Testicular Cancer

HEALTHY MALE
ANDROLOGY AUSTRALIA

The GP's role

GPs are typically the first point of contact for men who have noticed a testicular lump, swelling or pain. The GP's primary role is assessment, referral and follow-up.

- All suspected cases must be thoroughly investigated and referred to a urologist.
- Treatment frequently requires multidisciplinary therapy that may include the GP.
- Most patients will survive, hence the importance of long-term regular follow-up.

Note on screening: There is little evidence to support routine screening. However, GPs may screen men at higher risk, including those with a history of previous testicular cancer, undescended testes, infertility or a family history of testicular cancer.

Overview

- Testicular cancer is the second most common cancer in Australian men aged 20-39 years[1]. It accounts for about 20% of cancers in men aged 20-39 years and between 1% and 2% of cancers in men of all ages.
- The majority of tumours are derived from germ cells (seminoma and non-seminoma germ cell testicular cancer).
- More than 70% of patients are diagnosed with stage I disease (pT1)[2].
- Testicular tumours show excellent cure rates of > 95%, mainly due to their extreme chemo- and radio-sensitivity.
- A multidisciplinary approach offers acceptable survival rates for metastatic disease.

Benign cysts

Epididymal cysts, spermatocele, hydatid of Morgagni and hydrocele are all non-cancerous lumps that can be found in the scrotum. Diagnosis can be confirmed via an ultrasound.

Epididymal cysts	Common fluid-filled cysts which feel slightly separate from the testis and are often detected when pea-sized. Should be left alone when small, but can be surgically removed if they become symptomatic.
Spermatocele	Fluid-filled cysts containing sperm and sperm-like cells. These cysts are similar to epididymal cysts except they are typically connected to the testis.
Hydatid of Morgagni	Small common cysts located at the top of the testis. They are moveable and can cause pain if they twist. These cysts should be left alone unless causing pain.
Hydrocele	A hydrocele is a swelling in the scrotum caused by a buildup of fluid around the testes. Hydroceles are usually painless but gradually increase in size and can become very large. Hydroceles in younger men may be a warning of an underlying testis cancer, albeit rarely. In older men, hydroceles are almost always a benign condition, but a scrotal ultrasound will exclude testicular pathology.

Diagnosis and management

Medical history

- Scrotal lump.
- Genital trauma.
- Pain.
- History of subfertility or undescended testis.
- Sexual activity/history of urine or sexually transmitted infection.

Physical examination

- Perform a clinical examination of the testes and general examination to rule out enlarged nodes or abdominal masses.

Clinical notes

On clinical examination it can be difficult to distinguish between testicular and epididymal cysts. Lumps in the epididymis are rarely cancer. Lumps in the testis are nearly always cancer.

Refer to Clinical Summary Guide 1: Step-by-Step Male Genital Examination

Ultrasound

- Organise ultrasound of the scrotum to confirm testicular mass (urgent, organise within 1-2 days).
- Always perform in young men with retroperitoneal mass.

Investigation and referral

- Advice on next steps for investigation and treatment.
- Urgent referral to urologist (seen within 2 weeks).
- CT scan of chest, abdomen and pelvis.
- Serum tumour markers (AFP, hCG, LDH) before orchidectomy: may be ordered by GP prior to urologist consultation.
- Semen analysis and hormone profile (testosterone, FSH, LH).
- Discuss sperm banking with all men prior to treatment.
- Fine needle aspiration: scrotal biopsy or aspiration of testis tumour is not appropriate or advised.

Clinical notes

The urologist will form a diagnosis based on inguinal exploration, orchidectomy and en bloc removal of testis, tunica albuginea, and spermatic cord. Organ-sparing surgery can be attempted in specific cases (solitary testis or bilateral tumours) in specialist referral centres.

Follow-up

Patient follow-up (in consultation with treating specialist) for:

- Recurrence
- Monitoring the contralateral testis by physical examination
- Management of complications, including fertility.

