

A.A. Zebentaev, P.V. Plotnikov

UROLOGY

**Lecture course
for students of medical Universities**

Vitebsk, 2017

**Ministry of Health Care of the Republic of Belarus
Higher Educational Establishment
“Vitebsk State Medical University”**

A.A. Zebentaev, P.V. Plotnikov

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ABBREVIATIONS LIST

5-AR - 5 alfa - reductase
5-ARI - 5 alfa - reductase inhibitors
AAST - American Association for the Surgery of Trauma
ABP - acute bacterial prostatitis
ACE - angiotensin converting enzyme
ADH - antidiuretic hormone
ADPKD - autosomal dominant polycystic kidney disease
AFP - alpha - fetoprotein
AGN - acute glomerulonephritis
AML - angiomyolipoma
APCs - antigen-presenting cells
ARB - angiotensin receptor blocker
ARF - acute renal failure
ARPKD - autosomal recessive polycystic kidney disease
ART - assisted reproductive techniques
ASAP - atypical small acinar proliferation
ATN - acute tubular necrosis
ATP - adenosine triphosphate
AUR - acute urinary retention
AUS - artificial urinary sphincter
BC - bladder cancer
BCG - bacillus Calmet – Geren
bFGF - basic fibroblastic growth factor
BOO - benign outlet obstruction
BPE- benign prostatic enlargement
BPH - benign prostatic hyperplasia
BT - brachytherapy
BUN - blood urea nitrogen
CBP - chronic bacterial prostatitis
CIS - carcinoma in situ
CISC - clean intermittent self catheterisation
CKD - chronic kidney disease
CMV - cytomegalovirus
CPPS - chronic pelvic pain syndrome
CRF - chronic renal failure
Cr - creatinine
CT - computer tomography
CTLs - cytotoxic T lymphocytes
CXR - chest X-Ray
DHT - dihydrotestosterone
DIC - disseminated intravascular coagulopathy
DM - diabetes mellitus

DMSA - dimercaptosuccinic acid
DRE - digital rectal examination
DSD - detrusor-sphincter dysynergia
DTPA - ^{99m}Tc-labeled diethylenetriaminepentaacetic acid
EAU - European Association of Urology
EBRT - external beam radiotherapy
ECD - expanded criteria donor
ED - erectile dysfunction
EDTA - ethylene diamine tetra-acetic acid
EGF - epidermal growth factor
e-GFR - estimated GFR
EMG - sphincter electromyography
EPS - expressed prostatic secretions
ESRD - end-stage renal disease
ESRF - end stage renal failure
ESWL - extracorporeal shock waves lithotripsy
FVC - frequency volume chart
FSGN - focal segmental glomerulosclerosis
FSH - follicle stimulating hormone
GAG - glycosaminoglycan
GCT - germ cell tumours
GFR - glomerular filtration rate
GIT - gastrointestinal tract
GN - glomerulonephritis
GU, NGU - gonococcal, non-gonococcal urethritis
GUT - genitourinary tract
hCG - human chorionic gonadotrophin
HD - hemodialysis
HIFU - high-intensity focused US
HIV - human immunodeficiency virus
HLA - human leukocyte antigen
HPF - high-powered field
HPV - human papillomavirus
HU - Hounsfield units
Hz - hertz
IC - interstitial cystitis
ICSI - intracytoplasmic sperm injection
ICU - intensive care unit
IGCN - intratubular germ cell neoplasia
IIEF- International index of erectile function
IPSS - International prostate symptom score
ISD - intrinsic sphincter deficiency
IUI - intrauterine insemination
IVC - inferior vena cava
IVF - in vitro fertilization
IVU - intravenous urography

LDH - lactate dehydrogenase
LHRH - luteinizing hormone-releasing hormone
LUTS – lower urinary tract symptoms
MAB - maximal androgen blockade
MAG3 - 99mTc-labeled mercaptoacetyltriglycine
MAR test - mixed agglutination reaction test
MCD - medullary cystic disease
MCDK - multicystic dysplastic kidney
MCUG - micturating cystourethrography
MESA - microsurgical epididymal sperm aspiration
MET - medical expulsive therapy
MHC - major histocompatibility complex
MMC - mitomycin C
MRT - magnetic resonance tomography
MS - multiple sclerosis
MSU - midstream specimen of urine
NK - natural killer
NMIBC - non muscle invasive BC
NS - non-seminomatous
NSAIDs - non-steroid anti-inflammatory drugs
NSI - nosocomial infection
OAB - overactive bladder
OP - open prostatectomy
PC - prostate cancer
PCNL - percutaneous nephrolithotomy/tripsy/lapaxy
PCR - polymerase chain reaction
PD - peritoneal dialysis
PDE5 - phosphodiesterase type-5 inhibitors
PESA - percutaneous sperm aspiration
PFS - pressure-flow studies
PGE1 - prostaglandin E1
PIN - prostatic intraepithelial neoplasia
PNS - percutaneous nephrostomy
PSA - prostate specific antigen
PUJ - pyeloureteric junction
PUJO - pelviureteric junction obstruction
PUV - posterior urethral valve
PVR - post – void residuals
Qmax - maximum flow rate
RBC - red blood cells
RBF - renal blood flow
RCC - renal cell carcinoma
rHu-EPO - recombinant human erythropoetin
RP - radical prostatectomy
RPF - renal plasma flow rate
RPGN - rapidly progressive glomerulonephritis

RPLND - retroperitoneal lymph node dissection
RRF residual renal function
RT - radiotherapy
SBP - systolic blood pressure
SCC - squamous cell carcinoma
SCr - serum Cr
SD - standard deviations
SHBG - sex hormone binding globulin
SIRS - systemic inflammatory response syndrome
STD - sexually transmitted disease
SUI - stress urinary incontinence
TB - tuberculosis
TC - testicular cancer
TCC - transitional cell carcinoma
TCrCl - total Cr clearance
TESA - testicular sperm aspiration
TESE - testicular sperm extraction
TGF - transforming growth factors
Th - helper T cells
TOT - transobturator tape
TRUS - transrectal ultrasonography
TS - tuberous sclerosis
TUVP - transurethral electrovaporization of the prostate
TUMT - transurethral microwave thermotherapy
TUNA - transurethral radiofrequency needle ablation
TUR - transurethral resection
TURP - transurethral resection of the prostate
TVT - tension-free vaginal tape
TZ - transition zone
TWC - trial without catheter
UDT - undescended testes
UI - urinary incontinence
URS - ureterorenoscopy
US - ultrasound
UTIs - urinary tract infections
UUI - urge urinary incontinence
UHN - uretero hydronephrosis
VHL - von Hippel Lindau syndrome
VUJ - vesicoureteric junction
VUR - vesicoureteric reflux
WBC - white blood cells
WHO - World Health Organization
WW - watchful waiting.

1.1. SYMPTOMS

The medical history is the cornerstone of the evaluation of the urologic patient and a well-taken history will frequently elucidate the probable diagnosis. The urologist must lead the patient through detailed and appropriate questioning to obtain accurate information.

1.1.1. Systemic manifestations

Symptoms of fever and weight loss should be checked. The presence of fever associated with other symptoms of UTIs may be helpful in evaluating the site of the infection. Acute pyelonephritis or prostatitis will lead to high temperatures, often accompanied by chills. Infants and children who have acute pyelonephritis may have high temperatures without other localizing symptoms or signs. A history of unexplained attacks of fever occurring even years before may represent otherwise asymptomatic pyelonephritis. The absence of fever does not rule out renal infection. Chronic pyelonephritis does not cause fever. Weight loss is expected in the advanced stages of cancer, but it may be noticed also when there is CRF. In children who have low weight and less than average height, chronic obstruction, UTIs or both should be suspected. General malaise may be noted with tumors, chronic pyelonephritis or CRF. The presence of many of these symptoms may be compatible with HIV infection. RCC sometimes causes fever.

Paraneoplastic syndromes

Paraneoplastic syndromes are defined as a collection of symptoms and clinical signs occurring in cancer patients and involving systemic effects taking place remotely from the tumor. They are not related either to its local invasion or distant metastasis and are not caused by infection, nutritional deficiency or treatment.

A paraneoplastic syndrome etiology:

- Biologically active substances (hormonal peptides or hormone-like substances, biologic amines, growth factors) aberrantly produced by the tumor;
- Stimulation of the immune system via autoimmunity, immune complexes production and immune suppression;

Detection of this syndrome can lead to the diagnosis of a previously undetected neoplasm. It can dominate the clinical picture and thus lead to errors with respect to the origin and type of primary tumor. It can follow the clinical course of the tumor and thus be useful for monitoring its evolution.

All GUT tumors may cause this syndrome, even though RCC is the most frequent urological malignancy involved. Although some syndromes, such as polycythemia and hypertension, are more typical of RCC, others, such as hypercalcemia and Cushing's syndrome, are common to other GUT cancers. PC is the second urological tumor associated with paraneoplastic syndrome. This syndrome is uncommon in BC and rare in TC. Paraneoplastic hypercalcemia represents the most common case.

When evaluating an individual with new onset nonurological symptoms suggestive of paraneoplastic syndrome, clinicians should consider the presence of an underlying malignancy, including GUT carcinomas. Imaging studies may be useful to detect the primary tumor in patients. The most effective treatment strategy is represented by the radical therapy of the underlying cancer.

Gynecomastia

Often idiopathic, gynecomastia is common in elderly men, particularly those taking estrogens for PC. It is also seen in association with TC. Certain endocrinologic diseases, for example, Klinefelter syndrome, may also cause gynecomastia. Male patients with obesity have false gynecomastia.

Urosepsis

Patients with urosepsis should be diagnosed at an early stage, especially in the case of a complicated UTI. The systemic inflammatory response syndrome, known as SIRS (temperature $>38^{\circ}\text{C}$ or $<36^{\circ}\text{C}$), hyperleukocytosis or leukopenia (WBC >12000 cells/ mm^3 or <4000 cells/ mm^3 or $>10\%$ immature forms), tachycardia (>90 bpm), tachypnoea (respiratory rate >20 breaths/min or $\text{PaCO}_2 <32$ mmHg), is recognised as the first event in a cascade to multi-organ failure. SIRS is response to a wide variety of clinical insults, which can be infectious, as in sepsis but may be non-infectious in etiology (e.g. burns or pancreatitis). The prognosis of urosepsis is globally better than that of sepsis from other infectious sites.

The clinical evidence of UTI is based on symptoms, physical examination, sonographic and radiological features and laboratory data, such as bacteriuria and leukocyturia. Infection is presence of organisms in a normally sterile site that is usually, but not necessarily, accompanied by an inflammatory host response. Bacteraemia is presence of bacteria in blood as confirmed by culture, which may be transient and not necessary for diagnosis of urosepsis.

Sepsis is activation of the inflammatory process due to infection.

Severe sepsis is associated with organ dysfunction, hypoperfusion or hypotension. Hypoperfusion and perfusion abnormalities may include but are not limited to lactic acidosis, oliguria or acute alteration of mental status.

Septic shock is sepsis with hypotension despite adequate fluid resuscitation along with the presence of perfusion abnormalities. Patients who are on inotropic or vasopressor agents may not be hypotensive at the time that perfusion abnormalities are measured. Refractory septic shock lasts for $>1\text{h}$ and does not respond to fluid administration or pharmacological intervention. Mortality is considerably increased when severe sepsis or septic shock are present.

There are combination of treatment options for management of urosepsis. The drainage of any obstruction in the urinary tract is essential as first-line treatment. Urologists are recommended to treat patients in collaboration with ICU. Most nosocomial urosepsis can be avoided by reduction of hospital stay, early removal of indwelling urethral catheters and avoidance of unnecessary catheterisations, using of closed catheter systems and attention to simple daily aseptic techniques to avoid cross-infection.

1.1.2. Flank pain

This can present suddenly as severe acute pain in the flank reaching a peak within minutes or hours. Alternatively, it may have a slower course of onset as a chronic loin pain, developing over weeks or months. Loin pain is frequently presumed to be urological in origin. However, other non-urologic organs are located in this region. Diseases of non-urological organs may be the source of the pain and pain arising from extra-abdominal organs may radiate to the loins as a “referred” pain.

The most common cause of sudden onset of severe acute loin pain in the flank is the passage of a stone formed in the kidney, down through the ureter. Ureteric stone pain characteristically starts very suddenly. This pain is colicky in nature. Waves of increasing severity are followed by a reduction in severity, although seldom going away completely. It radiates to the groin as the stone passes into the lower ureter. The pain may change in location, from flank to groin, but its location does not provide a good indication of the position of the stone, except where the patient has pain or discomfort in the penis and a strong desire to void, which suggests that the stone has moved into the distal part of the ureter. The patient cannot get comfortable. They often roll around in agony. Those with peritonitis lie still.

Flank pain: non-stone urological causes

A clot may form from a bleeding source within the kidney (e.g. RCC and injury). Similarly, a ureteric cancer may cause ureteric obstruction and acute loin pain. Loin pain and hematuria are often assumed to be due to a stone, but it is important to do investigation of such patients from the perspective of upper urinary tract cancer.

