

U.B. TUMOURS

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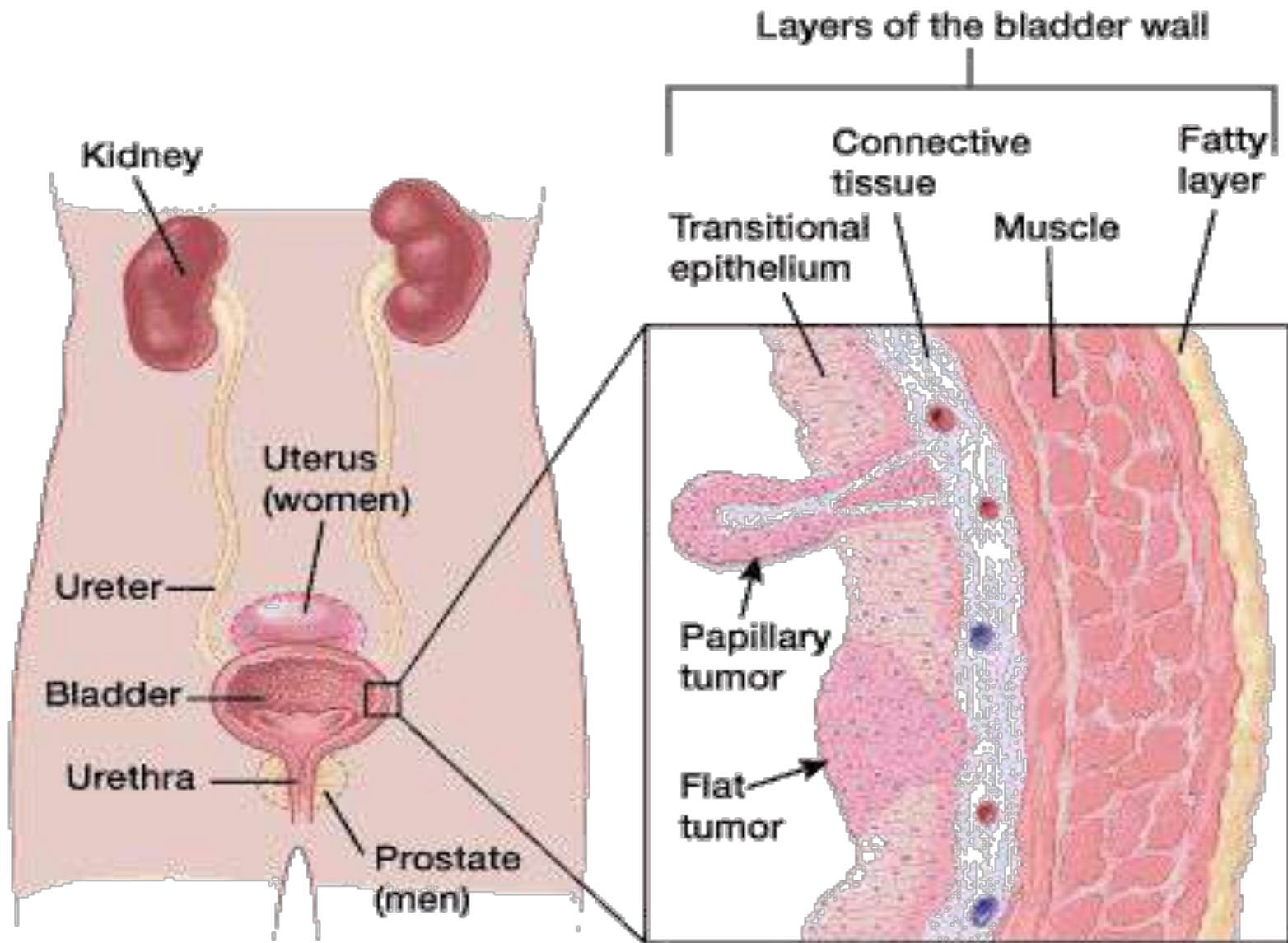
Consultant, Shifa hospital

The wall of the bladder has 4 main layers.

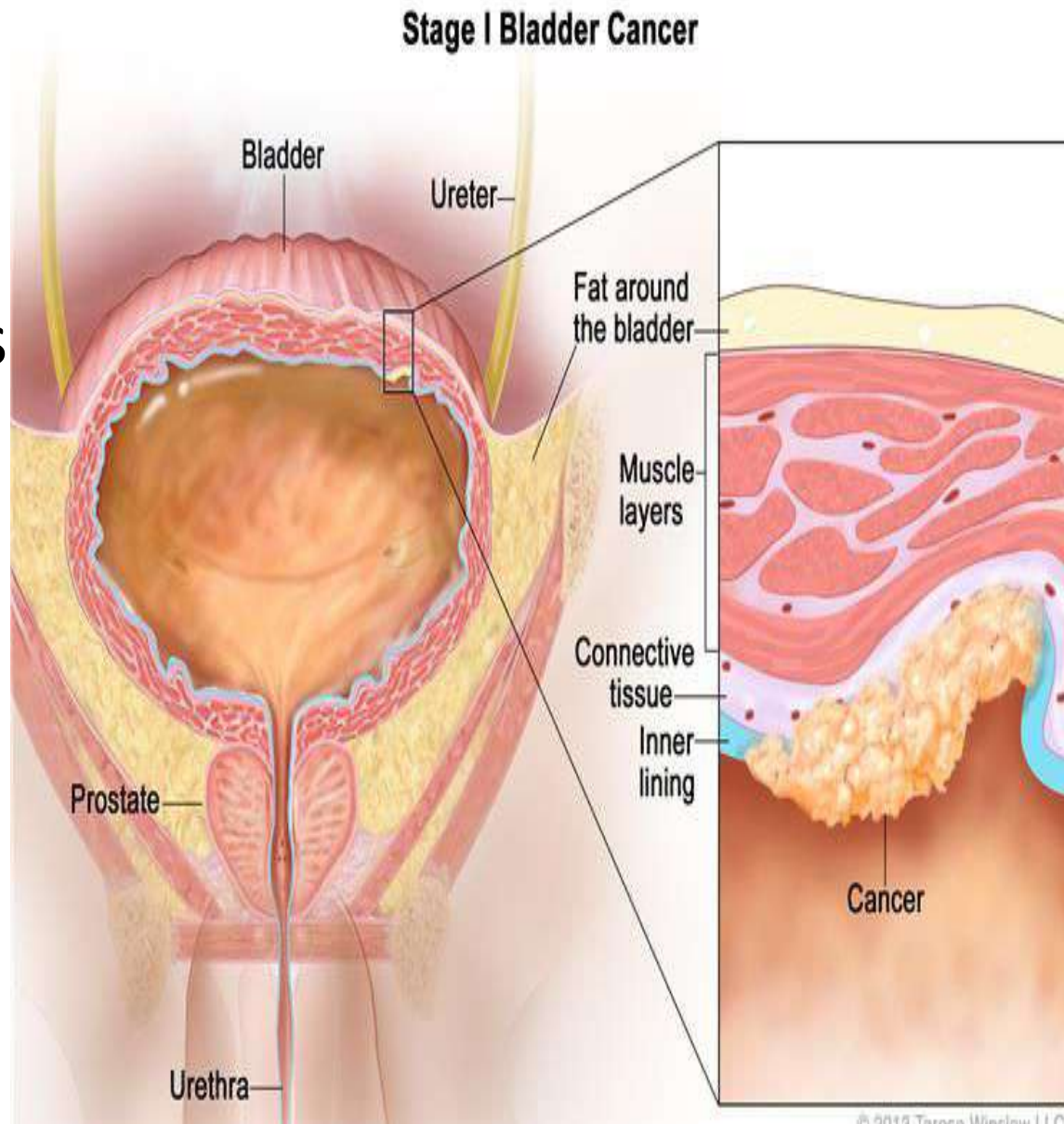
- ① The innermost lining is called the urothelium or transitional epithelium.
- ② Beneath the urothelium is a thin layer of connective tissue, blood vessels, and nerves.
↳ called sub epith. C.T. or lamina propria...
- ③ Next is a thick layer of muscle. called detrusor muscle...
- Outside of this muscle, a layer of fatty connective tissue separates the bladder from other nearby organs.

