ESSENTIAL UROLOGY FOR MEDICAL STUDENTS

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Assistant Professor Charles Chabert
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Assistant Professor Charles Chabert

As a final year medical student at Bond University, it was a pleasure working with Dr Chabert in Urology, and my experiences and knowledge attained have been reflected in this book, which I hope will serve as a tool for all medical students. It contains the essential Urology facts that a student must know in a clear and concise format, so enjoy reading.

Nishanth Krishnananathan
1. Acute Scrotal Pain

2. Prostate Specific Antigen.


4. Localised Prostate Cancer.

5. Macroscopic Haematuria.


7. Urothelial Cancer.

8. Renal Cell Carcinoma.

Acute Scrotal Pain is the presenting symptom for a wide spectrum of surgical conditions which may present in adolescents to adults. The aim of evaluation is to identify testicular torsion due to the threat of irreversible testicular ischemia and subsequent infarction.

**Differential Diagnoses**

1. **Testicular Torsion** (16.0–39.5%)\(^1\)
2. **Torsion of Testicular Appendages**
3. **Epididymo-orchitis**
4. **Testicular Trauma**
5. **Testicular Neoplasm(s)**

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**TESTICULAR TORSION (TT)**

**IMPORTANT** ➔ *Acute scrotal swelling in children indicates torsion of the testis until proven otherwise*.\(^2\)

**Definition:**
- Twisting or rotation of the testis on the axis of the spermatic cord.
- **Surgical emergency** as it causes strangulation of the gonadal blood supply with subsequent testicular necrosis and atrophy
- Torsion can be partial or complete (vary from 180–720°)

**Incidence:**
- Neonates/young adolescents (12-18, with a peak at 14), but can occur at any age. The prevalence is 1 in 4000 males less than 25 yrs old.\(^3\)

**Types:**
- **Extravaginal** (the whole cord and its investing layers twist, 5% of all torsions). More commonly associated with the neonatal age group.
- **Intravaginal** usually occurs in older children (also referred to as the Bell Clapper Deformity).

**Causes:**
- **Bell-Clapper Deformity** (12% of all males\(^5\)), a congenital abnormality in which the testicle lacks the normal attachment to the tunica vaginalis (permitting increased mobility) and rests transversely within the scrotum.
- Other: physical/sexual activity, trauma (4-8%\(^6\)).
Presentation:

1. Clinical features
   - Acute unilateral severe sudden onset testicular pain.
   - Nausea and vomiting (1/3 of patients, higher in paediatric population) \(^7\)
   - Abdominal pain (20-30\%) \(^8\)
   - Fever (16\%) \(^9\)
   - Urinary frequency (4\%) \(^10\)

2. Physical examination
   - Asymmetrically high-riding testis on the affected side with horizontal lie.
   - Diffuse testicular tenderness
   - Testicular oedema + scrotal erythema
   - Ipsilateral loss of the cremasteric reflex.
   - Prehn’s sign negative i.e. scrotal elevation relieves pain in epididymitis but not torsion.


Diagnosis:

- Clinical
- Colour Doppler Ultrasound (94% sensitivity, 96% specificity.) \(^\)\(^11\)

Treatment:

- Urgent surgical de-torsion and fixation (orchidopexy) of both testicles due to risk of contralateral torsion in the future
- A salvage rate of 90-100\% is found in patients who undergo de-torsion within 6 hours of onset of pain - the viability rate falls to 20\% and 50\% after 12 hours; and 0-10\% if de-torsion is delayed greater than 24 hours \(^12\).

TORSION OF TESTICULAR APPENDAGES (TTA)

Definition:

- The appendix testis (Hydatid of Morgagni), a mullerian duct remnant located at the superior pole of the testicle, is the most common appendage to undergo torsion (92\%) \(^13\).

Incidence:

- 7-14 y.o. (80\%), with a mean age of 10.6 \(^14\).

Presentation:

1. Clinical features:
   - Acute/Subacute onset of testicular pain (less severe and more gradual in onset when compared to Testicular Torsion) \(\rightarrow\) Pain at superior pole of testicle.
   - Patients may endure pain for several days before seeking medical attention.
   - Absence of systemic symptoms (nausea/vomiting) and urinary symptoms.

2. Physical examination:
   - Localised tenderness (upper pole of the testis)
   - Blue dot sign \(\rightarrow\) paratesticular nodule. Seen in 21\% of people \(^15\) (mainly light-skinned boys, or children due to their thin scrotal skin).
   - Normal vertical lie

Diagnosis:

1. Mainly clinical.
2. Testicular Ultrasound (TU)
3. Other: Colour Doppler Ultrasound (95.7% sensitivity and 48.7% specificity\textsuperscript{16})

**Treatment:**
- Conservative i.e. rest, analgesia and scrotal support to alleviate swelling.
- Pain should resolve in 5-10 days with surgery reserved for patients with persistent pain\textsuperscript{17}.

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**EPIDIDYMO-ORCHITIS**

**Definition:**
- Acute epididymitis is the inflammation of the epididymis, and when the infection extends down to the adjacent testicle, it is referred to as acute epididymo-orchitis

**Incidence:**
- Bi-modal age distribution i.e. younger sexually active males or older population with BPH/LUTS (See Chapter 3)

**Causes:**

a.) Epididymitis:
- Prepubertal males: **E-Coli**.
- Sexually active males/males <35: **Chlamydia Trachomatis** (50-60\textsuperscript{\%})\textsuperscript{18}, Nisseria Gonorrhoea.
- Older males/males >35: **E-Coli**

b.) Orchitis:
- Viral (most common cause) \(\rightarrow\) **Mumps**. It presents mainly unilaterally (70\%\textsuperscript{19}) in the paediatric population. General presentation is recent mumps infection/parotitis with testicular oedema (4/5 are pre-pubertal males\textsuperscript{20}).
- Bacterial infections (as above) can cause orchitis.

c.) Other causes:
- Viral (infectious mononucleosis, Coxsackie virus)
- Drugs (3-11\% of people taking Amiodarone\textsuperscript{21})
- Obstruction (BPH in older males)
- Tb (immuno-compromised people)
- Vasculitic Syndromes (Sarcoidosis)
- Post surgery or catheterisation.

**Presentation:**

1. **Clinical features** (dependent on cause)
   - **Acute/sub-acute onset of moderate unilateral scrotal pain** (bilateral in 5-10\%\textsuperscript{22}).
   - Pain localizes to posterior testicle (+/- radiation to the flanks/abdomen).
   - History of **frequency, urgency, dysuria, urethral discharge** (10\%\textsuperscript{23})
   - Nausea and/or low grade fever and chills (25\% of adults, 71\% of children\textsuperscript{24}) – not as common as testicular torsion.
   - Blood in semen.
   - Painful intercourse + ejaculation

2. **Physical examination**:
   - Erythematous, oedematous hemi-scrotum
   - Epididymis is engorged, swollen and tender
   - The affected testis has a normal vertical lie
- **Cremasteric reflex is intact.**
- **Prehn’s sign is positive**
- Scrotal oedema is present in 50% of cases\(^{25}\)
- Enlarged inguinal lymph nodes

3. **Complications:**
   - Scrotal abscess, pyocele, testicular infarction, chronic epididymitis, infertility, cutaneous fistulisation.

**Diagnosis:**
1. Mainly Clinical
2. Full Blood Count (FBC) \(\rightarrow\) Leukocytosis
3. Urine M/C/S (Pyuria) + Urethral Swab Culture
4. Colour Doppler Ultrasonography (CDU) : sensitivity of 91-100% for epididymitis +/- orchitis\(^{26}\)

**Treatment:**
- Antibiotics i.e. Ceftriaxone + Doxycycline for Chlamydia/Gonorrhoea
  - Trimethoprim-Sulfamethoxazole to cover coliforms in Pre-pubertal boys\(^{27}\)
- Analgesics + NSAIDS
- Scrotal support + elevation + bed rest.
- Pain generally self resolving (one week)
- Surgery considered for complications.

