INTRAVESICAL THERAPY FOR TCC BLADDER

Dr. Sanjeev Bandi

AIM: Prevent recurrence and progression of superficial TCC.

USED: Prophylaxis, persistent tumour, CIS.

RISK RECURRENCE:

* Tumour grade and stage
* Number of tumours
* Duration disease > 1 yr
  (ie. frequent recurrences)
* Positive cytology

TUMOR PROGRESSION

(muscle invasion or metastases)

	G1	G2	G3
Ta	2%	6%	25%
T1	N.A.	25%	50%

INDICATIONS - ? all T1 tumours

- T_a tumors - multifocal, high grade

- CIS

AGENTS - CHEMOTHERAPY: - Thiotepa,

Adriamycin,

Mitomycin C

- IMMUNOTHERAPY - BCG

Chemotherapy - Delays recurrences only, but by 5 yrs.

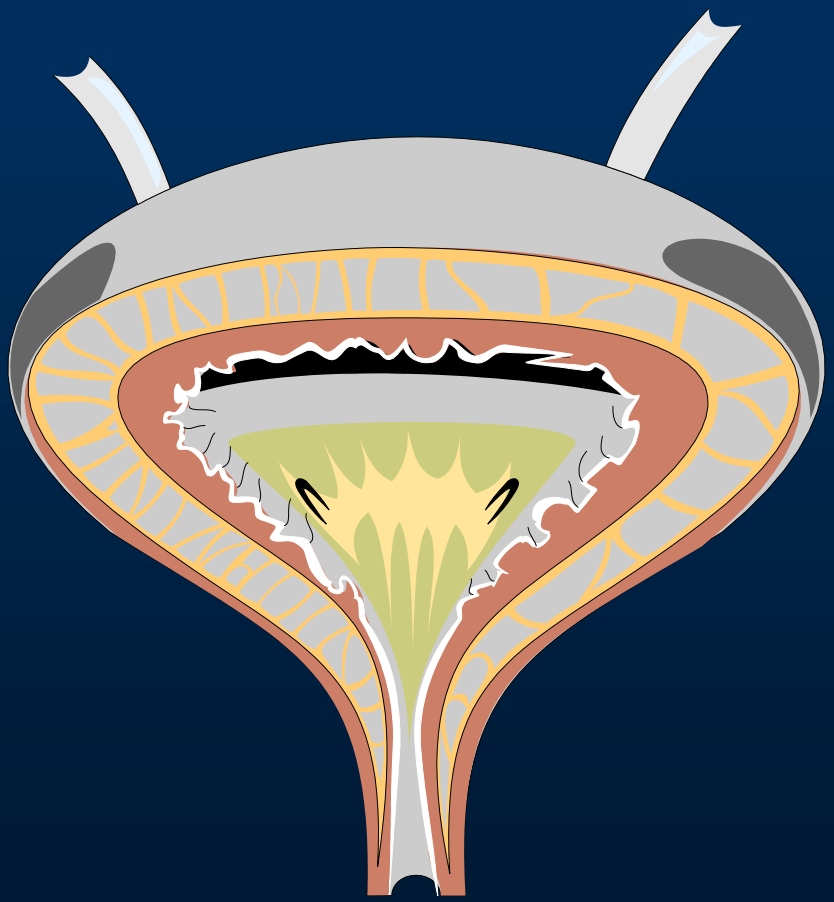
incid recurrences treated pts equals

controls. DOES NOT alter progression.

BCG - ↑ response rates + ↑ duration

↓ progression ie. alter natural history.

INTRAVESICAL BCG



Definition: Attenuated live culture preparation of the bacillus Calmette-Guerin strain of M.bovis.

Dose: Usually 5 - 7x10^{8} CFU's / ampoule = 50mg wet weight.

Mechanism Action: 2 step

1. Attachment to fibrinectin - inhib by anticlotting agents.
2. Effector events - probably immunological (not direct toxicity or acute inflamm.)

Probably antigenic recognition of BCG AG → cascade events → kill tumour cells.

Acts through DTH response:

- ↑ natural killer cells
- ↑ mononuclears - chronic

Inflamm reaction with granulomas is required.