American Joint Committee on cancer staging of testicular cancer[3, 4]

pT – Primary Tumour*

pTX	Primary tumour cannot be assessed.
pT0	No evidence of tumour.
pTis	Germ cell neoplasia in situ.
pT1	Tumour limited to testis (including rete testis invasion) without vascular/lymphatic invasion (LVI).
T1a	Pure seminoma < 3 cm in size.
T1b	Pure seminoma [> =] 3 cm in size.
pT2	Tumor limited to testis (including rete testis invasion) with LVI, or tumor invading hilar soft tissue or epididymis or penetrating visceral mesothelial layer covering the external surface of tunica albuginea with or without LVI.
pT3	Tumour invades spermatic cord with or without LVI.
pT4	Tumour invades scrotum with or without LVI.

Regional lymph nodes*

NX	Regional lymph nodes were not assessed.
N0	No positive regional nodes.
N1	Metastasis with a lymph node mass [> =] 2 cm in greatest dimension, or multiple lymph nodes, none more than 2 cm in greatest dimension.
N2	Metastasis with a lymph node mass more 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.
N3	Metastasis with a lymph node mass > 5 cm in greatest dimension.

*Clinical (based on clinical examination and histological assessment) or Pathological (based on histological examination post-orchidectomy) lymph node classifications may be made, denoted by the prefix 'c' or 'p', respectively (e.g. pN1, cN2).

Distant metastasis

MX	Distant metastasis cannot be assessed.
M0	No distant metastasis.
M1	Distant metastasis.
M1a	Nonretroperitoneal nodal or pulmonarymetastases.
M1b	Nonpulmonary visceral metastases.

Serum markers†

Sx	Serum markers not available or not performed.
S0	Serum marker study levels within normal limits.
S1	LDH < 1.5 x Normal* and hCG < 5000 mIU/mL and AFP < 1000 ng/mL.
S2	LDH 1.5-10 x Normal or hCG 5000-50,000 mIU/mL or AFP 1000-10,000 ng/mL.
S3	LDH > 10 x Normal or hCG > 50,000 mIU/mL or AFP > 10,000 ng/mL.

† LDH, lactate dehydrogenase; hCG, human chorionic gonadotrophin; AFP, alpha fetoprotein

* Upper limit of normal for LDH assay

Treatment options for localised testicular cancer

Orchidectomy cures almost 85% of stage I seminoma patients and 70-80% of stage I non-seminomatous germ cell tumour (NSGCT) patients. Adjuvant treatments may reduce the risk of metastases in those not cured by orcidectomy, but this comes at the cost of possible adverse effects. Surveillance is another management option. A risk-adapted approach is now used to determine subsequent management.

pT1 Seminoma

- Surveillance is recommended (if facilities are available and the patient willing and able to comply).
- Carboplatin-based chemotherapy decreases recurrence rates by 75% or 90%, for one or two courses, respectively[5].
- Adjuvant treatment not recommended for patients at very low risk (< 4 cm size, absence of rete testis invasion).
- Radiotherapy is not recommended as adjuvant treatment, although it is a treatment option.

pT1 Non-Seminomatous Germ Cell Tumour (NSGCT)

Low risk

(No Lymphovascular invasion, Embryonal component < 50%, Proliferative index < 70%).

- If the patient is able and willing to comply with a surveillance policy, long-term (at least 5 years) close follow-up should be recommended.
- In patients not willing (or unsuitable) to undergo surveillance, adjuvant chemotherapy or nerve-sparing retroperitoneal lymph node dissection (RPLND) are options[5].

High risk

(Lymphovascular invasion, pT2-pT4)

- Adjuvant chemotherapy with one or two courses of bleomycin, etoposide and cisplatin (BEP) is recommended.
- If the patient is not willing to undergo chemotherapy or if chemotherapy is not feasible, nerve-sparing RPLND or surveillance with treatment at relapse (in about 50% of patients) are options[6].

Treatment of metastatic disease (pT2-pT4)

The treatment of metastatic germ cell tumours[6] depends on:

- The histology of the primary tumour and
- Prognostic groups as defined by the International Germ Cell Cancer Collaborative Group (IGCCCG)[7].

Seminoma

- Radiotherapy (30Gy), or chemotherapy (BEP) can be used with the same schedule as for the corresponding prognostic groups for NSGCT.
- Any pT, N3 seminoma is treated as "good prognosis" metastatic tumour with three cycles of BEP or four cycles of EP.
- PET scan plays a role in evaluation of post-chemotherapy masses larger than 3 cm.

