INTRAVESICAL THERAPY
FOR TCC BLADDER

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**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)*

<table>
<thead>
<tr>
<th></th>
<th>G1</th>
<th>G2</th>
<th>G3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ta</td>
<td>2%</td>
<td>6%</td>
<td>25%</td>
</tr>
<tr>
<td>T1</td>
<td>N.A.</td>
<td>25%</td>
<td>50%</td>
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</table>
INDICATIONS - all T1 tumours

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

Dose: Usually $5 \cdot 7 \times 10^8$ 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 \( \rightarrow \) kill tumour cells.

Acts through DTH response:

- natural killer cells
- mononuclears - chronic

Inflamm reaction with granulomas is required.

- lymphokines (1L - 2)
Relative Contraindications:

- 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

<table>
<thead>
<tr>
<th></th>
<th>Rec rate prophylaxis (%)</th>
<th>Eliminate Existing Disease (%)</th>
<th>Eliminate CIS (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CONTROLS</td>
<td>50</td>
<td>60</td>
<td>70</td>
</tr>
<tr>
<td>BCG</td>
<td>20 (50% 5 yrs)</td>
<td>60</td>
<td>70</td>
</tr>
<tr>
<td>MITC</td>
<td>30</td>
<td>50</td>
<td>40</td>
</tr>
<tr>
<td>Adria</td>
<td>40</td>
<td>30</td>
<td>25</td>
</tr>
<tr>
<td>Thiotepa</td>
<td>45</td>
<td>35</td>
<td>15</td>
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</tbody>
</table>

Some evidence of ↓ progression rate + ↑ survival with BCG. (Gp pts High G1 Tₐ /T₁ (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.
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.
• 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.
• 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.
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 PRINCIPLES

• 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.
• 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.
• 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.
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.
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.