Diseases of Testes and Scrotum 2018-2019

Prof.Murtadha Almusafer

At the end of 2 lectures of scrotal diseases, the student should be able to:

1. Know different diseases affecting the scrotum & testis including congenital, inflammatory, traumatic, carcinomatous, and miscellaneous conditions.
2. Diagnose each condition (symptoms by history taking, signs by doing examination, investigations & imaging)
3. Know the emergency conditions like trauma , epididymo-orchitis with it's complications, testicular torsion. He should know the subsequent steps of management.
4. Know the treatment of each condition.
5. Know the possible complications of each condition.

Testicular maldescent

1.Incomplete descent of the testis: the testis is arrested in some part of it's path to the scrotum.

2.Ectopic testis: the testis is abnormally placed outside this path.

Incompletely descended testis

Incidence:

1. About 4% of full-term boys have unilateral or bilateral undescended testes(cryptorchidism).
2. The incidence is higher in preterm infants because the testis descends through inguinal canal during the third trimester of pregnancy. The prevalence of cryptorchidism is 30% in premature male neonates.
3. In 10% of unilateral cases there is a family history.
4. About 70% of cryptorchid testicles spontaneously descend within the first year of life (most occurring in the first 3 months of life).

Predisposing Factors:

prematurity, low birth weight, small size for gestational age, twinning, and maternal exposure to estrogen during the first trimester.

Aetiology

1.Abnormal descent of gubernaculums.
2.Intrinsic testicular defect: insensitive to gonadotropins.
3.Deficient maternal gonadotropic hormonal stimulation.

Presentation

1.More common on the right side.
2.Bilateral in 20% of cases.
3. Approximately 80% of undescended testes are palpable and 20% are nonpalpable. Nonpalpable testes may be intra-abdominal or absent. Palpable testes may be undescended, ectopic, or retractile.
4.Hypoplastic hemiscrotum.

Treatment

Treatment choices may include
1.watchful waiting,
2. hormonal treatment, or
3. surgery.
In clinical practice, the choice of initial therapy is often selected on the basis of age at presentation and the location of the cryptorchid testicle. Treatment should be started at the age of six months. After that age, undescended testes rarely descend . Any kind of treatment leading to a scrotally positioned testis should be finished by twelve months, or eighteen months at the latest, because histological examination of undescended testes at that age has already revealed a progressive loss of germ cells and Leydig cells
Watchful waiting may be used in boys,1 year of age with lower-lying testis in whom spontaneous descent is still a realistic possibility. Hormonal and surgical options are primarily selected on the basis of location and appearance of the undescended testicle. Hormonal treatment with luteinizing hormone releasing hormone (LHRH) analogs and/ or human chorionic gonadotropin (hCG) could theoretically increase circulating androgens that may, in turn, promote testicular descent. Surgical options include various forms of orchiopexy or orchiectomy.

Hazards of Incomplete descent

1.Sterility in bilateral cases
2.Pain as a result of trauma
3.An associated indirect inguinal hernia is often present
4.Torsion
5.Epididymo-orchitis in an incompletely descended right testis can mimic appendicitis.

6.Atrophy of an inguinal testis before puberty may be possibly caused by recurrent minor trauma.
7.Increased liability to malignant disease.

Ectopic testis

The **sites** of ectopic testis are:
1.At the superficial inguinal ring
2.In the perineum
3.At the root of the penis
4.In the femoral triangle.

Absent testis

1.Vanishing testis describes a condition in which a testis develops but disappears before birth.The most likely cause is prenatal torsion.
2.True agenesis of the testis is rare.

Retractile Testis

1.Common requiring no treatment but only monitoring.
2.Occur due to strong cremasteric contraction in cold weather, excitement, and physical activity.
3.Normally developed scrotum
4.Able to bring testis to the normal position.

Torsion of the testis:

Predisposing causes:

1.An abnormally high attachment of the tunica vaginalis predispose to torsion- the bell-clapper.
2.Separation of the testis from the epididymis- torsion about the pedicle between them.
3.Torsion of the appendages of the testis.

Clinical Features

1. Is most common between 10-25 years of age although a few cases occur in infancy.
2. Symptoms vary with degree of torsion most commonly there is sudden agonizing pain in the groin and lower abdomen.
3. Nausea and may be vomiting.
4. O/E: the testis seems high and the tender twisted cord can be palpated above it.
5. Elevation of testis worsing pain.Prehn's sign describes the (relief of pain with elevation of the testicle and) was once to be touted as a method to distinguish epididymitis from

torsion since the pain associated with torsion is usually not relieved with elevation of the testicle (ie, positive Prehn's = epididymitis). However, this sign is not reliable in differentiating these two entities.