- lymphokines (1L - 2)

INTRAVESICAL BCG.....contd

Relative Contraindications:

Rel. c/1 - no direct contact - muscle invasion

- prostatic urethra

- immune compromised - HIV

- I/S

- steroids

- anticoagulants

- UTI - recent endoscopic biopsy - traumatic catheterisation

- current antibiotics: - TMP-SMX, Noroxin

CARE WITH PREPARATION

- minimise splash + needlestick
- use within 4 hrs of preparation
- wash areas with chlorine disinfectant
- Dispose - toilet with bleach for 6 hours
- avoid intercourse 24 hours

TREATMENT PROTOCOLS

- Usually 6 x weekly installations
- Commence 2 - 4 weeks after cystoscopy and biopsy
- Remember - protocols are arbitrary only. Aim is to achieve an inflamm response. ie. can stop or delay further doses once inflamm reaction achieved or even ↓ dose if excessive local reaction.

Some institutions keep giving (up to 12 doses or till next C/E) until inflamm response achieved.

TREATMENT PROTOCOLS

Maintenance - some evid of ↑ CR rate esp with BCG

- 6 x weekly then monthly for 1 yr
- 6 x weekly - gap - 6 x weekly
- 12 x weekly

but ↑ local S/E with maintenance

COMPLETE RESPONSE AT > 1 YR

	Rec rate prophylaxis (%)	Eliminate Existing Disease (%)	Eliminate CIS (%)
CONTROLS	50		
BCG	20 (50% 5 yrs)	60	70
MITC	30	50	40
Adria	40	30	25
Thiotepa	45	35	15

Some evidence of ↓ progression rate + ↑ survival with BCG.
(Gp pts High G1 T_a /T_1 (50% concomitant CIS)
- progression 90% controls + 50% BCG.
Pt not failure unless develops inflamm reaction - Some correlation with PPD skin test conversion + devpt inflamm response, but some pts never convert.

COMPLICATIONS OF BCG

1. Side Effects

- frequency, dysuria, low grade fever + flu like symptoms after 2-3 installations (frequent)

2. Significant Adverse Reactions

- high fever (3%) - if persists consider INH, check CXR + LFT's.
- GRANULOMATOUS PROSTATITIS (0.9%) symptomatic.

  (if Bx prostate 40% have pathological prostatitis)

  - assoc with ↑ PSA (measure PSA + DRE prior to Bx)
- PNEUMONITIS, HEPATITIS (0.7%)

  - granulomas - usually no M/O on AFB stains

  - probably H/S reactions not infections.
- BCG SEPSIS (0.4%) ~ 10 reported deaths

  Associated with intravascular absorption due to traumatic IDC, UTI, installation at time of tumour resection.
- S & S - high fever, ↓ BP, confusion, ↓ WCC, resp failure.

  Treat with INH, Rifampicin, Cycloserine & Genta/Amp.

COMPLICATIONS OF BCG.....contd

- Migratory Arthralgia + Rash (0.5%)
- Abscess - epididymitis, orchitis (0.4%)
- Ureteral obstruction (0.3%) assoc with reflux
- Acontractile bladder

Rare - GN, nephrogenic adenoma, adenitis, mycotic aneurysm

RENAL TUBERCULOSIS

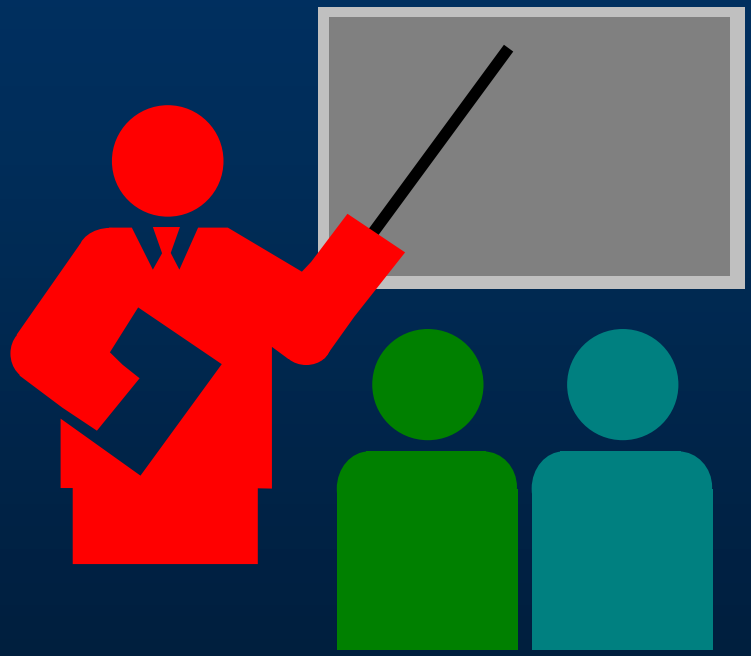
- Incidence decreased during the last half of this century in most developed countries.
- AIDS and immigration have been cited as an explanation for its resurgence.
- After 5-8 years, approximately 8-10% of patients with pulmonary tuberculosis develop genitourinary tuberculosis.