PUJO may present acutely with flank pain severe enough to mimic a ureteric stone. Investigations will demonstrate hydronephrosis, with a normal calibre ureter below the PUJ and no stone.

Patient may have acute loin pain if there is UTIs (acute pyelonephritis or pyonephrosis). These patients have a high fever and no signs of obstruction. On the contrary, ureteric stone patients with obstructive pyelonephritis are often systemically very unwell. History, physical examination, US and radiological methods are clearly important for distinguishing urological from non-urological loin pain. Palpate the abdomen for signs of peritonitis (abdominal tenderness and/or guarding) and examine for abdominal masses. Examine the patient’s back, chest and testicles. In women, do a pregnancy test and gynecological exam.

Flank pain: non-urological causes

There are many causes for non-urological pain syndrome:

- Pneumonia;
- Myocardial infarction;
- Ovarian pathology (e.g. twisted ovarian cyst, adnexitis);
- Ectopic pregnancy;
- Leaking abdominal aortic aneurysm;
- Acute appendicitis;
- Inflammatory bowel disease (Crohn’s, ulcerative colitis);

- Diverticulitis;
- Burst peptic ulcer;
- Bowel obstruction;
- Spinal cord disease.

1.1.3. Scrotal symptoms

Scrotal pain may be observed by torsion of the testicles and testicular appendages, epididymo-orchitis, testicular tumours and as a referred pain by ureteric colic and prostatitis.

Ischaemic pain by testicular torsion is severe. Torsion presents with sudden onset of pain in the hemiscrotum. Pain may radiate to the groin and/or loin. There is sometimes a history of mild trauma to the testis. Similar episodes may have occurred in the past, with spontaneous resolution of the pain, suggesting torsion/spontaneous detorsion. The testis is very tender and “high-riding”, lying at a higher than normal position in the testis. Testis may lie horizontally and there is scrotal erythema.

Patient with epididymo-orchitis has similar presenting symptoms as testicular torsion. Tenderness is usually localized to the epididymis (posterior part of the testis).

Patient with testicular tumour rare present with testicular pain. Testicular swelling may occur rapidly. An secondary hydrocele is common. A hydrocele in a young person should always be investigated with an US to determine whether the underlying testis is normal. Approximately 10-15% of testis tumours present with signs suggesting inflammation. Often there are signs suggesting a diagnosis of epididymo-orchitis with a tender, swollen testis, with redness in the overlying scrotal skin and a fever.

Lumps in the scrotum and in the groin may be observed in patients with hydrocele, epididymal cyst, testicular tumour, varicocele, TB, epididymo-orchitis and inguinal hernia.

A hydrocele is an abnormal collection of peritoneal fluid between the parietal and visceral layers of the tunica vaginalis. Normally the processus vaginalis becomes obliterated along its entire length, apart from where it surrounds the testis. Hydrocele may be primary and secondary. Primary hydrocele usually painless. A hydrocele has a smooth surface and it is difficult or impossible to feel the testis which is surrounded by the tense, fluid collection. Unless, rarely, the hydrocele is very lax. The superior margin can be palpated. It is possible to transilluminate a hydrocele. The light from a torch applied on one side can be seen on the other side of the hydrocele. Primary hydroceles develop slowly and there is no precipitating event such as epididymo-orchitis or trauma and the underlying testis appears normal on US. Secondary hydroceles may be due to infection, tumour and trauma represent an effusion between the layers of the tunica vaginalis. In filariasis, obstruction of the lymphatics of the spermatic cord give rise to the hydrocele.

Epididymal cyst also known as a spermatocele. Derived from the collecting tubules of the epididymis and contain clear fluid. They develop slowly, lie within the scrotum and usually lie above and behind the testis. They are often multiple.

In the absence of involvement of the epididymitis, inflammation of the testis is due to a viral infection e.g. mumps. Often occurs with enlargement of the salivary glands.

Tuberculous epididymo-orchitis is infection of the epididymis by TB, which has spread from the blood or urinary tract. The absence of pain and tenderness is noticeable. The epididymis is hard and has an irregular surface. The spermatic cord is thickened and the vas deferens also feels hard and irregular as a “string of beads”.

Testicular tumour is a solid mass, arising from within the scrotum and may extend up into the spermatic cord. They may present with symptoms of an acute epididymo-orchitis. They may have undergone an orchidopexy for UDT. The lump is usually hard and may have a smooth or irregular surface. Abdominal and supraclavicular lymph nodes are examined.

Varicocele is the dilatation of the pampiniform plexus more common on the left side. They may cause a dragging sensation or ache in the scrotum. Patients with III stage of the disease feel like a “bag of worms” in the scrotum. Primary varicocele disappears when the patient lies down.

An indirect inguinal hernia often extends into the scrotum. It usually expands on coughing. This hernia usually reduces with direct pressure or on lying down. It is not possible to get above the lump. Since inguinal and femoral hernias arise from within the abdomen and descend into the groin, it is not possible to get above them. For lumps that arise from within the scrotum, the superior edge can be palpated. Once a hernia has protruded through the abdominal wall, it can expand in any direction in the subcutaneous tissues and therefore the position of the unreduced hernia cannot be used to establish whether it is inguinal or femoral. Inguinal hernia reduces through the abdominal wall at a point above and medial to the pubic tubercle. An indirect inguinal hernia often descends into the scrotum, but direct inguinal hernia rarely does. Femoral hernia reduces through the abdominal wall at a point below and lateral to the pubic tubercle.

1.1.4. Penile and urethral symptoms

Phimosis is a condition in which the contracted foreskin cannot be retracted over the glans. Chronic infection from poor local hygiene is its most common cause of secondary phimosis. Calculi and SCC may develop under the foreskin. Phimosis can occur at any age. In diabetic older men, chronic balanoposthitis may lead to phimosis and may be the initial presenting complaint. Children under 2 years of age seldom have true phimosis. Their relatively narrow preputial opening gradually widens and allows for normal retraction of foreskin over the glans. Edema, erythema and tenderness of the prepuce and the presence of purulent discharge usually cause the patient to seek medical care.

Paraphimosis is the condition in which the foreskin, once retracted over the glans, cannot be replaced in its normal position. This is complication of the phimosis. The skin ring causes venous congestion leading to edema and enlargement of the glans with significant risk of necrosis.

Peyronie’s disease is plastic induration of the penis and is a well-recognized clinical problem affecting middle-aged and older men. Patients present with com-

plaints of painful erection and curvature of the penis. The penile deformity may be so severe that it prevents satisfactory vaginal penetration. The patient has no pain and no curvature when the penis is non-erect. Examination of the penile shaft reveals a palpable dense, fibrous plaque of varying size involving the tunica albuginea. Multiple plaques are sometimes seen. In severe cases, calcification and ossification are noted. Although the cause of Peyronie's disease remains obscure, the dense fibrous plaque is microscopically consistent with findings of Dupuytren's contracture of the tendons of the hand.

Priapism – is painful, persistent, prolonged erection of the penis more than 4 hours and not related to sexual stimulation. There are two broad categories - low-flow (most common) and high-flow. Low-flow priapism may be due to hematological disease and malignant infiltration of the corpora cavernosa or papaverine injection intracavernosly. Priapism is painful because the corpora are ischaemic. High-flow priapism is painless and may arise due to perineal trauma, which creates an arteriovenous fistula. Diagnosis is usually obvious from the history and examination of the erect, tender penis in low-flow priapism. Characteristically, the corpora cavernosa are rigid and the glans is flaccid.

Acquired urethral stricture is common in men but rare in women. Most acquired strictures are due to infection or trauma. Although GU is seldom a cause of stricture today, UTIs remains a major cause, particularly infection from long-term use of indwelling urethral catheters. Large catheters and instruments are more likely to cause ischemia and internal trauma. External trauma, for example, pelvic fractures can partially or completely sever the membranous urethra and cause severe and complex urethral obliterations. Straddle injuries can produce bulbar strictures. These narrowings restrict urine flow and cause dilation of the proximal urethra and prostatitis. The bladder muscle may become hypertrophic and increased PVR may be noted. Severe, prolonged obstruction can result in VUR, UHN and CRF. Chronic urinary stasis makes UTIs likely. Urethral fistulas and periurethral abscesses commonly develop in association with chronic, severe strictures.

Condylomata acuminata are uncommon in the urethra and are almost always preceded by lesions on the penile skin. They are wart-like papillomas caused by a papilloma virus and are usually transmitted by direct sexual contact but may be transmitted nonsexually. Patients commonly complain of bloody spotting from the urethra and occasionally have dysuria and urethral discharge. Examination of the urethral meatus often reveals a small, protruding papilloma. If a lesion is not found in this location, the meatus should be separated with the examining fingers so that the distal urethra can be inspected. The sexual partner must also be examined and treated if necessary.

1.1.5. Urinary incontinence

Stress urinary incontinence is the complaint of involuntary leakage of urine on effort of exertion, sneezing or coughing. A diagnosis of urodynamic SUI is made during filling cystometry when there is involuntary leakage of urine during a rise in abdominal pressure induced by coughing, in the absence of a detrusor contraction. SUI occurs as a result of bladder neck/urethral hypermobility and/or neuro-

muscular defects causing ISD. It is called sphincter weakness incontinence. As a consequence, urine leaks whenever urethral resistance is exceeded by an increased abdominal pressure.

Urge urinary incontinence is the complaint of any involuntary leakage of urine accompanied by or immediately preceded by urgency. UUI may be due to neurogenic or idiopathic OAB or more commonly due to pathology that irritates the bladder (infection, tumour, stone).

Mixed urinary incontinence is a combination of SUI and UUI.

Overflow incontinence is bedwetting in an elderly man usually indicates high pressure chronic retention due to presence of BOO.

A constant leak of urine suggests a fistulous communication between the bladder and vagina due to surgical injury at the time of hysterectomy or caesarian section or, rarely, the presence of an ectopic ureter draining into the vagina. In this case the urine leak is usually low in volume, but lifelong. It is called false incontinence.

1.1.6. Nocturia and nicturia

Nicturia is empirically defined as the production of more than one-third of 24-h urine output between midnight and 8 a.m. Nicturia may lead to sleep disturbance. Nicturia is associated with endocrine, renal and cardiovascular disease (CRF, DM, central and nephrogenic diabetes insipidus, primary polydipsia, hypercalcaemia, drugs, autonomic failure).

Nocturia can be due to urological disease and this is a frequent urinations during the night due to BPH, OAB or incomplete bladder emptying.

Ask the patient to complete a FVC, which is a voiding diary that records time and volume of each void over a 24-h period for 7 days. Polyuria is defined empirically as >3 L of urine output per 24 h. Polyuria may be due to either a solute diuresis or a water diuresis. Measure urine osmolality: <250 mOsm/kg = water diuresis, >300 mOsm/kg = solute diuresis. Excess levels of various solutes in the urine, such as glucose in the poorly controlled diabetic, lead to a solute diuresis. A water diuresis occurs in patients with primary polydipsia as an appropriate physiological response to high water intake and diabetes insipidus due to ADH deficiency or resistance.

1.2. PHYSICAL EXAMINATION OF THE UROLOGICAL PATIENT

1.2.1. Abdominal examination of the patient with urological disease

Because of their retroperitoneal (kidneys, ureters) or pelvic location (bladder and prostate) these organs are relatively inaccessible to the examining hand when compared with, for example, the spleen, liver or bowel. For the same reason, for the kidneys and bladder to be palpable implies a fairly advanced disease state.

It is important that the urologist appreciates the characteristics of other intra-abdominal organs when involved with disease, so that they may be distinguished from urological organs.

Characteristics and causes of an enlarged kidney (RCC, hydronephrosis, pyo-

nephrosis, perinephric abscess, polycystic disease): the mass lies in a paracolic gutter, it moves with respiration, is dull to percussion and can be felt bimanually. It can also be balloted between your hands, one placed on the anterior abdominal wall and one on the posterior abdominal wall.

Characteristics and causes of an enlarged bladder (BPH, PC, urethral stricture): arises out of the pelvis, dull to percussion, pressure of examining hand may cause a desire to void.

Enlarged inguinal lymph nodes are palpated as a firm, non-compressible, nodular lump in the groin and abdomen. Look for pathology in the skin of the scrotum and penis, the peri-anal area and anus, the skin and superficial tissues of the thigh and leg.

Testis may be on the correct anatomical path, but may have failed to reach the scrotum if there are abdominal or inguinal UDT. Testis have descended away from the normal anatomical path is called ectopic testis. The lump is smooth, oval, tender to palpation, non-compressible and there is no testis in the scrotum.

1.2.2. Digital rectal examination

Prostate is located on the anterior part of the rectum. The DRE is the mainstay of prostatic examination.

