such as the prostate, vagina, ovaries, womb or back passage (rectum). It may also be in a lymph node in the pelvis, near to the bladder.

Advanced

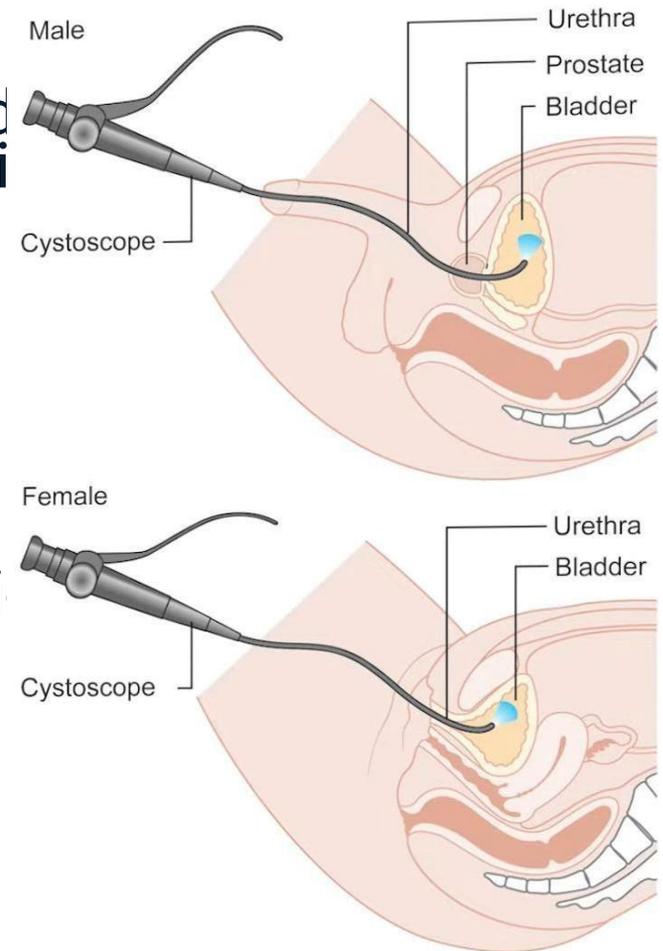
This is when the cancer has spread to other parts of the body, such as the liver, lungs or bones, or to the lymph nodes further from the bladder.