RENAL TUBERCULOSIS
PATHOGENESIS 1

- M. tuberculosis and M. bovis are the most likely cause of renal tuberculosis.
- Atypical organisms can cause disease clinically, radiologically and histologically indistinguishable from the above but the patient usually has had previous treatment with steroids or immunosuppressive drugs or AIDS.
- Renal tuberculosis is the result of the dissemination of the tubercle bacilli via the bloodstream, usually from the lungs but the site could be the GI tract.

RENAL TUBERCULOSIS
PATHOGENESIS 2

- There will be foci of infection in both kidneys though the disease is manifested usually unilaterally.
- The primary lesion is in the glomerulus and it may heal rapidly or progress.
- Subsequent granuloma formation and giant cells may lead to caseous necrosis through the wall of the calyx forming the first radiologically visible lesion.



RENAL TUBERCULOSIS
PATHOGENESIS 3

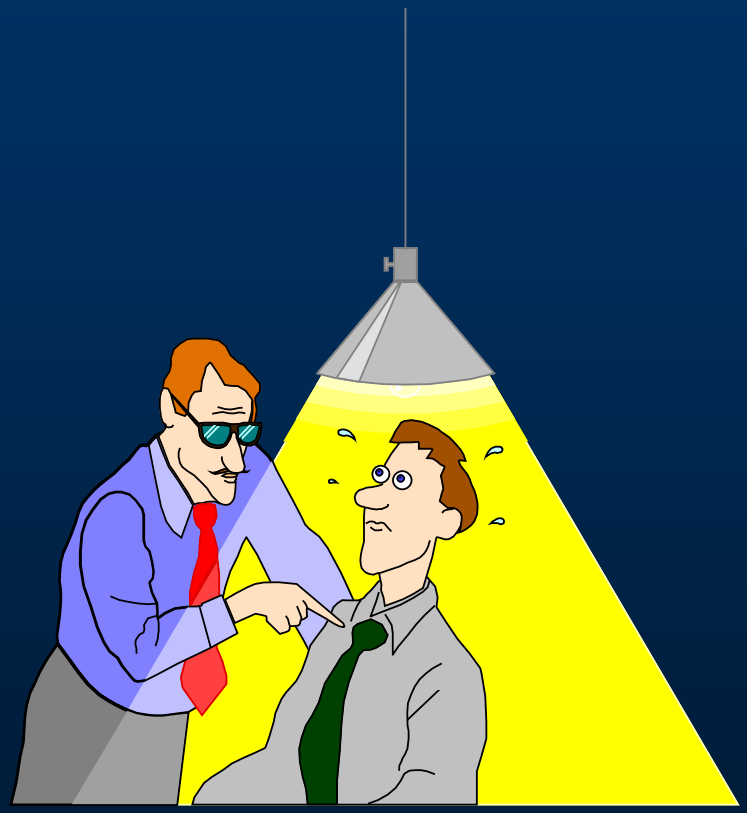
- Further spread occurs along the mucosal surfaces of the renal pelvis and calyces down the ureter to the bladder.
- Healing is characterised by fibrosis and later calcification-leading to distortion of renal pelvis - leading to partial or autonephrectomy(putty kidney).
- Fibrosis affects the ureter and strictures occur at the UVJ,UPJ, the mid ureter or in females where it crosses the broad ligament.

RENAL TUBERCULOSIS
PATHOGENESIS 4

- An early stricture of the ureter may lead to a non-functioning kidney in several weeks.
- The bladder heals by fibrosis and a severely contracted bladder may result(thimble bladder).
- Renal blood supply may be impaired and the fibrosis occurring may result in hypertension.
- Tuberculous prostatitis and epididymitis usually is secondary to renal TB but may be blood borne.