Rules of the DRE. The anal region is examined for fistulae and fissures. Lubricant gel is applied to the gloved finger. Index finger is inserted gently and slowly into the anal canal, then into the rectum. Prostate is palpated anteriorly with the pulp of finger. Consistency (normal or firm), surface (smooth or irregular) are noted and size is estimated. It can be helpful to relate its size to common objects. A normal prostate is the size of a walnut. A moderately enlarged prostate has the appearance of a tangerine. A big prostate has the size of an apple or orange. The normal bilobed prostate has a median sulcus between the two lobes and in PC this groove may be obscured. Prostatic tenderness is best elicited by gentle pressure on the prostate with the examining finger. If there is acute prostatitis, prostate gland is very tender. By prostatic abscess there is a hole and fluctuation. DRE should be avoided in acute prostatitis because of septicaemia risk and in patients with an anal fissure, where DRE would be very painful.

The integrity of the sacral nerves that innervate the bladder and of the sacral spinal cord can be established by eliciting the bulbocavernosus reflex during a DRE. The sensory side of the reflex is elicited by squeezing the glans of the penis or the clitoris. In catheterized patients reflex is estimated by gently pulling the balloon of the catheter onto the bladder neck. The motor side of the reflex is tested by feeling for contraction of the anus during this sensory stimulus. Contraction of the anus represents a positive reflex and indicates that the afferent and efferent nerves of the sacral spinal cord (S2-S4) and the sacral cord are intact.

1.3. URINE EXAMINATION

1.3.1. Dipstick testing

Analysis for pH, blood, protein, glucose and WBC can be done with dipstick test-

ing. Urinary pH varies between 4.5 and 8, averaging between 5.5 and 6.5. Normal urine contains <3 RBCs per HPF. Positive dipstick for blood indicates the presence of hemoglobin in the urine. Sensitivity of urine dipsticks for identifying hematuria is >3 RBCs/HPF is >90%. Specificity is lower. Higher false positive rate with the dipstick may be due to contamination with menstrual blood, dehydration.

Hematuria due to a urological cause does not elevate urinary protein. Hematuria of nephrological origin often occurs in association with casts and there is almost always significant proteinuria. Normal, healthy adults excrete about 80-150 mg of protein per day in their urine. Normal protein concentration <20 mg/dl. Proteinuria suggests the presence of renal disease (glomerular, tubulo-interstitial, renal vascular) or multiple myeloma, but it can occur following strenuous exercise. Dipstick test is based on a tetrabromophenol blue dye colour change and green colour develops in the presence of protein of >20 mg/dL.

Leukocyte esterase activity detects the presence of WBC in the urine. Leukocyte esterase is produced by neutrophils and causes a color change in a chromogen salt on the dipstick. Not all patients with bacteriuria have significant pyuria. False negatives causes: concentrated urine, glycosuria, presence of urobilinogen, consumption of large amounts of ascorbic acid. False positives causes: contamination.

Nitrites in the urine suggest the possibility of bacteriuria. They are not normally found in the urine. Many species of gram negative bacteria can convert nitrates to nitrites and these are detected in urine by a reaction with the reagents on the dipstick, which form a red azo dye. The specificity of the nitrite dipstick for detecting bacteriuria is >90%. False positive nitrite testing may be due to contamination. Sensitivity is 35-85%. Test is less accurate in urine containing fewer than 10^5 organisms/ml. Cloudy urine that is positive for WBC and nitrite is very likely to be infected.

1.3.2. Urine microscopy

Urine microscopy is performed with help of phase-contrast microscopy. RBCs derived from the glomerulus are dysmorphic because of their passage through the glomerulus. RBCs derived from tubular bleeding by tubulointerstitial disease and those due to urinary tract diseases have a normal shape. Glomerular bleeding is suggested by the presence of dysmorphic RBCs, casts and proteinuria.

A protein coagulum formed in the renal tubule has an appearance of "cast" in the shape of the tubule. The protein matrix traps tubular luminal contents. If the cast contains only mucoproteins it is called a hyaline cast seen after exercise, heat exposure, pyelonephritis or CRD. RBCs casts contain trapped erythrocytes and are diagnostic of glomerular bleeding, most often due to GN. WBCs casts are seen in acute GN, acute pyelonephritis and acute tubulointerstitial nephritis.

Specific crystal types may be seen in urine and help diagnose stone disease. Cystine crystals establish the diagnosis of cystinuria. Calcium oxalate, uric acid and cystine are precipitated in acidic urine. Crystals precipitated in alkaline urine include calcium phosphate and triple-phosphate.

1.3.3. Urine cytology

Exfoliated cells lying in urine for several hours are degenerated. Such urine specimens are not suitable for cytological interpretation. Cytological examination can be performed on bladder washings with normal saline obtained from the bladder at cystoscopy or following catheterization or from the ureter via a ureteric catheter or ureteroscopy. The urine is centrifuged and the specimen obtained is fixed in alcohol and stained by the Papanicolaou technique. Normal urothelial cells are shed into the urine and under the microscope their nuclei appear regular and monomorphic with diffuse, fine chromatin pattern and single nucleolus.

Causes of a positive cytology report may be by urothelial malignancy (TCC, SCC, adenocarcinoma), previous radiotherapy, previous cytotoxic drug (e.g. cyclophosphamide, busulfan, ciclosporin) treatment and urinary tract stones.

High-grade TCC and CIS exfoliate cells, which look very abnormal. Abnormal urothelial cells have high nuclear/cytoplasmic ratio, hyperchromatic and prominent nuclei.

1.4. ENDOSCOPY

1.4.1. Urethroscopy

To identify and aid in treating urethral pathology, endoscopic inspection via a urethrocytoscope with a 0° lens is helpful. Strictures are characterized by circumferential narrowing. It is difficult to identify the true extent and depth of a stricture solely by vision because scarring can involve deeper tissues. Urethral diverticulum, BPH, bladder neck sclerosis, chronic inflammation can be identified with urethroscopy. Urethroscopy can be used for identification and extraction of foreign bodies or calculi and to access biopsy-suspicious lesions. Urethroscopy allows endoscopic treatment of urethral condylomata.

1.4.2. Cystoscopy

Endoscopic inspection of the bladder requires irrigation, illumination and optics. To optimize a complete examination, the rigid endoscope should be rotated and 0°, 30°, 70° lenses may be required. Suprapubic pressure facilitates inspection of the anterior wall of the bladder. Bladder dome frequently has an air bubble. A systematic approach is required when evaluating the urethra, prostate, bladder walls, dome and neck and ureteral orifices, including location, number, shape and character of efflux. The bladder should be evaluated at different levels of filling. It is only after full distention of the bladder characteristic glomerulations and echymoses are seen in patients with interstitial cystitis. Cystoscopy is informative, especially in assessing prostate size and length of prostatic urethra. Rigid endoscopy results in discomfort, which can be minimized with 1% lidocaine per urethra as a local anesthetic.

Flexible endoscopes decrease patient discomfort and allow for instrumentation in the supine rather than the dorsal lithotomy position. They are now used routinely in an office setting for hematuria/tumor surveillance and double-J stent retrieval. Videoendoscopy with flexible scopes allows patients to visualize normal

and abnormal anatomy and thus helps them understand their pathology. Videendoscopy reduces fluid contact to the urologist. However, there are disadvantages. Flexible scopes have smaller irrigating ports. As a result, changing lenses, assessing residual urine and repeat evacuation of irrigant cannot be completed without entirely removing the endoscope. Rigid endoscopy allows for a greater variety of instrumentation, better optics and increased durability. Endoscopic inspection allows for identification of calculi, foreign bodies and tumors and also is used for catheterization of ureters.

1.4.3. Ureterorenoscopy

URS is endoscopy of the ureter up to the renal pelvis for both diagnostic evaluation and therapeutic intervention. Ureterorenoscopes are endoscopes for retrograde insertion into the ureter. However, they also may be used in an antegrade fashion via a percutaneously established nephrostomy tract. Technical improvements in the last decade have led to the introduction of smaller caliber, more versatile instruments. Rigid ureterorenoscopes are available in sizes 6.9-12.6F and semi-rigid fiberoptic ureterorenoscopes and flexible ureterorenoscopes may be found in sizes 6.2-9.3F. The smallest instruments are for diagnostic procedures only. Larger instruments, with a 3-6F working channel, can accept stone baskets, wire graspers, stone forceps, biopsy forceps and probes for stone disintegration. Flexible ureterorenoscopes follow the topographic anatomy of the ureter more easily and facilitate inspection of middle and lower renal calyces if a deflecting mechanism for the tip of the instrument is provided. Newer flexible ureterorenoscopes have 270° deflecting tips, that allow access to virtually every calyx of the collecting system. However, the use of instrumentation through flexible nephroscopes is limited by the size and flexibility of working instruments such as stone forceps and flexible ureterorenoscopes do not offer the optical quality and durability of rigid instruments.

Indications for Ureterorenoscopy:

Diagnostic indications:

- Lesions of ureter or renal pelvis;
- Hematuria from upper tract;

Therapeutic indications:

- Ureteral stone treatment;
- Direct vision internal ureterotomy of ureteral strictures;
- Endoscopic resection and coagulation of ureteral tumors.

1.5. ULTRASOUND

Sound is the mechanical propagation of pressure changes or waves, through a deformable medium. A wave frequency of 1 cycle/s (cps) is called a Hz. Sound frequencies greater than 20 kHz are beyond the range of human hearing and are called US. Medical sonography uses US to produce images. The frequencies commonly used in medical sonography are between 3.5 and 15 MHz. US waves for imaging are generated by transducers, devices that convert electrical energy to sound energy and vice versa.

These transducers are special piezoelectric crystals that emit US waves when they are deformed by an electrical voltage and, conversely, generate an electrical potential when struck by reflected sound waves. Thus, they act as both sonic transmitters and detectors. In general concept, medical sonography resembles naval submarine sonar. US images are reflection images formed when part of the sound that was emitted by the transducer bounces back from tissue interfaces to the transducer. The sound, reflected by stationary tissues forms the data set for anatomic gray-scale images. The sound reflected by moving structures (eg, flowing blood in a vessel) has an altered frequency due to the Doppler effect. By determining the Doppler shift, vascular flow direction and velocity can be encoded graphically with spectral Doppler or by color Doppler. A more sensitive method of detecting flow, called power mode Doppler, is available on modern equipment. This technique displays the integrated power of the Doppler signal rather than the mean Doppler frequency shift. Direction or velocity of flow is not displayed in the power mode. Reflected sound received by the transducer is converted into electrical signals that are analyzed by computer algorithms and rapidly converted into video images viewed directly on a real-time display. Images are rapidly updated on the display, giving an integrated cross-sectional anatomic depiction of the site studied. Individual frames may be frozen during an examination for motion-free analysis and recording or continuous images may be recorded as digital or conventional video.

US is commonly used for the evaluation of the GUT organs. US is useful for assessing renal size and growth. For example, small echogenic kidneys suggest renal parenchymal disease, whereas a dilated pelvocaliceal system indicates an obstruction. Renal US is useful in detection and characterization of renal masses. US provides an effective method of distinguishing benign cortical cysts from potentially malignant solid renal lesions. US may also be used to follow up mildly complicated cysts detected on CT, for example, hyperdense cysts or cysts with thin septations. The differential diagnosis for echogenic renal masses includes renal stones, AML, renal cortical neoplasms, abscesses and hematomas. All echogenic renal masses should be correlated with clinical history and, if necessary, confirmed with another imaging modality or follow-up US. Thin-section CT showing fat within the renal lesion characterizes it as a benign AML and no further investigation is required. Echogenic lesions smaller than 1 cm are more difficult to characterize by CT owing to partial volume averaging. In the correct clinical setting, follow-up US rather than repeat CT may be more useful.

Doppler sonography is useful for the evaluation of renal vessels, vascularity of renal masses and complications following renal transplant. It can detect renal vein thrombosis, renal artery stenosis and ureteral obstruction prior to the development of hydronephrosis, arteriovenous fistulas and pseudoaneurysms. Perinephric fluid collections following renal transplantation, ESWL or acute obstructions are reliably detected by US.

Applications of bladder sonography include assessment of bladder volume, wall thickness, detection of bladder calculi and tumors. The suprapubic transabdominal approach is most commonly used.

US of the testis has become an extension of the physical examination. The location of the testis allows the use of a high-frequency transducer (10-15 MHz),

which produces excellent spatial resolution. The addition of color Doppler sonography provides simultaneous display of morphology and blood flow. Normal low-resistance intratesticular arterial blood flow is consistently detected with power or color Doppler. US is highly accurate in differentiating intratesticular from extratesticular disease and in the detection of intratesticular pathology. US is commonly used to evaluate acute scrotum syndrome. It can distinguish between inflammatory processes, inguinal hernias and testicular torsion. In addition, epididymitis not responding to antibiotics within 2 weeks should be investigated further with scrotal US to exclude TC.

Developments in other imaging modalities have decreased the use of US in several clinical scenarios. Most patients with suspected renovascular hypertension are evaluated with CT or MRT rather than Doppler US. Unenhanced helical CT is now the initial procedure of choice for the evaluation of the patient with acute flank pain and suspected urolithiasis. In addition to rapidly and sensitively detecting renal stones without the need for i.v. contrast medium, helical CT also has the potential for identifying other causes of flank pain such as appendicitis and diverticulitis. In the past, a combination of KUB and US was advocated for the evaluation of hematuria, but recent studies indicate that, CT with IVU are the preferred modalities to evaluate this common clinical problem.