Bladder cancer diagnosis

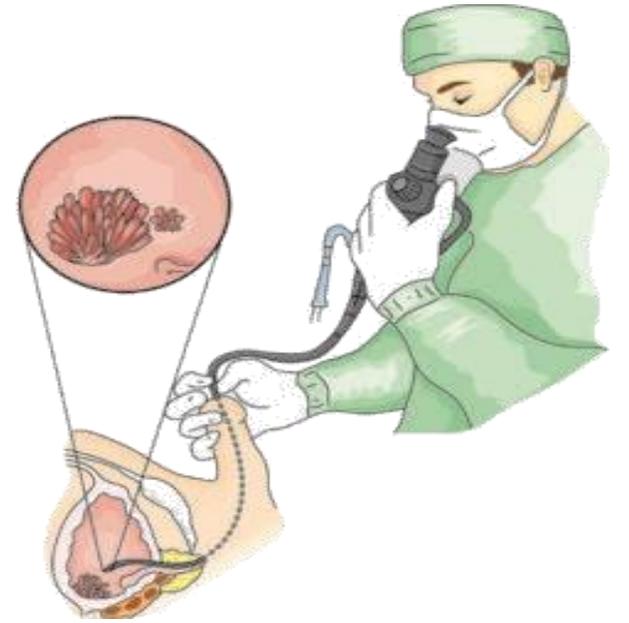
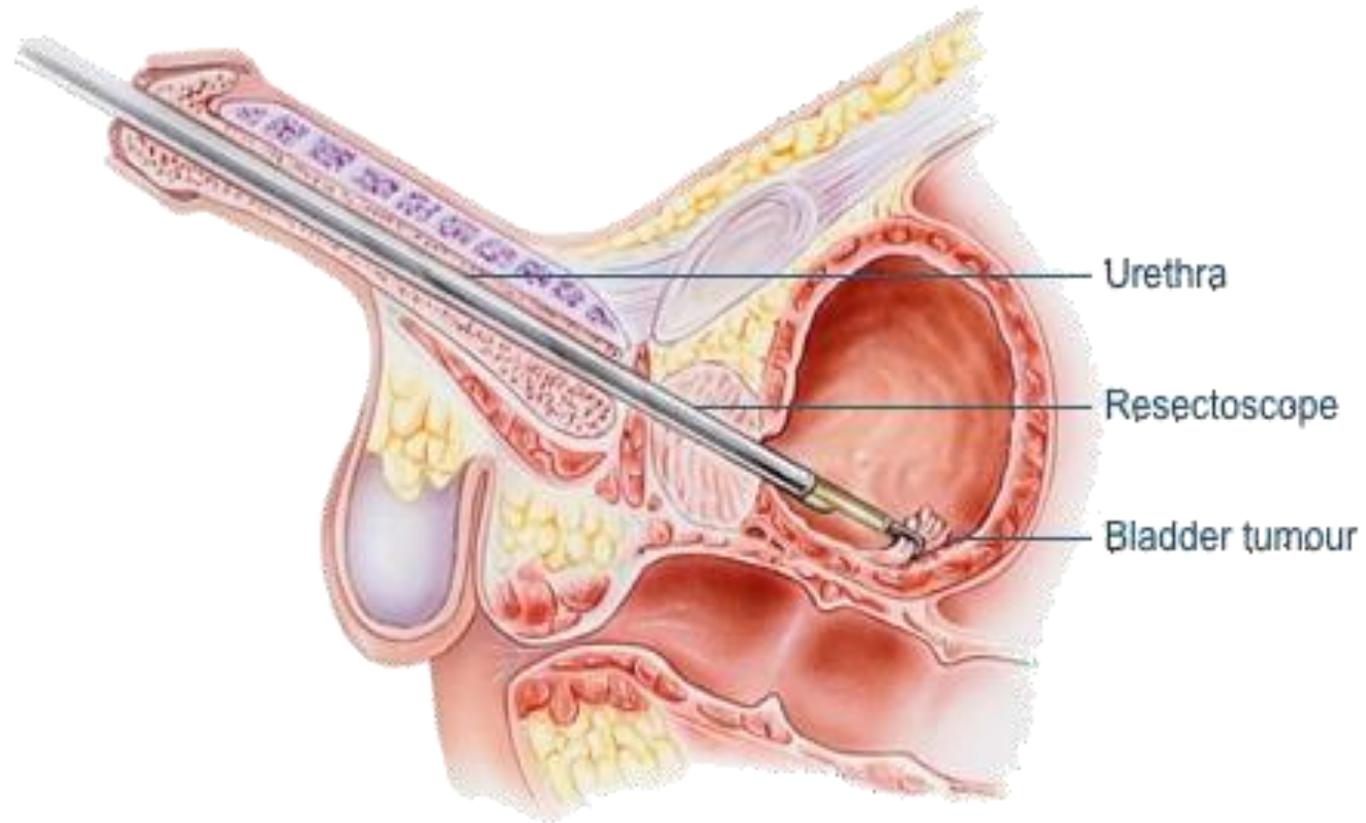
After a urinary tract infection has been excluded or treated all patients with microscopic or macroscopic haematuria require investigation. Usually, **flexible cystoscopy, performed under local anesthesia, are first-line investigation.**

As a part of the work up , an IVU or CT scan and urine cytology are justified second-line investigations. As we need to investigate upper tracts, kidney , and ureter.

- Patients with predominantly filling-type LUTS, suprapubic pain, or recurrent UTI/pneumaturia should also have **urine cytology and cystoscopy.**



Transurethral Resection of Bladder Tumor (TURBT)



- False - ve cytology is frequent (40-70%) in patients with papillary TCC, but more sensitive (90-100%) in patients with high-grade TCC and CIS.
- False +ve cytology can arise due to
 - Infection
 - Inflammation
 - Instrumentation
 - chemotherapy.

Staging investigations

are usually reserved for patients with biopsy-proven muscle-invasive bladder cancer unless clinically indicated, since superficial TCC and CIS disease are rarely associated with metastases.

Pelvic CT or MRI may demonstrate extra-vesical tumor extension or iliac lymphadenopathy, reported if $>8\text{mm}$ in maximal diameter.

Chest X-ray

Isotope bone scan is obtained in cases being considered for radical treatment.

Staging lymphadenectomy (open or laparoscopic) may be indicated in the presence of CT-detected pelvic lymphadenopathy if radical treatment is under consideration.

- **CT scan before and after IV contrast is becoming the first-line radiological investigation of haematuria.** It is faster and more sensitive than ultrasound or IVU in the detection of renal (parenchymal and urothelial) and ureteric tumours. However, it carries a higher radiation dose and is more expensive.
- CT scan also detects some bladder tumours, but may overcall bladder wall hypertrophy as tumour and will miss flat CIS and urethral pathology. Thus it cannot replace cystoscopy.
- If there is hydronephrosis in association with a bladder tumour, it is likely that the tumour is causing the obstruction to the distal ureter. This tends to be caused by muscle-invasive disease rather than superficial TCC.
- If all investigations are normal, consideration should be given to nephrological disorders that may cause haematuria, such as glomerulonephritis.