NSGCT

- Low volume NSGCT with elevated markers (good or intermediate prognosis), three of four cycles of BEP; if no marker elevation, repeat staging at 6 weeks surveillance to make final decision on treatment.
- Metastatic NSGCT with a good prognosis, primary treatment three courses of BEP.
- Metastatic NSGCT with intermediate or poor prognosis, four courses of BEP and inclusion in clinical trial recommended.
- Surgical resection of residual masses after chemotherapy in NSGCT is indicated in case of visible residual mass and when tumour marker levels are normal or normalising.

IGCCCG Prognostic- based staging system for metastatic germ cell cancer[7]

Prognosis	Seminoma	Non-Seminoma
Good (If ALL criteria are met)	Any primary site. • No non-pulmonary metastases. • Normal AFP/normal LDH, low hCG.	If all criteria are met: • Testis/retroperitoneal primary • No non-pulmonary metastases (e.g. liver and/or brain) • Lower levels of tumour markers.
Intermediate (If ALL criteria are met)	If all criteria are met: • Any primary site • No non-pulmonary metastases • Normal AFP/normal LDH, medium hCG.	If all criteria are met: • Testis/retroperitoneal primary • No non-pulmonary metastases (e.g. liver and/or brain) • Medium levels of tumour markers.
Poor (If ANY criteria are met)	No seminoma carries poor prognosis.	If any criteria are met: • Non-pulmonary metastases (e.g. liver and/or brain) • Higher level of tumour markers • Mediastinal primary for NSGCT.

Additional Investigations

Serum tumour markers

Post-orchidectomy half-life kinetics of serum tumour markers.

- The persistence of elevated serum tumour markers 6 weeks after orchidectomy may indicate the presence of metastases, while its normalisation does not necessarily mean an absence of tumour.
- Tumour markers should be assessed until they are normal, as long as they follow their half-life kinetics and no metastases are revealed on scans.

Other examinations

Assessment of abdominal and mediastinal nodes and viscera (CT scan) and supraclavicular nodes (physical examination).

- Other examinations such as brain or spinal CT, bone scan or liver ultrasound should be performed if metastases are suspected.
- Patients diagnosed with testicular seminoma who have a positive abdominal CT scan are recommended to have a chest CT scan.
- A chest CT scan should be routinely performed in patients diagnosed with NSGCT because in 10% of cases small. subpleural nodes are present that are not visible radiologically.

Classification and risk factors

There are three categories of testicular epithelial cancer. Germ cell tumours account for 90-95% of cases of testicular cancer[8].

1. Germ cell tumours

a. Seminoma

b. Non-seminoma (NSGCT)
- Embryonal carcinoma.
- Yolk sac tumour.
- Choriocarcinoma.
- Teratoma.

2. Sex cord stromal tumours

3. Non-specific stromal tumours

Prognostic risk factors

Pathological (pT1-pT4)

- Histopathological type.
- For seminoma.
  - Tumour size (> 4 cm).
  - Invasion of the rete testis.
- For non-seminoma
  - Vascular/lymphatic invasion or peri-tumoural invasion.
  - Percentage embryonal carcinoma > 50%.
  - Proliferation rate (MIB-1) > 70%.

Clinical (for metastatic disease)

- Primary location.
- Elevation of tumour marker levels (AFP, hCG, LDH).
- Presence of non-pulmonary visceral metastasis.
- Only clinical predictive factor for metastatic disease in seminoma.

Staging of testicular tumours

The Tumour, Node, Metastasis (TNM) system[3] is recommended for classification and staging purposes. The IGCCCG staging system is recommended for metastatic disease.

Treatment

- The first stage of treatment is usually an orchidectomy: removal of the diseased testis via an incision in the groin, performed under general anaesthetic. Men can be offered a testicular prosthesis implant during or following orchidectomy.
- Further treatment depends on the pathological diagnosis (seminoma vs non-seminoma and the stage of disease) and may include surveillance, chemotherapy or radiotherapy[9].
  - Men with early stage seminoma have treatment options of surveillance, chemotherapy or radiotherapy. The treatment is based on patient and tumour factors.
  - Men with early stage non-seminoma have treatment options of surveillance, chemotherapy or further surgery. The treatment is again based on patient and tumour factors.
  - Men with early stage disease who relapse and men with advanced disease are generally referred for chemotherapy. If chemotherapy leaves residual masses, these may contain cancer and usually will need surgical removal.
- If a man has a bilateral orchidectomy (rare) he will require ongoing testosterone replacement therapy.