* The UB tumor

- ↳ superficial Bladder tumor [non muscle invasive]...
→ treated by trans urethral incision (تحت الجلد) Bladder tumor ١)
- ↳ deep Bladder tumor [muscle invasive]...
→ treated by radical cystectomy ↳ Lo T₂ or more



- Nearly all bladder cancers start in the lining or urothelium.
- As the cancer grows into or through the other layers in the bladder, it becomes more advanced (the stage goes up).



EPIDEMIOLOGY

- The 4th most common cancer in men.
- The average age of diagnosis is 55 -73 years and the incidence increases with age. [>60 y/o]

^{M:F}
- 3:1 male to female predominance

But ..

- women are more likely to be seen initially with more advanced tumors and less favorable prognosis. [more aggressive]
- Bladder cancer is more common in whites than in blacks; however, blacks have a worse prognosis than whites. [more aggressive]

Risk factors:

- Genetics
- Hereditary (pt. with lynch syndrome)
- **Cigarette smoking** *most important risk factor*
- Age: rare in less than 30 years old and more common over 60 year old.
- Occupational risk : associated with industrial exposure to aromatic amines , rubber workers , painters , dye , tobacco
- Radiation exposure
- Schistosomiasis *or stone or catheter or infection → lead to Bladder irritation ... [make Sq. metaplasia → then SCC]..*
- Medications: **Cyclophosphamide**, analgesics (Phenacetin). *chemotherapy*
...risk for Bladder tumor ... نظر ال Acrolein مرتزقه وبقه . فكل ال ...
...itself not affect on the Bladder But its metabolite [Acrolein] lead to Bladder metaplasia - dysplasia ...etc
...نذلك فكل cyclophosphamide فكل ... mesna فكل ... ال Acrolein مرتزقه وبقه . نظر ال ...

Histopathology

- Of all bladder cancers, 95% are epithelial malignancies, predominantly transitional cell carcinomas (TCCs). $\Rightarrow$ urothelial cancer سرطانة

occur with the Trans urethral resection of Bladder tumor [TURBT]

في القمم بـ أكثر بأجزاء من
[endemic for schistosoma]..

- About 5% are adenocarcinomas, squamous cell 17% carcinomas, neuroendocrine tumors, and other histologic subtypes <5%

-Non-urothelial primary bladder tumors are rare and may

include small cell carcinoma, carcinosarcoma, primary lymphoma, and sarcoma.

③

④

①

③

- * The Bladder adenocarcinoma types :-
- ↓
- we find ↑ mucin in urine analysis
+ ↑ Carcinoembryonic Ag
- ① metz [2ry] from any other cancer...
 - ② ly [from it self]
 - ③ urachal adenocarcinoma [from urachus canal]

Urothelial (Transitional Cell) Carcinoma

- Approximately 90% of all bladder cancers are TCCs.
- These are now more commonly referred to as urothelial carcinomas.
- These tumors most commonly appear as papillary

In areas of **endemic schistosomiasis**, most bladder cancers are **squamous cell cancers**, although this parasitic infection may produce transitional cell cancer .

Tumors may be classified by growth patterns

- Papillary (70%) *we see papillary growth in the cystoscope...*
- Sessile or mixed (20%)
- Nodular (10%)

PRESENTATION AND WORKUP

■ History and physical examination :

- ① ^{painless} **gross hematuria** is present in 85% of patients (is classically painless and commonly is intermittent)
 - ^{↑RBC in urine analysis} **microscopic hematuria** is present in nearly all patients. ② **LUTS :-**
 - **Irritative voiding symptoms** (e.g., frequency, urgency) also may be signs of Bladder Ca, especially those with carcinoma in situ (CIS). ^{lead to flank pain - hydronephrosis..}
 - **Upper urinary tract obstruction** is rare on initial presentation and is a sign of advanced disease in 50% of cases .
^{↳ wt loss - chaxcia..etc}
 - **Mets sx**
- * 60 y/o heavy smoker male pt presented with LUTS → Firstly think about prostate cancer...
But if the same pt presented with painless hematuria → Firstly think about UB cancer...

* The History :-

in brief (ask about: smoking - occupational exposure - drugs hx - LUTS - B symptom)

* The physical exam :-

① The general exam:- vital sign - abdomen for palpable abdominal mass - metastatic lymph node mass - or palpable flank mass ..

② The local exam:- Bimanual examination of the Bladder [ask the pt to empty his Bladder]
digital rectal or per vaginal examination ↴
↳ to reduce the pain...

① Consistency of the mass

② fixation and mobility of the mass

imaging - بظرفا ١، ٢

Investigations :

- CBC , Urinalysis , urine culture * Chemistry...
در معاینات
- KFT. → imaging of choice is CT + Contrast + urine - to see if there is RCC or not...
- Upper tract imaging
- Cystoscopy
→ urethral cells from pelvic calyces, ureter - Bladder
- urine cytology in patients with gross hematuria. ✓
→ to see if there is malignant cells in the urine [indicate TCC]...

* CT with contrast is the imaging of choice for hematuria...
[IV]

* 1st thing we do in cystoscopy is panoramic viewing [imaging] of the Bladder...
→ The Bladder walls :- If lateral - Rt lateral - Ant. - Post. wall - dome of the Bladder...
و اگر مشکلی در پروستات
cystoscope to do planing of the
resection...
↳ we start from easy one ...

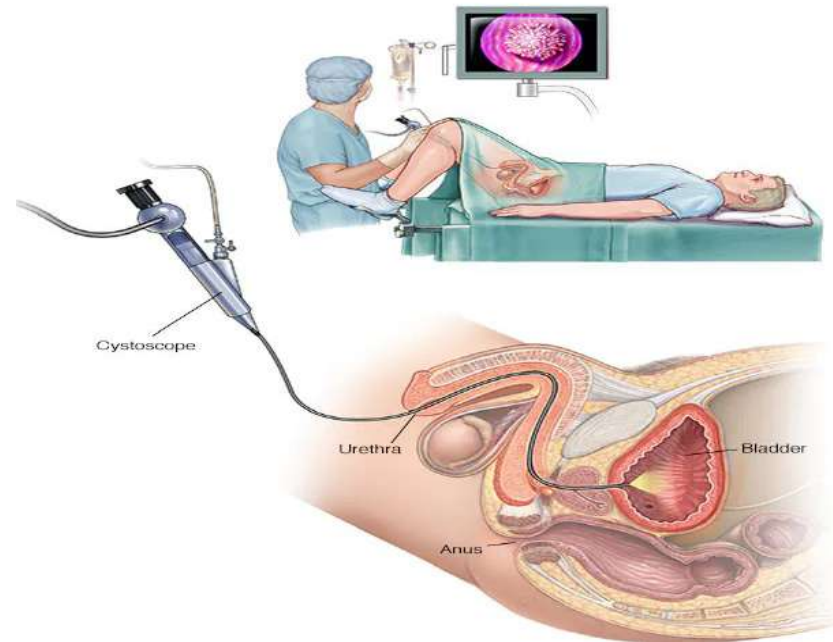
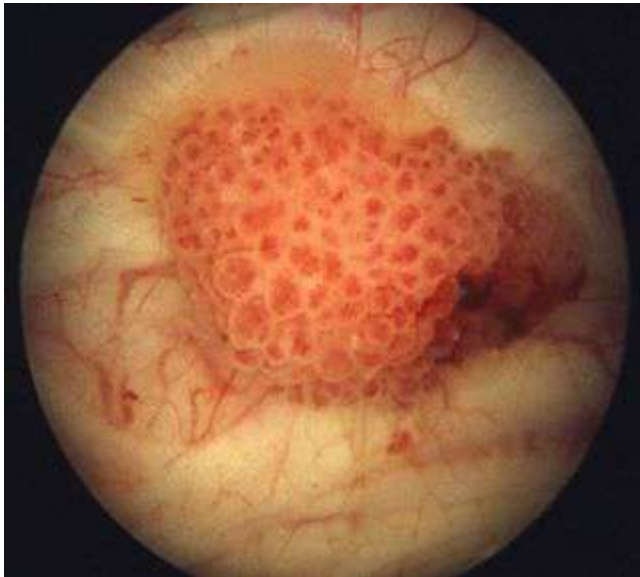
Cystoscopy

we do it to confirm the dx - to see if there is other cancer...

the target is to do total resection of
Bladder tumor [TURBT]

The gold-standard test for the diagnosis of Bladder Ca is **cystoscopy**.