**SUMMARY**

<table>
<thead>
<tr>
<th>Acute Scrotum</th>
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</thead>
<tbody>
<tr>
<td><strong>Condition</strong></td>
</tr>
<tr>
<td>Testicular Torsion</td>
</tr>
<tr>
<td>TTA</td>
</tr>
<tr>
<td>Epididymo-orchitis</td>
</tr>
</tbody>
</table>
REFERENCES


L.Galejs, E.Kass, *Diagnosis and Treatment of the Acute Scrotum*, American Family Physician, Feb 1999,


Dugani S., Lam D, *Toronto Notes 2009*, Mcgraw Hill Professional; Canada, 2009
Prostate Specific Antigen (PSA)

Prostate specific antigen is a serine protease produced specifically by the prostate. It can be increased by inflammation, benign prostatic hyperplasia (BPH), or by cancer of the prostate.

Role in Body
PSA liquefies the seminal fluid.

PSA Test
PSA is a blood test used to detect early prostate cancer (increased in 25-92% of people\(^1\)); however elevation of PSA is not specific for cancer; it can also be increased due to inflammation or BPH.

Causes for an elevated PSA include:
- BPH (increased in 30-50% of people\(^2\))
- Recent rectal examination, prostate massage, prostatitis, UTI, urinary catheterization,
- Acute urinary retention, ejaculation and acute renal failure.

Evaluation of different aspects of PSA allows improvements in the utility of the test. These include:
- Age specific value
- Median value
- Free-total ratio
- Velocity, increase the utility of the test
- PSA density

1. **Age- Reference values + Median values.**

<table>
<thead>
<tr>
<th>Age</th>
<th>Median PSA</th>
<th>Normal Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>40-49</td>
<td>0.7ng/ml</td>
<td>0-2.5ng/ml</td>
</tr>
<tr>
<td>50-59</td>
<td>0.9ng/ml</td>
<td>0-3.5ng/ml</td>
</tr>
<tr>
<td>60-69</td>
<td>1.4ng/ml</td>
<td>0-4.5ng/ml</td>
</tr>
<tr>
<td>70+</td>
<td></td>
<td>0-6.5ng/ml</td>
</tr>
</tbody>
</table>

2. **Free-Total ratio**
PSA is bound to alpha 1 antichymotrypsin in plasma. When produced by malignant disease, it has a higher affinity for this protein than benign produced PSA. As a result, there is an inverse correlation between F/T ratio and prostate cancer risk.
- Risk of CAP is 55% if F/T ratio <10%
- Risk of CAP 7% if F/T ratio >25\(^3\)
3. **Velocity.**
PSA velocity is calculated over a period of 12 months with at least 3 measurements.
- A velocity of \(0.75\text{ng/ml/yr}\) increases the risk of CAP.
- A velocity of \(0.35\text{ng/ml/yr}\) is consistent with BPH.

**Prostate Biopsy**
Abnormalities of PSA and DRE are evaluated further through a Trans-Rectal Ultrasound (TRUS) biopsy. See Cancer of the Prostate (CAP) for further information.

**Pros + Cons of PSA Testing**

**Positives**
- Allows early detection of CAP
- Decreased risk of CAP death.
- Decreased risk of metastasis.
- Reassurance (if negative)
- Early intervention.
- The PSA test itself is inexpensive, and there are minimal side effects.

**Negatives**
- The positive predictive value of a PSA test is only 30%, and when combined with a DRE is 38-50%\(^5\).
- The PSA test has a sensitivity of 34.9% and the specificity is 63.1%\(^6\).
- Only one in three men with a high PSA level will have cancer\(^7\).
- False positives can create anxiety for the patient and his family.
- False negative rate of 25%
- Can lead to overtreatment of indolent disease.
- Further evaluation for CAP risk involves a TRUS biopsy introducing the potential for complications such as a 1% chance of infection\(^8\).
REFERENCES

(1,2) D.Provan, A.Krentz, Oxford Handbook of Clinical and Laboratory Investigation, 2002, UK, p 90.


(5) S.Brosman, Prostate Specific Antigen, E-medicine Urology, April 2009, last viewed on March 24 2010.


(Table) C.Chabert, Laparoscopic Urology Australia, 2010.


CHAPTER 3

Benign prostatic hyperplasia (BPH)

BPH is the most common prostate disease in men in Australia\(^1\). It is the hyperplasia of stroma and epithelium in peri-urethral area of prostate (transition zone)\(^2\). The prevalence of histopathologic BPH is age dependent, with initial development usually after 40 years of age\(^3\). By 60 years of age, its prevalence is greater than 50% and by age 85 is as high as 90% (incidence is proportional to age)\(^4\). The exact aetiology of BPH is unknown, although there is a possible correlation with testosterone production, impaired apoptosis, and other growth factors.\(^5\)

Clinical Presentation

BPH causes lower urinary tract symptoms (LUTS). These can be broadly classified into obstructive and overactive bladder (OAB) symptoms.

<table>
<thead>
<tr>
<th>Obstructive symptoms</th>
<th>Irritative symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hesitancy</td>
<td>Frequency</td>
</tr>
<tr>
<td>Weak stream</td>
<td>Urgency</td>
</tr>
<tr>
<td>Straining (stranguria)</td>
<td>Nocturia</td>
</tr>
<tr>
<td>Feeling of incomplete bladder emptying</td>
<td></td>
</tr>
<tr>
<td>Dribbling (Post-micturition)</td>
<td></td>
</tr>
<tr>
<td>Intermittent flow</td>
<td></td>
</tr>
</tbody>
</table>

Objective assessment is carried out by ‘The International Prostate Symptom Score’\(^6\) (IPSS) questionnaire which assesses the severity of symptoms and their effects on the patient’s quality of life. (Appendix 1)

Complications secondary to BPH are:
- Urinary retention
- Renal insufficiency
- Recurrent urinary tract infections
- Macroscopic haematuria
• Bladder calculi
The presence of these complications requires to bladder outlet surgery.

Prognosis
The prognostic features for BPH progression are:
1. PSA>1.4
2. Prostate Volume>40cc
3. Age>65
4. PVR>150mls.

Clinical assessment includes an abdominal examination and a digital rectal examination (DRE). A DRE should be done to assess prostate size and consistency, to detect nodules, indurations, and asymmetry. The prostate is usually smooth, rubbery and symmetrically enlarged in patients with BPH (median sulcus remains palpable).

Investigations
Investigating BPH includes combining History and DRE with Urinalysis, Blood tests, Imaging and occasionally a cystoscopy.
1. DRE: Assess prostate size, consistency and detect nodules, indurations, and asymmetry, all of which raise suspicion for malignancy.
2. Urinalysis: assess for the presence of blood, leukocytes, bacteria, protein, or glucose.
3. Urine M/C/S: assess for infection.
4. Urine flow studies: Evaluate max flow rate combined with post-void residual volume determination.
5. Prostate Specific Antigen: Refer to PSA testing in booklet.
8. TRUS Prostate: may be required for the exclusion of prostate cancer in the presence of persistent elevation of PSA levels.

Treatment
Treatment for BPH involves conservative measures, pharmacological treatments or surgical interventions depending on the severity of symptoms and degree of bother.
1. Patients with mild symptoms/minimal bother.
   -> Watchful waiting - 40% of patients improve spontaneously.\(^7\)
   -> Includes lifestyle changes (e.g. evening fluid restriction, reducing consumption of mild diuretics such as caffeine and alcohol, planned voiding).
   -> Herbal Therapies: Saw Palmetto\(^8\)

2. Medical treatment
   -> Alpha-1-adrenergic antagonists (e.g. tamsulosin/Flomax, Doxazosin) reduce stromal smooth muscle tone. SEs: orthostatic hypotension and dizziness.
   -> 5-Alpha-reductase inhibitors (e.g. finasteride and dutasteride) decrease the conversion of testosterone to DHT (dihydrotestosterone). It is the second line
medical treatment and has greater efficacy when combined with Alpha-1 blockers.\textsuperscript{9} SEs: Impotence, decreased libido.

