Pan-Birmingham NHS
Cancer Network

Coversheet for Network Site Specific Group Agreed Documentation*

Document Title	Guideline for the Management of Testicular Cancer
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Document Purpose	• The referral of patients presenting with symptoms suspicious of testicular cancer. • The management of patients with testicular cancer.
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References	See document
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Cancer Network

Guideline for the Management of Testicular Cancer

Version History:

Version	Summary of change	Date Issued
2	Endorsed by the Governance Committee	Sept 2007
2.1	Discussed and updated by NSSG and sent to Mike Cullen to review and update	Feb 2010
2.2	With Mike Cullen's comments	13 April 2010
2.3	Reformatted by LB, for review by Alan Fergusson and Mike Cullen, Andrew Stanley and the Urology NSSG.	14 April 2010
2.4	With MC changes. Sent to the urology NSSG	14 April 2010
2.5	With final amendments from MC awaiting comments from NJ	20.08.10
2.6	With Professor Nick James' comments	31.08.10
2.7	Reviewed at Sub Group meeting	21.09.10
3.0	Updated with changes from Paul Hutton	Sept 2010

Changes made since version 2

- *An update to the trials available for the teratoma.*
- *Clarity over surgery for patients with bilateral testicular cancer, or when the tumour is in the patient's only testis.*
- *Adjustment to radiotherapy section and flowchart on appendix 2.*

1 Scope of the Guideline

This Guidance has been produced to support the following:

- The referral of patients presenting with symptoms suspicious of testicular cancer.
- The management of patients with testicular cancer.

2 Guideline Background

These guidelines are based on the Two Week Wait Guidelines for Referral[1], Improving Outcomes for Urological Cancer – The Manual[2], and the European Association of Urology Clinical Guidelines[3]. They have been written by the Pan Birmingham Cancer Network, Network Site Specific Group which consists of local urology teams based at; University Hospital Birmingham Foundation Trust (UHBFT), Sandwell and West Birmingham Hospital, Heart of England Foundation Trust and Walsall Hospital NHS Trust.

In line with the Improving Outcomes Guidance for Urology[2] the Pan Birmingham Cancer Network and Greater Midlands Cancer Network have

agreed to refer all patients requiring treatment for testicular cancer to UHBFT (The Regional Testicular Tumour Centre). Where appropriate, arrangements for the shared care of patients may be made on an individual patient basis.

Guideline Statements

3 Referral

3.1 Patients with suspected urological cancer should be referred from GPs to local urology units, urgently, according to the 2 week wait criteria[1] (outlined below):

a. Any patient with a swelling or mass in the body of the testis.
b. Any patient with ultrasound scan suspicion of testis cancer.

3.2 Referrals deemed inappropriate by consultant urologists will be notified to the referring GP, and to the relevant PCT, according to agreed protocols.

3.3 GPs will be notified of the diagnosis of cancer within 24 hours of the diagnosis being made, and will be kept informed of all aspects of the patients care at all times.

3.4 See appendix one for the referral form.

3.5 Referral for Family History Assessment.

3.5.1 Individuals (affected or unaffected with cancer) who have two or more relatives with testicular cancer at any age should be referred to the West Midlands Regional Clinical Genetics Unit, Birmingham Women's Hospital for risk assessment.

3.5.2 The individuals will be assessed and managed using the West Midlands Family Cancer Strategy guidelines. Further details and referral form can be found at www.bwhct.nhs.uk/wmfacs.

4 Diagnosis and Staging

4.1 An urgent ultrasound should be considered in men with a scrotal mass that does not transilluminate and/or when the body of the testis cannot be distinguished.

4.2 90% of cancers can be confirmed with ultrasound. Occasionally a mass cannot be clearly categorised as either benign or malignant on USS. The options for the management of this small group of patients include follow-up scanning or surgery. On the rare occasion that the diagnosis is in doubt, representative samples may be sent for frozen section[4].

4.3 An FNA or percutaneous biopsy **should not be carried out** under any circumstances.

4.4 When a cancer is diagnosed on ultrasound:

4.4.1 Blood should be taken prior to surgery for tumour markers (AFP, HCG) and LDH.

4.4.2 An Urgent CT of chest, abdomen and pelvis should be booked.

4.4.3 Surgery (orchidectomy) should be offered, and can be carried out at the cancer unit except:

a. When the tumour is apparently in the patient's only testis or there are bilateral tumours. In these cases partial testicular preservation may be possible.

b. When there are clear signs or symptoms of metastatic germ cell cancer (generally unwell, have multiple lung metastases, AFP above >1000ng/ml, HCG> 5000iu/ml, or renal obstruction).