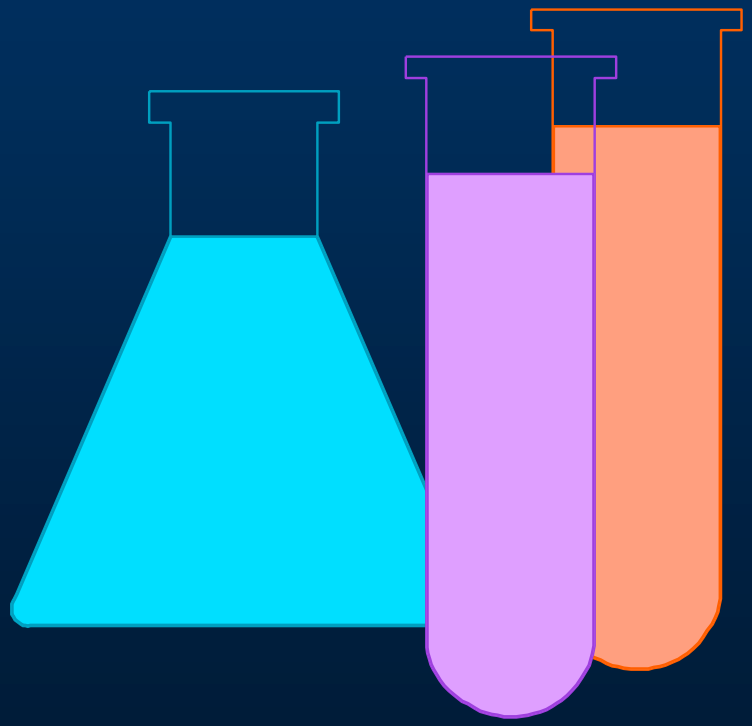
RENAL TUBERCULOSIS
CLINICAL PRESENTATION

- Renal TB has no classic clinical presentation.
- Vast majority of patients are born abroad and the most common symptoms are frequency, nocturia and dysuria.
- Next most common complaint is tender epididymis which may at times form draining sinuses.
- Symptoms may be few or absent even with advanced disease.
- Physical examination may be unremarkable apart from chronic draining epididymal sinuses, a beaded and indurated vas and a shrunken, irregular and hard nodular prostate.



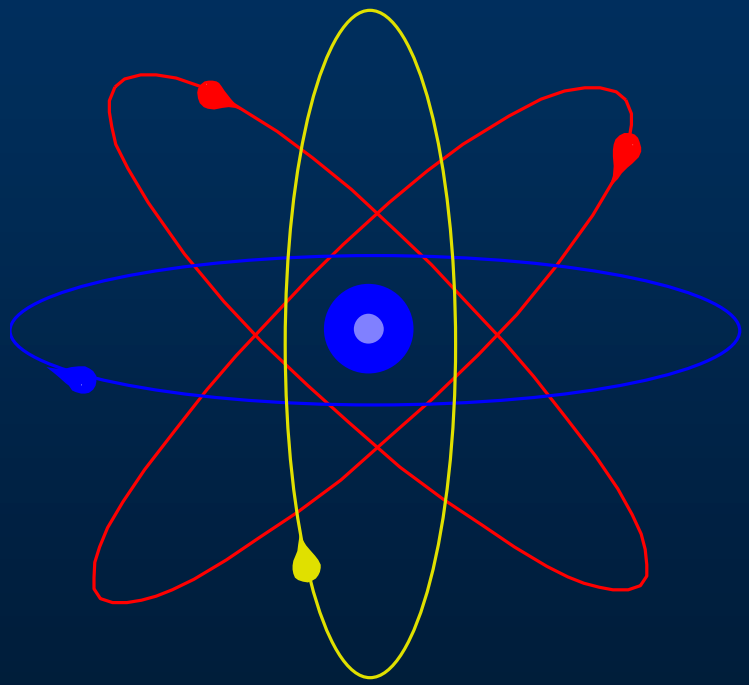
RENAL TUBERCULOSIS
DIAGNOSIS 1

- Skin testing and CXR are important initial studies.
- Urinary test results may vary considerably but STERILE ACID PYURIA is the classical finding.
- Secondary infections are often observed but sterile pyuria will persist after treatment.
- A minimum of 3 clean catch fresh early morning urine samples are required for confirmation of diagnosis.
- These should be cultured and stained for AFB.