3 Surgical Treatments

\begin{itemize}
  \item \textbf{Green Light Laser Prostatectomy}: Minimally invasive option with lower incidence of complications when compared to TURP.
  \item \textbf{TURP} (Transurethral resection of the prostate).
  \item \textbf{Open Prostatectomy}
\end{itemize}
REFERENCES

(1) Andrology Australia URL: <www.andrologyaustralia.org>


(5) Dugani S., Lam D, Toronto Notes 2009, Mcgraw Hill Professional; Canada, 2009


(7) URL: <http://www.nutrition2000.com/Q&A_BPH.cfm>


<http://www.emedicinehealth.com/enlarged_prostate>


F.Gardiner, Prostate Enlargement Fact Sheet, Andrology Australia, March 2006.
<http://www.andrologyaustralia.org/docs/Factsheet_ProstateEnlargement.pdf>


APPENDIX

(1) C. Chabert, Laparoscopic Urology Australia

Assessing Prostate Symptoms

By filling in this form, you will help your doctor to assess if you have an enlarged prostate, and how badly it is affecting you. An enlarged prostate is a common and benign (non-cancerous) condition that often occurs in older men. (The results do not help to diagnose prostate cancer.)

1. The International Prostate Symptom Score (IPSS)

Please answer the following questions about your urinary symptoms. Write your score for each question at the end of each row.

<table>
<thead>
<tr>
<th>Over the past month, how often have you...</th>
<th>Not at all</th>
<th>Less than 1 time in 5</th>
<th>Less than half the time</th>
<th>About half the time</th>
<th>More than half the time</th>
<th>Almost always</th>
<th>Your Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. ...had a sensation of not emptying your bladder completely after you finished urinating?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>2. ...had to urinate again less than two hours after you finished urinating?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>3. ...stopped and started again several times when you urinated?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>4. ...found it difficult to postpone urination?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>5. ...had a weak urinary stream?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>6. ...had to push or strain to begin urination?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td></td>
</tr>
</tbody>
</table>

And finally...

<table>
<thead>
<tr>
<th>None</th>
<th>Once</th>
<th>Twice</th>
<th>3 times</th>
<th>4 times</th>
<th>5 times or more</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>

7. Over the past month, how many times did you most typically get up to urinate from the time you went to bed at night until the time you got up in the morning?

Add up your total score and write it in the box.

Supplementary question - Quality of life due to urinary symptoms.

If you were to spend the rest of your life with your urinary condition the way it is now, how would you feel about that? (Please tick which best describes how you would feel.)

0. Delighted
1. Pleased
2. Mostly satisfied
3. Mixed - about equally satisfied and dissatisfied
4. Mostly dissatisfied
5. Unhappy
6. Terrible

Total
CHAPTER 4

Localised Prostate Cancer

Prostate Cancer is the most common cancer in Australian men and is the second most common cause of cancer deaths in men\(^1\). Almost all prostate cancers arise from the secretory glandular cells in the prostate. 95% are Adenocarcinomas\(^2\). Spread may be local (seminal vesicles, bladder, rectum) via lymphatics or haematogenously (sclerotic bone lesions).

Of prostate cancer cases, 70% arise in the peripheral zone, 15-20% arises in the central zone, and 10-15% arises in the transitional zone.\(^3\)

**Risk factors**

1. **Age**: One in 11 Australian men will develop Cancer of the Prostate (CAP) by age 70.\(^4\)
2. **Race**: African-American men are 1.6 times more likely than white men to develop prostate cancer.\(^5\) (Young African American men have testosterone levels that are 15% higher\(^6\))
3. **Diet**: *High fat diet* (Low vegetable intake, omega-6 fatty acids is a positive stimulant)
4. **Family History**: - Men with BRCA2 gene have almost four times the risk of developing prostate cancer\(^7\). BRCA1 mutation causes a lesser increase in risk.\(^8\) - Family history of breast or ovarian cancer. - Men more likely to present 6-7 years earlier.\(^9\) - A man with a first-degree relative who has been diagnosed with prostate cancer (brother or father) has at least twice the risk\(^10\). If two or more first-line relatives are affected, the risk increases 5- to 11-fold.\(^11\) - Early age of onset in a family member also increases the risk.\(^12\)
5. **Industrial exposure**: Exposure to *herbicides and pesticides*. Certain occupations such as farming and work in industrial chemical industry place patient at higher risk.
6. **Demographics**: Men in rural and regional Australia have a 21% higher prostate cancer mortality rate than men in capital cities.\(^13\)
7. **Sexually Transmitted Infections**: 1.4 times greater chance of men developing the disease as compared to the general population.\(^14\)
8. **Hormone levels**: Serum concentrations of androgens and insulin-like growth factor-I (IGF-I) have been studied as possible risk factors for prostate cancer.\(^15\)

**Clinical Presentation**

1. **Localised** \rightarrow **Asymptomatic**. Detected by an increase in PSA and abnormal DRE.
2. **Locally advanced** \rightarrow **Obstructive lower urinary tract symptoms** such as difficulty voiding and increased frequency.
3. **Metastatic** \rightarrow **Bone pain** from metastases (most commonly vertebral bodies, pelvis, and long bones in legs), **weight loss**, loss of appetite, fatigue, malaise, oedema (due to
obstruction of venous and lymphatic tributaries by nodal metastasis) and uremic symptoms can occur from ureteric obstruction.

**Assessment**

1. **DRE** (Digital Rectal Examination): An *irregular firm prostate or nodule* can be palpable. (Possible *indurations, asymmetry, enlargement*). When cancer is palpable, 60-70% has spread beyond the prostate.  
2. **PSA** (Prostate Specific Antigen): There are 4 aspects to PSA – age-specific reference value, median, free-total percentage, and velocity to evaluate risk of person having prostate cancer. (Refer to PSA topic in booklet). PSA may also be elevated due to inflammation or BPH. The Urological Society of Australia and NZ recommend a PSA test at age 40 years.  
3. **TRUS** (Transrectal ultrasonography) + **Biopsy** - main utility of ultrasonography is to guide prostate biopsy, and provide an assessment of gland size. Prostate biopsy is the gold standard for prostate cancer diagnosis – It is peripherally weighted with a minimum of 12 cores. CAP grading is by way of the Gleason grading system (See Appendix 1). Complications of TRUS Biopsy:  
   - 1% chance of infection.  
   - If patients are on anti-platelet or anticoagulant therapy, it is discontinued 7 to 10 days prior to biopsy to minimize the risk of bleeding complications.  
   - Haematospermia (51 percent), haematuria (23 percent longer than three days), fever (3.5 percent) and rectal bleeding (1.3 percent).  

**Staging + Grade**  
**CT Scan intermediate and high risk prostate cancer**  
**Technetium (Tc 99m) bone scan** are reserved for intermediate to high risk patients. **Staging** of CAP is done via the Tumour, nodes, metastasis (**TNM**) classification (Appendix 2). **Grading** of CAP is done via The **Gleason Score** (Appendix 1) The Stage, Grade and the PSA value are combined to give a pre-treatment risk stratification score i.e. low, intermediate, high risk according to the **D’Amico Risk Stratification Score** (See Appendix 3).  

**Treatment**  
Treatment for prostate cancer depends on the staging, the grade and the histological subtype. Conservative measures:  
1. **Watchful Waiting**: Aim is to delay therapy until demonstrable signs of progression (development of LUTS or PSA concern). Ideal for elderly patients with less than 10 years life expectancy. Androgen deprivation (ADT) is commenced upon disease progression.  
2. **Active surveillance**: Deferred local therapy until disease progression or patient anxiety lead to definitive local therapy. Aims to avoid potential complications of local therapy without compromising cancer control. Suitable for patients with greater than 10 years life expectancy with low volume low risk disease. Requires compliance with regular PSA and periodic repeat TRUS biopsy.
3. **Radical Prostatectomy**: definitive therapy – done either laparoscopically, open, perineally or with robotics. Excellent treatment option with established outcomes. Ideal for men with at least 10 years life expectancy with low and intermediate risk disease. Nerve-sparing surgery in selected cases facilitates recovery of spontaneous erectile function. Urinary incontinence is now a rare long term complication. Radical Prostatectomy is the only treatment option with a demonstrable survival advantage.  