Both these groups should be referred immediately to the specialist MDT (at the Regional Testicular Tumour Centre at UHBFT).

4.4.4 All patients should be offered the insertion of a prosthesis at the time of primary surgery.

4.4.5 Histology slides should be sent to UHBFT for review at the time of referral to the lead pathologist for testicular cancer.

5 Management of Testicular Cancer – All Patients.

5.1 Initial treatment is usually with radical orchidectomy (but see 4.4.3 above), and the local urology team should perform this.

5.2 All patients with proven urological malignancy will be discussed by an MDT. Normally this will be the local MDT in the first instance, and the overall responsibility for the patient's management rests with the local MDT until referral has been agreed.

5.3 Once diagnosis is confirmed, or strongly suspected, the patient should be referred to the regional testicular tumour centre at UHBFT for discussion at the UHBFT Specialist Testicular MDT, and for further treatment planning.

5.4 All non-surgical treatment of these patients is led by the specialist team at UHBFT. 5.5 In limited circumstances there may be a requirement for shared care:

a. Children under the age of 16 with teratoma are treated at the Children's Hospital.

b. Patients aged between 16 and 25 that require inpatient treatment are offered a bed on the young persons unit.

c. Older patients and those that prefer not to be treated on the young persons unit are admitted to the 5 day treatment unit for inpatient care.

5.6 Where relevant, patients should be offered sperm banking regardless of treatment plan.

5.7 At 12 months following treatment all patients should be offered sperm analysis to determine the need for continued storage of their sperm samples.

5.8 Please see appendix two for an algorithm for the management of testicular germ cell neoplasms by histopathology, stage and IGCCC grouping

6 Management of non- seminomatous germ cell and combined (mixed) seminoma plus non-seminomatous tumours - Stage 1 (see section 9 for seminoma stage 1)

6.1 <u>High Risk Patients</u> (that is those with lymphovascular space invasion [LVS] on histology). These are those with an increased risk of recurrence; that is > 45% chance of relapse on surveillance only.

Stage 1 adjuvant treatment for high risk patients:

a. 111 Trial: A single group trial evaluating one cycle of adjuvant BEP chemotherapy in high risk, stage 1 non-seminomatous germ cell tumours of the testis (NSGCTT) should be offered to all these patients.
b. BEP x 2 cycles should be offered to patients declining 111 trial, or those who are ineligible.
c. The Chemotherapy rota reference for these is: o-rota 03 (BEP 120 – adjuvant).

6.2 Low Risk Patients

Patients with stage I disease who do not possess LVS invasion factors management options include:

a. Surveillance which should be undertaken in **Regional Testicular Tumour Centre** (UHBFT) according to schedule shown below (12.6.1).
b. Adjuvant chemotherapy BEP x 2 cycles.

On surveillance their risk of recurrence is 15 – 20%. This is reduced to <2% with adjuvant chemotherapy.

7 Management of metastatic malignant teratoma (stage 2 and above):

7.1 Poor Prognosis

factors include:
a. Mediastinal primary or
b. Non-pulmonary visceral metastases (NPVM) or
c. AFP>10,000 ng/L or
d. HCG>50,000 iu/L or
e. LDH >10 x upper limit of normal

Treatment
The primary treatment will be 4 cycles BEP/EP (5 day regimen) plus interval Bleomycin, followed by reassessment after 4 cycles. Depending on outcome, proceed to 2 further cycles, elective surgery or no further action.

7.2 Intermediate Prognosis:

Testicular or retro-peritoneal primary, no NPVM and:
a. *AFP >1000 + <10 000 or*
b. *HCG > 5000 + < 50 000 or*
c. LDH > 1.5 x upper limit of normal + < *10 x upper limit of normal.*

Treatment
The primary treatment will be 3-4 cycles BEP/EP (BEP-165) plus interval Bleomycin, followed by reassessment. Depending on outcome, proceed to 2 further cycles, elective surgery or no further action.