RENAL TUBERCULOSIS
DIAGNOSIS 2

- An IVU may show punctate calcification or large areas of renal calcification on plain film.
- The contrast study may show delayed excretion , moth eaten calyces, exclusion of 1 or more calyces, parenchymal cavitation & scarring, ureteral strictures and hydroureteronephrosis, bladder wall thickening and contraction.



RENAL TUBERCULOSIS
DIAGNOSIS 2

- A CT scan is often the initial modality to suggest the inflammatory nature of the mass seen on IVU.
- Cystoscopy may reveal the classic “pepper-and-salt” pattern around 1 or both ureteric orifices.
- Retrograde pyelography may be required if the kidneys are poorly functioning.

RENAL TUBERCULOSIS

MEDICAL TREATMENT- THE BASIC PRICIPLES

- Multidrug therapy is required.
- Treatment should be continued for 6 MONTHS or longer if necessary.
- PATIENT COMPLIANCE is of the utmost importance in following this prolonged medical regimen.

RENAL TUBERCULOSIS
STANDARD CHEMOTHERAPY

- ISONIAZID 300mg/d
- RIFAMPICIN 600mg/d
- PYRAZINAMIDE 1000mg/d
- PYRIDOXINE(Vitamin B6) 25mg/d to prevent the occurrence of peripheral neuropathy with ISONIAZID.
- This regimen for 2 months and if no unusual findings on tests continue ISONIAZID & RIFAMPICIN for 4 months more.

RENAL TUBERCULOSIS
MEDICAL FOLLOWUP

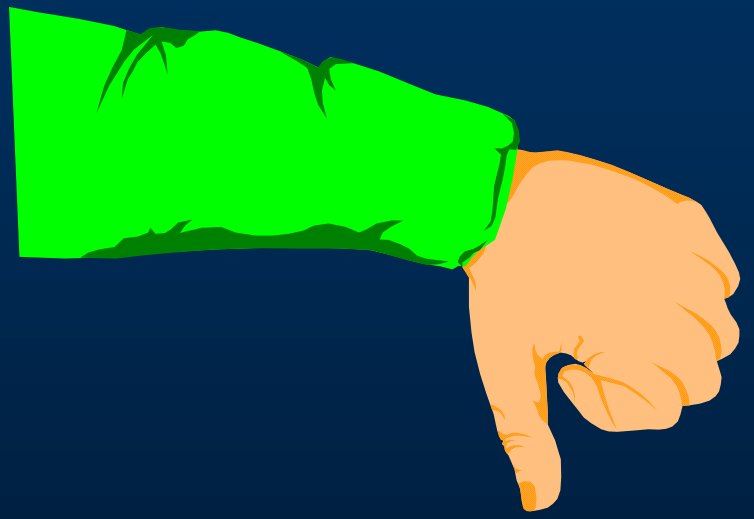
- During medical therapy, cultures are performed every 2 months and then every 6 months for 3 years.
- Renal scans and ultrasonography are performed on a 2 monthly basis to determine the degree of renal function as well as development or progression of hydronephrosis.
- After treatment, U/S is performed every year for 3 years.

RENAL TUBERCULOSIS
DRUG TOXICITY

- Hepatic toxicity from INH, Rifampicin and Pyrazinamide - patient may present with malaise, jaundice,fever, anorexia & vomiting.
- Asymptomatic rise in AST, ALT and Alkaline phosphatase.
- Rifampicin induced interstitial nephritis.
- Uric acid nephropathy.
- Rifampicin induced stimulation of liver enzymes may effect the drug kinetics of cardiac glycosides, anticoagulants, oral contraceptives, oral antidiabetics, narcotics, corticosteroids and analgesics.