6. Several studies have found **loss of the cremasteric reflex** to be the most accurate sign of testicular torsion. This reflex is elicited by stroking the ipsilateral thigh which leads to reflex elevation of the ipsilateral testicle by greater than 0.5cm.

Diagnosis

1.History & physical examination
2.Doppler U/S scan will confirm absence of blood supply to affected testis.

Treatment:

1.In the first hour it may be possible to untwist the testis by gentle manipulation.
2.Definitive treatment is Surgical Exploration with orchidopexy of the affected and the contralateral sides.
3.Orchidectomy for non-viable infarcted testis.

Epididymo-orchitis

Epididymitis is inflammation confined to the epididymis. Infection spreading to the testis is epididymo-orchitis.

Mode of infection

1.Infection reaches epididymis via vas from primary infection of urethra, prostate or seminal vesicle.

2.In men with outer flow obstruction, epididymitis may result from secondary urinary infection.

3.In young men the most common sexually transmitted infection causing epididymitis is now Chlamydia but gonococcal epididymitis is still prevalent both cause urethritis.

4.Blood borne infections are less common.

Causes:

1.Urethral instrumentation and urethral catheterization with urinary tract infection.

2.Urethral stricture.

3.Post-prostatectomy.

4.Tuberculosis.

5.Mumps

Presentation

1.The initial symptoms are those of urinary infection, later an ache in the groin and fever hearald onset of epididymitis.

2.The epididymis and testis swell and become painful and scrotal wall at first red, oedematous and shiny.

3.occasionally an abscess may form and discharge of pus may occur through scrotal skin.

Diagnosis

1.History & physical examination

2.GUE and Culture

3.Colour Doppler ultrasound

Treatment

1.Antibiotics

2.Elevation and scrotal support.

3.If suppuration occur, drainage is necessary.

Varicocele

The term varicocele specifically refers to dilatation and tortuosity of the pampiniform plexus, which is the network of veins that drain the testicle.

The small vessels of the pampiniform plexus normally range from 0.5–1.5 mm in diameter. Dilation of these vessels greater than 2 mm is called a varicocele.

Aetiology

1.**Idiopathic varicocele**: occurs when the valves within the veins along the spermatic cord do not work properly.

2. 98% of idiopathic varicoceles occur on the **left side**, apparently because the left testicular vein connects to the renal vein (and does so at a 90-degree angle), while the right testicular vein drains at less than 90-degrees directly into the significantly larger inferior vena cava. Isolated right sided varicoceles are rare.

3. **Secondary varicocele** is due to compression of the venous drainage of the testicle. A pelvic or abdominal malignancy is a definite concern when a right-sided varicocele is newly diagnosed in a patient older than 40 years of age. The most common cause is renal cell carcinoma (hypernephroma) followed by retroperitoneal fibrosis or adhesions. One non-malignant cause of a secondary varicocele is the so-called "Nutcracker syndrome", a condition in which the superior mesenteric artery compresses the left renal vein, causing increased pressures there to be transmitted retrograde into the left pampiniform plexus.

Diagnosis

1.Palpating a varicocele can be likened to feeling **a bag of worms**. When one is lying down, gravity may allow the drainage of the pampiniform plexus and thus make the mass not obvious.

2. The testicle on the side of the varicocele may or may not be smaller compared to the other side.

3.Grades of varicocele

Grade 1 The varicocele is only felt when the patient bears down.
Grade 2 The varicocele can be felt, but not seen.

Grade 3 The varicocele is large enough to be visible.

4.Varicocele can be reliably diagnosed with ultrasound which will show dilation of the vessels of the pampiniform plexus to greater than 2 mm. Doppler ultrasound is a technique of measuring the speed at which blood is flowing in a vessel. An ultrasound machine that has a Doppler mode can see blood reverse direction in a varicocele with a Valsalva, increasing the sensitivity of the examination.

Treatment

1. Varicocelectomy, the surgical correction of a varicocele.
2. An alternative to surgery is embolization, a minimally invasive treatment for varicocele that is performed by an interventional radiologist. This involves passing a small wire through a peripheral vein and into the abdominal veins that drain the testes.

Hydrocele

Is an abnormal collection of serous fluid in a part of processus vaginalis, usually the tunica.