7.3 Good Prognosis

Testicular or retro-peritoneal primary, no NPVM and:
a. AFP <1,000 ng/L **and**
b. HCG <5,000 iu/L **and**
c. LDH <1.5 x upper limit of normal

Treatment
The primary treatment will be 3 cycles BEP (BEP-165)

7.4 The chemotherapy rota references are:
a. Poor prognosis: o-rota 04 (BEP 5 day) & o-rota 04a (B)
b. EP 5 (day)
c. Good prognosis & intermediate: o-rota 05 (BEP 165 metastatic) & 05a (B)
d. EP (165 metastatic)

8 Post Chemotherapy Residual Disease in non-seminomatous germ cell tumours

Surgical resection of residual para aortic nodes after chemotherapy should be considered in all cases where a residual mass exceeds 1cm and is indicated where the residual lymph node mass is ≥ 2cm. These patients should be discussed at the Specialist MDT and referred to the Lead Consultant Urologist/Retroperitoneal surgeon.

9 Seminoma Stage 1

Surveillance is not a practical option for stage 1 Seminoma. Treatment with either chemotherapy or radiotherapy results in a reduction in recurrence rate from 20% to less than 2-3%.

9.1 Chemotherapy.

Patients should be offered a single cycle of carboplatin AUC7 (based on EDTA Clearance)

9.2 Radiotherapy

9.2.1 A few patients, for whom chemotherapy is inappropriate or who decline it, may be offered 20 Gy/10# / daily for 2 weeks

9.2.2 Localisation
a. Patient supine
b. CT scan plan to ensure localisation of kidneys.

9.2.3 Clinical Target Volume (CTV)
a. Abdominal para-aortic lymph nodes
b. Renal hilar nodes ipsilateral to tumour
c. Patients with prior surgery to groin / scrotum (excluding vasectomy), CTV to include common iliac, external iliac & femoral nodes ipsilateral to tumour.

9.2.4 Planning Target Volume (PTV)
Typical limits to cover the above CTV will be:

a. Superiorly - T10 / T11
b. Laterally - Ipsilateral renal hilum, contra-lateral tips of transverse processes
c. Inferior - L5 / S1
d. Typical width around 8cm

However, with CT definition of the CTV, these limits are purely indicative as a check and should not be the primary sources for planning purposes.

10 Seminoma Stage IIa and IIb

10.1 Radiotherapy may be appropriate if RT volume permits curative doses, if not, chemotherapy with cisplatin and etoposide should be offered.

10.2 Localisation
CT localisation as for Stage I disease.

10.3 CTV
Macroscopic tumour + node chains superiorly & inferiorly 5 cm from gross tumour volume. 2cm laterally.

There is no indication for routine post-chemotherapy radiotherapy.

11 Seminoma stage III / IV / bulk disease

4 cycles cisplatin + etoposide should be offered.

12 Follow-up and recurrent disease.

12.1 In testis tumours the aims of follow-up are:

a. To detect relapse as early as possible in all stages
b. To detect an asynchronous contra lateral carcinoma of the testis in an early phase.
c. To encourage healthy lifestyles, particularly important is smoking cessation counselling.

12.2 The intensity of follow-up is dictated by the risk of recurrence over time. A series of follow-up schedules have been developed to reflect these differences in patient groups. Shared care may be appropriate in some circumstances.

12.3 Whether in early or advanced stages follow-up attendances should include:

a. Enquiry concerning testicular self-examination (TSE), and advice to report any concerns promptly, not necessarily waiting for next scheduled appointment.

b. Physical examination is only required routinely in symptomatic patients, those who are concerned about an abnormality on TSE or those where investigations raise concerns.
c. Serum Tumour Markers determination (AFP, beta-hCG and LDH),
d. Chest, Abdominal and pelvic CT (see schedules in 12.5 below).
e. Post chemotherapy semen analysis at 12 months or at other times if requested and indicated.
f. Brain CT or MRI in case of neurological symptoms and bone scan in case of suspicious bone pain.

12.4 Surveillance should continue for 5 years for teratoma and seminoma.
12.5 Patients who have been recruited into a clinical trial will be followed up as defined in the protocol.

12.6 Follow-up schedules

12.6.1 Five year Follow-up Stage 1 non-seminoma germ cell tumour Surveillance

Procedure	Year 1	Year 2	Year 3	Year 4	Year 5
Patient self-examination reminder	12 times	6 times	4 times	3 times	twice
LH, FSH, Testosterone	twice (3 and 12 months)	If indicated	If indicated	If indicated	If indicated
Tumour markers	12 times	6 times	4 times	3 times	twice
Chest X-ray	10 times	6 times	4 times	3 times	twice
CT scan chest, abdomen and pelvis	twice (3 and 12 months)	none	none	none	none