4. **Radiation therapy**: Can be delivered as external beam (EBRT) with or without a HDR (high dose rate brachytherapy) boost. Is suitable for more elderly patients or those with significant medical co-morbidities with 10 years life expectancy with intermediate or high risk disease. Is combined with neo-adjuvant ADT of 3-6 months prior to treatment.  

5. **LDR Brachytherapy**: This involves the placement of radioactive iodine seeds into the prostate. Suitable for low and intermediate risk cancers with gland sizes less than 50cc with minimal urinary symptoms. Limited data for patients less than 55 years of age.  

**Prognosis + Follow up**  
For men who have undergone radical prostatectomy, radiation therapy, or both, follow-up care is important to detect recurrence of cancer.  
1. PSA levels should be checked every three months for one year, every six months for the second year, and annually after that. Biochemical free survival is defined as a PSA less than 0.2 ng/ml after radical prostatectomy.
REFERENCES

(1, 4, 7) Prostate Cancer Foundation of Australia, URL: <www.prostate.org.au>


APPENDIX

1. The Gleason Score (www.prostate.org.au)

<table>
<thead>
<tr>
<th>Gleason Score</th>
<th>Aggressiveness of prostate cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-4</td>
<td>Low</td>
</tr>
<tr>
<td>5-6</td>
<td>Moderate</td>
</tr>
<tr>
<td>7</td>
<td>Intermediate</td>
</tr>
<tr>
<td>8-10</td>
<td>High</td>
</tr>
</tbody>
</table>


<table>
<thead>
<tr>
<th>TABLE 1: TNM staging system of prostate cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Localized disease</strong></td>
</tr>
<tr>
<td>T1a Tumor incidental histologic finding in ≤ 5% of resected tissue; not palpable</td>
</tr>
<tr>
<td>T1b Tumor incidental histologic finding in &gt; 5% of resected tissue</td>
</tr>
<tr>
<td>T1c Tumor identified by needle biopsy (e.g., because of elevated PSA level)</td>
</tr>
<tr>
<td>T2a Tumor involves one-half of one lobe or less</td>
</tr>
<tr>
<td>T2b Tumor involves more than one-half of one lobe but not both lobes</td>
</tr>
<tr>
<td>T2c Tumor involves both lobes</td>
</tr>
<tr>
<td><strong>Local extension</strong></td>
</tr>
<tr>
<td>T3a Extracapsular extension (unilateral or bilateral)</td>
</tr>
<tr>
<td>T3b Tumor invades seminal vesicle(s)</td>
</tr>
<tr>
<td>T4 Bladder invasion, fixed to pelvic side wall, or invasion of adjacent structures</td>
</tr>
<tr>
<td><strong>Metastatic disease</strong></td>
</tr>
<tr>
<td>N1 Positive regional lymph nodes</td>
</tr>
<tr>
<td>M1 Distant metastasis</td>
</tr>
</tbody>
</table>

PSA = prostate-specific antigen

3. **D’Amico Risk Stratification Score** (J. Moul et al. *Prostate Cancer* 09)

<table>
<thead>
<tr>
<th>Risk Level</th>
<th>Criteria</th>
</tr>
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<tbody>
<tr>
<td>Low risk</td>
<td>Diagnostic PSA &lt; 10.0 ng/mL and highest biopsy Gleason score ≤ 6 and clinical stage T1c or T2a</td>
</tr>
<tr>
<td>Intermediate risk</td>
<td>Diagnostic PSA &gt; 10 but &lt; 20 ng/mL or highest biopsy Gleason score = 7 or clinical stage T2b</td>
</tr>
<tr>
<td>High risk</td>
<td>Diagnostic PSA &gt; 20 ng/mL or highest biopsy Gleason score ≤ 8 or clinical stage T2c/T3</td>
</tr>
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*PSA = prostate-specific antigen*
Macroscopic Haematuria

Definition
Macroscopic Haematuria is the evidence of visible blood in the urine, and can present as pink, red, brownish-red, or tea-coloured urine. Haematuria can be of glomerular or non-glomerular origin.

- Brown-coloured urine, RBC casts, and dysmorphic (small deformed, misshapen, sometimes fragmented) RBCs and proteinuria are suggestive of glomerular haematuria.
- Reddish or pink urine, passage of blood clots, and eumorphic (normal sized, biconcavely shaped) erythrocytes are suggestive of a non-glomerular bleeding site.

Causes
- **Cancer**: transitional cell cancer of the bladder (TCC), kidney (adenocarcinoma), Transitional Cell Cancer, Prostate cancer
- **Stones**: kidney, ureteric, bladder
- **Infection**: bacterial, mycobacterial (TB), parasitic (schistosomiasis), infective urethritis
- **Inflammation**: cystitis, interstitial cystitis
- **Trauma**: kidney, bladder, urethra (e.g. traumatic catheterization), pelvic fracture causing urethral rupture
- **Renal cystic disease** (e.g. medullary sponge kidney)
- **Other urological causes**: BPH (rarely causes isolated haematuria)
- **Nephrological causes** of haematuria tend to occur in children or young adults and include, commonly → IgA nephropathy, post-infectious glomerulonephritis.
- **Psuedohaematuria**: menses, endometriosis, dyes (beetroot, rhodamine B in drinks, candy and juices).

History
Evaluation of Macroscopic Haematuria involves a history which is both urologic specific and general. The main set of questions are related to
1. **Pain** i.e. Nature, Location, Radiation, Onset, Duration, Aggravating/Relieving factors, Severity.
   e.g. unilateral flank pain → suggests calculus.
PAINLESS Macroscopic HEMATURIA → TRANSITIONAL CELL CARCINOMA.

2. **Lower Urinary Tract Symptoms**: Both obstructive and irritative symptoms. Ask the patient if he/she has seen **clots in the blood** (suggests an extraglomerular cause of haematuria).

3. **Systemic features**: Fever or Suprapubic pain (in acute onset) → Suggestive of UTI.

General History should include:

4. A **positive family history** of renal disease.
5. Any history of a **bleeding disorder**
6. **Travel or residences** in certain areas (Schistosoma haematobium, or tuberculosis).
7. **Presence of risk factors for TCC**

**Investigations**

Evaluation of Macroscopic Haematuria includes physical examination, urinalysis, blood tests, imaging and a possible biopsy dependent on the cause.

1. **Physical Examination**: Assess for haemodynamic compromise
2. **Urine dipstick** → sensitivity in identifying haematuria is >90%.
3. **Urine M/C/S**
4. **Urine cytology** → most sensitive for carcinoma of the bladder (90%)
5. **Blood Tests** → FBC, EUC, Coagulation studies
6. **CT KUB Triple Phase** → Non-Contrast allows assessment of stones, nephrogram phase allows assessment of Renal Cell Carcinoma, and delayed phase allows assessment of urothelial abnormalities.
7. **Cystoscopy**: allows direct inspection of the lower tract

**Management**

1. Acute → Resuscitation with fluids, blood transfusion if necessary.
2. Definitive → Depending on the underlying cause.
REFERENCES


CHAPTER 6

Nephrolithiasis

Types
1. Calcium Stones (most common – 80-85%)
   - Composed of either Calcium oxalate or phosphate
   - Radio-dense (i.e. visible on abdominal radiograph)
   - Occurs secondary to hypercalcuria (more common) and hyperoxaluria.
   - Causes of Hypercalcuria →
     1. Hypercalcemia.
     2. Excessive dietary intake of calcium.
     3. Excessive resorption of calcium e.g. from prolonged immobilization.
     4. Medical conditions: Primary hyperparathyroidism, Sarcoidosis, Malignancy, Vitamin D excess
   - Causes of Hyperoxaluria →
     1. Excessive dietary intake of food high in oxalate e.g. rhubarb, spinach, and tea.
     2. Dietary restriction of calcium, leading to compensatory increase of absorption of oxalate.
2. Uric Acid Stones (2nd most common – 10%)
   - Radiolucent (cannot be seen on abdominal radiograph)
   - Causes → Associated with Hyperuricemia.
   - Also seen in patients who have had Gastric or intestinal bypass surgery, as patients with ileostomies are at higher risk of dehydration and from the loss of bicarbonate from gastrointestinal secretions leading to the production of acidic urine.
3. Struvite Stones (Staghorn stones – 5-10%)
   - Radio-dense
   - Causes → Often seen in patients with recurrent UTI’s due to urease producing organisms (such as Proteus and Klebsieilla).
   - The presence of urease-producing bacteria leads to the hydrolysis of urea into ammonium and hydroxyl ions, The resulting increase in ammonium and phosphate concentrations combined with the alkalotic urine (pH >7.2) is necessary for struvite and carbonate apatite crystallization.
4. Cystine stones (rare – 1%)
   - Cystinuria (autosomal recessive)

Risk Factors
1. Diet: Low fluid intake (most common and preventable risk factor), Diet with high levels of animal protein or sugars.
2. Family History - the risk of stones is increased 3 fold.
3. Male Gender (3:1)
4. Medical Conditions that predispose to stone formation
E.g. Gout, Primary hyperparathyroidism, Crohn’s disease, Diabetes mellitus, Renal tubular acidosis, Primary renal disease such as Polycystic kidneys and Medullary sponge kidney.