Obtain biopsy samples of suspicious lesions during cystoscopy. Attempt to include the bladder muscle in the biopsy specimen. This allows the pathologist to determine whether the tumor is muscle invasive.



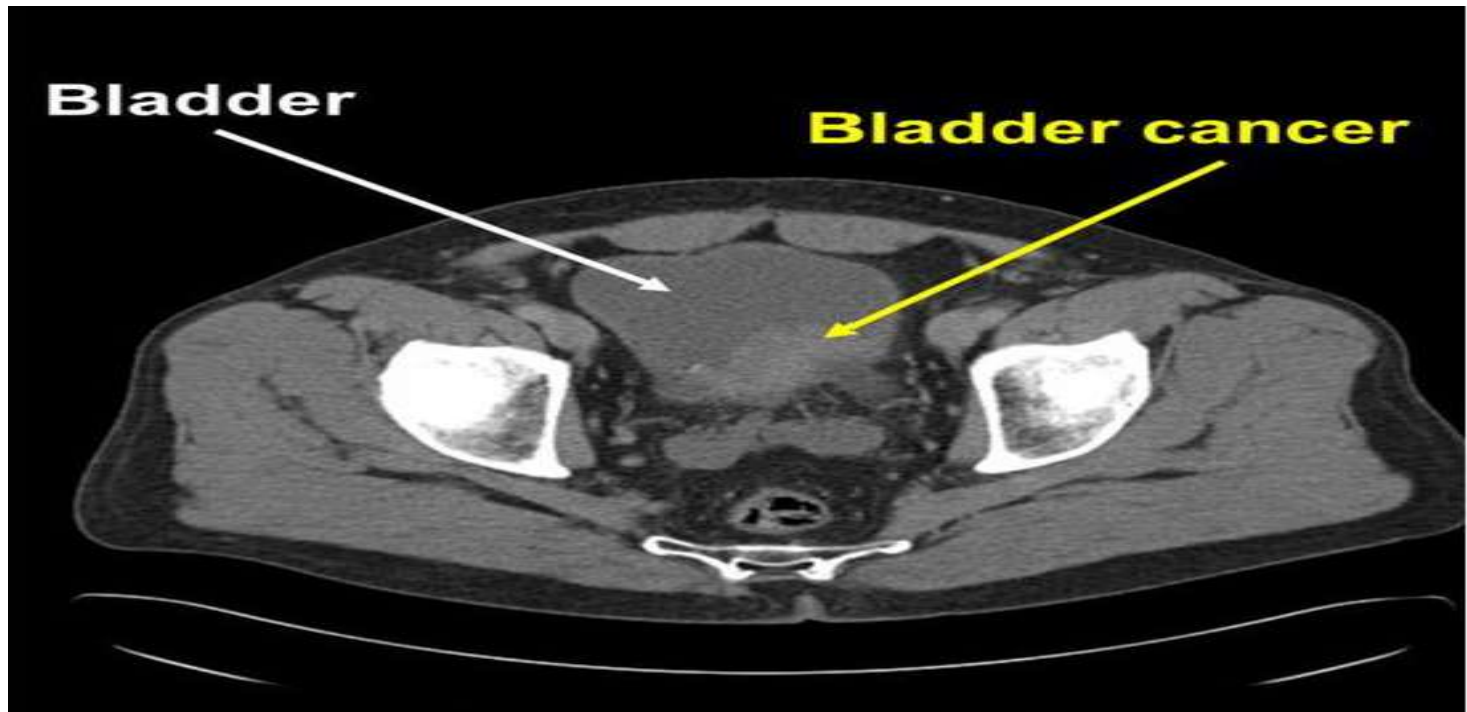
Urine cytology

- Cells for microscopic examination are collected from voided urine or bladder washings.
- Urinary cytologic study is excellent for detecting carcinoma in situ and high-grade lesions (90%).

Radiologic examination

if we see mass the next step is cystoscopy...

CT is very useful for clinical staging of patients with more advanced



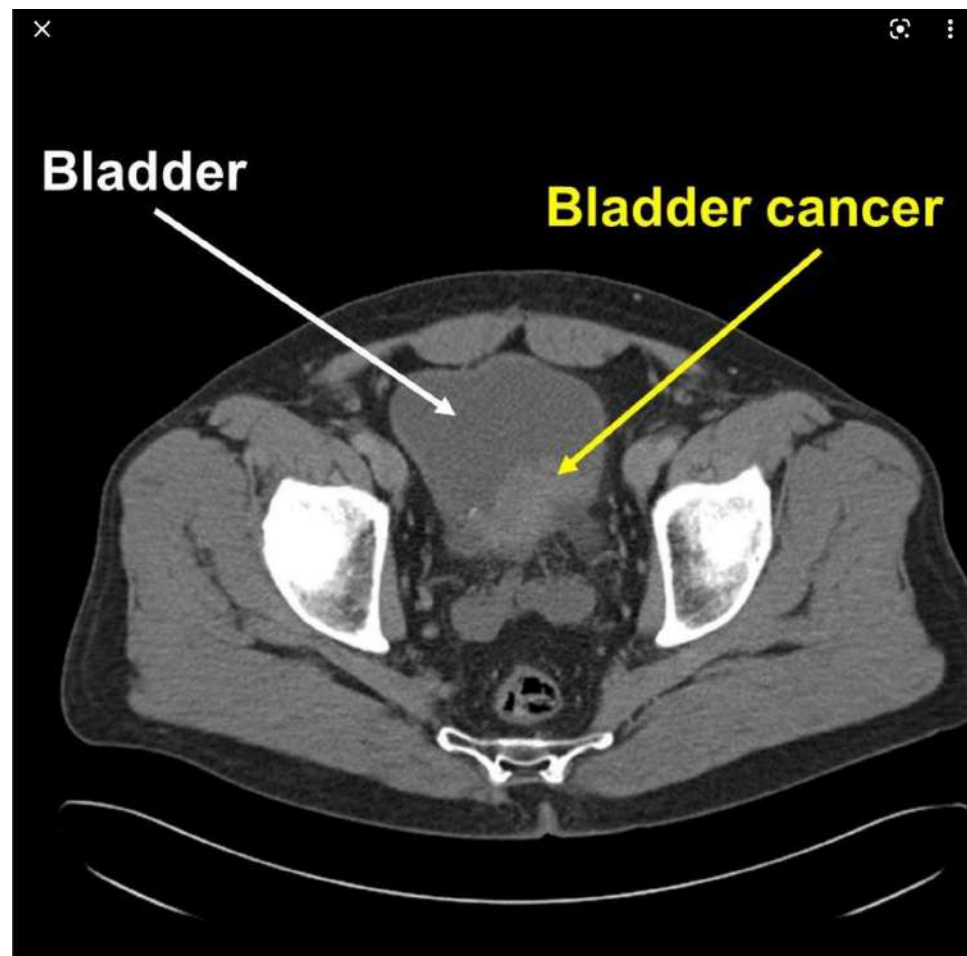


filling defect [indicate Bladder tumor]...