12.6.2 Five year follow-up schedule post adjuvant chemotherapy for Stage 1 non seminoma germ cell tumour

Procedure	Year 1	Year 2	Year 3	Year 4 and 5
Patient self-examination reminder	4 times	3 times	Twice	Once/year
Tumour markers	4 times	3 times	Twice	Once/year
FBC, UE's	Once	Once	If indicated	If indicated
LH, FSH, Testosterone	Twice (3 and 12 months)	Once	If indicated	If indicated
Chest X ray	Once	Once	none	none
CT scan chest, abdomen and pelvis	Once (twelve months)	If indicated	If indicated	If indicated

12.6.3 Five year follow up protocol for testicular seminoma: Stage 1 Post-Adjuvant and >stage 1 CR post -therapy

Procedure	Year 1	Year 2	Year 3-4	Year 5
Patient self-examination reminder	Four times	Three times	Twice	Once
Tumour markers	Four times	Three times	Twice	Once
FBC, UE's	Once	Once	Once	If indicated
LH, FSH, Testosterone	Once	Once	Once	If indicated
Chest X-ray	Twice	Twice	Once	Once
CT abdomen and pelvis + CXR (as above)	Twice (6 and 12 months)	Once (24 months)	none	none

12.6.4 Five year follow up for NSGCTT: >stage 1 CR post chemotherapy + / - RPLND

Procedure	Year 1	Year 2	Year 3	Year 4	Year 5
Patient self-examination reminder	Bimonthly	Four times	Three times	Twice	Twice
Tumour markers	Bimonthly	Four times	Three times	Twice	Twice
FBC, UE's	Twice	Once	If indicated	If indicated	If indicated
LH, FSH, Testosterone	Once	Once	Once	If indicated	If indicated
Chest X-ray	Once	none	none	none	none
CT scan chest, abdomen and pelvis	Twice (6 and 12 months)	Once (24 months)	If indicated	If indicated	If indicated

12.6.5 Seven year follow up for Residual Radiological abnormalities Post-chemotherapy + / - Surgery / RT

Procedures	Year 1	Year 2	Year 3	Year 4	Year 5	Years 6-7
Patient self-examination reminder	Bimonthly	Four times	Twice	Twice	Twice	Once yearly
Tumour markers	Bimonthly	Four times	Three times	Twice	Twice	Once yearly
FBC, UE's	Twice	Once	Once	Once	Once	If indicated
LH, FSH. Testosterone	Twice	Once	If indicated	If indicated	If indicated	If indicated
Chest X-ray	Once	If indicated	If indicated	If indicated	Once	If indicated
CT scan chest, abdomen and pelvis	Three	Twice	Once	Once	If indicated	If indicated

13 Recurrence

13.1 Recurrence following primary treatment of stage 1 germ cell cancers is curable in the vast majority of cases and management is generally with chemotherapy in the first instance. Referral to the regional testicular tumour centre is required in all cases.

13.2 Recurrence following treatment of metastatic disease is also treated with curative intent with chemotherapy (e.g. POM-ACE, TIP, Gem-TIP trial), surgery or radiotherapy alone, or in combination. Referral to the Regional Testicular Tumour Centre is required in all cases.

13.3 Contralateral tumours

The risk of a second contralateral tumour is about 1%. Management varies enormously between individuals based on prospects and wishes for maintaining fertility and an endogenous androgen source whilst maximising the chance of cure. Radical orchidectomy is usually, but not invariably required. Urgent referral to the Regional Testicular Tumour Centre prior to orchidectomy is required to discuss options for individualised care.

14 Patient Information and Counselling

14.1 All patients, and with their consent, their partners will be given access to appropriate written information during their investigation and treatment, and on diagnosis will be given the opportunity to discuss their management with a clinical nurse specialist who is a member of the relevant MDT. The patient should have a method of access to the team at the regional testicular tumour centre at all times.

14.2 Access to psychological support will be available if required. All patients should undergo a Holistic Needs Assessment and onward referral as required.

15 Palliative Care

Palliative care services will be made available to all patients as deemed appropriate by the MDT.

16 Clinical Trials

16.1 Wherever possible, patients who are eligible should be offered the opportunity to participate in National Institute for Health Research portfolio clinical trials and other well designed studies.

16.2 Where a study is only open at one Trust in the Network, patients should be referred for trial entry. A list of studies available at each Trust is available from Pan Birmingham Cancer Research Network. Email: PBCRN@westmidlands.nhs.uk .