Pathophysiology ana Aetiology

A hydrocele can be produced in 4 different ways:

1.Excessive production of fluid within the sac e.g secondary hydrocele(acute and chronic epididymo-orchitis, torsion, and testicular tumours)..

2.Defective absorption of fluid. This appears to be the explanation for most primary hydroceles.?

3.Interference with lymphatic drainage of scrotal structures.

4.Connection with peritoneal cavity (Congenital).

Hydrocele fluid contains albumin and fibrinogen.

Clinical Features

1.**Primary vaginal hydrocele** is most common in middle and later life but can also occur in older children.
2.Painless Scrotal swelling and the testis may be palpable within a lax hydrocele.
3.O/E: Hydrocele typically translucent and is possible to ' get above the swelling'.
4.In **congenital hydrocele**, the processus vaginalis is patent and connect with peritoneal cavity and the fluid may drain into peritoneal cavity when the child is lying down.
5.**Encysted hydrocele** of the cord is a smooth oval swelling near the spermatic cord.
6.**Hydrocele of canal of Nuck** : the cyst lies in relation to the round ligament in females.

Complications:

1.Infection
2.Transformation into hematocele after trauma or spontaneous bleeding into the sac.
3.Rupture is rare.
4.The sac may calcify.

Treatment

1.Congenital hydrocele is treated by herniotomy.
2.Established acquired hydrocele: Surgery**(Lord's operation and Jaboulay's)**
3.Secondary hydrocele subsides when the primary lesion resolves.

Spermatocele

Is a unilocular cyst and typically lies above and behind the upper pole of testis.It transilluminates and it's fluid contains spermatozoa and resembles barely water in appearance.

Treatment

Small spermatoceles can be ignored. Larger ones should be aspirated or excised.

Diseases of Scrotum

Idiopathic Scrotal Gangrene (Fournier's Gangrene)

It is a vascular disaster of infective origin that is characterized by:

1.Sudden scrotal inflammation.

2.Rapid onset of gangrene leading to exposure of the scrotal contents.

3.The absence of any obvious cause in over half the cases.

Predisposing Factors

Diabetes mellitus, it can follow minor injuries or procedures in the perineal area such as bruise, scratch, urethral dilatation, injection of hemorrhoids, or opening of a periurethral abscess.

Causative Organisms

Hemolytic streptococci are associated with other organisms(staphylococcus, E.coli, Clostridium welchi) in a fulminating inflammation of the subcutaneous tissue, which results in an obliterative arteritis.

Clinical Features:

1.Sudden pain in the scrotum.

2.prostration.

3.pallor and pyrexia.

4.Cellulitis spreads until the entire scrotal covering sloughs, leaving the testes exposed but healthy.

5.Crepitus which may spreads along the fascial planes.

Treatment

1.Swab for culture and sensitivity.

2.Antibiotics like gentamicin and cephalosporin until the bacteriological report is available.

3.Wide local excision of the necrotic scrotal skin

Testicular Tumors

Testicular cancer represents 1% of male neoplasms and 5% of urological tumours.

At diagnosis, 1-2% of cases are bilateral and the predominant histology is GCT (90-95% of cases) . Peak incidence is in the third decade of life for non-seminoma, and in the fourth decade for pure seminoma.

Testicular cancers (TC) show excellent cure rates based on their chemosensitivity especially to cisplatin-based chemotherapy

Epidemiological risk factors for the development of testicular tumours are 1.components of the testicular dysgenesis syndrome (i.e. cryptorchidism, hypospadias, decreased spermatogenesis evidenced by sub- or infertility)

2. Familial history of testicular tumours among first-grade relatives and

3.The presence of a contralateral tumour or GCNIS .

4. A recent systematic review confirmed the association between height and TGCT with an odds ratio (OR) of 1.13 per 5 cm increase in height

Pathological classification

3.2. Pathological classification

The recommended pathological classification shown below is based on the 2016 update of the World Health Organization (WHO) pathological classification [34].