5. **Medications** e.g. Loop diuretics, Antacids, glucocorticoids → all promote calcium formation. Chemotherapeutic drugs, thiazides, salicylates → promote uric acid stone formation.

6. **UTIs**.

**Clinical Presentation**

1. Patients can be **Asymptomatic**.
2. **Colicky pain** – typically begins in the flank and radiates inferiorly and anteriorly towards the groin. It can vary from mild discomfort to severe excruciating pain. (The pain generated by renal colic is primarily caused by the dilation, stretching, and spasm caused by the acute ureteral obstruction).
3. **Haematuria** (90% of cases): Can be microscopic or macroscopic.
4. Other: **Nausea and Vomiting**.

**Diagnosis**

1. **History + physical examination**.
2. **Urinalysis (Urine M/C/S)**
   - Evidence of Haematuria.
   - Evidence of Pyuria or bacteruria if UTI present.
   - Examine urinary sediment for crystals.
   - Determine urinary ph – alkaline urine may suggest struvite stones, acidic urine may suggest uric acid stones.
3. **Serum chemistry (FBC and EUC)** – Base line renal function and also calcium, uric acid, magnesium and phosphate levels.

**Imaging includes:**

4. **Plain abdominal radiograph KUB** – to accompany all CT scans to discern radiolucent from radio-opaque calculi.
5. **Helical CT KUB without contrast** – most sensitive test for detecting stones.

**Treatment**

Treatment of Stones is best divided into acute, definitive and preventative measures.

**Acute** → 1st line management of a patient with stones is:

1. **Pain management** i.e. adequate analgesia i.e. IV morphine or NSAIDS.
2. **Fluid hydration**
3. **Antibiotics** if infection is present.
4. **Decompression of Renal unit** via stent or nephrostomy if: failure of conservative measures or evidence of sepsis.

**Definitive**

Depends on:

- Stone factors i.e. size, location and composition.
- Patient factors
- Hospital resources
The options of surgery are:
   1. *Ureteroscopy/pyeloscopy and laser lithotripsy*
   2. *Extracorporeal shock wave lithotripsy (ESWL)*
   3. *Percutaneous nephrolithotomy.*

**Prevention**

1. **Dietary measures**
   - High fluid intake (keep urine volume at 2-3L/day).
   - Decreased animal protein intake in patients with hyperuricosuria (uric acid stones) via red meat.
   - Decreased Dairy intake (calcium)
   - Decreased green vegetables.
   - Decreased Coke intake (contains oxalate)

2. **Pharmacological measures**
   - Refer to *renal physician* if recurrent stones for 24hr urinalysis +/- pharmacological measures such as thiazide diuretics (reduce urinary calcium), Allopurinol (patients with high uric acid levels in the blood), Penicillamine (cystine stones).

The Risk of Recurrence of stones is 10% per year.
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(1,2,3,4) S. Agabegi, E. Agabegi, Step up to medicine: Second edition, Lippincott Williams & Wilkins, USA, 2008, p. 284-287.


CHAPTER 7

Urothelial Cancer

Bladder cancer is the most common malignancy involving the urinary system. It is the fourth most common cancer in men and the tenth most common cancer in women in Australia.\(^1\)

**Types**
1. *Transitional Cell Carcinoma* (TCC) (80-90%)\(^2\) – can occur anywhere from the kidney to bladder.
2. *Squamous Cell Carcinoma* (5%)\(^3\) – is more prevalent in Middle East.
3. *Adenocarcinoma* (1-2%)\(^4\)

Nearly all Adenocarcinomas and Squamous Cell Carcinomas are invasive.

**Epidemiology**
1. *Race*: Bladder cancer is more common in whites than in blacks; however, blacks have a worse prognosis than whites.
2. *Age*: The median age at diagnosis is 69 years for men and 71 years for women, and the incidence increases with age\(^5\). (80% between 50-80 years old)
3. *Gender*: The male-to-female ratio is 3:1\(^6\). Women generally have a worse prognosis than men
4. *Location* – TCC highest in Western Europe and North America\(^7\).

**Risk Factors**
1. *Smoking* - 2/3 of men and 30% of women\(^8\).
2. Industrial carcinogens - *Aromatic amines* in dyes, paints, solvents, leather dust, inks, combustion products, rubber, and textiles
3. *Cyclophosphamide* - used as long term treatment for other cancer(s) may cause hemorrhagic cystitis and increase the risk of TCC.
4. *Radiation*
5. Analgesics – *Phenacetin*.
6. Chronic irritation (cystitis, chronic catheterization, bladder stones) (associated with SCC)
7. *Family History* – chromosome 17 (high grade), chromosome 9 (low grade)
8. Spinal cord injuries - Patients with spinal cord injuries who have long-term indwelling catheters have a 16- to 20-fold increased risk of developing SCC of the bladder.
10. Coffee, Tea, Artificial sweeteners – Weak correlation
11. Arsenic in water or long-term consumption of chlorinated water (increased risk in men)
Clinical Presentation
1. **Painless Macroscopic Haematuria** → Presentation of 80-90% of people. Haematuria is typically intermittent, gross and present throughout micturition.

2. **Voiding Symptoms** → 20-30% of people present with irritative voiding symptoms (e.g., daytime and/or nocturnal frequency, urgency, dysuria, or urge incontinence). Obstructive symptoms are less common.

3. **Constitutional symptoms** → Symptoms such as fatigue, weight loss, anorexia, and failure to thrive are usually signs of advanced or metastatic disease and denote a poor prognosis. Patients with advanced disease can present with pelvic or bony pain, lower-extremity oedema from iliac vessel compression, or flank pain from ureteral obstruction. Approximately 5% of patients present with metastatic disease, which commonly involves the lymph nodes, lung, liver, bone, and central nervous system.

Staging + Grade
Staging of Bladder Cancer is via the Tumour, nodes, metastasis (TNM) classification (Appendix 1).

Investigations
Evaluation of Bladder Cancer involves:
1. History and Physical Examination
2. Full Blood Count – may reveal anaemia due to chronic blood loss.
3. **Urinalysis and urine culture** – to rule out infection.
4. **Urine cytology** – to detect malignant cells (has a 95% accuracy rate for diagnosing high-grade carcinoma and CIS).
5. **Triple-Phase CT Scan KUB** – for staging.

Other: Chest X ray — an initial staging tool
Bone Scan - assess the presence of bone metastasis in patients with invasive or locally advanced tumours

Treatment
Treatment of the patient depends upon staging, the grade and the histological subtype of the tumour.

1. **Non–muscle-invasive disease (Ta, T1, CIS)**
   Trans-urethral resection of bladder tumour/TURBT +/- intravesical immunotherapy: Bacillus Calmette-Guérin (BCG) + Mitomycin C.

2. **Muscle-invasive disease (T2 and greater)**
   Radical Cystectomy + Pelvic lymphadenectomy (with urinary diversion via a conduit, Indiana pouch or neo-bladder) + Neo-Adjuvant Chemotherapy (Cisplatin combination).