Bladder Carcinoma. CT urogram. CT of the abdomen with contrast reformatted in the coronal projection shows a filling defect in the left lateral wall of the urinary bladder (red arrow) .representing a papillary urothelial tumor of the bladder







Definitive diagnosis

The definitive diagnosis is made on biopsy, which is commonly taken with a rigid cystoscope or resectoscope under anaesthesia.

- Bladder muscle must be included in the biopsy to exclude or confirm muscle invasion

Histological types and grading

Transitional cell and squamous cell cancers of the bladder are described by histopathologists in three grades:

- G1 (well differentiated) ✓
 - G2 (moderately differentiated) ✓
 - G3 (poorly differentiated). ✓
- تصنيف تدريجي
- G1 → well diff. دالة طلياً خفياً هنا
- G2 → poorly diff.

-They have prognostic value and different treatment pathways.

- Bladder tumors are now classified as either low or high grade.
- Almost all invasive bladder tumors are high grade

Staging

↳ depend on the histopathology...

- Clinical staging (T category) is established by **bimanual examination at cystoscopy and biopsy under anaesthetic** .
- Biopsies can be staged only up to stage pT2a, as staging higher than this requires a whole specimen from cystectomy

- non muscle invasive [treated by CRBT + follow up after 3 month] *د جـ لـ و ~ ٥*
- **Ta and T1 tumors and CIS** were once *د جـ لـ و د جـ لـ و د جـ لـ و*
considered **superficial** bladder tumors. *CRBT...*

- muscle invasive [treated by radical cystectomy; ultramajor surgery]
- **T2, T3, and T4** tumors were traditionally
described as **deep** **invasive** bladder cancer

* In Male radical cystectomy we resect:-

- 1- Bladder w/US...
- 2- Prostate...
- 3- Seminal vesicle...
- 4- vas deference...
- 5- Bilateral lower ureter...

* In female radical cystectomy we resect:-

- 1- lower ureter...
- 2- Bladder
- 3- total abdominal histrectomy + Bilateral
slingo oophorectomy + Ant. vaginal wall resect

T_a: superficial ...

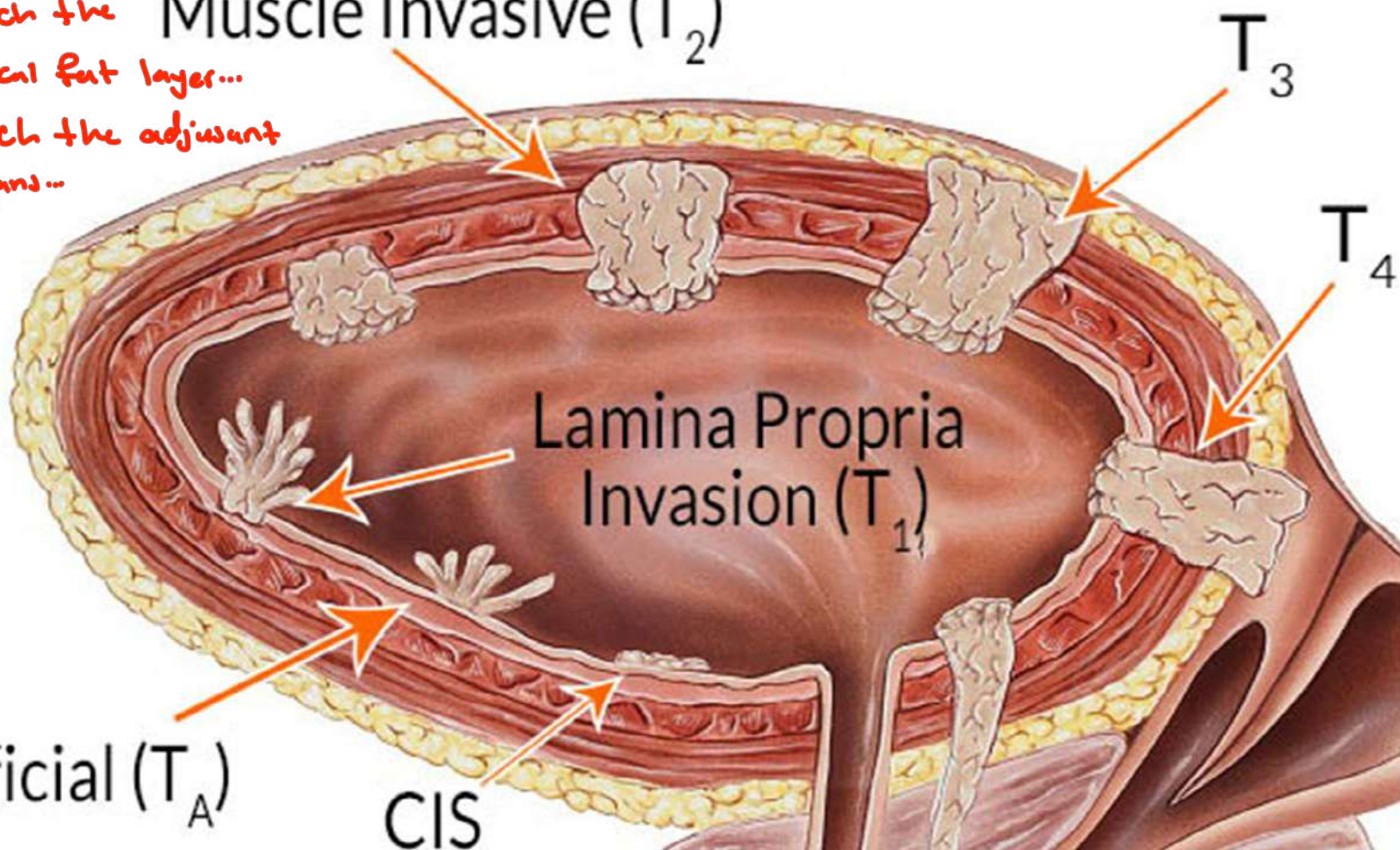
T₁: reach the lamina propria...

T₂: reach the muscle...

T₃: reach the perivesical fat layer...

T₄: reach the adjacent organs...

Muscle Invasive (T₂)



Clinical staging

Stage	Description
T1	Impalpable before and after resection
T2	Palpable before but not after resection
T3	Palpable before and after resection
T4	Involving a neighbouring organ

مسند مطلوب

Pathological staging

Stage	Description	Bladder cancer
PTa	Confined to urothelium; basement membrane not breached	Superficial
pT1	Invasion into lamina propria	Superficial (invasive)
PTis	Overtly malignant cells form a layer that replaces urothelium	
pT2a	Invasion into muscularis propria (detrusor)	Muscle invasive
pT2b	Deep invasion into muscularis propria (detrusor)	Muscle invasive
pT3a	Microscopic extravesical spread	Muscle invasive
pT3b	Macroscopic extravesical spread	Muscle invasive
pT4	Involves neighbouring organ	

Involved lymph nodes

Nodal disease indicates a very poor prognosis. The TNM classification classifies it as follows:

- N1: single node <2 cm
- N2: single node >2 cm, multiple nodes <5 cm
- N3: >5 cm

Metastases

The TNM classification classifies soft tissue or bony metastases as follows:

- M1: presence of metastases

-The most significant prognostic factors for bladder cancer are:
grade, depth of invasion, and the presence of CIS

- * The presence of **CIS** indicate very Bad prognosis + has very Bad response of Ht ...
- Presented with irritative LUTS just [no hematuria] →
- has ↑ risk of recurrence + progression if it not well treated may 60 % ✓
 - may be it is normal mucosa [there is no visible tumor] in cystoscope
 - normal workup except the urine cytology
 - vilvud apperance [diagnostic criteria...
 - Ht : intravesical immunotherapy [BCG]
- 60%, in 80% + become invasive cancer

MANAGEMENT OF NONMUSCLE INVASIVE BLADDER CANCER

- Approximately 70%–80% of BlCa cases are nonmuscle-invasive bladder cancer (NMIBC) at presentation with 60%–70% as stage Ta
- 20%–30% as T1
- approximately 10% as CIS
- Risk of recurrence is typically approximately 40%–60%

← من أين بدأ الـ malignant cell؟ من مكانة في urine cytology بعمل :-

① repeat the urine cytology ...