The main advantages of US are ease of use, high patient tolerance, non-invasiveness, lack of ionizing radiation, low relative cost and wide availability. Disadvantages include a relatively low signal-to-noise level, tissue non-specificity, limited field of view and dependence on the operator's skill and the patient's habitus.

Indications:

- Assessment of hematuria;
- Determination of nature of renal masses: US can differentiate simple benign cysts (smooth, well-demarcated wall, reflecting no echoes) from solid masses (almost always malignant cystic masses with solid components or multiple septae or calcifications are malignant), from those casting an 'acoustic shadow';
- The presence/absence of hydronephrosis in patients with abnormal renal function;
- US guided nephrostomy insertion in patients with hydronephrosis and renal impairment or with infected, obstructed kidneys;
- US guided placement of a suprapubic catheter;
- TRUS investigation of prostate size and pathology;
- To assist prostate biopsy;
- Investigation of azoospermia;
- To image the urethra and establish the depth and extent of spongiofibrosis in urethral stricture disease;
- To differentiate benign lesions (hydrocele, epididymal cyst) from malignant testicular tumours (solid, echo poor or with abnormal echo pattern);
- To establish the presence/absence of testicular blood flow when combined with power Doppler in suspected torsion;
- Assessment of testicular trauma;

- Investigation of infertility in the patients with varicoceles and testicular atrophy;
- PVR urine volume measurement.

1.6. RADIOLOGICAL IMAGING

1.6.1. A plain film

A plain film of the abdomen, frequently called a KUB film, is the simplest uro-radiologic examination. It is generally the preliminary film in extended radiologic examinations. It may demonstrate osseous abnormalities, abnormal calcifications or large soft-tissue masses. Kidney outlines usually can be seen on the plain film, so that their size, number, shape and position can be assessed. The length of the kidney is the most widely used and most convenient radiographic measurement. The average adult kidney is about 12-14 cm long. In children older than 2 years of age, the length of a normal kidney is approximately equal to the distance from the top of the first to the bottom of the fourth lumbar vertebral body. Patterns of calcification in the urinary tract may help to identify specific diseases.

KUB is used for detection of stones and determination of their size and their location within the kidneys, ureters and bladder. If there is intrarenal calcification and it moves with the kidney, this is renal stone. If in doubt get an US. Stone has the characteristic 'acoustic shadow' within the kidney. IVU or CT will confirm diagnosis. CTU or IVU, which relate the position of the opacity to the anatomical location of the ureters, are required to make a definitive diagnosis of a ureteric stone. However, once the presence of a ureteric stone has been confirmed by another imaging study (CTU or IVU) and as long as it is radio-opaque enough and large enough to be seen, plain radiography is a good way of following the patient to establish whether the stone is progressing distally, down the ureter. It is not useful for 'following' ureteric stones that are radiolucent, small (generally a stone must be 3-4 mm to be visible on plain X-ray) or when the stones pass through the ureter as it lies over the sacrum. Ability of KUB X-ray to 'see' stones is also dependent on amount of overlying bowel gas. Opacities that may be confused with stones on plain radiography are: calcified lymph nodes and pelvic phleboliths (round, lucent centre, usually below the ischial spines).

1.6.2. Intravenous urography

A KUB is obtained before contrast is given to look for calcification overlying the region of GUT organs. Intravascular contrast is administered followed by a series of examinations, to image their anatomy and pathology and to give some indication of renal function. Nephrogram phase is first phase of IVU. Film taken immediately following i.v. administration of contrast shows peak nephrogram density. The contrast medium is concentrated in the pelvicalyceal system and thus this 'pyelogram' phase is much denser than the nephrogram phase. The pyelogram phase can be made more dense by dehydrating the patient prior to contrast administration.

Side-effects of administration of i.v. contrast media occur in 1% of patients given non-ionic and 5% given ionic contrast media. The most serious reactions

represent an anaphylactic reaction - hypotension with flushing of the skin (marked peripheral vasodilatation), edema (face, neck, body and limbs), bronchospasm, urticaria. Rarely, cardiac arrest can occur. A contrast reaction is more likely to occur in patients with an iodine allergy, previous contrast reaction, asthma, multiple other allergies and heart disease and is less likely with non-ionic contrast media. Steroid premedication at least 12 h before can reduce the risk of a contrast reaction. Contrast media are also nephrotoxic. 10% of patients with a raised Cr will develop an increase in Cr after an IVU. This is more likely in DM, with dehydration and with large contrast doses. The increase in Cr usually resolves spontaneously.

Indications for imaging:

- Investigation of hematuria: detection of renal masses, filling defects within the collecting system of the kidney and within the ureters, which may be stones or TCCs;
- Localization and confirmation of calcification overlying the urinary tract;
- Investigation of patients with loin pain and suspected ureteric colic;
- Identification of congenital urinary tract abnormalities;
- Identifying of strictures.

1.6.3. Retrograde urography

This is a invasive procedure that requires cystoscopy and the placement of catheters in the ureters. A radiopaque contrast medium is introduced into the ureters or renal collecting structures through the ureteral catheters and radiographs of the abdomen are taken. Some type of local or general anesthesia should be used. Retrograde urograms may be necessary if IVU or CT urogram are unsatisfactory, if the patient has a history of adverse reaction to i.v. contrast media or if other methods of imaging are unavailable or inappropriate.

1.6.4. Antegrade urography

Outlining the renal collecting structures and ureters by percutaneous urography is occasionally done when excretory or retrograde urography has failed or is contraindicated or when there is a PNS tube in place and delineation of the collecting system is desired.

1.6.5. Cystography

Retrograde filling of the bladder, via a catheter, with contrast. Identifies vesicocolic and vesicovaginal fistulae, extraperitoneal and/or intraperitoneal bladder injuries.

1.6.6. Urethrography

The urethra can be imaged radiographically by retrograde injection of radiopaque fluid or in antegrade fashion with VCUG. The antegrade technique is required when lesions of the posterior urethra, for example, posterior urethral valves, are suspected. The retrograde technique is more useful for examining the anterior urethra in the patients with anterior urethral stricture.

1.7. COMPUTED TOMOGRAPHY

In CT scanning, a thin, collimated beam of X-rays is passed through the patient and captured by an array of solid-state or gas detectors.

The interconnected X-ray source and detector system are rapidly rotated in the gantry around the patient. Computers integrate the collected X-ray transmission data to reconstruct and show a cross-sectional tomogram.

Spiral CT uses a slip-ring gantry that rotates continuously while the patient moves constantly through the collimated X-ray beam. Spiral CT technology affords the ability to image during specific phases of contrast bolus enhancement, including the ability to perform CT angiography and allows improved image reformations. Multidetector or multislice, helical CT scanners have an array of multiple rows of detectors in a helical scanner such that multiple scan images can be acquired per gantry rotation and as a by-product thinner sections and higher resolution achieved. Such systems are optimally paired with powerful computer workstations so that high-quality 3D and multiplanar reformations can be quickly generated and analyzed.

Renal CT is most commonly used in the evaluation of acute flank pain, hematuria, renal abscess and trauma and in the characterization and staging of renal neoplasm. CT evaluation of renal anatomy and pathology generally requires i.v. injection of iodinated contrast media. Noncontrast scans are needed, however, when renal or perirenal calcification, hemorrhage or urine extravasation is suspected, since scans obtained after the administration of contrast media may mask these abnormalities. Also, pre- and postcontrast scans are required to determine whether a mass is solid or cystic. A nephrogram phase with medullary enhancement is reached within 60 seconds. Excretion of contrast material into the collecting structures can be expected within 2–3 minutes after initiation of contrast administration.

Although CT can detect ureteral tumors, the current role of CT in the evaluation of the ureters is predominantly for tumor staging and evaluation of the cause and level of obstruction. Helical CT without oral or i.v. contrast is the preferred imaging modality for patients with renal colic or suspected urolithiasis.

In the evaluation of the urinary bladder, CT is used primarily in staging bladder tumors and in diagnosing bladder rupture following trauma. Performing CT after filling the bladder with dilute contrast medium (CT cystography) improves the sensitivity of this modality for detecting tumors and bladder rupture.

For prostate diseases, CT is used for detection of lymphadenopathy and to delineate prostatic abscesses. CT is used for detection of the abdominal location of suspected UDT, for staging of testicular tumors and in the search for nodal or distant metastasis. The addition of delayed CT imaging 10–15 minutes post i.v. contrast-enhanced CT shows high sensitivity and specificity in characterizing adrenal lesions. Benign adenomas, including lipid poor adenomas, show brisk contrast washout. CT or MRT are replacing conventional angiography for diagnostic examinations.

The main advantages of CT include a wide field of view, the ability to detect subtle differences in the X-ray attenuation properties of various tissues, good spatial resolution, anatomical cross-sectional images and operator independence. A

considerable amount of diagnostic information available from CT scans depends on patterns of contrast enhancement, so a carefully tailored examination is essential. Reformatted helical image data in different planes and in 3D has made renal CT imaging, with renal angiography and urography, valuable in preoperative planning, such as for partial nephrectomy.

Limitations of CT include restriction to the transaxial plane for direct imaging, tissue nonspecificity, low soft-tissue contrast resolution and the need for contrast media. Finally, radiation exposure is a consideration with multisequence CT imaging. On average, current CT urography technique exposes the patient to approximately 1.5 times the radiation dose of conventional urography. Ongoing studies evaluating reduced exposure and modifying protocols are under way.

1.8. MAGNETIC RESONANCE TOMOGRAPHY

Clinical MRT has its basis in the nuclear properties of the hydrogen atoms in the body. Hydrogen nuclei, when considered as aggregates, sometimes referred to as "protons," behave like tiny magnets, with net polarity (positive and negative) oriented along an axis at any given point in space. Ordinarily, the axes of the hydrogen nuclei in the body are randomly oriented. However, if the nuclei are placed in a strong magnetic field, like that produced in an MRT scanner, they precess and wobble like a spinning top around the lines of magnetic force. When hydrogen nuclei in a strong magnetic field are additionally stimulated by short, pulsed radio waves of appropriate frequency, they absorb energy and invert their orientation with respect to the magnetic field. At the termination of radiofrequency pulses, the hydrogen nuclei return at various rates to their original orientation within the magnetic field, emitting energy in the form of radio waves. This phenomenon is called nuclear magnetic resonance. The emitted weak radio signals from the resonating hydrogen nuclei are received by sophisticated antenna or coils and transformed with various computer programs into cross-sectional images. Different MR signal intensities reflect different hydrogen densities in body tissues, as well as differing physical, cellular and chemical microenvironments and also flow characteristics.

Applications for MR in renal imaging include demonstration of congenital anomalies, diagnosis of renal vein thrombosis and diagnosis and staging of RCC. MR angiography is useful in evaluating renal transplant vessels, renal vein tumor or thrombosis and renal artery stenosis. The use of contrast media in MRT of the kidney has broadened clinical applications. Using bolus injection of gadolinium and rapid sequence imaging, both anatomy and function of the kidney can be assessed. Gadolinium, similar to iodine contrast media, is an extracellular contrast agent primarily excreted by glomerular filtration. Compared to iodinated contrast media, gadolinium has superior renal tolerance in patients with preexisting CRF. Iodinated contrast agents used in radiography and CT increase attenuation linearly with their concentration. The effect of gadolinium on MR tissue signal intensity is more complex, though in general at lower concentrations gadolinium causes an increase in signal intensity. The use of gadolinium has extended the application of MRT to the evaluation of renal obstruction and the detection and characterization of renal

tumors. Gadolinium enhanced MRT is useful for assessing renal artery stenosis and for evaluating potential renal donors. MRT is used primarily to stage bladder tumors and to differentiate between benign bladder wall hypertrophy and infiltrating malignant neoplasm. In imaging the prostate gland, MRT is principally used to stage patients with PC. MRT of the testis is appropriate when other imaging studies are inconclusive and is applicable to the evaluation of UDT, trauma, epididymoorchitis and tumors. This technique is commonly used to characterize adrenal masses.

Advantages of MRT include direct imaging in any plane desired, choice of large or small field of view, excellent soft-tissue contrast, imaging without exposure to ionizing radiation and less operator dependence. MRT can image blood vessels and the GUT without contrast material. MR scanning, however, is not without drawbacks. The scanning time is relatively slow and as a result image clarity is often inferior compared with CT. Absolute contraindications to MRT include the presence of intracranial aneurysm clips, unless the referring physician is certain that the clip is made of a nonferromagnetic material, intraorbital metal fragments and any electrically, magnetically or mechanically activated implants. Relative contraindications such as pregnancy should always be viewed in the light of risk versus benefit of the examination.

1.9. RADIOISOTOPE IMAGING AND RENAL FUNCTION ASSESSEMENT

Glomerular filtration rate

When we talk about measuring kidney function, what we mean is measurement of GFR. This is regarded as the best measure of kidney function and we grade the degree of renal impairment and renal failure according to the GFR. Normal GFR in young men is approximately 130 ml/min per 1.73 m² of body surface area. In young women it is 120 ml/min per 1.73 m² of body surface area.