1. **Germ cell tumours**
   - Derived from germ cell neoplasia *in situ* (GCNIS)
   - Germ cell neoplasia *in situ* (GCNIS)
   - **Seminoma**
   - Embryonal carcinoma
   - Yolk sac tumour, post-pubertal type
   - Trophoblastic tumours
   - Teratoma, post-pubertal type
   - Teratoma with somatic-type malignancies
   - Mixed germ cell tumours

2. **Germ cell tumours unrelated to GCNIS**
   - Spermatocytic tumour
   - Yolk sac tumour, pre-pubertal type
   - Mixed germ cell tumour, pre-pubertal type

3. **Sex cord/stromal tumours**
   - Leydig cell tumour
     - Malignant Leydig cell tumour
   - Sertoli cell tumour
     - Malignant Sertoli cell tumour
     - Large cell calcifying Sertoli cell tumour
     - Intratubular large cell hyalinising Sertoli cell neoplasia

on

- Granulosa cell tumour
  - Adult type
  - Juvenile type
- Thecoma/fibroma group of tumours
- Other sex cord/gonadal stromal tumours
  - Mixed
  - Unclassified
- Tumours containing both germ cell and sex cord/gonadal stromal
  - Gonadoblastoma

4. Miscellaneous non-specific stromal tumours

- Ovarian epithelial tumours
- Tumours of the collecting ducts and rete testis
  - Adenoma
  - Carcinoma
- Tumours of paratesticular structures
  - Adenomatoid tumour
  - Mesothelioma (epithelioid, biphasic)
  - Epididymal tumours
- Cystadenoma of the epididymis
- Papillary cystadenoma
- Adenocarcinoma of the epididymis
- Mesenchymal tumours of the spermatic cord and testicular adnexae.

Table 4.2: TNM classification for testicular cancer (UICC, 2017, 8th edn. [34])

pT -	Primary Tumour[1]	
	pTX	Primary tumour cannot be assessed (see note 1)
	pT0	No evidence of primary tumour (e.g. histological scar in testis)
	pTis	Intratubular germ cell neoplasia (carcinoma *in situ*)
	pT1	Tumour limited to testis and epididymis without vascular/lymphatic invasion; tumour may invade tunica albuginea but not tunica vaginalis*
	pT2	Tumour limited to testis and epididymis with vascular/lymphatic invasion, or tumour extending through tunica albuginea with involvement of tunica vaginalis
	pT3	Tumour invades spermatic cord with or without vascular/lymphatic invasion
	pT4	Tumour invades scrotum with or without vascular/lymphatic invasion
N -	**Regional Lymph Nodes - Clinical**	
	NX	Regional lymph nodes cannot be assessed
	N0	No regional lymph node metastasis
	N1	Metastasis with a lymph node mass 2 cm or less 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 more than 5 nodes positive, none more than 5 cm; or evidence of extranodal extension of tumour
	N3	Metastasis with a lymph node mass more than 5 cm in greatest dimension dimension
Pn	**Regional Lymph Nodes - Pathological**	

Pn -	Regional Lymph Nodes - Pathological	
	pNX	Regional lymph nodes cannot be assessed
	pN0	No regional lymph node metastasis
	pN1	Metastasis with a lymph node mass 2 cm or less in greatest dimension and 5 or fewer positive nodes, none more than 2 cm in greatest dimension
	pN2	Metastasis with a lymph node mass more than 2 cm but not more than 5 cm in greatest dimension; or more than 5 nodes positive, none more than 5 cm; or evidence or extranodal extension of tumour
	pN3	Metastasis with a lymph node mass more than 5 cm in greatest dimension
M -	**Distant Metastasis**	
	MX	Distant metastasis cannot be assessed
	M0	No distant metastasis
	M1	Distant metastasis
		M1a Non-regional lymph node(s) or lung metastasis
		M1b Distant metastasis other than non-regional lymph nodes and lung

S -	Serum Tumour Markers			
	SX	Serum marker studies not available or not performed		
	S0	Serum marker study levels within normal limits		
		LDH (U/l)	**hCG (mIU/mL)**	**AFP (ng/mL)**
	S1	< 1.5 x N and	< 5,000 and	< 1,000
	S2	1.5-10 x N or	5,000-50,000 or	1,000-10,000
	S3	> 10 x N or	> 50,000 or	> 10,000

The mean serum half-life of AFP and hCG is five to seven days and two to three days, respectively . Tumour markers need to be re-evaluated after orchiectomy to determine half-life kinetics. Marker decline in patients with clinical stage (CS) I disease should be assessed until normalisation has occurred. Markers before the start of chemotherapy are important to classify the patient according to the IGCCCG risk classification . The persistence of elevated serum tumour markers after orchiectomy might indicate the presence of metastatic disease (macro- or microscopically), while the normalisation of marker levels after orchiectomy does not rule out the presence of tumour metastases. During chemotherapy, the markers should decline; persistence has an adverse prognostic value . Slow marker decline in patients with poor prognosis during the first cycle of standard bleomycin, etoposide and cisplatin (BEP) chemotherapy can be used as an indication for early chemotherapy dose intensification [39].