② Random Bladder Biopsy يعني كل مكانة نأخذ عينة - ...

③ target Biopsy [by inject the bladder material called hexa amino-

!! - وهو تم بنقله بالحقن في مكانة Biopsy من مكانة highly vascularized - مكانة - false the result ...

Table 20.2 American Urological Association Risk Stratification
for **Nonmuscle-Invasive Bladder Cancer**

criteria for recurrence and progression...

LOW RISK	INTERMEDIATE RISK	HIGH RISK
① LG ^{single} solitary Ta ≤3 cm ② PUNLMP ↓ <i>Papillary urothelial neoplasm low malign. potential</i>	Recurrence within 1 year, LG Ta Solitary LG Ta >3 cm LG Ta, multifocal HG Ta, ≤3 cm LG T₁	HG <u>T₁</u> ① Any recurrent, HG Ta HG Ta, <u>>3 cm</u> (or <u>multifocal</u>) ② Any CIS Any BCG failure in HG patient Any variant histology Any LVI Any HG prostatic urethral involvement

□ Endoscopic Surgical Management

^[TUR] Transurethral Resection of Bladder Tumor.

TURBT is intended to be diagnostic and therapeutic by providing specimens to allow for pathological determination of stage and grade.

-Traditionally, TURBT has been performed with monopolar loop using sterile water or glycine

solution. (using non ionic solution [no Na^+ - no Cl^-] to avoid the pain...
side effect :- may absorbed and lead to TUR syndrome [volume over load - hyponatremic])

- The use of bipolar loop allows use of saline irrigation, which can decrease risk of transurethral resection (TUR) syndrome in cases of perforation and if the resection is prolonged. fatal

* The ~~ttt~~ if there is Bladder perforation [intra peritoneal] and peritonitis is :-ex ploration...
But if there is no sign of peritonitis we do conservative ~~ttt~~ . Follow up
But the ~~ttt~~ of the extra peritoneal Bladder perforation is : Catheter drainage...

Complications of Transurethral Resection of Bladder Tumor and Bladder Biopsy

Common side effects in the immediate postoperative period :

- Minor bleeding or Bladder perforation or urethral injury due to trauma [infection → late]
- irritative symptoms.

Major complications :

- uncontrolled hematuria
 - Clinical bladder perforation
- occur in 1%–6.7% of cases

Extraperitoneal bladder perforation during TURBT can typically be managed with prolonged urethral catheter drainage.

Intraperitoneal perforation is less likely to close spontaneously and usually requires open or laparoscopic surgical repair.

Bladder Repeat Transurethral Resection of Tumor

AUA guidelines recommend repeat TURBT of primary tumor site, to include muscularis propria.

- within 6 weeks of the initial TURBT in patients with : *redo 2nd TURBT*

- incomplete initial resection ✓
 - stage T1 disease *→ in 25% of T₁ has up staging to T₂
↳ in 30% after resection we find residual tumor...*
 - high-risk, high-grade Ta tumors. ✓
- indication of 2nd TURBT*

❑ Intravesical Therapy

immuno therapy [to ↓ recurrence and ↓ progression]...
chemo therapy [to ↓ recurrence but not has any effect on the progression] 6 stage..

Perioperative Intravesical Therapy :

- in a patient with suspected or known low- or intermediate-risk

Bladder Ca .

- administration of a **single postoperative instillation of intravesical chemotherapy (e.g., gemcitabine, mitomycin C) within 24 hours of TURBT.**

Lo mc chemo therapy.

- resulted in a 13% absolute reduction in tumor recurrence from 50%–37%,

- local irritative symptoms are the most common complications of postoperative instillation

- **And rare deaths** have also occurred, especially in patients with perforation during resection

* we give the intravesical chemotherapy to the Ta tumor within 24 hr of TURBT
[ideally within 6 hr after the TURBT]...

Intravesical immunotherapy ([BCG] immunotherapy):

as BCG sepsis [TBT]
immuno therapy [has ↑ side effect more than chemotherapy so we don't use it routinely]
- **BCG** is recommended for CIS, T1 tumors, and high-risk Ta tumors (large, high- grade, recurrent, or multifocal tumors). **The intravesical immune therapy absolute contraindication is active infection... sepsis & ...*

-Treatments are typically **started 2–4 weeks after tumor resection**, allowing time for *BCG sepsis, حادثة سقادی* reepithelialization of the bladder after TURBT, thereby minimizing the potential for intravasation of live bacteria .

- Patients receive a 6-week induction course followed by three weekly instillations at 3 and 6 months and every 6 months thereafter for 3 years (maintenance therapy) .

- **Intravesical BCG decreases both tumor recurrence and progression.**

Box 20.1 Contraindications to Bacille Calmette-Guérin (BCG) Therapy

ABSOLUTE CONTRAINDICATIONS

Immunosuppressed and immunocompromised patients^a
Immediately after transurethral resection on the basis of the risk of intravasation and septic death
Personal history of BCG sepsis ✓
Gross hematuria (intravasation risk)
Traumatic catheterization (intravasation risk)
Total incontinence (patient will not retain agent)

RELATIVE CONTRAINDICATIONS

Urinary tract infection (intravasation risk) ✓
Liver disease (precludes treatment with isoniazid if sepsis occurs)
Personal history of tuberculosis (risk theorized but unknown)
Poor overall performance status
Advanced age

NO OR INSUFFICIENT DATA ON POTENTIAL CONTRAINDICATIONS

Patients with prosthetic materials have not been shown to have increased risk of infectious or other complications in limited literature (Rosevear et al., 2010)
Ureteral reflux
Antitumor necrosis factor medications (theoretically predispose to BCG sepsis)

.Intravesical Chemotherapy

Optimization of mitomycin delivery can be achieved by eliminating residual urine volume, fasting overnight, using sodium bicarbonate to reduce drug degradation .

- in a **low-risk patient**, a clinician should **not administer induction** intravesical therapy.
- In an **intermediate risk patient** a clinician should consider administration of a 6-week course of induction intravesical chemotherapy or immunotherapy .
- a **high-risk patient** with newly diagnosed CIS, high-grade T1, or high-risk Ta urothelial carcinoma, a clinician should administer a 6-week induction course of BCG.

Management of Refractory High-Grade Disease

- If the initial treatment was intravesical chemotherapy, a course of BCG should be considered.
- For patients who have failed BCG, a second course still gives a 30%–50% response.
 - A second course of BCG is recommended for patients with intermediate- or high-risk disease if persistent or recurrent Ta disease or CIS is noted after a single course of intravesical BCG.
- Patients who cannot tolerate BCG for any reason may be considered for **salvage chemotherapy**, but the risk of failure and progression is high.
- pembrolizumab for the treatment of patients with BCG unresponsive high-risk NMIBC with CIS with or without papillary tumors who are ineligible for or have elected not to undergo cystectomy.

Role of “Early” Cystectomy

we make diversion [orthotopic - enterotopic]

- **radical cystectomy** in patients who are fit for surgery and have persistent high-grade T1 disease on repeat resection or T1 tumors with associated CIS .

- These guidelines also suggest cystectomy in high-risk patients with persistent or recurrent disease within 1 year after treatment with two induction cycles of BCG or BCG maintenance.