The ideal filtration marker is excreted by filtration alone. Exogenous markers that can be used to measure include inulin, iothalamate, EDTA, iohexol. Measurement of GFR using exogenously administered markers is complex and expensive and is difficult to do in routine clinical practice.

Urinary clearance of endogenous markers, such as Cr, can be used to estimate GFR. Cr is freely filtered at the glomerulus. A timed urine collection and measurement of serum Cr concentration allows calculation of GFR according to the formula:

$$\text{Clearance (GFR)} = U \times V / P,$$

where U is the concentration of Cr in urine, P the concentration in plasma and V is the urine flow.

As an alternative, estimation of GFR can be made from simple measurement of serum Cr, since the main mechanism of Cr excretion is by glomerular filtration and GFR has a reciprocal relationship with serum Cr. Thus, as GFR falls, indicating worsening renal function, Cr rises. However, Cr is not the ideal filtration marker, since it is also excreted by proximal tubular secretion, as well as by glomerular filtration and therefore Cr clearance exceeds GFR, i.e. Cr clearance tends to overestimate GFR.

A variety of organic compounds can be “labeled” with a radioactive isotope that emits gamma rays, allowing the radiation to penetrate through tissues and reach a “gamma” camera placed adjacent to the patient. The most commonly used radioisotope is technetium 99Tc. The excretion characteristics of the organic compound to which the 99Tc is bound determine the clinical use. 99Tc is bound to mercaptoacetyl triglycine. Over 90% MAG3 becomes bound to plasma proteins following i.v. injection. It is excreted from the kidneys principally by tubular secretion. Following i.v. injection MAG3 is very rapidly excreted. Appearing in the kidney within 15 s. of the injection and starting to appear in the bladder within about 3 min. Approximately 2/3 of the injected dose of MAG3 is taken up by the kidneys with each passage of blood through the kidney. The radioactivity over each kidney thus increases rapidly. The peak of radioactivity represents the point at which delivery of MAG3 to the kidney from the renal artery is equivalent to excretion of MAG3. The radioactivity starts to decline as excretion outstrips supply. Thus, a time-activity curve can be recorded for each kidney. This time-activity curve is known as a renogram.

Images are collected onto a film at 30 s. intervals for the first 3 min and then at 5 min intervals for the remainder of the study (usually a total of 30 min).

A normal renogram has 3 phases. First phase: a steeply rising curve lasting 20-30 s. Second phase: a more slowly rising curve, rising to a peak. If the curve does not reach a peak the second phase is said to rise continually. A normal second phase ends with a sharp peak. Third phase: a curve that descends after the peak. There can be no third phase if there is no peak. No comment is made about the first phase. The second phase is described as being absent, impaired or normal. The third phase is described as being absent, impaired or normal.

The time to the peak depends on urine flow and level of hydration and is a crude measure of the time it takes the tracer to travel through the parenchyma of the kidney and through the renal pelvis. The time to the peak of the renogram normally varies between 2 and 4.5 min.

If the renogram continues beyond the time at which the peak should normally occur, then there may be a distal obstruction. In this situation, an injection of 40mg of furosemide is given and if the curves start to fall rapidly, this is taken as proof that there is no obstruction. If it continues to rise, there is obstruction. If it remains flat (neither rising or falling), this is described as an “equivocal” result.

Renography is used to characterize “split” renal function. This is % of function contributed by each kidney. Determination of presence of renal obstruction based on shape of renogram curve.

There is also radioisotope imaging with DMSA, which is labelled with 99Tc. It is taken up by the proximal tubules and retained there, with very little being excreted in the urine. A “static” image of the kidneys is thus obtained. It demonstrates whether a “lesion” contains functioning nephrons or not.

Renography with DMSA is used also to characterize “split” renal function and detection of scars in the kidney. These appear as defects in the cortical outline, representing areas in which the radioisotope is not taken up.

Radioisotope imaging with 99Tc -labelled MDP is used in clinical situa-

tions, where there is increased blood supply and increased osteoblastic activity in areas of bone. There are many causes of a focal increase in isotope uptake - bone metastases, site of fractures, osteomyelitis, TB, benign bone lesions. Metastases from PC are characterized by their predilection for the spine and the fact that they are multiple.

1.10. UROFLOWMETRY

Uroflowmetry is used for measurement of flow rate. Provides a visual image of the “strength” of a patient’s urinary stream. Urine flow rate is measured in ml/s and is determined using electronic flowmeters. These flowmeters are able to provide a print-out recording the voided volume, Qmax and time taken to complete the void, together with a record of the flow pattern. Maximum flow rate, Qmax, is influenced by the volume of urine voided, by the contractility of the patient’s bladder and by the resistance of their urethra.

Uroflowmetry alone cannot tell you why the flow is abnormal. It cannot distinguish between low flow due to BOO and that due to a poorly contractile bladder.

1.11. CYSTOMETRY, PRESSURE FLOW STUDIES AND VIDEOCYSTOMETRY

Cystometry is the recording of bladder pressure during bladder filling. PFS is the simultaneous recording of bladder pressure during voiding. Videocystometry is fluoroscopy (X-ray screening) combined with PFS during voiding.

These techniques provide the most precise measurements of bladder and urethral sphincter behaviour during bladder filling and during voiding. Cystometry precedes the PFS. Bladder pressure (Pves, measured by a urethral or suprapubic catheter) and abdominal pressure (Pabd, measured by a pressure line inserted into the rectum) are recorded as the bladder fills (cystometric phase) and empties (voiding phase) and flow rate is simultaneously measured during the voiding phase. The pressure developed by the bladder muscle (Pdet), cannot be directly measured, but it can be derived by subtracting abdominal pressure from the pressure measured within the bladder (the intravesical pressure). This allows the effect of rises in intra-abdominal pressure caused by coughing or straining to be subtracted from the total (intravesical) pressure, so that a “pure” detrusor pressure is obtained.

All pressures are recorded in cm H₂O and flow rate is measured in ml/s. The pressure lines are small-bore, fluid-filled catheters attached to an external pressure transducer or catheter-tip pressure transducers can be used.

A computerized print-out of intravesical pressure (Pves), intra-abdominal pressure (Pabd) and detrusor pressure (Pdet) and flow rate (Qmax) is obtained. During bladder filling, the presence of OAB contractions can be detected. During voiding, the key parameters are Qmax and the detrusor pressure at the point at which Qmax is reached, Pdet Qmax. This pressure, relative to Qmax, can be used to define the presence of BOO by using a variety of nomograms.

1.12. PSA

PSA is a 34KD glycoprotein enzyme produced by the columnar acinar and ductal prostatic epithelial cells. It is a member of the human kallikrein family and its function is to liquefy the ejaculate, enabling fertilization. PSA is present in both benign and malignant cells, although the expression of PSA tends to be reduced in malignant cells and may be absent in poorly differentiated tumors. Large amounts are secreted into the semen and small quantities are found in the urine and blood.

The function of serum PSA is unclear, although it is known to liberate the insulin-like growth factor type 1 from one of its binding proteins. 75% of circulating PSA is bound to plasma proteins (complexed PSA) and metabolized in the liver, while 25% is free and excreted in the urine. Complexed PSA is stable, bound to alpha-1 antichymotrypsin and alpha-2 macroglobulin. Free PSA is unstable, recently found to consist of two iso-forms: pro-PSA is a peripheral zone precursor, apparently elevated in the presence of PC and BPSA is the TZ precursor and associated with BPH. The current normal range for the serum PSA assay in men is 2,5-3,0 ng/mL. Though this varies with age, prostatitis, BPH, ejaculation, prostate massage. In the absence of PC, serum PSA concentrations also vary physiologically, according to race and prostate volume.

2.1. KIDNEY STONES

The prevalence of renal stone disease is determined by endogenous and environmental factors. A combination of factors and genetic predisposition often contribute to risk of stone formation.

Endogenous factors:

- The peak incidence of stones occurs between the ages of 20-50 years;
- Males are affected 3 times as frequently as females;
- Urinary tract abnormalities with urine stasis;
- UTIs;
- Genetic factors and metabolic abnormalities. It is reported that 1/4 of patients with kidney stones has a family history of stone disease.

Environmental factors:

- Geographical location and climate: while renal stone disease is more common in hot climates, some endogenous populations of hot climates have a low incidence of stones and many temperate areas have a high incidence of stones. Ureteric stones become more prevalent during the summer, presumably because of higher urinary concentration in the summer encourages crystallization. Concentrated urine has a lower pH, encouraging cystine and uric acid stone formation. Exposure to sunlight may also increase endogenous vitamin D production, leading to hypercalciuria;
- Low fluid intake (<1000 ml/day) predisposes to stone formation. Increasing water “hardness” with high calcium content may reduce risk of stone formation, by decreasing urinary oxalate;
- High animal protein intake increases risk of stone disease due to high urinary oxalate and uric acid, low pH and low urinary citrate.
- High salt intake causes hypercalciuria.
- Contrary to conventional teaching, low calcium diets predispose to calcium stone disease and high calcium intake is protective;
- Sedentary lifestyle predispose to stones compared with active life.

Types and predisposing factors of the kidney stones

Stones may be classified according to composition, X-Ray appearance, size and shape.

Other rare radiolucent stone types: indinavir (a protease inhibitor used for treatment of HIV), triamterene (a relatively insoluble potassium sparing diuretic, most of which is excreted in urine), xanthine stones.

Three broad categories of stones are described, based on their X-Ray appearance. This gives some indication of the likely stone composition and helps, to some extent, to determine treatment options.

Table 2.1. Stones classification

Stones	Frequency
Calcium oxalate	80-85%
Uric acid stones	5-10%
Calcium phosphate + calcium oxalate	8-10%
Pure calcium phosphate	Rare
Struvite (infection stones)	5-20%
Cystine stones	1%

Radio-opaque

Opacity implies the presence of substantial amounts of calcium within the stone. Calcium phosphate stones are the most radiodense stones, being almost as dense as bone. Calcium oxalate stones are slightly less radiodense.

Relatively radiolucent

Cystine stones are relatively radiodense because they contain sulphur. Magnesium ammonium phosphate (struvite) stones are less radiodense than calcium containing stones.

Completely radiolucent

Uric acid, cystine, triamterene, xanthine and indinavir stones are radiolucent. Stones can be characterized by their size. Stones which grow to occupy the renal collecting system are known as staghorn calculi. They are most commonly composed of struvite - magnesium ammonium phosphate and being caused by UTIs and forming under the alkaline conditions induced by urea-splitting bacteria. They may be composed of uric acid, cystine or calcium oxalate monohydrate.

Mechanisms of formation

Most common urine is saturated with calcium and oxalate, when the product of the concentrations of calcium and oxalate exceeds the solubility product. Above the solubility product, crystals of calcium and oxalate should form, but they do not because of the presence of inhibitors of crystallization. However, above a high concentration of calcium and oxalate, inhibitors of crystallization become ineffective and crystals of calcium oxalate start to form. The concentration of calcium and oxalate at which crystallization starts is known as the formation product and the urine is said to be supersaturated with the substances.

The ability of urine to hold more solute in solution than can pure water is due to the presence of various inhibitors of crystallization. Citrate forms a soluble complex with calcium, preventing it from combining with oxalate or phosphate to form stones. Other inhibitors of crystallization include magnesium, glycosaminoglycans and Tamm-Horsfall protein.

Periods of intermittent supersaturation of urine with various substances can occur as a consequence of dehydration and following meals.

The earliest phase of crystal formation is known as nucleation. Crystal nuclei usually form on the surfaces of epithelial cells and proteins or on other crystals. Aggregation - is formation of clumps. Citrate and magnesium not only inhibit crystallization but also inhibit aggregation.

Symptoms, signs and diagnosis

Kidney stones may present with acute or chronic symptoms or be found incidentally during investigation of other problems. Presenting symptoms include pain or hematuria (microscopic or macroscopic). Struvite staghorn calculi classically present with recurrent UTIs. Malaise, weakness and loss of appetite can also occur if patient has CRF. Less commonly, struvite stones present with infective complications (abscess, purulent pyelonephritis, pyonephrosis, urosepsis).

Plain X-Ray: calculi that contain calcium are radiodense. 15-20% of stones are radiolucent.

Sensitivity of renal US for detecting of renal calculi is ~90-95%. A combination of plain X-Ray and renal US is a useful screening test for detection of renal calculi.

IVU will detect "filling defect, but increasingly being replaced by CT.

CT is a very accurate method of diagnosing all stones. Allows accurate determination of stone size, location and good definition of pelvicalyceal anatomy.

Treatment

Watchful waiting

The traditional indications for intervention are pain, UTIs and obstruction. It is not necessary to treat every kidney stone. As a rule, the younger the patient, the larger the stone and the more symptoms it is causing, the more inclined are we to recommend treatment. "Silent" stones could drop into the ureter causing ureteric colic or it could increase in size and affect kidney function or cause pain.

Another factor determining the need for treatment is the patient's job. It is sensible to warn any one whose job entrusts them with the safety of others (pilots, drivers) that they are not fit to carry out these occupations until stone free.