DIAGNOSTIC EVALUATION

Clinical examination

Testicular cancer usually presents as a painless, unilateral testicular scrotal mass, as a casual US finding or is revealed by a scrotal trauma . Scrotal pain may be the first symptom in 20% of cases and it is present in up to 27% of patients with TC. Gynaecomastia appears in 7% of cases (more common in non-seminomatous tumours). Back and flank pain due to metastasis is present in about 11% of cases.

Diagnosis is delayed in around 10% of cases of TC that mimic epididymo-orchitis , physical examination reveals the features of the mass and must always be carried out together with a general examination to find possible (supraclavicular) distant metastases, a palpable abdominal mass or gynaecomastia. Ultrasound must be performed in any doubtful case. A correct diagnosis must be established in all patients with an intrascrotal mass.

Imaging of the testis

Currently, US is used to confirm the presence of a testicular mass and explore the contralateral testis. Ultrasound **sensitivity is almost 100%,** and US has an important role in determining whether a mass is intra- or extra-testicular . Ultrasound is an inexpensive test and should be performed even in the presence of clinically evident TC. Ultrasound of the testis should be performed in young men with retroperitoneal or visceral masses and/or elevated serum hCG or AFP and/or consulting for fertility problems and without a palpable testicular mass .

Magnetic resonance imaging of the scrotum offers higher sensitivity and specificity than US in the diagnosis of TC, but its high cost does not justify its routine use for diagnosis.

Serum tumour markers at diagnosis

Serum tumour markers are prognostic factors and contribute to diagnosis and staging . The following markers should be determined before, and five to seven days after orchiectomy:

1. Alpha-fetoprotein (produced by yolk sac cells);

2. Human chorionic gonadotrophin (expression of trophoblasts);

3. Lactate dehydrogenase.

Tumour markers are of value for diagnosis (before orchiectomy) as well as for prognosis (after orchiectomy). They are increased in approximately every second patient with TC. Alpha-fetoprotein and hCG are increased in 50-70% and in 40-60% of patients with NSGCT, respectively. About 90% of NSGCT present with a rise in one or both of the markers. Up to 30% of seminomas can present or develop an elevated hCG level during the course of the disease .

Lactase dehydrogenase is a less specific marker, its concentration being proportional to tumour volume. Its level may be elevated in 80% of patients with advanced TC. Of note, negative marker levels do not exclude the diagnosis of a GCT. Placental alkaline phosphatase (PLAP), is an optional marker in monitoring patients with pure seminoma, but not recommended in smokers.

Cytogenetic and molecular markers are available in specific centres, but at present only contribute to research. There is preliminary evidence that micro-RNAs from two clusters (miR-371-373 and miR-302-367) or a composite panel display higher accuracy in the diagnosis of residual and recurrent GCT than conventional markers. They may be useful in diagnostic, monitoring and prognostication in the future.

Inguinal exploration and orchiectomy

Every patient with a suspected testicular mass must undergo inguinal exploration with exteriorisation of the testis within its tunics. Orchiectomy with division of the spermatic cord at the internal inguinal ring must be performed if a malignant tumour is found. If the diagnosis is not clear, a testicular biopsy (and enucleation of the intraparenchymal tumour) is taken for frozen (fresh tissue) section histological examination. Even though only limited data are available, it has been shown that during orchiectomy, a testicular prosthesis can be inserted without increased infectious complications or rejection rates .

In cases of life-threatening disseminated disease, life-saving chemotherapy should be given up-front, especially when the clinical picture is very likely TC, and/or tumour markers are increased. Orchiectomy may be delayed until clinical stabilisation occurs or in combination with resection of residual lesions.

Organ-sparing surgery

Although organ-sparing surgery is not indicated in the presence of non-tumoural contralateral testis, it can be attempted in special cases with all the necessary precautions.

1.In synchronous bilateral TCs, metachronous contralateral tumours,

2.Or in a tumour in a solitary testis with normal pre-operative testosterone levels, organ preserving surgery can be performed when tumour volume is less than approximately 30% of the testicular volume and surgical rules are respected. In those cases, the rate of associated GCNIS is high (at least up to 82%)

In cases of undetermined testicular masses (< 1 cm, non-palpable, multiple or of unusual presentation), frozen section examination (FSE) has proven reliable and highly concordant with final histopathology. Frozen section examination may be considered as a selection tool for organ sparing surgery.