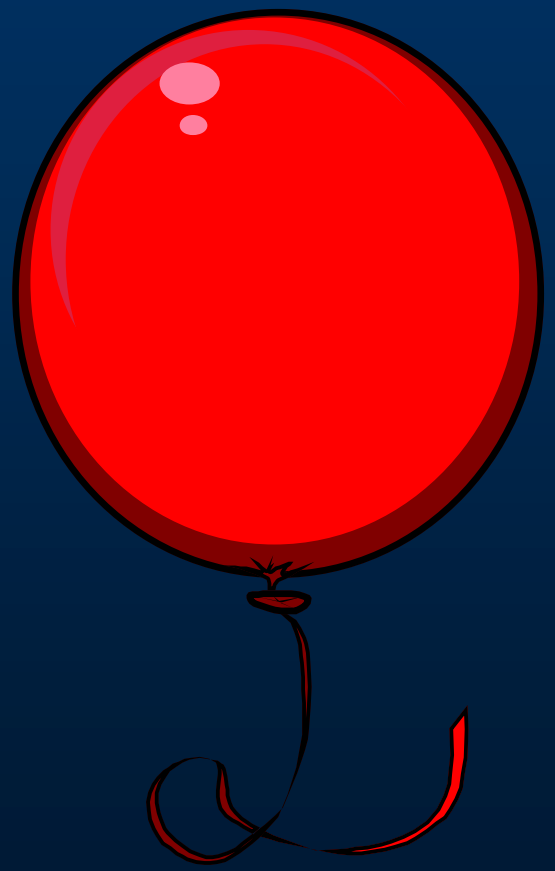
RENAL TUBERCULOSIS
SURGICAL TREATMENT

- **NEPHRECTOMY is performed in patients with intractable pain, uncontrollable fever, persistent haematuria, bacterial resistance or uncontrollable HTN caused by a poorly functioning kidney not responding to antihypertensive drugs.**
- **Patient should at least have 3 weeks of anti TB therapy prior to surgery.**
- **Extraperitoneal approach**
- **Dissection may be difficult**
- **Artery and vein are poorly defined so mass ligature of pedicle with absorbable suture needed.**



RENAL TUBERCULOSIS
URETERAL STRICTURE

- The lower ureter is most commonly involved.
- Balloon dilatation and insertion of JJ stent for 3-6 weeks initially.
- If this fails, ureteroneocystostomy with or without psoas hitch or Boari flap.
- PUJ strictures are best handled with a dismembered pyeloplasty.
- No open operative procedure should be performed until 3 weeks of anti TB therapy.



RENAL TUBERCULOSIS

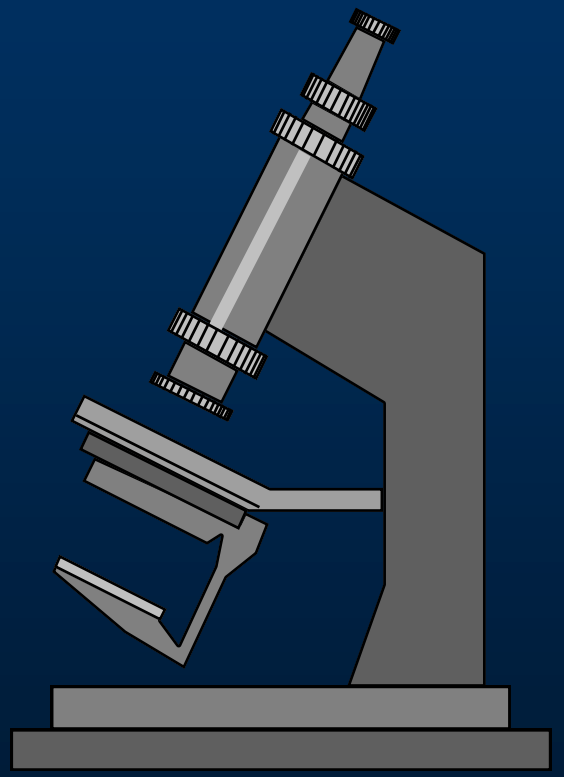
TUBERCULOUS CYSTITIS

- In a few patients with GU TB, extensive fibrosis of the urinary bladder may occur during the healing process.
- The bladder has a markedly reduced capacity and may develop ureteral obstruction or vesicoureteric reflux.
- Bladder augmentation may be performed with the caecum or sigmoid.
- Bladder neck or urethral strictures may require endoscopic incision.

RENAL TUBERCULOSIS

TUBERCULOUS EPIDIDYMITIS & PROSTATITIS

- Epididymitis may be the first manifestation of genitourinary TB.
- If chronic sinuses or painful epididymitis persists it may require epididymectomy.
- TB prostatitis can easily be confused for prostate cancer. Abnormal DRE after appropriate treatment may require percutaneous biopsy.



RENAL TUBERCULOSIS

- THE INITIAL THERAPY FOR GENITOURINARY TUBERCULOSIS IS CHEMOTHERAPY & SURGERY IS REQUIRED ONLY IN SPECIAL CLINICAL SETTINGS.