Some stones are definitely not suitable for watchful waiting. Untreated struvite staghorn calculi will eventually destroy the kidney if untreated and are a significant risk to the patient's life. Watchful waiting is therefore not recommended for staghorn calculi unless patient co-morbidity is such that surgery would be a higher risk than watchful waiting. Historical series suggest that many patients with staghorn calculi who did not undergo surgical removal died of CRF, urosepsis, pyonephrosis, perinephric abscess.

Medical therapy

Uric acid and cystine stones are potentially suitable for dissolution therapy, but calcium within either stone type reduces the chances of successful dissolution.

Urine of patients with purine - rich diet is frequently supersaturated with uric acid. Many patients who form uric acid stones have gout. The other do so because of a high protein and low fluid intake.

Uric acid stones form in concentrated, acid urine. Dissolution therapy is based on hydration, urine alkalinization, allopurinol and diet. The aim being to reduce urinary uric acid saturation. It is recommended to maintain a high fluid intake with urine output 2-3L per day, "alkalinization" the urine to pH 6.5-7. In those with hyperuricemia or urinary uric acid excretion >1200 mg/day, allopurinol 300-600 mg/day is used, which inhibits conversion of hypoxanthin and xanthine to uric acid. Dissolution of large stones is possible with this regimen.

Cystinuria is an inherited defect for the amino acids cystine ornithine, arginine and lysine transport, leading to excessive urinary excretion of cystine. Most cystinuric patients excrete about 1g of cystine per day, which is well above the solubility of cystine by acidic pH. Patients with cystinuria most common present with renal calculi. It is recommended the reduction of cystine excretion. Dietary restriction of the cystine precursor amino acid methionine and also of sodium intake to excretion <100 mg/day. Options are: alkalinization of the urine to >pH 7,5 to increase solubility of cystine, maintenance of a high fluid intake and use of drugs which convert cystine to more soluble compounds. Cystine stones are very hard and are therefore relatively resistant to ESWL. Nonetheless, for small cystine stones, a substantial proportion will still respond to ESWL. Flexible URS and PCNL are used where ESWL fragmentation has failed.

ESWL

This is technique of focusing externally generated shock waves at a stone. There are many methods of shock waves generations.

By electromagnetic method there are two electrically conducting cylindrical plates, which are separated by a thin membrane of insulating material. Passage of an electrical current through the plates generates a strong magnetic field between them, the subsequent movement of which generates a shock wave. An "acoustic" lens is used to focus the shock waves.

X-ray and US or a combination of both are used to locate the stone on which the shock waves are focused.

Likelihood of fragmentation with ESWL depends on stone size and location, anatomy of renal collecting system, degree of obesity and stone composition. ESWL is most effective for stones <2 cm in diameter and less effective for stones >2 cm diameter, lower pole stones, stone in a calyceal diverticulum with absent drainage and those very hard cystine or calcium oxalate monohydrate stones.

Stone free rates for solitary kidney stones are app. 80% for stones <1 cm in diameter, 60% for those between 1-2 cm and 50% for those >2 cm in diameter. Lower stone free rates as compared with open surgery or PCNL are accepted because of the minimal morbidity of ESWL.

ESWL causes a certain amount of structural and functional renal damage. Microscopic or macroscopic hematuria and edema are common, perirenal hematoma less so.

Absolute contraindications: pregnancy, uncorrected blood clotting disorders, UTIs, obstruction, high blood pressure.

Flexible URS and laser lithotripsy

The development of small-calibre ureteroscopes with active deflecting mechanisms and instrument channels, in combination with the development of laser technology, small-diameter laser fibres and stone baskets and graspers, has opened the way for intracorporeal, endoscopic treatment of kidney and urethral stones. Access to the entire collecting system is possible with modern instruments. The holmium: YAG laser has a minimal effect on tissues at distances of 2-3 mm from the laser tip and so “collateral” tissue damage is minimal with this laser type.

Flexible URS and laser fragmentation offers a more effective treatment option compared with ESWL, with a lower morbidity than PCNL, but usually requires a general anaesthetic. It can also allow access to areas of the kidney where ESWL is less efficient or where PCNL cannot reach. It is most suited to stones <2 cm in diameter.

PCNL

PCNL is the removal of a kidney stone via a “track”, developed between the surface of the skin and the collecting system of the kidney. The first step requires “inflation” of the renal collecting system (pelvis and calyces) with fluid or air instilled via a ureteric catheter inserted cystoscopically. This makes subsequent percutaneous puncture of a renal calyx with a nephrostomy needle easier. Once the nephrostomy needle is in the calyx, a guide wire is inserted into the renal pelvis to act as a guide over which the “track” is dilated. An access sheath is passed down the track and into the calyx and through this a nephroscope can be advanced into the kidney. An ultrasonic or laser lithotripsy probe is used to fragment the stone and remove the debris.

A posterior approach is most commonly used: below the 12th rib to avoid the pleura and far enough away from the rib to avoid the intercostal vessels and nerve. The preferred approach is through a posterior calyx, rather than into the renal pelvis, because this avoids damage to posterior branches of the renal artery which are closely associated with the renal pelvis. General anaesthesia is usual, though regional or even local anaesthesia can be used.

PCNL is generally recommended for stones >3 cm in diameter, those that have failed ESWL and/or an attempt at flexible URS and laser treatment. It is the first-line option for staghorn calculi, with ESWL and/or repeat PCNL being used for residual stone fragments.

For stones 2-3 cm in diameter, options include ESWL with a JJ stent in situ, flexible URS with laser treatment and PCNL. PCNL gives the best chance of complete stone clearance with a single procedure, but this is achieved at a higher risk of morbidity. Some patients will opt for several sessions of ESWL or flexible URS/laser treatment and the possible risk of ultimately requiring PCNL because of failure of ESWL or laser treatment, rather than proceeding with PCNL “up front”.

For small stones, the stone-free rate after PCNL is in the order of 90-95%. For staghorn stones, the stone-free rate of PCNL, when combined with post-operative ESWL for residual stone fragments, is in the order of 80-85%.

Open stone surgery

Indications are very limited:

- Complex stone burden;
- Failure of endoscopic treatment;
- Anatomic abnormality that precludes endoscopic surgery;
- Body habitus that precludes endoscopic surgery;
- Patient request for a single procedure where multiple PCNLs might be required for stone clearance;
- Non-functioning kidney, nephrosclerosis and pyonephrosis (nephrectomy).

2.2. URETERIC STONES

Symptoms and signs

Ureteric stones usually present with sudden onset of severe flank pain which is colicky in nature. It may radiate to the groin as the stone passes into the lower ureter. The patient moves around, trying to find a comfortable position. Patients with conditions causing peritonitis (e.g. appendicitis, a ruptured ectopic pregnancy) lie very still: movement and abdominal palpation are very painful.

Many patients with ureteric stones have microscopic or macroscopic hematuria, but 10-30% have no blood in their urine (complete unilateral block). Remember, blood in the urine on dipstick testing or microscopy may be a coincidental finding because of non-stone urological disease (e.g. neoplasm, UTIs).

The most important aspect of examination in a patient with a ureteric stone confirmed on imaging is to measure their temperature. If the patient has a stone and a fever, they have obstructive pyelonephritis. A fever in the presence of an obstructing stone is an indication for urine and blood culture, i.v. fluids and antibiotics and drainage (stenting or nephrostomy) if the fever does not resolve within a matter of hours.

Diagnosis

The IVU for many years the mainstay of imaging in patients with flank pain. Currently IVU has been replaced by CT urography.

If you only have access to IVU, remember that it is contraindicated in patients with a history of previous contrast reactions and should be avoided in those with high fever, a strong history of allergies or asthma. Patients with allergies will require high-dose steroids 24h before the IVU. Patients taking metformin for DM should stop this for 48h prior to an IVU. Clearly, being able to perform an alternative test, such as CT in such patients, is very useful.

Abdominal US is used in all patients, who present with flank pain suggestive of a possible stone, to exclude serious pathology such as a leaking abdominal aortic aneurysm and to demonstrate any other gross abnormalities due to non-stone associated flank pain. There is hydronephrosis due to ureteric obstruction.

Plain abdominal X-Ray and renal US are not sufficiently sensitive or specific for their routine use for diagnosing ureteric stones.

Treatment

While appropriate imaging studies are being organized, pain relief should be given: NSAIDs (e.g. diclofenac) by intramuscular or i.v. injection, by mouth or per rectum. This drug provides rapid and effective pain control. Analgesic effect may be partly anti-inflammatory, partly by reducing ureteric peristalsis. Where NSAIDs are inadequate, opiate analgesics are added. There is no need to encourage the patient to drink copious amounts of fluids, nor to give them large volumes of fluids i.v. in the hope that this will “flush” the stone out. Excess urine output will tend to cause a greater degree of hydronephrosis in the affected kidney, which may make ureteric peristalsis even less efficient than it already is.

Watchfull waiting

In many instances, small ureteric stones (3-5 mm) will pass spontaneously within days or a few weeks, with analgesic supplements for exacerbations of pain. Chances of spontaneous stone passage depend principally on stone size. 68% of stones 5 mm or less will pass spontaneously and 47% of stones 6-10 mm in diameter will pass spontaneously. Average time for spontaneous stone passage for stones 4-6 mm in diameter is 3-4 weeks. Stones that have not passed in 1 month are unlikely to do so. Therefore, accurate determination of stone size on plain abdominal X-Ray or by CT helps predict chances of spontaneous stone passage.

Medical expulsive therapy

There is growing evidence for the efficacy of alpha adrenoreceptor blockers in patients with lower ureteric stones. These increase spontaneous stone passage rates, reduce stone passage time and reduce frequency of ureteric colic. MET is contraindicated where there is clinical evidence of obstructive pyelonephritis and urosepsis or deteriorating renal function. If a trial of MET is used, warn patients of the risks (drug side effects, possible need for intervention in the form of ESWL, URS or JJ-stenting). Arrange periodic plain X-Ray or US to monitor stone position.

Relieving of the obstruction

Temporary relief of the obstruction can be obtained by insertion of a JJ stent or PNS tube. JJ stent insertion or PNS tube can be done quickly, but the stone is still present. It may pass down and out of the ureter with a stent or nephrostomy in situ, but in many instances it simply sits where it is and subsequent definitive treatment is still required. While JJ stents can relieve stone pain, they can cause bothersome irritative bladder symptoms with pain in the bladder, frequency and urgency. JJ stents do make subsequent stone treatment in the form of URS technically easier by causing passive dilatation of the ureter.

Indications for drainage:

- Pain that fails to respond to analgesics or recurs and cannot be controlled with additional pain relief;
- Bacteriuria in the presence of an obstructing stone can lead to the development of pyelonephritis and urosepsis. Where intervention is planned (ESWL or ureteroscopy), appropriate antibiotics should be given in advance of the treatment

- Obstructive pyelonephritis: have a low threshold for draining the kidney (both stenting and PNS);
- Impaired renal function and anuria due to solitary kidney obstructed by a stone, bilateral ureteric stones or pre-existing renal impairment which gets worse as a consequence of a ureteric stone;
- Prolonged unrelieved obstruction: this can result in long-term loss of renal function. Generally speaking the period of watchful waiting for spontaneous stone passage tends to be limited to 4-6 weeks;
- Social reasons: young, active patients may be very keen to opt for surgical treatment because they need to get back to work or their childcare duties. Airline pilots and some other professions are unable to work until they are stone free.

Treatment options for ureteric stones:

- ESWL in situ or after JJ stent insertion;
- URS;
- Open ureterolithotomy;
- Laparoscopic ureterolithotomy;
- Percutaneous antegrade URS

Nowadays, the advent of ESWL and of smaller ureteroscopes with efficient stone fragmentation devices has made stone treatment and removal a far less morbid procedure, with a far smoother and faster post-treatment recovery. It is easier for both the patient and the surgeon to opt for intervention, in the form of ESWL or surgery, as a quicker way of relieving them of their pain.

It is clearly important for the surgeon to inform the patient of the outcomes and potential complications of intervention, particularly given the fact that many of stones would pass spontaneously if left a little longer, particularly now there is evidence for MET.

Blind or under radiographic “basketing of stones” is a historical treatments because of the potential for serious ureteric injury is significant.

Smaller ureteroscopes with improved optics and larger instrument channels and the advent of holmium laser lithotripsy have improved the efficacy of ureteroscopic stone fragmentation and reduced its morbidity. As a consequence, many surgeons and patients will opt for URS, with its potential for a “one-off” treatment, over ESWL where more than one treatment will be required and post-treatment imaging is required to confirm stone clearance.

There are no great differences in stone free rates between ESWL and URS. Precisely which technique one uses will depend to a considerable degree on local resources and local expertise at performing URS, particularly for upper tract stones.

Open and laparoscopic ureterolithotomy are used in the rare cases for very impacted stones, where ESWL or URS have been tried and failed or were not feasible.

2.3. BLADDER STONES

There are struvite (infection stones) or uric acid (in non-infected urine). Bladder calculi are predominantly a disease of men aged >50 and with BOO due to BPE.