** we should do pelvic L.N dissection with the radical cystectomy...*

MANAGEMENT OF MUSCLE-INVASIVE BLADDER CANCER

- 20- 30% of patients present with muscle-invasive bladder cancer (MIBC) at the time of initial presentation.
- MIBC is a highly lethal entity and if left untreated will result in mortality within 2 years of diagnosis in 85% of cases.
- TUR is the gold standard method for establishing the diagnosis of MIBC.
- Bimanual examination under anesthesia remains an important aspect of primary tumor assessment.
- A high suspicion for extravesical disease is warranted when hydronephrosis is noted on cross-sectional imaging

○ Radical Cystectomy and Pelvic Lymph Node Dissection for Muscle-Invasive Bladder Cancer

- For patients with cT2–T4a, N0, M0 disease, radical cystectomy and bilateral pelvic lymph node dissection remains the gold standard therapy

○ Bilateral Pelvic Lymph Node Dissection.

- Bilateral pelvic lymphadenectomy should be performed in **all patients**, including those with unilateral bladder wall involvement, due to documented crossover risk to the contralateral lymphatic chain.

○ Intraoperative Decision Making

Grossly Positive Nodes and T4b Disease.

- For patients with clinically positive lymph nodes, the standard of care is **cisplatin** based systemic chemotherapy.
- Patients who do achieve a complete response appear to have a significant survival advantage with 5-year cancer-specific survival rates of 63%.

Oncologic Outcomes Following Radical .Cystectomy

Pathologic tumor stage and presence of nodal metastasis are the strongest predictors of recurrence and survival following cystectomy

○ Adjuvant Therapy for Muscle-Invasive Bladder Cancer.

Current AUA guidelines favor neoadjuvant chemotherapy instead of adjuvant chemotherapy based on higher-level evidence data.

However, guidelines suggest considering adjuvant chemotherapy in the setting of pT3/T4 or node-positive disease .

○ Urinary Diversion ↑morbidity rate.

The current body of published literature is insufficient to conclude that any form of urinary diversion is superior to another on the basis of health-related quality-of-life outcomes.



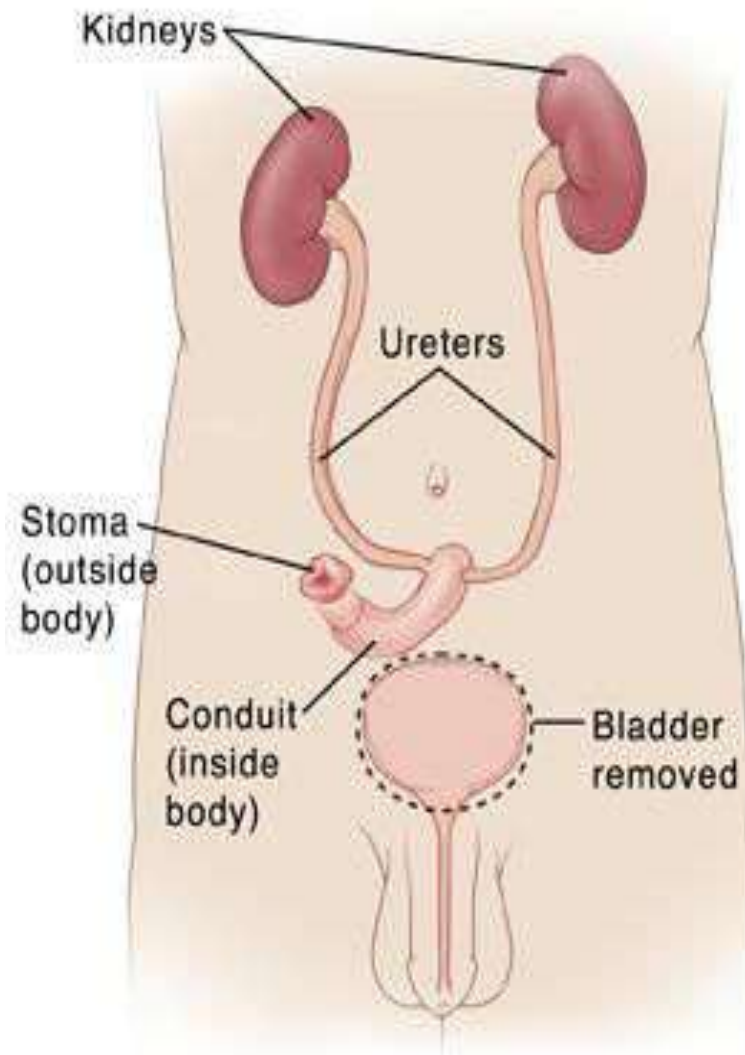
Different types of urinary diversion

1. Ileal Conduit :

بخیه جزد صمد ileum دینطوع در distal end تغه
در proximal end بنترها...

- Is the most commonly utilized urinary diversion using a short segment of distal ileum.
- The preservation of the most distal 15 cm can reduce issues related to absorption of vitamin B12, fat-soluble vitamins, and bile salts.
- It is not advisable to use ileum for a conduit in
 - patients with a short bowel syndrome
 - patients with inflammatory small bowel disease
 - those whose ileum has received extensive irradiation

Ileal Conduit



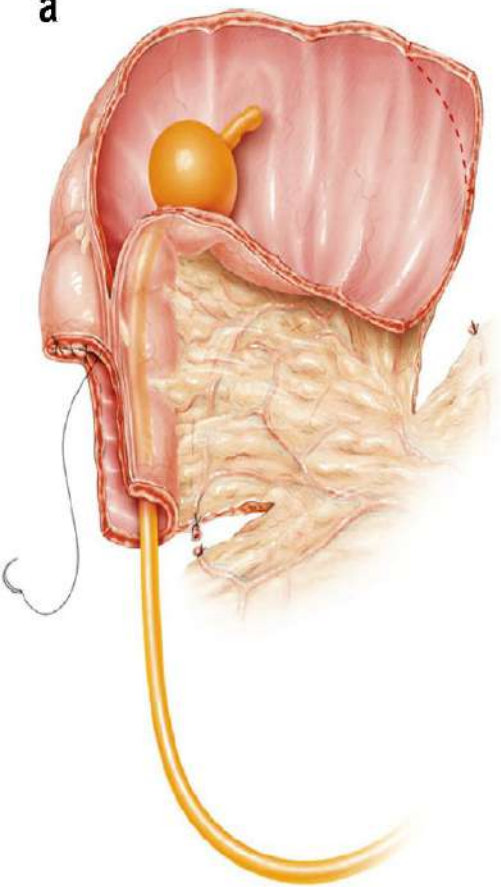
Long-term complications of ileal conduits

- stomal stenosis *-mucus plaque -infection- etc*
- peristomal hernia
- Pyelonephritis
- calculus formation
- ureteral obstruction
- renal deterioration.
- Metabolic complications of intestine interposed in the urinary tract include :
 - electrolyte abnormalities
 - altered sensorium
 - Osteomalacia
 - growth retardation, persistent
 - recurrent urinary tract infection
 - formation of calculi
 - short gut
 - development of urothelial or intestinal cancers

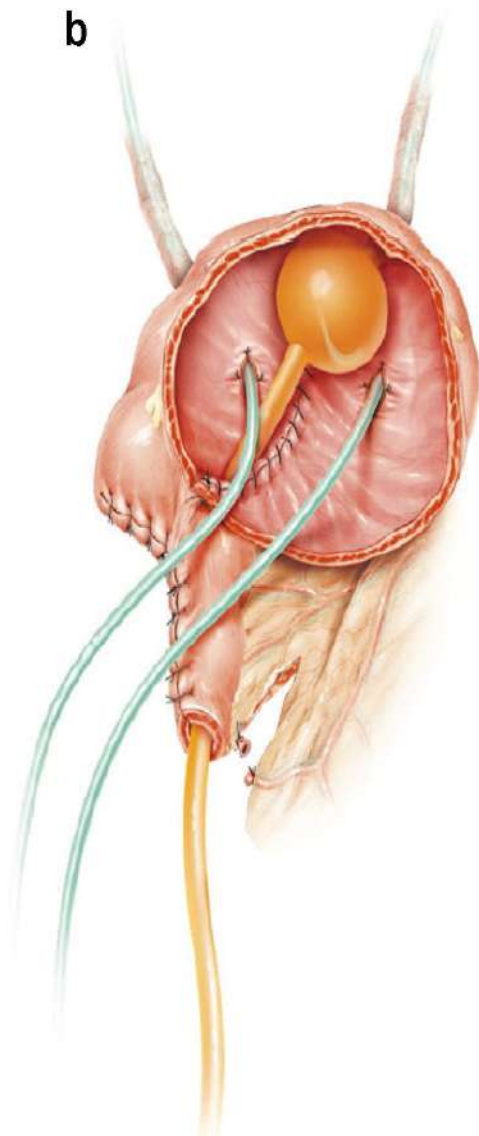
2. Continent Cutaneous Urinary Diversion.