16.3 Teratoma:

a. NCRI

111 – A single group trial evaluating one cycle of adjuvant BEP chemotherapy in high risk, stage 1 non-seminomatous germ cell tumours of the testis (NSGCTT) (recruiting)

b. NRCI Testis Clinical Studies Group – Phase II multicentre trial of salvage chemotherapy with Gem- TIP for relapsed germ cell cancer (approved).

16.4 Seminoma:

a. NRCI Testis Clinical Studies Group – Phase II multicentre trial of salvage chemotherapy with Gem- TIP for relapsed germ cell cancer (approved).

17 References

1 Department of Health, 2000. Referral guidelines for suspected cancers (www.dh.gov.uk),

2 NICE, 2002. Improving Outcomes in Urological Cancers - The Manual (www.nice.org.uk)

3 European Association of Urology, 2006. Guidelines on Testicular Cancer(www.uroweb.org).

4 Clinical Oncology (2000) 12:S181-182, Royal College of Radiologists

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Approval Date of Network Site Specific Group Date: 30 June 2010
Approval Date by the Clinical Governance Committee Date: 21Sept. 2010

Approval Signatures

Pan Birmingham Cancer Network Clinical Governance Committee Chair

Name: Doug Wulff

Signature Date 21 Sept. 2010

Pan Birmingham Cancer Network Manager

Name: Karen Metcalf

Signature Date 21 Sept. 2010

Network Site Specific Group Clinical Chair

Name: Dev Sarmah

Signature Date 21 Sept. 2010

Appendix 1

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Pan-Birmingham NHS Cancer Network

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URGENT REFERRAL FOR SUSPECTED UROLOGICAL CANCER

(Version 2.0)

If you wish to include an accompanying letter, please do so. **On completion please FAX to the number below.**

These forms should only be used for suspected cancer and in conjunction with the NICE Referral Guidelines for Suspected Cancer, June 2005

Patient Details	**GP Details (inc Fax Number)**
Surname Forename D.O.B. Gender Address Postcode Telephone NHS No Hospital No Interpreter Y / N First Language	Fax No: **Date of Decision** **Date of Referral**

Suspected cancer:	**Symptoms:**
Prostate ☐	Hard irregular prostate on DRE ☐
PSA value _____ng/ml	Significant symptoms (inc. symptoms of metastases) and raised PSA ☐
	Raised age-related PSA ☐

Age related cut-off measurements : 50-59 > 3.0 ng/ml ; 60-69 > 4.0 ng/ml; 70-80 > 5.0ng/ml
Elderly patients (over 80yrs) or those with significant co-morbidity do not require urgent referral for mildly elevated PSA in the absence of symptoms. PSA measurements are NOT valid in the presence of urinary tract infection and need to be repeated once the infection has resolved.

Bladder or Renal ☐	**Symptoms:** PAINLESS macroscopic haematuria (any age) ☐ Haematuria associated with PERSISTENT UTI (over 40) ☐ Unexplained microscopic haematuria (over 50) ☐ Palpable renal mass or solid renal mass on U/S scan ☐
Testicular ☐	**Symptoms:** Swelling / mass in BODY of testicle ☐
Penile ☐	**Symptoms:** Ulceration / mass in the glans or the prepuce ☐

Clinical Details:
History/Examination/Investigations……

Medication ……

For Hospital Use
Appointment Date Clinic Attending
Was the referral appropriate Yes No (if no please give reason)

UROLOGY CLINICS WITH RAPID ACCESS FACILITIES

Hospital	Tel	Fax
City	**0121 507 5805**	**0121 507 5075**
Good Hope	**0121 424 7476**	**0121 7376**
Heart of England	**0121 424 5000**	**0121 424 5001**
Queen Elizabeth (UHBFT)	**0121 627 2485**	**0121 460 5800**
Walsall Manor	**01922 721172 ext 6876 or 7227**	**01922 656773**
Sandwell	**0121 507 3834**	**0121 507 3723**

The age-specific cut-off PSA measurements recommended by the Prostate Cancer Risk Management Programme are as follows: aged 50−59 years ≥ 3.0 ng/ml; aged 60−69 years ≥ 4.0 ng/ml; aged 70 years and older ≥ 5.0 ng/ml. (Note that there are no age-specific reference ranges for men aged over 80 years. Nearly all men of this age have at least a focus of cancer in the prostate. Prostate cancer only needs to be diagnosed in this age group if it is likely to need palliative treatment.)

Appendix 2: Algorithm for the Management of Testicular Germ Cell Neoplasms by Histopathology, Stage and IGCCC Grouping