Patient support

Diagnosis and treatment can be extremely traumatic for the patient and family. Regular GP consultations can offer patients a familiar and constant person with whom to discuss concerns (e.g. about treatment, cancer recurrence, and the effects of testis removal on sexual relationships and fertility). Referral to a psychologist may be required.

Patient follow-up

- Regular follow-up is vital, and patients with testicular cancer should be watched closely for several years. The aim is to detect relapse as early as possible, to avoid unnecessary treatment and to detect asynchronous tumour in the contralateral testis (incidence 5%).
- Plan follow-ups in conjunction with the urologist/oncologist. Follow-up schedules are tailored to initial staging and treatment, and can involve regular physical examination, tumour markers and scans to detect recurrence. The timing and type of follow-ups need to be determined for each patient in conjunction with the treating urologist/oncologist.

Semen storage

- **Men w**ith testicular cancer often have low or even absent sperm production even before treatment begins[10, 11]. Chemotherapy or radiotherapy can, but does not always, lower fertility further[2]. All men should be offered pre-treatment semen analysis and storage as semen can be stored long-term for future use in fertility treatments. Men who have poor sperm counts may need to visit the sperm-banking unit on 2 or 3 occasions or, in severe cases, an Andrology referral may be required. Surgical removal of one testis does not affect the sperm-producing ability of the remaining testis.
- Provide prompt fertility advice to all men considering chemotherapy or radiotherapy, to avoid delaying treatment. It is highly recommended that men produce semen samples for sperm storage prior to treatment.
- Sperm storage for teenagers can be a difficult issue requiring careful and delicate handling. Coping with the diagnosis of cancer at a young age and the subsequent body image problems following surgery can be extremely difficult. Fatherhood is therefore not likely to be a priority concern. Producing a semen sample by masturbation can also be stressful for young men in these circumstances.
- Refer the patient to a fertility specialist or a local infertility clinic. These clinics usually offer long-term sperm storage facilities.

References

1. https://www.canceraustralia.gov.au/affected-cancer/cancer-types/testicular-cancer/statistics Accessed 9 March 2021
2. Cheng et al., 2018. Testicular cancer. *Nature Reviews Disease Primers*
3. Amin et al. (eds) AJCC Cancer Staging Manual. 8th ed.
4. Cornejo et al., 2020. Updates in Staging and Reporting of Genitourinary Malignancies. *Archives of Pathology & Laboratory Medicine*
5. Oldenburg et al., 2015. Personalizing, not patronizing: the case for patient autonomy by unbiased presentation of management options in stage I testicular cancer. *Annals of Oncology*
6. Laguna et al., 2020. EAU guidelines on testicular cancer. ISBN 978-94-92671-07-3
7. Mead et al., 1997. The International Germ Cell Consensus Classification: a new prognostic factor-based staging classification for metastatic germ cell tumours. *Clinical Oncology (R Coll Radiol)*
8. Gilligan et al., 2019. Testicular Cancer, Version 2.2020, NCCN Clinical Practice Guidelines in Oncology. *Journal of the National Comprehensive Cancer Network*
9. International Germ Cell Cancer Collaborative Group, 1997. International GermCell Consensus Classification: a prognostic factor-based staging systemfor metastatic germ cell cancers. *Journal of Clinical Oncology*
10. Berthelsen., 1984. Andrological aspects of testicular cancer. *International Journal of Andrology*
11. Skakkebaek, N.E., 2017. Sperm counts, testicular cancers, and the environment. *British Medical Journal*
12. Weibring et al., 2019. Sperm count in Swedish clinical stage I testicular cancer patients following adjuvant treatment. *Annals of Oncology*

Date reviewed: October 2020
Clinical review by Dr Gideon Blecher, Alfred Health

© Healthy Male (Andrology Australia) 2007

Australian Government
Department of Health

HEALTHY MALE
ANDROLOGY AUSTRALIA