- A low-pressure detubularised ileal reservoir can be used for self catheterization.
- day-time and night-time continence approaching 93%.
- stomal stenosis was seen in 23.5% of patients with an appendix stoma and 15% of those with an efferent intussuscepted ileal nipple.
- Stone formation in the pouch occurred in 10% of patients.

a

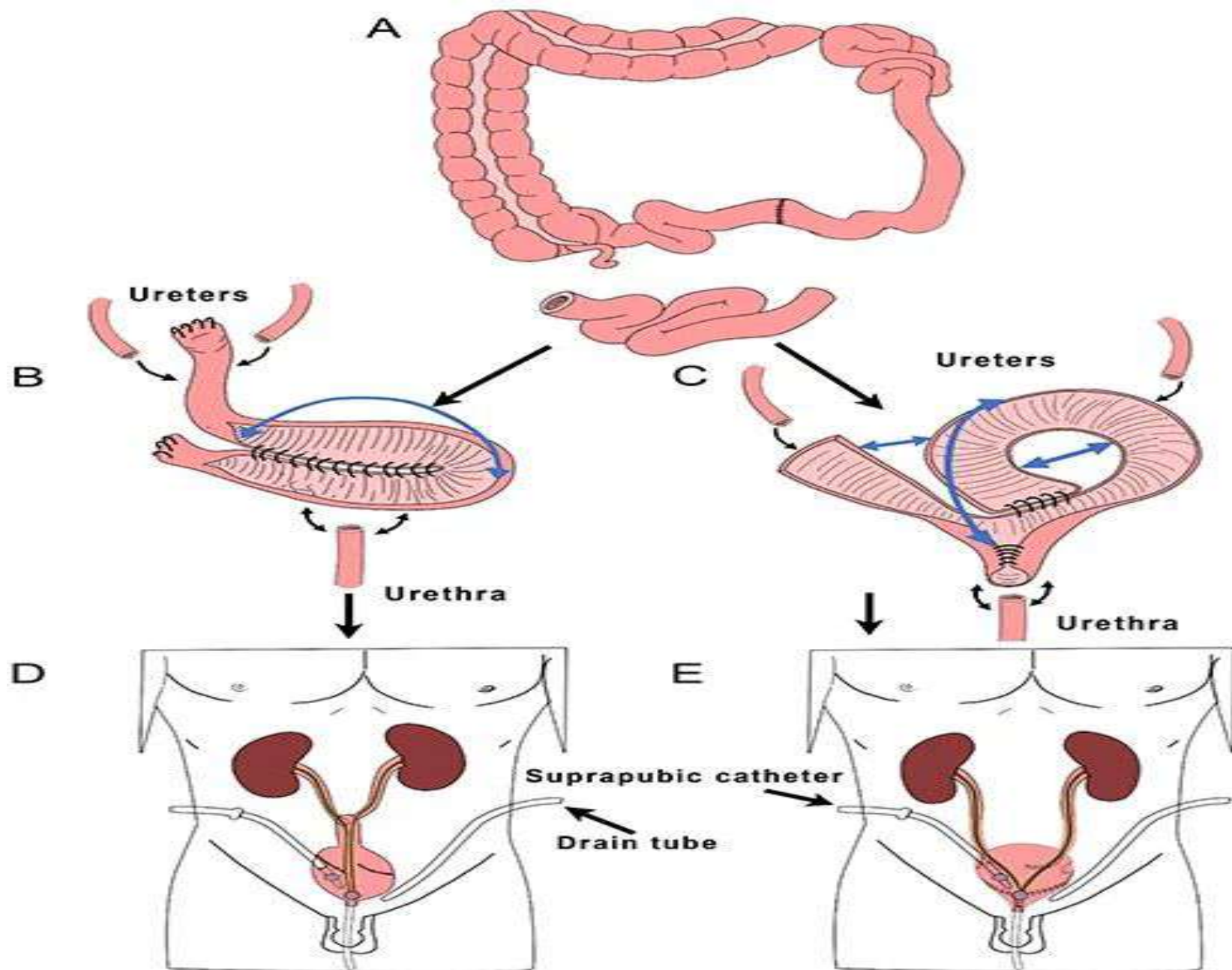


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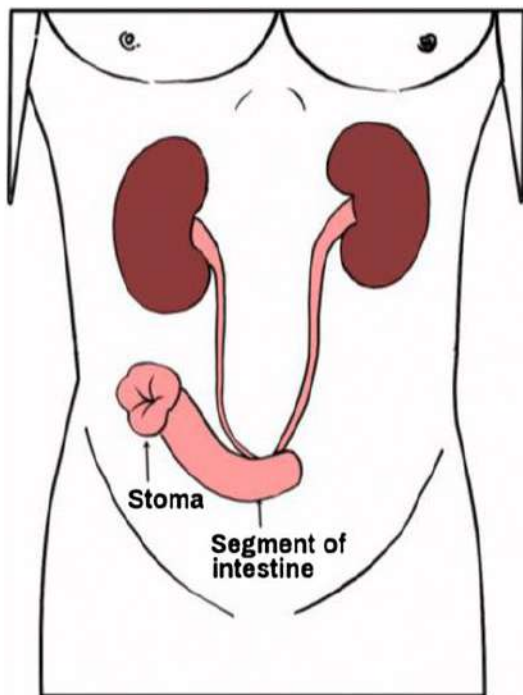


3. Orthotopic neobladder: بنتیل جزء من اړ intestine ډېرېځله په شکل Bladder [sphere] ډېرېځه غبرګون اړ ureter دندو لخوا پار urethra ډکله هدا بیا ضد دقت...

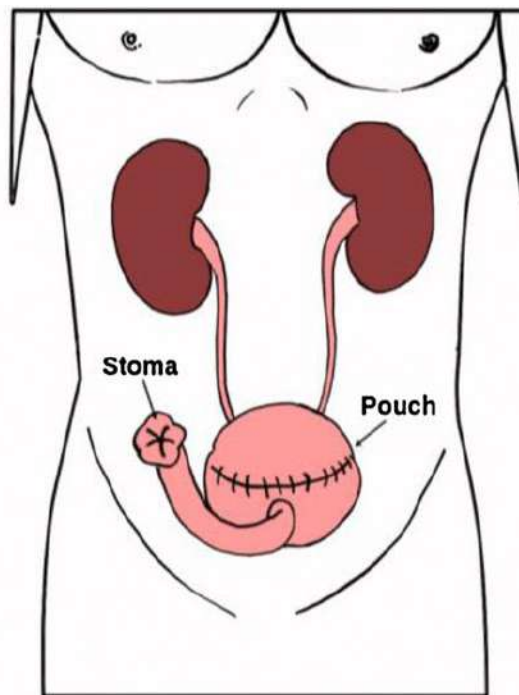
- commonly used both in men and women.
- The terminal ileum is the most often used.
- Emptying of the reservoir anastomosed to the urethra requires abdominal straining, intestinal peristalsis, and sphincter relaxation.