They also occur in the chronically catheterized patient with spinal cord injury patients.

Bladder stones may be symptomless in patients with incidental finding on investigations. This is the common presentation in spinal patients who have limited or no bladder sensation. In the neurologically intact patient there are suprapubic or perineal pain, hematuria, urgency and/or urge incontinence, recurrent UTIs, LUTS. If a bladder stone is suspected, they will be visible on KUB X-ray, renal US or cystoscopy.

Most stones are small enough to be removed cystoscopically with the help of endoscopic cystolitholapaxy, using stone - fragmenting forceps for stones that can be engaged by the jaws of the forceps and electrohydraulic or pneumatic lithotripsy for those that cannot. Multiple and large stone/es (>3cm) can be also removed by open surgery.

Etiology and pathophysiology

BPH is characterized by an increase in epithelial and stromal cell numbers in the periurethral area. New epithelial gland formation is normally only seen during fetal development. The development of new glands in the adult prostate has given rise to the concept of “reawakening” of the inductive effect of the prostatic stroma on the prostatic epithelium cells.

The increase in prostate cell number could reflect proliferation of epithelial and stromal cells, impairment of apoptosis or a combination of both. During the early phases of development of BPH, cell proliferation occurs rapidly. In established BPH, cell proliferation slows down and there is impairment of programmed cell death. Androgens and oestrogens imbalance actively inhibit apoptosis.

The role of androgens in BPH

Testosterone can bind directly to the androgen receptor or may be converted to a more potent form, DHT, by the enzyme 5AR. There are two isoforms of 5AR. Type I or “extra-prostatic” 5AR, which is absent in prostatic tissue and present in, for example, skin and liver. Type II or “prostatic” 5AR, which is found exclusively on the nuclear membrane of stromal cells, but not within prostatic epithelial cells. Type I 5AR is not inhibited by finasteride, whereas type II 5AR is.

Testosterone diffuses into prostate gland. Within epithelial cells it binds directly to the androgen receptor. In prostate stromal cells a small proportion binds directly to the androgen receptor, but the majority binds to type II 5AR on the nuclear membrane, is converted to DHT and then binds with greater affinity and therefore greater potency than testosterone to the androgen receptor in the stromal cell. The androgen receptor/testosterone or androgen receptor/DHT complex then binds to specific binding sites in the nucleus, thereby inducing transcription of androgen-dependent genes and subsequent protein synthesis.

It is thought that stromal/epithelial interactions may be mediated by soluble growth factors that stimulate or inhibit cell division and differentiation. Most common growth stimulating factors are bFGF, EGF and other. TGF normally inhibit epithelial cell proliferation and it is possible that in BPH, TGF is downregulated.

The principle cause of BOO in men is BPH. Less common causes are urethral stricture and PC. BOO in women is altogether less common, the causes including pelvic prolapse, urethral stricture, urethral diverticulum and pelvic masses. In either sex, neurological disease (DM, spinal cord injury, spina bifida...) can cause failure of relaxation of the external sphincter during voiding.

The pathophysiological basis of BOO due to BPE secondary to BPH has been studied more than any other type of obstruction.

BPO has dynamic and static components:

- Dynamic component of BPO: alfa-1-adrenoceptors mediated prostatic smooth muscle contraction. Smooth muscle accounts for approximately 40% of the

area density of the hyperplastic prostate and human prostate contracts following administration of alpha adrenergic agonists. This effect is the rationale for alpha-blockers treatment for symptomatic BPO;

- Static component of BPO: mediated by the volume effect of BPE.

The disease of the bladder arising from BOO is increased irritability and its consequences, by which it admits of little distension, becomes quick in its action and thick and strong in its coats. BOO causes thickening of the bladder wall. Microscopically smooth muscle cells enlarge and there is an increase in connective tissue between the smooth muscle bundles. In some cases this may lead to poor compliance, with development of high bladder and intrarenal pressures. Progressive UHN can develop, with impairment of renal function and even CRF due to high pressure chronic urinary retention.

Experimentally created BOO causes development of OAB with unstable bladder contractions during bladder filling. This may be due to prolonged increased intravesical pressure during voiding causing ischaemia and leading to ischaemic damage to neurons within the bladder. Symptomatically, many patients with BOO develop LUTS.

Symptoms and signs

There are many guidelines, developed to standardize the approach to diagnosis and treatment of men presenting with symptoms suggestive of BPH.

The classic “prostatic” symptoms of frequency, urgency, nocturia, hesitancy, poor and intermittent flow, terminal dribbling traditionally said to indicate the presence of BOO due to BPE were shown to bear little relationship to prostate size, flow rate, PVR or indeed urodynamic evidence of BOO. Age-matched elderly men and also women have similar LUTS, despite the fact that women have no prostate and rarely have BOO.

The term “Prostatism” has therefore been replaced by the term “LUTS” which avoids any implication about the cause of these symptoms. Urinary symptoms may have non-prostatic causes.

There are many symptoms in patients with BPH:

- Marked frequency and urgency, particularly when also combined with bladder pain;
- Bedwetting: suggests the presence of high pressure chronic retention. Look for distension of the abdomen due to a grossly enlarged bladder which is tense on palpation and dull to percussion;
- Macroscopic hematuria: sometimes due to a large vascular prostate, but exclude other causes (bladder and kidney cancer and stones);
- Back pain and neurological symptoms (sciatica, lower limb weakness or tingling). Rarely, LUTS can be due to neurological disease.

High pressure chronic renal failure

This is maintenance of voiding, with a bladder volume of >800ml, accompanied by UHN. Over time this leads to CRF. When the patient is suddenly unable to pass urine, acute-on-chronic high pressure retention of urine has occurred.

A man with high pressure retention who continues to void spontaneously may be unaware that there is anything wrong. He will often have no sensation of incomplete emptying and his bladder seems to be insensitive to the gross distension. Often the first presenting symptom is that of bedwetting. This is such an unpleasant and disruptive symptom that it will cause most people to visit their doctor. Visual inspection of the patient's abdomen may show marked distension due to a grossly enlarged bladder. The diagnosis of chronic retention can be confirmed by palpation of the enlarged, tense bladder, which is dull to percussion.

The serum Cr is elevated and an US will show UHN with a grossly distended bladder if the scan is done before relief of retention.

Diagnosis

As mentioned above, a history should be taken and an examination performed and all recommend assessment of symptom severity using the IPSS. High-quality guidelines, based on results of randomized trials, recommend few diagnostic tests: urine analysis, completion of a voiding diary, measurement of serum Cr. They regard flow rate measurement and assessment of PVR as optional tests.

Digital rectal examination and PSA

Done to detect nodules which may indicate an underlying PC and to provide a rough indication of prostate size. Size alone is not an indication for treatment, but if surgical treatment is contemplated, marked prostatic enlargement can be confirmed by TRUS. Prostate volume in the order of 80 ml or more increases the likelihood of an open prostatectomy. Discuss the pros and cons of PSA testing with the patient.

Serum Cr

Baseline measure of renal function and to detect renal failure secondary to high pressure urinary retention.

Post-void residual urine volume

Varies considerably on the same or on different days. Along with serum Cr it indicates whether watchful waiting is safe. It is safe not to operate where the PVR volume is <150-200 ml, since the majority of men show no worsening of Cr, no increase in PVR, no worsening of symptoms and do not require TURP.

Flow rate measurement

This is variously regarded as optional, recommended and obligatory prior to undertaking surgical treatment for BPH. $Q_{max} > 15$ ml/s in norm. Like PVR, measurement flow rate varies substantially on a given day, cannot distinguish between BOO and a poorly contractile bladder.

Renal ultrasonography

To detect UHN and kidney disease if serum Cr is elevated, measurement of PVR and prostate volume.

Treatment

Watchful waiting

No particular early symptoms are specific for PC. Even if it later turns out that he does have PC, a patient's symptoms might be due to coexistent BPH or some other pathology. If patient is concerned about the possibility of PC, PSA testing and prostate biopsy are performed.

Many patients are understandably concerned that their urinary symptoms may be a harbinger for the development of AUR. This may influence their decision to seek help for symptoms which they may perceive as indicating a risk of subsequent retention and it may affect the type of treatment they choose.

Once reassured that the likelihood of urinary retention and PC is low, patient may not want treatment for symptoms which on the surface may appear quite bad and he may be happy to adopt a policy of watchful waiting.

A number of studies have shown that in a substantial proportion of men, symptoms do not progress, even for those with severe symptoms. Almost a quarter of men who initially presented with severe symptoms noted an improvement in their symptoms, to mild or moderate.

On the basis of these studies we can say that symptoms, even if severe, do not necessarily get worse even over fairly long periods of time. This forms the foundation of watchful waiting as an option for many patients, even if the symptoms at baseline are severe.

Conservative treatment

As described earlier, BOO is caused partly by alpha-1 adrenoceptors mediated prostatic smooth muscle contraction and this is the rationale treatment of symptomatic BPH.

Alpha blockers are categorized by their selectivity (non-selective or selective) for adrenoceptors and by their elimination half-life. Indications for treatment: bothersome LUTS where WW has failed or the patient wishes to have treatment. Most studies describe response rates of 30-40%. A some proportion of men stop taking their medication either because of side-effects or because of a perceived lack of effectiveness. Side-effects: asthenia and weakness, dizziness, headache and postural hypotension and retrograde ejaculation.

5 ARI blocks the conversion of testosterone to DHT, the more potent androgen in the prostate. This causes shrinkage of the prostatic epithelium and therefore a reduction in prostate volume, thereby reducing the "mechanic" component of BPH. This takes some months to occur, so urinary symptoms will not improve initially. Finasteride is a competitive inhibitor of the type II 5 alpha-reductase, which converts testosterone to DHT. Finasteride therefore lowers serum and intraprostatic DHT levels. Dutasteride is a dual inhibitor of 5 alpha-reductase. A number of large studies have shown symptom improvement over placebo in the IPSS scores and improvements in flow rates. The data also shows a small reduction in the risk of AUR. Shrinking large vascular prostates probably helps reduce the frequency of hematuria in men with BPH. Side-effects are rare sexual problems with loss of libido, impotence, reduced volume of ejaculate.

A combination of an alpha blocker and a 5 ARI prevented progression of BPH. Progression being defined as a worsening of symptom score by 4 or more or the development of complications such as UTIs or AUR.

For a man with frequency, urgency and urge incontinence symptoms suggestive of an OAB consider prescribing an anticholinergics (e.g. oxybutynin, tolterodine, trospium chloride, solifenacin). There is the concern that these drugs could precipitate urinary retention in men with BOO, but the risk of this occurring is probably very low, even in men with urodynamically proven BOO.

An alternative drug treatment for BPH symptoms is phytotherapy. 50% of all medications consumed for BPH symptoms are phytotherapeutic ones. These agents are derived from plants and include the *Pygeum africanum*, purple cone flower (*Echinacea purpurea*), South African star grass (*Hipoxis rooperi*) and saw palmetto berry (*Serenoa Repens*). These plant extracts contains an anti-inflammatory, antiproliferative, oestrogenic components and produces improvements in LUTS and flow rates. Beta-sitosterol may induce apoptosis in prostate stromal cells, by causing elevated levels of TGF.

Operative treatment

TURP – electrosurgical removal of the obstructing tissue of BPH or obstructing PC from within the prostatic urethra till prostatic capsule. An electrically heated wire loop is used, through a resectoscope, to cut the tissue and diathermy bleeding vessels. The cuted “chips” of BPH are pushed back into the bladder by the flow of irrigating fluid and at the end of resection are evacuated.

Indications for TURP:

- LUTS which fail to respond to changes in life style or medical therapy;
- Recurrent AUR;
- Renal impairment due to BPH;
- Recurrent hematuria due to BPE;
- Bladder stones due to prostatic obstruction.

Open prostatectomy indications:

- Large prostate (>80g);
- TURP not technically possible;
- Urethra too long for the resectoscope to gain access to the prostate;
- Presence of bladder stones which are too large for endoscopic cystolitholapaxy (>3 cm), combined with marked enlargement of the prostate.

Transvesical open prostatectomy is the preferred operation if there is a grossly enlarged prostate gland. The bladder is opened, the mucosa around the protruding BPH is incised and the finger between the node and capsule is inserted to enucleate this disease. A 22Ch urethral and a suprapubic catheter are left. The urethral catheter is removed in 3 days. Suprapubic drain can be removed on the 10 postoperative day.

Simple retropubic prostatectomy compared with the transvesical approach allows more precise anatomic exposure of the prostate, thus giving better visualization of the prostatic cavity which allows more accurate removal of the BPH, better control of bleeding and more accurate division of the urethra, so reducing the risk of inconti-

nence. The retropubic approach should not be employed when the middle lobe is very large because it is difficult to get behind the middle lobe and so to incise the mucosa distal to the ureters. The prostate is exposed by a Pfannenstiel or lower midline incision. Hemostasis is achieved before enucleating the prostate, by ligating the dorsal vein complex with sutures placed deeply through the prostate. The prostatic capsule and BPH are incised transversely with the diathermy just distal to the bladder neck. The plane between the capsule and BPH is found with scissors and developed with a finger. Sutures are used for hemostasis. A wedge of bladder neck is resected. A catheter is inserted and left for 7-10 days and the transverse capsular incision is closed.