Prognosis
Prognosis ranges from a 5 year survival rate of 80-90% for lesions not involving bladder muscle to 5% for those presenting with metastases. The high rate of disease recurrence and progression in non–muscle invasive bladder cancer underscores the need for careful follow-up studies.
REFERENCES

(1) AIHW and AACR, AIHW National Mortality Database, Australia’s Health 2004, AIHW.


(5,7,8) S.Daneshmand, T.Becker, D.Raghavan, M.Ross, Epidemiology and etiology of urothelial bladder cancer, UpToDate, June 2008.


R.Hedgepeth, S.Campbell, J.Jones, D.Raghavan, M.Ross, Screening for bladder cancer, UpToDate, June 2008.

APPENDIX

(1) M. Hurwitz et al., *Urothelial and Kidney Cancers* 09.

<table>
<thead>
<tr>
<th>TABLE I: TNM staging of urothelial tract cancers</th>
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<tbody>
<tr>
<td><strong>Primary tumor (T)</strong></td>
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<tr>
<td>Tx</td>
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<tr>
<td>T0</td>
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<tr>
<td>Ta</td>
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<td>pT2a</td>
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<td>T3</td>
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<td>pT3a</td>
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<td>pT3b</td>
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<tr>
<td>T4</td>
</tr>
<tr>
<td>T4a</td>
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<tr>
<td>T4b</td>
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<table>
<thead>
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<th>Regional lymph nodes (N)</th>
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<tbody>
<tr>
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</tr>
<tr>
<td>N1</td>
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<td>N2</td>
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<table>
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<th>Distant metastasis (M)</th>
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<tbody>
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<table>
<thead>
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<td>Stage III</td>
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<td>Stage IV</td>
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Renal Cell Carcinoma

Renal cell carcinomas (RCC) make up 80-85% of all primary renal neoplasms in adults and are commonly seen in adults over 40, with the mean age of presentation being 55 years old (the peak incidence occurs between 60 and 70 years of age). Australians have a 1 in 74 risk of developing RCC during their lifetime.

Types
1. Clear cell carcinoma (80-90%)
2. Papillary (10-15%)
3. Chromophobe (4-5%)
4. Collecting Duct (1-2%)
5. Unclassified

Risk Factors
1. Cigarette Smoking: doubles the risk of renal cell carcinoma and contributes to as many as one third of all cases.
2. Gender: Males 1.6:1
3. Obesity
4. Hypertension
5. Exposure to heavy metals: Increased in workers exposed to asbestos, cadmium, petroleum products, dry-cleaning solvents, as well as those who work in the iron and steel industries.
7. Acquired Cystic disease: Acquired cystic disease develops in a large percentage of chronic dialysis patients (approximately 35 to 50 percent), approximately 6 percent of whom eventually develop RCC.
8. Chronic dialysis
10. Race: More common in Northern European ancestry (Scandinavians) and North Americans.
11. Genetic: include von-Hippel Lindau (VHL) syndrome and Birt-Hogg-Dube syndrome etc.
12. Childhood Chemotherapy.
13. Previous radiation therapy: Renal cell carcinoma caused by radiation occurs in less than 1% of cases of RCC.

Clinical Presentation
1. Asymptomatic - Many renal masses remain asymptomatic and non-palpable until late in the natural course of the disease. More than 50% of RCCs are detected
incidentally using non-invasive imaging to evaluate a variety of non-specific symptom complexes.\(^7\)

2. The Classic Triad (Robson’s) \(\rightarrow\) **flank pain** (40%), **haematuria** gross or microscopic (40%), and a **palpable abdominal renal mass**. (25%)\(^8\)

   Occurs in only 6-10% of patients\(^9\) and when present, it strongly suggests locally advanced disease.

3. **Paraneoplastic syndrome** (30% of people)\(^10\) \(\rightarrow\) Weight loss, Fever, Night sweats, Malaise, Anorexia, Hypertension, Hypercalcemia, Varicocele (2% - majority left sided)\(^11\), Amyloidosis (3-5%)\(^12\), Abnormal liver function, Polycythemia (5%)\(^13\), erythrocytosis.

4. **Metastatic disease** (25-30% of people)\(^14\) \(\rightarrow\) Anaemia (29-88%)\(^15\), bone pain, persistent cough. Organs involved include: Lung (75%), Soft tissues (36%), Bone (20%), Liver (18%), Cutaneous sites (8%), Central nervous system (8%).\(^16\)

### Investigations

Assessment of RCC involves:

1. **Medical History** looking at presenting symptoms and **Physical Examination** looking for palpable abdominal mass, palpable cervical lymphadenopathy, non-reducing varicocele, and bilateral lower extremity oedema which suggests venous involvement.

2. **Laboratory Investigations** include:
   - Full Blood Count \(\rightarrow\) Haemoglobin, Calcium, ESR.
   - EUC
   - Liver function tests (ALP for metastasis)

3. **Urinalysis + Urine M/C/S**

4. Radiological investigations
   - **Triple-Phase CT with contrast** (Best evaluation test) \(\rightarrow\) assesses primary tumour extension with extra renal spread and provides information on venous involvement, enlargement of locoregional lymph nodes, and condition of adrenal glands and the liver. Chest CT \(\rightarrow\) accurate for chest staging if involvement.\(^17\)
   - **MRI** \(\rightarrow\) to delineate extent of caval thrombus, and is reserved primarily for patients with locally advanced malignancy or allergy to intravenous contrast.\(^18\)

Further evaluation in the presence of metastasis involves a bone scan and brain CT.

### Treatment

Treatment of RCC depends on the tumour stage (see ‘Classification’ below) and involves either conservative, surgical or immunotherapy measures.

Around 40% of tumours smaller than 1cm are found to be benign\(^19\). For this reason, conservative management with regular monitoring ("watchful waiting") is the most appropriate treatment option for these patients.

For patients with a resectable stage I, II, or III tumour, surgery is the best possible option.

1. **Nephron-sparing surgery** \(\rightarrow\) For patients with a solitary tumour of <4 cm maximum diameter. Partial nephrectomy which can be performed either laparoscopically or open.

2. **Laparoscopic radical nephrectomy** \(\rightarrow\) for >T1b tumours and possible T3a tumours. 5% have inferior vena cava involvement, Lymph nodes involved in 10-25% patients.\(^20\)

3. **Tumour nephrectomy + immunotherapy + radiotherapy** \(\rightarrow\) for metastatic RCCs.
1st line immunotherapy for metastatic RCCs is Sunitinib/Bevacizumab + IFN-alpha for low-intermediate risk patients and Temsirolimus for high risk patients.

**Classification**

Classification of RCC involves the Tumour Node Metastases (TNM) Stage Classification System (Appendix 1) or the Robson System (Appendix 2).

**Prognosis**

Prognosis of RCC depends on anatomical, histological, clinical and molecular factors. The 5 year survival rate is 60-70% with tumours confined to the renal parenchyma, 15-35% with lymph node involvement, and only approximately 5% in those who have distant metastases.

The follow up of a patient with RCC depends on their risk stratification group i.e. risk of tumour recurrence or systemic tumour progression.
REFERENCES


(12,15) M. Atkins, J. Richie, M. Ross, *Clinical manifestations, evaluation, and staging of renal cell carcinoma*, UpToDate, Jan 2007.


APPENDIX

1. TNM Classification (M.Hurwitz et al., *Urothelial and Kidney Cancers* 09)

![TABLE 3: TNM staging of renal cell carcinoma](image)

2. Robson Staging (J.Richie et al., *Renal Cell Carcinoma*, 03)

![Stage](image)
CHAPTER 9

Testicular Cancer

Testicular cancer is the second most common form of cancer in men aged 18-39, and is diagnosed in around 680 Australians each year. It has a very good cure rate (95%) if found and treated early. There has been a steady increase (2% each year) in the number of men diagnosed with testicular cancer in Australia since 1982.