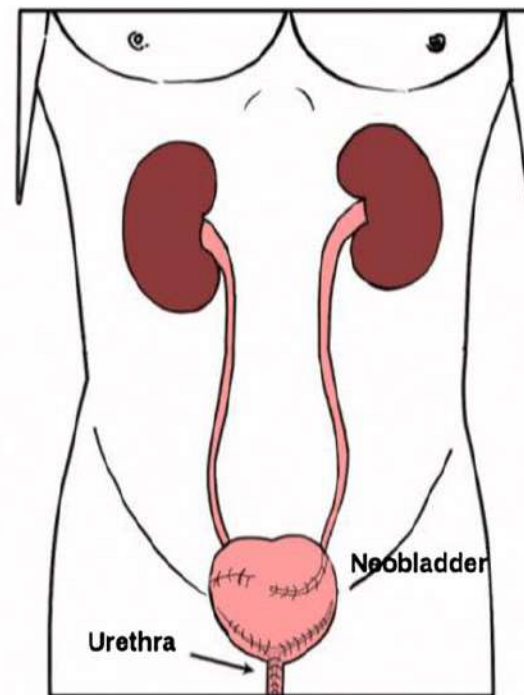
- Early and late morbidity in up to 22%.
- **long-term complications** included:
 - _ diurnal incontinence 8-10%.
 - _ nocturnal incontinence 20-30%.
 - _ metabolic disorders.
 - _ vitamin B12 deficiency
 - _ urinary retention
 - _ urinary tract infection
 - _ ureteroileal or afferent limb obstruction
 - _ urethral stricture
 - _ upper tract and pouch stones
 - _ vaginal fistula, and pouch rupture.



ILEAL CONDUIT
(incontinent
diversion to skin)



**CONTINENT
CUTANEOUS
RESERVOIR**
(continent diversion
to skin)



**ORTHOTOPIC
NEOBLADDER**
(continent diversion
to urethra)

Bladder-sparing treatments for localised disease [trimodal]

④ TURBT:

- should only be considered when the patient is unfit for cystectomy, or refuses open surgery, or as part of a multimodality bladder-preserving approach.

Recommendation	Strength rating
Do not offer transurethral resection of bladder tumour alone as a curative treatment option as most patients will not benefit.	Strong

② External beam radiotherapy (EBRT):

- Important prognostic factors for outcome include response to RT, tumour size, hydronephrosis, completeness of the initial TURB, age and stage.
- External beam radiotherapy alone should only be considered as a therapeutic option when the patient is unfit for cystectomy or as part of a multimodality bladder-preserving approach.

- Radiotherapy can also be used to stop bleeding from the tumor when local control cannot be achieved by transurethral manipulation because of extensive local tumor growth.

Recommendations	Strength rating
Do not offer radiotherapy alone as primary therapy for localised bladder cancer.	Strong

③ Chemotherapy:

قبل الجراحة neoadjuvant
بعد الجراحة adjuvant [Cis for T4 stage or true LN disease]

- Complete and partial local responses have been reported with cisplatin-based chemotherapy as primary therapy for locally advanced tumours in highly selected patients.
neoadjuvant improve the survival rate 5% + should give it as a adjuvant
Contraindicated in the Renal impairment [has nephrotoxicity]...

Recommendations	Strength rating
Do not offer chemotherapy alone as primary therapy for localised bladder cancer.	Strong



* if the histopathology is **SCC** ^{sq.}, whatever the stage → **Radical cystectomy**
↳ radio chemo resistant + has ↑ progression ...

radical cystectomy: $\geq T_2$ ← stage 1 & 2 → **TCC** 1, 2, 3
urethral resection: $< T_2$ ←

* if the histopathology is **Small cell Cancer** we should do **more work up**
metz work up, ~b~ up **chemotherapy** ∴ next step 1, ~b~ 2 ~b~ -ve all path ~b~
up is -ve. [not exclude the micro metz]...

* if the histopathology is **pheochromocytoma** we should do **partial cystectomy**
↳ rare - Benign - presented with paroxysmal
[↑BP] during urination

* if the histopathology is **adenocarcinoma** we should do **more work up**
end block + **Radical cystectomy**: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100
excision of urachus and umbilicus...

Bladder -preserving treatment

- Bladder preserving therapy should be offered to : -
 - patients with newly diagnosed MIBC who desire to retain their bladder
 - for those with significant comorbidities (radical cystectomy is not a treatment option) .
- Choices include : multimodal therapy, maximal TURBT, partial cystectomy with lymphadenectomy, and primary radiation therapy.

Trimodality therapy

It involves :

1. a maximal safe complete TUR,
2. chemotherapy (cisplatin, or 5-fluorouracil, and mitomycin)
3. radiation.

Appropriate candidates are those with adequate normal bladder function and **limited disease burden** : .

- if the bladder tumor is unifocal and small (<4 cm in maximal dimension)
- without frank extravesicular extension on imaging (i.e., not cT3b),
- is not causing hydronephrosis
- and can be gross totally resected by TUR.

Partial Cystectomy

- Ideal candidates for partial cystectomy include those with small, solitary tumors amenable to wide resection with 2 cm margins.
- _ It is imperative that the tumor is in a location that allows for complete resection while maintaining adequate functional bladder capacity

MANAGEMENT OF METASTATIC BLADDER CANCER

- Systemic cisplatin-based combination chemotherapy is the standard of care for patients with metastatic urothelial cancer
- Although the majority of patients with metastatic disease (40%–70%) will experience an initial response to chemotherapy, most will ultimately progress with a median survival of 14 months and overall 5 year survival rates of 5%– 20%.

.

Patients who meets any of the following criteria **are not cisplatin candidates:**

1. WHO or Eastern Cooperative Oncology Group performance status > 2
 2. creatinine clearance < 60 mL/min
 3. $\geq$ grade 2 audiometric hearing loss
 4. $\geq$ grade 2 peripheral neuropathy
 5. a New York Heart Association class III or higher heart failure.
- When cisplatin therapy is contraindicated, **carboplatin** has been substituted with the benefit of improved tolerability but with the cost of decreased efficacy

❖ Second-Line Chemotherapy

- Salvage chemotherapy in this setting with conventional agents typically has a suboptimal response rate .
- Multiple novel single agents have been evaluated in patients with advanced Bladder Ca, typically with modest response rates of < 20%

◆ Immune Checkpoint Inhibitor Therapy

- Tumor cells may express PD-L1 as a mechanism to neutralize T-cell activation. These immune checkpoint inhibitors result in an increase in T-cell activation and proliferation, which may result in an antitumor response.
- The anti-PD-L1 and anti-PD-1 agents have been approved for platinum-resistant and cisplatin-ineligible metastatic urothelial cancer .
- Recently, avelumab has been approved as a maintenance therapy in patients with unresectable locally advanced or metastatic urothelial cancer who did not have disease progression with first-line chemotherapy

◆ Fibroblast Growth Factor Receptor Therapy

- Erdafitinib is a kinase inhibitor approved for patients with locally advanced or metastatic Bladder Ca that has susceptible genetic alteration
- Clinical trial showed that patients who received erdafitinib had response rate of 40% and median duration of response was 5.6 months

Prognosis

RATE OF PROGRESSION AND SURVIVAL BY TUMOR STAGE AND GRADE:

Stage	Grade	Progression	5 yr survival	10 yr survival
Ta	1	0-2%	100%	95%
	2	10-20%	95%	89%
	3	40-50%	95%	84%
T1	2	10-20%	90%	78%
	3	40-50%	70%	50%
CIS	3	30-50%	70%	55%

FOLLOW-UP

Time schedule for surveillance:

- guided by the principle that recurrences tend to occur within the first years following initial treatment.
- A schedule suggested by the EAU Guidelines Panel includes a CT scan (every 6 months) until the third year, followed by annual imaging thereafter.

Conclusion

1- Stage Ta, T1- grade 1,2

TURBT

follow up 3 month.

If recurrence – repeat mitomycin C.

2- Stage T1,grade3 +- Cis

BCG 2cycles

3- T2 + greater-

cystectomy- diversion

- neobladder

- conduit reservoir

4- Squamous/adenocarcinoma

cystectomy

5- patient unfit for surgery

Radio/chemotherapy

Thank you