TCC MANEGMENT

Bladder cancer (non-muscle invasive TCC): surgery and recurrence

TURBT

As a primary treatment, a visually complete tumor resection is adequate for 70% of newly presenting patients with Ta/T1 superficial disease. The remaining

30% of patients experience early recurrence, 15% with upstaging.

Because of this, it is **standard care that all new patients receive adjuvant treatment with a single dose of post-operative intravesical chemotherapy (usually mitomycin)**. Complications of TURBT **are uncommon, including bleeding, sepsis, bladder perforation, incomplete resection, and urethral stricture.**

Alternatives to TURBT

Transurethral cyst diathermy or laser are accepted, quicker and less morbid

procedure for ablating small superficial recurrences when obtaining tissue for histology is not considered necessary

Follow-up after TURBT

Second resection: an early repeat TUR (within 2-6 weeks) should be undertaken:

- (a) if the first resection was incomplete
- (b) when the pathologist reports that the resected specimen contains no muscularis propria
- (c) if a high-grade, but apparently non-invasive, T1 tumor has been reported since perhaps 10% (3-25%) of high grade T1 tumors are understaged T2 tumors. This strategy improves recurrence-free survival and prognosis while complications include bladder perforation.

ADJUVANT THERAPY

Intravesical chemotherapy (e.g. mitomycin C (MMC) [decreases rate of recurrence]

For many patients at **low risk of recurrence**, the risk reduction seen with single-dose postoperative chemotherapy is equivalent to that seen using weekly instillations for 6 weeks, commencing up to 2 weeks post-TURBT. Such longer courses are still recommended for patients at **higher risk of recurrence** or who have multifocal recurrences, excluding those with high-grade Ta/T1 TCC or CIS

ADJUVANT THERAPY

Intravesical BCG [decreases rate of progression]

BCG produces complete responses in 60-70% of patients. It is as effective as chemotherapy for adjuvant treatment of low- and intermediate risk TCC, therefore, is not often used (except as second-line) **because of the additional toxicity.**

Contraindications to intravesical BCG include:

- Immunosuppressed patients.
- Pregnant or lactating women.
- Patients with haematological malignancy.
- Following traumatic catheterization