Treatment

Seminoma Stage I

After modern staging procedures, less than 15% of stage I seminoma patients have subclinical metastatic disease, usually in the retroperitoneum, and will relapse after orchiectomy alone. The decision regarding adjuvant treatment should always be based on a thorough discussion with the patient, taking into account the described advantages and disadvantages, as well as the individual situation of the patient.

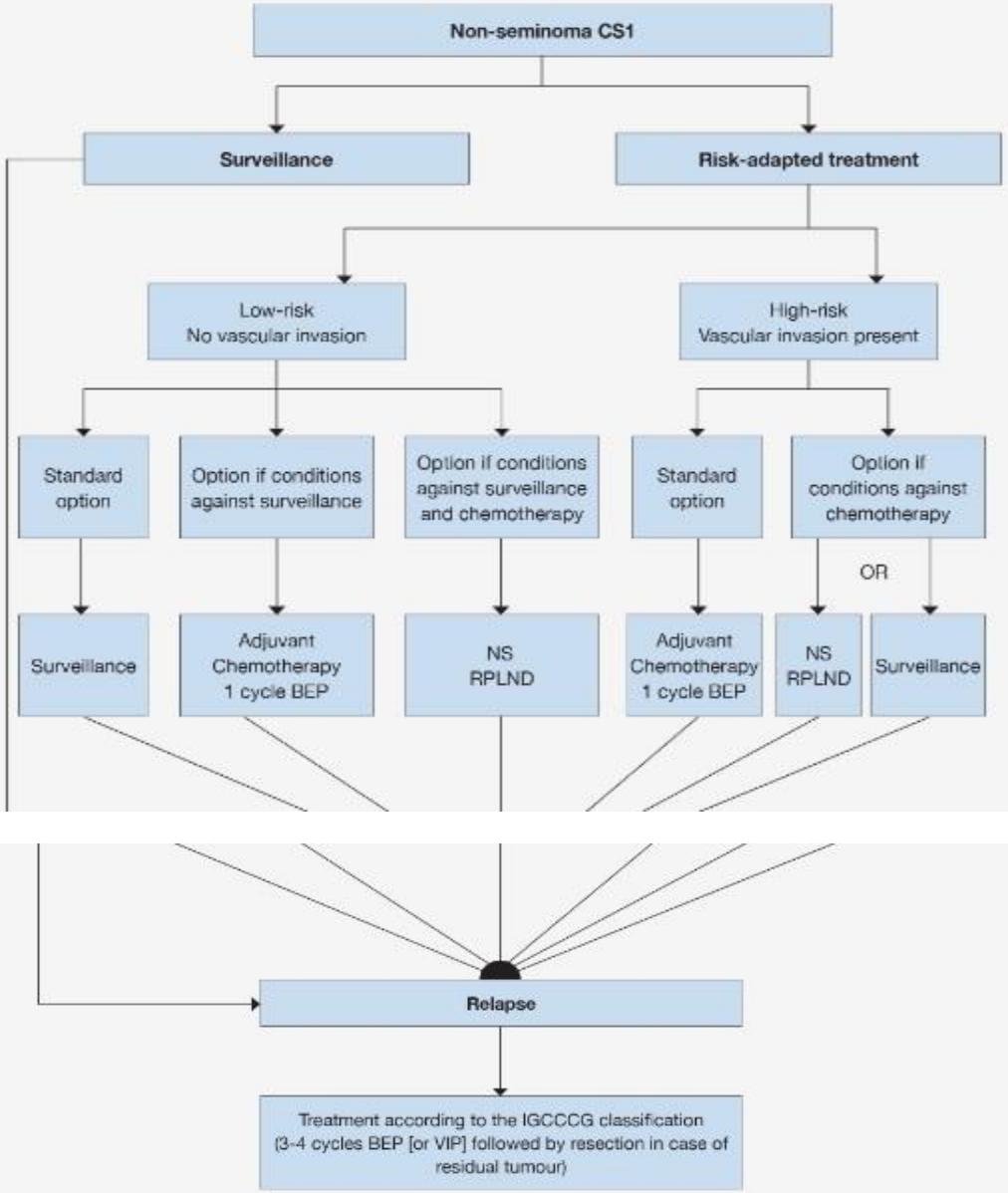
Surveillance

Several prospective non-randomised surveillance studies have been conducted during the past decade, the largest study from Canada with > 1,500 patients . Previous analyses from four studies showed an actuarial five-year relapse-free rate of 82.3%. The Princess Margaret Hospital series (n=1,559) showed an overall relapse rate in unselected patients of 16.8%. The actuarial relapse rate is in the order of 15-20% at five years, and most of the relapses are first detected in infra-diaphragmatic lymph nodes.