Risk factors
1. History of cryptorchidism/undescended testis: risk of developing germ cell tumour is increased 4-8 fold. About 1 in 10 men with testicular cancer have had undescended testes in childhood.
2. Infertility.
3. Familial history of testicular tumours among first-grade relatives (brothers, father): 1-3% of affected men have a family member with the disease. Genetic markers specifically i(12p) have been found in germ cell tumours.
4. Contralateral testicular tumour.
5. Down Syndrome or Klinefelter’s syndrome.
6. HIV infection (particularly seminomas).
7. Hypotrophic (< 12 ml) or atrophic testicle.

Types
Approximately 95% of testicular tumours are Germ Cell Tumors. These are divided into two types: pure seminoma (peak incidence in 4th decade of life) and non-seminomatous germ cell tumours (NSGCT) (peak incidence is in the 3rd decade of life). Mixed germ cell tumours (i.e. those containing two or more germ cell types) constitute approximately one third of testicular cancer, while yolk cell tumours are the most common testicular tumour in infants and young children. Determining the cell type is important for estimating the risk of metastasis and the response to chemotherapy. (See Appendix 1 for the World Health Organisation (WHO) classification of Testicular Cancer).

Clinical Presentation

Localised testicular cancer: Painless, unilateral intrascrotal mass (painful or tender in 10%, bilateral in 1-2%) is the most common finding. Other symptoms include:
- A dull ache or ‘heaviness’ in the lower abdomen, perianal area or scrotum. (33%)
- Gynaecomastia (7%) (more common in non-seminomatous tumours)
- Back and flank pain (11%)

Metastasis (10% of patients)
- A neck mass (supraclavicular adenopathy)
- Chest pain, cough or dyspnoea (pulmonary metastasis)
- Anorexia, nausea, vomiting, or gastrointestinal haemorrhage (retroduodenal metastasis)
- Lumbar back pain (bulky retroperitoneal disease involving the psoas muscle or nerve roots)
- Bone pain or CNS involvement are rare.

**Physical examination:**
Any solid, firm mass within the testis should be considered testicular cancer until proven otherwise. This involves a bimanual examination of the scrotal contents, starting with the normal contralateral testis. Any firm, hard, or fixed area within the substance of the tunica albuginea should be considered suspicious. There can also be a spread to the epididymis or spermatic cord (10-15%).

The examination should also include signs such as supraclavicular nodes, bone tenderness, and gynaecomastia that would suggest metastasis, and an evaluation of the abdomen for lymphadenopathy and hepatomegaly.

**Evaluation**
The diagnostic evaluation of men with suspected testicular cancer includes scrotal ultrasound followed by radiographic testing, blood chemistry workup (with serum tumour markers) and radical inguinal orchidectomy.

1. **Scrotal ultrasound** (100% sensitivity): When evaluating a palpable mass by ultrasound, the primary goal is localization of the mass (intraspecific versus extratesticular) and further characterization of the lesion (cystic or solid). With rare exception, solid intratesticular masses should be considered malignant.

   Ultrasounds are unreliable for staging purposes.

2. **Radiographic testing:** CT scan of the abdomen and pelvis and a Chest X/R are ordered as part of the initial staging workup. Regional metastases of testicular cancer first appear in the retroperitoneal lymph nodes, and can be visualised by CT (44% false negative rate).

3. **Serum tumour markers:** In addition to a complete blood chemistry workup (e.g. full blood count), three serum tumour markers should be ordered i.e. **AFP** (alpha fetoprotein, produced by yolk sac cells), **Beta-hCG** (expression of trophoblasts) and **LDH** (lactate dehydrogenase, a marker for tissue destruction).

   - Globally, there is an increase in these markers in 51% of cases of testicular cancer.
   - Serum levels of AFP and/or beta-hCG are elevated in approximately 80% to 85% of patients with NSGCTs, even when nonmetastatic.
   - Up to 30% of seminomas can present or develop an elevated hCG level during the course of the disease.
   - LDH is a less sensitive marker, and may be elevated in 80% of patients with advanced testicular cancer.
   - It is important to remember that elevation of serum beta-hCG and AFP levels, alone or in combination, are not sufficiently sensitive or specific to establish the diagnosis of testicular cancer in the absence of histological confirmation. They are used for determining diagnosis, staging, and prognosis and for following response to therapy.
4. **Inguinal exploration and orchidectomy**

Radical inguinal orchidectomy is the definitive procedure to permit histological evaluation of the primary tumour and provide local tumour control\(^\text{30}\). Thus, every patient with suspected testicular mass or abnormal ultrasound findings must undergo inguinal exploration, with orchidectomy performed if a tumour is found. For patients with a mass post-chemotherapy, retroperitoneal lymph node dissection (RPLND) is performed. This procedure is the gold standard for identifying nodal micro-metastases and provides accurate pathologic staging of the retroperitoneal disease\(^\text{31}\). Both the number and size of involved retroperitoneal lymph nodes have prognostic importance.

**Staging**

Staging for testicular cancer is done via the tumour, nodes, metastasis (TNM) classification as defined by the American Joint Committee on Cancer (AJCC) (See Appendix 2) and aids in risk classification.

**Treatment**

95% of testicular cancers are curable\(^\text{32}\). Initial therapy is selected according to IGCCC (International Germ Cell Cancer Collaborative Group) risk stratification (good, intermediate, or poor risk) (See Appendix 3) and histological subtype (seminoma versus non-seminoma).

Stage 1 seminoma patients are treated either by adjuvant radiotherapy to the para-aortic nodes or alternatively one dose of carboplatin therapy. NSGCT is treated with adjuvant chemotherapy (PEB - Cisplatin, Etoposide, and Bleomycin) or nerve-sparing RPLND\(^\text{33}\). Surveillance as an option for treatment is reserved for the low risk/low compliance patient.

The primary treatment of choice for advanced disease is three or four cycles of PEB combination chemotherapy (cycles dependent on prognosis).

**Prognosis**

The median time for recurrence is 7 months, and 90% of patients who experience recurrence do so within 2 years\(^\text{34}\). Hence, an intensive schedule of follow-up and imaging is required for the first 2 years, with timing of surveillance and associated tests varied depending on the type and outcome of testicular cancer found.
REFERENCES


(2,4,5) Andrology Australia <http://www.andrologyaustralia.org/pageContent.asp?pageCode=TESTICULARCANCER#>


(6,8,9) M. Michaelson, W. Oh, P. Kantoff, M. Ross, Epidemiology of and risk factors for testicular germ cell tumour, UpToDate, May 2008.


(14,18,20,24) G. Steele, J. Richie, W. Oh, M. Michaelson, P. Kantoff, M. Ross, Clinical manifestations, diagnosis, and staging of testicular germ cell tumours, UpToDate, Sept 2008.


Urology Sydney, Testicular Cancer <http://www.urologysydney.org/testis_cancer.htm>

APPENDIX

(1,2) Eble J.N., Sauter G., Epstein J.I., Sesterhenn I.A. (Eds.): World Health Organization Classification of Tumours. Pathology and Genetics of Tumours of the Urinary System and Male Genital Organs. IARC Press: Lyon 2004