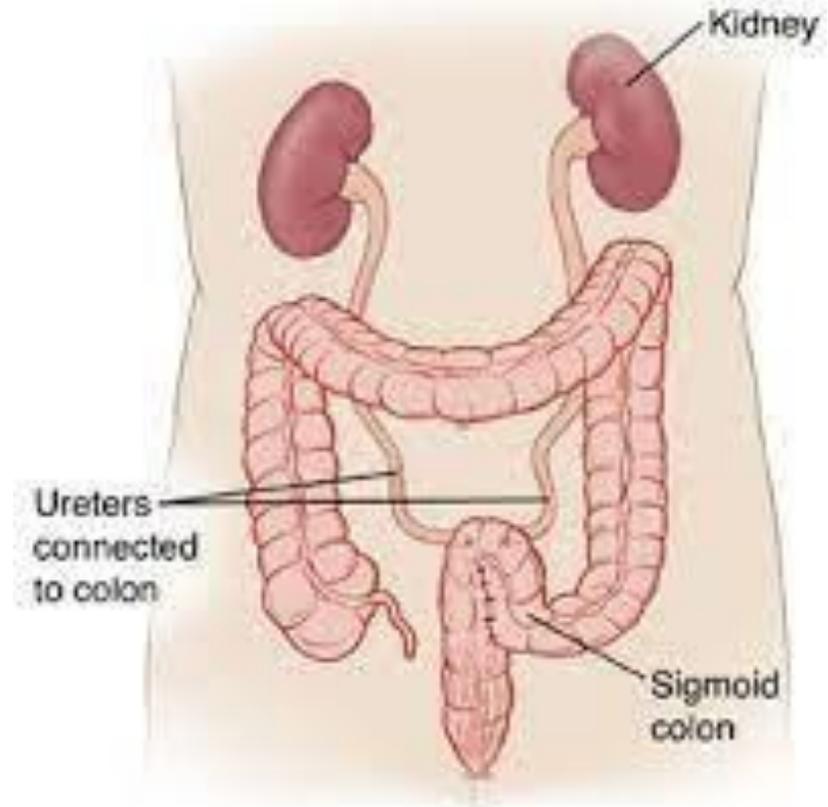
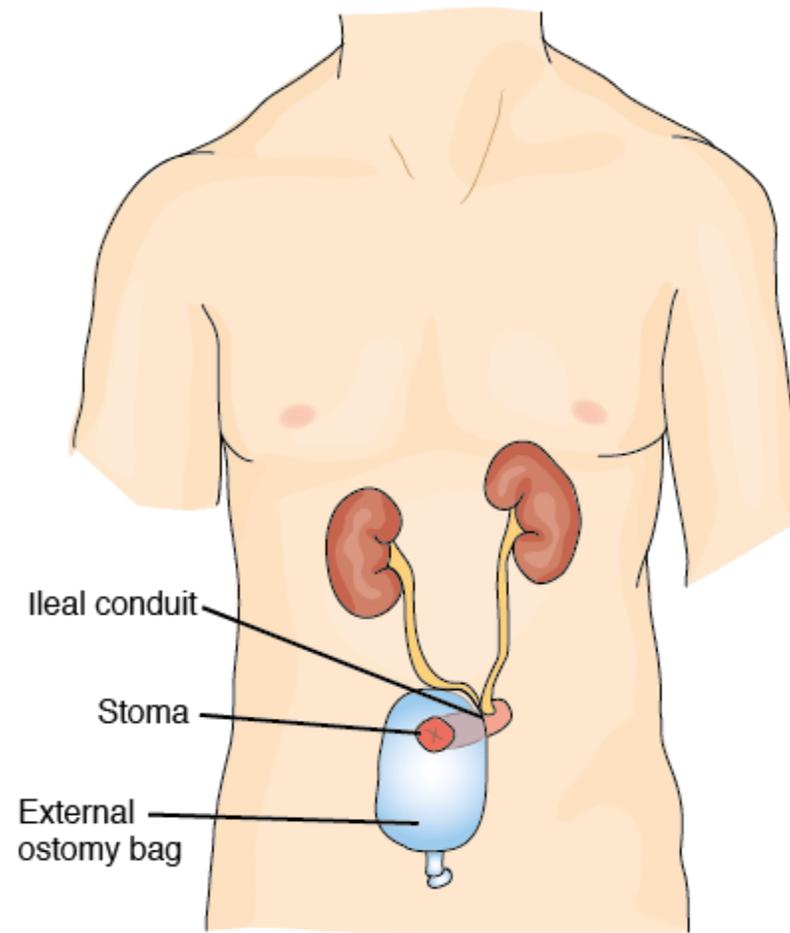
muscle invasive TCC

Radical cystectomy with:

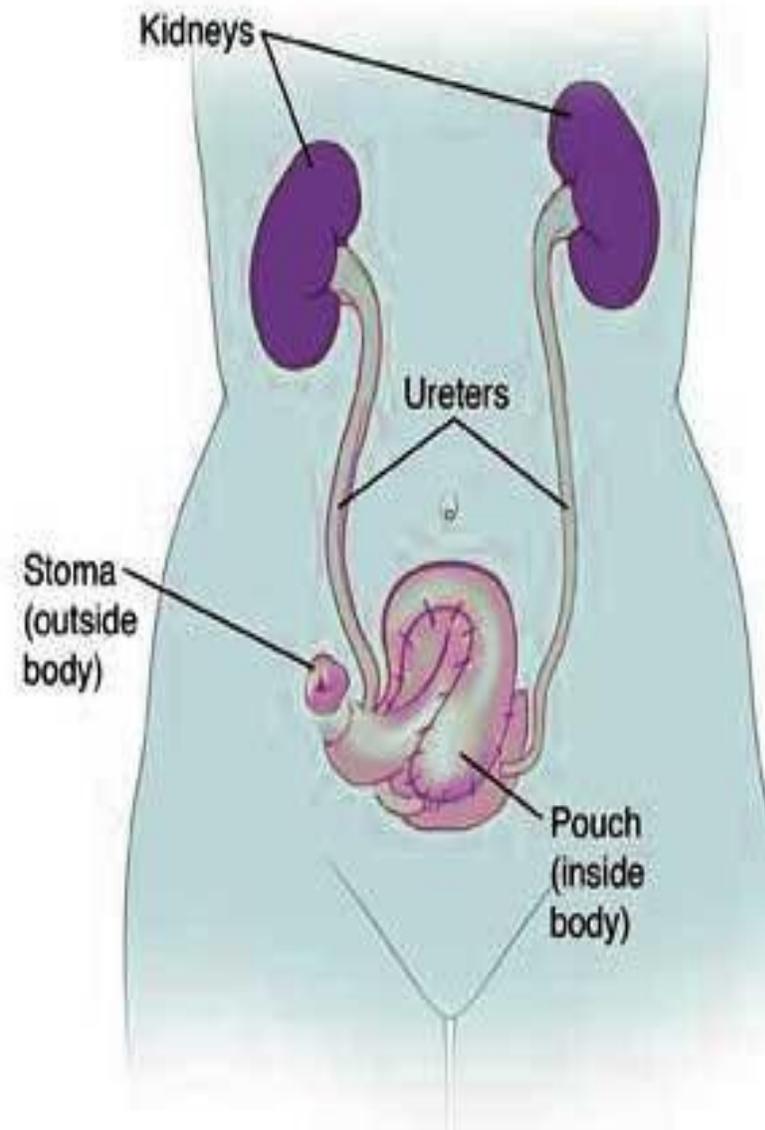
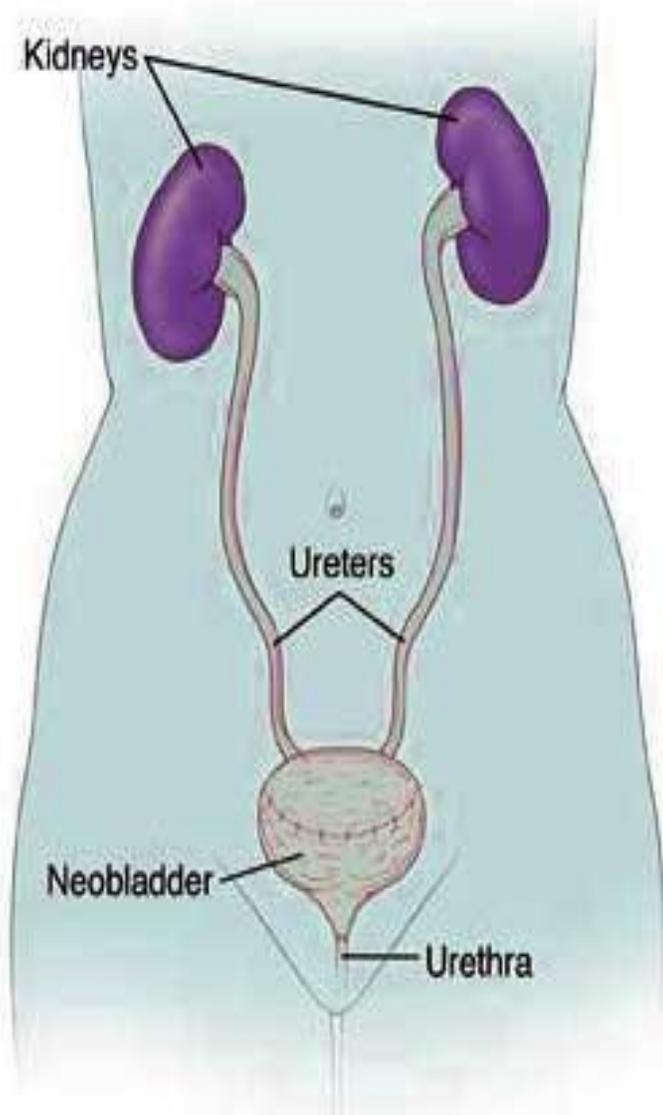
- Ileal conduit urinary diversion.
- Ureterosigmoidostomy urinary diversion.
- Continent urinary diversion.

Radical cystectomy :

- complete removal of the **urinary bladder**, pelvic **lymph nodes** ; external/ internal iliac LNs and obturator LNs , and **adjacent organs** ; (prostate, seminal vesicle and proximal part of urethra in **males** /ovaries , fallopian tubes , uterus , cervix and anterior vaginal wall in **females**)



Ileal conduit urinary diversion Ureterosigmoidostomy urinary diversion



Continent urinary diversion

Table 7.11 5y survival rates for cystectomy alone

Stage T1/CIS	90%+
Stages T2,T3a	55–63%
Stage T3b	31–40%
Stage T4a (into prostate)	10–25%
Stage TxN1–2	30%
Salvage T0	70%
Salvage T1	50%
Salvage T2, 3a	25%

Palliative treatment

RT is effective for *metastatic bone pain* or to palliate symptomatic (bleeding) local tumor.

Intractable haematuria may be controlled by intravesical formalin or a Alum, hyperbaric oxygen, bilateral internal iliac artery embolization or ligation, or palliative cystectomy/diversion.

Ureteric obstruction may be relieved by percutaneous nephrostomy .

Involvement of the palliative care team can be very helpful to the patient and family.

THANK YOU