In patients with low risk (tumour size < 4 cm and no rete testis invasion), the recurrence under surveillance is as low as 6% . Chemotherapy, according to the IGCCCG classification, is a possible treatment for seminoma relapse under surveillance. However, 70% of patients with relapse are suitable for treatment with radiotherapy (RT) alone because of small volume disease at the time of recurrence. Patients who relapse after salvage RT can be effectively treated with chemotherapy. The combination of carboplatin chemotherapy and modern RT for treatment of low-stage seminoma relapse (IIA/IIB) is under investigation.

The overall cancer-specific survival (CSS) rate reported under surveillance performed by experienced centres is 97-100% for seminoma stage I. The main drawback of surveillance is the need for more intensive follow-up, especially with repeated imaging examinations of the retroperitoneal lymph nodes.

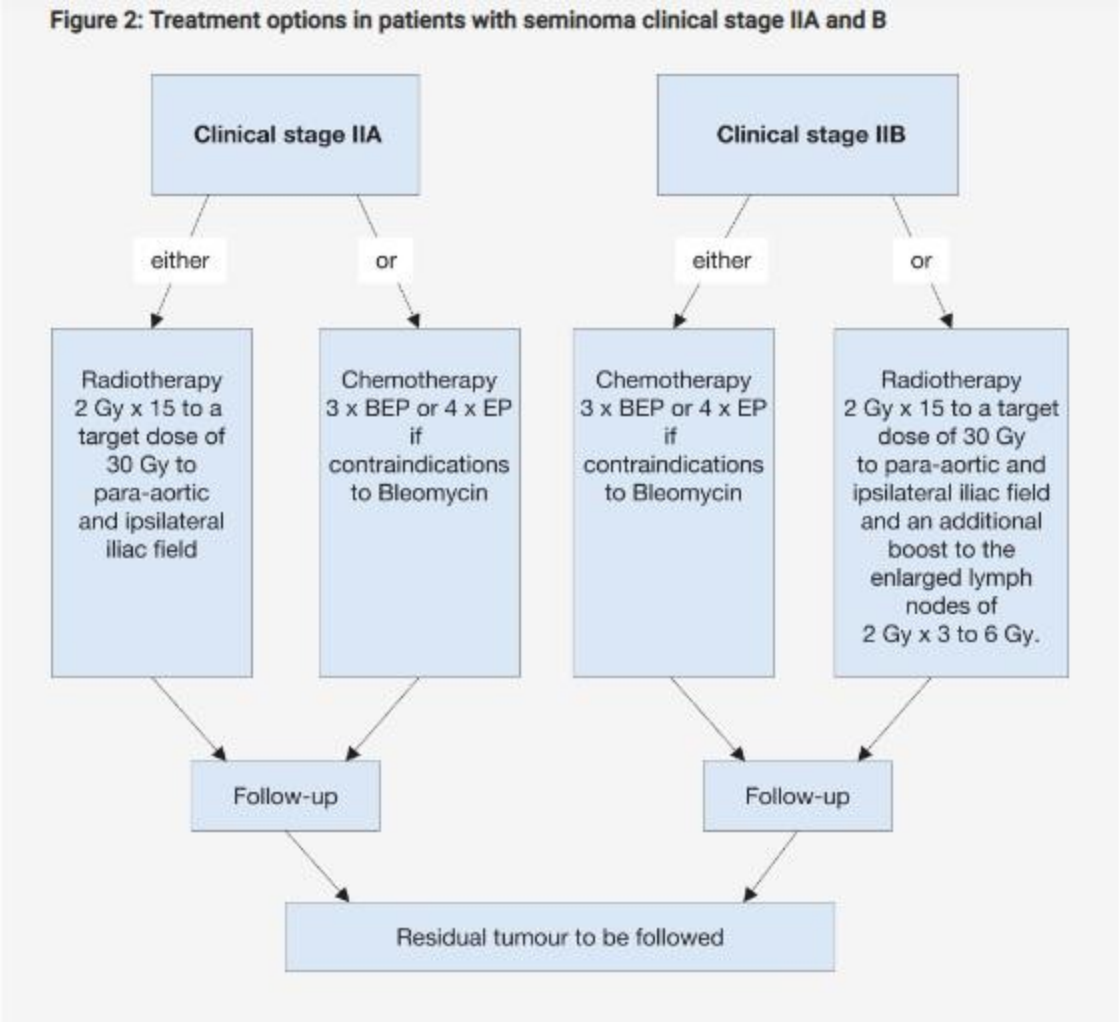
Figure 1: Risk-adapted treatment in patients with clinical stage 1 non-seminoma NSGCT CS1 [148]*