1. WHO histological classification of testis tumours

<table>
<thead>
<tr>
<th>Gem cell tumours</th>
<th>Sex cord/gonadal stromal tumour; incompletely differentiated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intratubular germ cell neoplasia, unclassified</td>
<td>9064/2</td>
</tr>
<tr>
<td>Other types</td>
<td></td>
</tr>
<tr>
<td>Tumours of one histological type (pure forms)</td>
<td></td>
</tr>
<tr>
<td>Seminoma</td>
<td>9061/3</td>
</tr>
<tr>
<td>Seminoma with syncytiotrophoblastic cells</td>
<td></td>
</tr>
<tr>
<td>Spermatocytic seminoma</td>
<td>9063/3</td>
</tr>
<tr>
<td>Spermatocytic seminoma with sarcoma</td>
<td></td>
</tr>
<tr>
<td>Embryonal carcinoma</td>
<td>9070/3</td>
</tr>
<tr>
<td>Yolk sac tumour</td>
<td>9071/3</td>
</tr>
<tr>
<td>Trophoblastic tumours</td>
<td></td>
</tr>
<tr>
<td>Choriocarcinoma</td>
<td>9100/3</td>
</tr>
<tr>
<td>Trophoblastic neoplasms other than choriocarcinoma</td>
<td></td>
</tr>
<tr>
<td>Monophasic choriocarcinoma</td>
<td></td>
</tr>
<tr>
<td>Placental site trophoblastic tumour</td>
<td>9104/1</td>
</tr>
<tr>
<td>Teratoma</td>
<td>9080/3</td>
</tr>
<tr>
<td>Dermoid cyst</td>
<td>9084/0</td>
</tr>
<tr>
<td>Monodermal teratoma</td>
<td></td>
</tr>
<tr>
<td>Teratoma with somatic type malignancies</td>
<td>9084/3</td>
</tr>
<tr>
<td>Tumours of more than one histological type (mixed forms)</td>
<td></td>
</tr>
<tr>
<td>Mixed embryonal carcinoma and teratoma</td>
<td>9081/3</td>
</tr>
<tr>
<td>Mixed teratoma and seminoma</td>
<td>9085/3</td>
</tr>
<tr>
<td>Choriocarcinoma and teratoma/embryonal carcinoma</td>
<td>9107/3</td>
</tr>
<tr>
<td>Others</td>
<td></td>
</tr>
<tr>
<td>Sex cord/gonadal stromal tumours</td>
<td></td>
</tr>
<tr>
<td>Pure forms</td>
<td></td>
</tr>
<tr>
<td>Leydig cell tumour</td>
<td>8650/1</td>
</tr>
<tr>
<td>Malignant Leydig cell tumour</td>
<td>8650/2</td>
</tr>
<tr>
<td>Sertoli cell tumour</td>
<td>8649/0</td>
</tr>
<tr>
<td>Sertoli cell tumour epithelial rich variant</td>
<td>8641/0</td>
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<tr>
<td>Sclerosing Sertoli cell tumour</td>
<td></td>
</tr>
<tr>
<td>Large cell calcifying Sertoli cell tumour</td>
<td>8642/1</td>
</tr>
<tr>
<td>Malignant Sertoli cell tumour</td>
<td>8643/0</td>
</tr>
<tr>
<td>Granulosa cell tumour</td>
<td>8632/0</td>
</tr>
<tr>
<td>Adult type granulosa cell tumour</td>
<td>8632/1</td>
</tr>
<tr>
<td>Juvenile type granulosa cell tumour</td>
<td>8632/2</td>
</tr>
<tr>
<td>Tumours of the thecoma/hibroma group</td>
<td></td>
</tr>
<tr>
<td>Thecoma</td>
<td>8630/0</td>
</tr>
<tr>
<td>Fibroma</td>
<td>8810/0</td>
</tr>
</tbody>
</table>

1. Morphology codes of the International Classification of Diseases for Oncology (ICD-O-3) and the Systematized Nomenclature of Medicine (http://icdmed.org). Behaviour is coded (0) for benign tumours, (2) for in situ carcinomas and grade I intratubular neoplasia, (3) for malignant tumours, and (1) for borderline or uncertain behaviour.
2. **TNM classification of germ cell tumours of the testis**

<table>
<thead>
<tr>
<th>Stage</th>
<th>pT1a</th>
<th>pT1b</th>
<th>pT2</th>
<th>pT3</th>
<th>pT4</th>
</tr>
</thead>
<tbody>
<tr>
<td>IA</td>
<td>N0</td>
<td>N0</td>
<td>N0</td>
<td>N0</td>
<td>N0</td>
</tr>
<tr>
<td>IB</td>
<td>N0</td>
<td>N0</td>
<td>N0</td>
<td>N0</td>
<td>N0</td>
</tr>
<tr>
<td>IIA</td>
<td>N0</td>
<td>N0</td>
<td>N0</td>
<td>N0</td>
<td>N0</td>
</tr>
<tr>
<td>IIB</td>
<td>N0</td>
<td>N0</td>
<td>N0</td>
<td>N0</td>
<td>N0</td>
</tr>
<tr>
<td>III</td>
<td>N0</td>
<td>N0</td>
<td>N0</td>
<td>N0</td>
<td>N0</td>
</tr>
<tr>
<td>IVA</td>
<td>N0</td>
<td>N0</td>
<td>N0</td>
<td>N0</td>
<td>N0</td>
</tr>
<tr>
<td>IV</td>
<td>N0</td>
<td>N0</td>
<td>N0</td>
<td>N0</td>
<td>N0</td>
</tr>
</tbody>
</table>

- **pN** = Regional lymph nodes
- **pNX** = Regional lymph nodes cannot be assessed
- **pNO** = No regional lymph node metastasis
- **pN1** = Metastasis with a lymph node mass 2 cm or less in greatest dimension or multiple lymph nodes, none more than 3 cm in greatest dimension
- **pN2** = Metastasis with a lymph node mass less than 2 cm but not more than 5 cm in greatest dimension, or multiple lymph nodes, any one mass more than 2 cm but not more than 5 cm in greatest dimension
- **pN3** = Metastasis with a lymph node mass more than 5 cm in greatest dimension

- **pM** = Distant metastasis cannot be assessed
- **pMX** = Distant metastasis
- **pMO** = No distant metastasis
- **pM1** = Distant metastasis
- **pM1a** = Non-regional lymph nodes or lung
- **pM1b** = Regional lymph nodes

**TNM classification**

- **pT1** = Primary tumour
- **pT2** = Tumour limited to testis and epididymis without extravasal growth
- **pT3** = Tumour extends into tunica albuginea or is fixed to other structures
- **pT4** = Tumour extends beyond testis or epididymis

**Risk Stratification**

<table>
<thead>
<tr>
<th>LDH</th>
<th>ICG (mU/m)</th>
<th>AFP (ng/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>S1</td>
<td>&lt;1.5 x N</td>
<td>&lt;5,000</td>
</tr>
<tr>
<td>S2</td>
<td>1.5 x N -10 x N</td>
<td>5,000-50,000</td>
</tr>
<tr>
<td>S3</td>
<td>&gt;10 x N</td>
<td>&gt;50,000</td>
</tr>
</tbody>
</table>

**IGCCCG Risk Stratification**

<table>
<thead>
<tr>
<th>Classification</th>
<th>Nonseminoma</th>
<th>Seminoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Good risk</td>
<td>Gonadal or retroperitoneal primary tumor</td>
<td>Any primary site</td>
</tr>
<tr>
<td></td>
<td>No nonpulmonary visceral metastases</td>
<td>No nonpulmonary visceral metastases</td>
</tr>
<tr>
<td></td>
<td>Good tumor markers (AFP &lt;1,000µg/L and hCG &lt;5,000 IU/L)</td>
<td>Normal AFP, any hCG, and any LDH</td>
</tr>
<tr>
<td></td>
<td>and LDH &lt;1.5 x N**</td>
<td></td>
</tr>
<tr>
<td>Intermediate risk</td>
<td>Gonadal or retroperitoneal primary tumor</td>
<td>Any primary site</td>
</tr>
<tr>
<td></td>
<td>No nonpulmonary visceral metastases</td>
<td>Nonpulmonary visceral metastases</td>
</tr>
<tr>
<td></td>
<td>Intermediate tumor markers (AFP 1,000-10,000µg/L)</td>
<td>Normal AFP, any hCG, and any LDH</td>
</tr>
<tr>
<td></td>
<td>or hCG 5,000-50,000IU/L or LDH 1.5-10 x N**</td>
<td></td>
</tr>
<tr>
<td>Poor risk</td>
<td>Mediastinal primary tumor or</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>Nonpulmonary visceral metastases or</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Poor tumor markers (AFP &gt;10,000µg/L or hCG &gt;50,000 IU/L)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>or LDH &gt;10 x N**</td>
<td></td>
</tr>
</tbody>
</table>

**NA** indicates the upper limit of normal for the LDH assay. Abbreviations: AFP = alpha-fetoprotein; GCT = germ cell tumour; IGCCCG, International Germ Cell Cancer Collaborative Group; LDH = lactate dehydrogenase; NA, not applicable.