**Discuss all treatment options with individual patients, to allow them to make an informed decision as to their further care.*

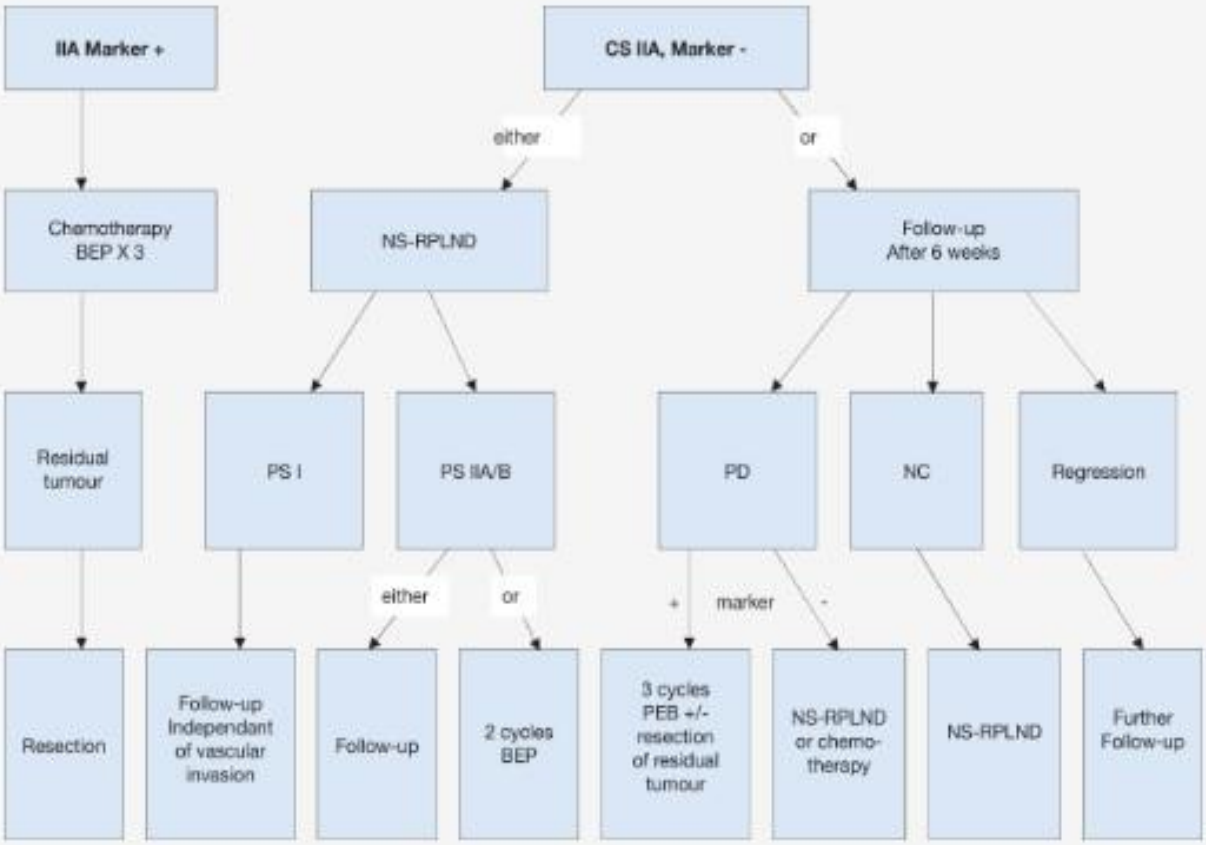
BEP=cisplatin, etoposide, bleomycin; CS=clinical stage; IGCCCG=International Germ Cell Cancer Collaborative Group; NS=nerve-sparing; RLNPD=retroperitoneal lymph node dissection; VIP=etoposide, cisplatin, ifosfamide.

Figure 2: Treatment options in patients with seminoma clinical stage IIA and B



BEP=cisplatin, etoposide, bleomycin; EP=etoposide, cisplatin.

Figure 3: Treatment options in patients with non-seminoma clinical stage IIA



BEP=cisplatin, etoposide, bleomycin; NS=nerve-sparing; RPLND=retroperitoneal lymph node dissection;

PS=pathological stage; PD=progressive disease; NC=no change.