Minimally invasive management of BPH

It is reported a seemingly higher mortality and re-operation rate after TURP when compared with open prostatectomy. This, combined with other studies suggesting that symptomatic outcome after TURP was poor in a substantial proportion of patients and that TURP was associated with substantial morbidity, prompted the search for less invasive treatments.

The two broad categories of alternative surgical techniques are minimally invasive (TUNA, TUMT, HIFU) and invasive (TUVP and laser prostatectomy). All are essentially heat treatments, delivered at variable temperature and power and producing variable degrees of coagulative necrosis of the prostate or vaporization of prostatic tissue.

Treatment of chronic renal failure

Suprapubic catheterization relieves the pressure on the kidneys and allows normalization of renal function. A large volume of urine is drained from the bladder. A small percentage of patients have a postural drop in SBP. It is wise to admit patients with such CRF for a short period of observation, until the diuresis has settled. Patients will require i.v. fluid replacement. Definitive treatment options are operation (open BPH-ectomy or TURP) or a long-term suprapubic catheter. A TWC is clearly not appropriate in cases where there is back pressure on the kidneys.

4.1. RENAL AND URETERAL ANOMALIES

Abnormalities of renal fusion and ascent occur in weeks 6-9 of gestation, when the embryonic kidney is 'ascending' to its definitive lumbar position in the renal fossa.

4.1.1. Horseshoe kidney

Most common example of renal fusion. Prevalence 1 in 400. Male to female ratio 2:1. The kidneys lie vertically and are joined at their lower poles by midline parenchymal tissue. Consequently, the horseshoe kidney lies lower in the abdomen. Normal rotation of the kidney is also prevented and therefore the renal pelvis lies anteriorly, with the ureters also passing anteriorly over the lower part of the kidneys, but entering the bladder normally. Blood supply is variable, usually from one or more renal arteries or their branches or from branches off the aorta or inferior mesenteric artery. A proportion of individuals with horseshoe kidneys have associated congenital urological and non-urological abnormalities.

Most patients with horseshoe kidneys remain asymptomatic. However, UTIs and stones may develop and cause symptoms. The diagnosis is usually suggested on renal US and confirmed by IVU. Renal function is usually normal or slowly reduced.

4.1.2. Ectopic kidney

The kidney fails to achieve its normal position and may be located in the thorax, abdomen, in iliac fossa or pelvis (on the contralateral side or crossed). The prevalence of renal ectopia is 1 in 900, with both sexes affected equally. The left kidney is affected more often than the right and bilateral cases are seen in <10%. The affected kidney is smaller, with the renal pelvis positioned anteriorly and the ureter is short, but enters the bladder normally. Pelvic kidneys occur in 1 in 2000–3000 and lie opposite the sacrum and below the aortic bifurcation and are supplied by adjacent vessels. Renal ectopia has an increased risk of congenital anomalies including contralateral renal agenesis and genital malformations.

Most are asymptomatic. Diagnosis is made on renal US, IVU or renography. Complications include hydronephrosis secondary to VUR or PUJO, stones and UTIs.

4.1.3. Renal agenesis

Unilateral renal agenesis is the absence of one kidney due to embryological abnormality or absence of the ureteric bud. This results in failure of the ureteric bud to contact the metanephric blastema with failed induction of nephrogenesis. The incidence is 1 in 1000, left side > right, males > females. Absence of a kidney may also be caused by involution of a multicystic dysplastic kidney in utero or postnatally. Many patients are asymptomatic. However, it is associated with other abnormalities. Often discovered as an incidental finding on US performed for other reasons or during investigation of associated abnormalities. Long-term

follow-up of renal function, urinalysis and blood pressure should be considered. Bilateral renal agenesis is rare, incompatible with life and is associated with severe other abnormalities.

4.1.4. Cystic kidney disease

Autosomal recessive polycystic kidney disease

A disease of infancy and childhood, where renal collecting tubules and ducts become cystically dilated and numerous small cysts form in the renal cortex and medulla bilaterally. Incidence of 1 in 10,000-40,000. Severe forms present early and have a poor prognosis. Prenatal US demonstrates large, "bright" homogeneously hyperechogenic kidneys, which can cause obstructed labour and respiratory problems. Neonates have large flank masses, limb and facial anomalies. All cases are associated with congenital hepatic fibrosis. Infants may develop fatal uraemia and respiratory failure. Older children present with CRF, hypertension and portal hypertension. Most develop ESRD by adulthood requiring hemodialysis, nephrectomy to control hypertension and subsequent renal transplantation.

Autosomal dominant polycystic kidney disease

An autosomal dominant inherited disorder involving multiple expanding renal parenchymal cysts. Incidence is 0.1-0.5%. 95% are bilateral. ADPKD can affect children and adults and accounts for 10% of all CRF, which usually manifests at >40 years old.

The kidneys reach an enormous size due to multiple fluid-filled cysts and can easily be palpated on abdominal examination. Expansion of the cysts results in ischaemic atrophy of the surrounding renal parenchyma and obstruction of normal renal tubules. Symptoms are hematuria, flank pain, flank mass, UTIs, proteinuria, hypertension and intracerebral bleeding, multiple cysts of other organs. The incidence of renal adenoma is 20%. However, the risk of RCC is the same as the general population. CRF may present with nausea, vomiting, anemia, confusion and seizures.

Investigations depend on the presenting symptoms. For suspected UTI culture urinalysis are used. For hematuria urine cytology, cystoscopy and renal US are needed. On US the kidneys are small and hyperechoic, with multiple cysts of varying size, many of which show calcifications. If the nature of the cysts cannot be determined with certainty on US, a renal CT or MRT are used.

CRF will be managed by a nephrologist. Anemia may occur, though ADPKD may cause increased erythropoietin production and polycythemia.

The aim of the treatment is to preserve renal function as long as possible. It is indicated to monitor and to control hypertension and UTIs. Infected cysts and abscesses should be drained. Persistent heavy hematuria can be controlled by embolization or nephrectomy. ESRD requires hemodialysis and ultimately renal transplantation.

Due to the high risk of inheritance of ADPKD, off-spring should be offered genetic testing or US screening.

Medullary cystic disease

MCD is an autosomal dominant condition, which develops in later childhood. Histology shows interstitial nephritis associated with corticomedullary cysts. Disease progression causes a reduction in kidney size. Features include polyuria and polydipsia due to a salt-losing nephropathy, anemia, growth retardation, hypertension and CRF. Initial treatment includes salt replacement. Hemodialysis and renal transplantation are later options.

Multicystic dysplastic kidney

The cysts of a “multicystic” kidney are not due to dilatation of renal collecting ducts as in polycystic disease, but instead, the entire kidney is dysplastic, with immature dysplastic stroma and cysts of various sizes. Bilateral disease is incompatible with life. The incidence of unilateral MCDK is 1 in 4000. Disease is usually detected on pre- or postnatal US. Neonates may present with an abdominal mass. Unilateral disease is often associated with VUR or PUJ obstruction in the contralateral kidney. Affected kidneys may undergo renal aplasia, where they spontaneously shrink to a tiny remnant. US and renogram with DMSA help to distinguish this condition from hydronephrosis. Most can be treated conservatively with close surveillance and US follow-up for the associated risks of hypertension and Wilms tumour, which would be indications for nephrectomy.

Multilocular cystic nephroma

Presents in young children with a flank mass, loin pain or hematuria. Diagnosis is on US or CT, demonstrating multilocular cysts in the renal parenchyma, which may extend into the collecting system. It is included in a spectrum of disease that is closely associated with tumours and so the recommended treatment is partial or full nephrectomy.

4.1.5. Upper urinary tract duplication

A duplex kidney has an upper pole and a lower pole, each with its own separate pelvicalyceal system and ureter. The two ureters may join to form a single ureter at the PUJ or more distally as a bifid ureter before entering the bladder through one ureteric orifice. The two ureters may pass down individually to the bladder. This is called complete duplication. In this case, the Weigert-Meyer rule states that the upper pole ureter always opens onto the bladder medially and inferiorly to the ureter of the lower pole, thereby predisposing to ectopic placement of the ureteric orifice and obstruction due to the longer intramural course of the ureter through the bladder wall. The lower pole ureter opens onto the bladder laterally and superiorly, reducing the intramural ureteric length, which predisposes to VUR.

Ureteric duplication occurs in 1 of 25 individuals. Female to male ratio is 2:1. Unilateral cases are more common than bilateral, with right and left sides affected equally. Risk of other congenital malformations is increased.

Patients have symptoms of UTIs, flank pain or incidental finding. Ectopic ureters are associated with upper renal pole hydronephrosis secondary to obstruction, renal hypoplasia or dysplasia and ureteroceles. Lower pole ureters are prone to

VUR, resulting in UHN. Bifid ureters can get urine continuously passing from one collecting system to the other predisposing to urinary stasis, UTIs and stone formation.

Renal US demonstrates ureteric duplication and UHN. IVU shows decreased contrast excretion from renal upper pole and UHN. Contrast in a ureterocele gives the appearance of a “cobra head”. MCUG will determine whether VUR is present. CT and MRT reveals detailed anatomical information. Isotope renogram assesses renal function.

Uncomplicated complete or incomplete ureteric duplication does not require any intervention. In symptomatic patients, the aim is to reduce obstruction and VUR and improve function. Where renal function is reasonable, ureteric re-implantation can treat both conditions. A poorly functioning renal unit, where upper pole associated with ectopic ureter and/or obstruction or lower pole associated with a VUR or ureterocele may require heminephrectomy and ureterectomy.

4.1.6. Pelviureteric junction obstruction

A obstruction of the ureter at the PUJ resulting in a restriction of urine flow. Childhood incidence is estimated at 1 in 1000. Boys are affected more than girls with ratio 2:1. The left side is more often affected than the right side with ratio 2:1 and there is bilateral obstruction in 10-50%.

In children, most PUJO is congenital, due to either an intrinsic narrowing secondary to aberrant development of ureteric/renal pelvis muscle or abnormal collagen or extrinsic causes with compression of the PUJ by aberrant vessels. Co-existing VUR is found in up to 30%.

PUJO is the most common cause of hydronephrosis found on prenatal and early postnatal US. Infants may also present with an abdominal mass, UTIs and hematuria. Older children present with flank or abdominal pain exacerbated by fluid consumption, UTIs. In some cases there are nausea, vomiting and hematuria following minor trauma.

If prenatal US has shown a large or bilateral hydronephrosis, a follow-up renal tract US should be performed soon after birth. If there is a prenatal unilateral hydronephrosis and the bladder is normal, the scan is deferred until day 3-7 to allow normal physiological diuresis to occur, which may spontaneously improve or resolve the hydronephrosis.

Children may be observed with US and renogram if they remain stable, with good renal function and no other complications such as persistent UTIs or stones.

Pyeloplasty is indicated if children are symptomatic, have a significant hydronephrosis with >30 mm anterior-posterior renal pelvis diameter or impaired renal function. Techniques include open or laparoscopic Anderson-Hynes dismembered pyeloplasty. Post-operative follow-up is with US and MAG3 renogram. Where renal function is poor on the side of the PUJO, options include temporary PNS drainage to assess the potential for recovery. Next will be pyeloplasty if function is improved or nephrectomy where the impairment is severe or irreversible.

4.1.7. Vesicoureteric reflux

VUR results from abnormal retrograde flow of urine from the bladder into the upper urinary tract. Overall incidence in children is 1-2%, younger>older with female:male ratio 5:1.

In normal conditions the ureter passes obliquely through the bladder wall (1-2 cm), where it is supported by muscular attachments, which prevent VUR during bladder filling and voiding. The normal ratio of intramural ureteric length to ureteric diameter is 5:1. VUR occurs when the intramural length of ureter is too short. The degree of reflux is graded from I to V.

Classification:

- Primary VUR results from a congenital abnormality of the VUJ. An anatomical cause is seen with duplex ureters. The Weigert-Meyer rule states the lower pole ureter enters the bladder proximally and laterally, resulting in a shorter intramural tunnel which predisposes to VUR.
- Secondary VUR results from urinary tract dysfunction associated with elevated intravesical pressures creating damage to the VUJ. Causes include PUV, urethral stenosis, neuropathic bladder, DSD. Inflammation associated with acute cystitis can also distort the VUJ causing VUR.

At presentation most common patients have symptoms of UTIs. VUR associated with UTIs can result in reflux nephropathy and nephrosclerosis, causing hypertension and progressive CRF.

Investigation are urinalysis and culture to diagnose UTIs, US, DMSA renogram to detect and monitor associated renal cortical scarring, MCUG to diagnose and grade VUR and establish reversible causes. Urodynamic investigation is used if there is suspicious of voiding dysfunction.

Treatment starts from eliminating of the problems contributing to secondary VUR. The majority (80-85%) of primary VUR grade I-II will resolve spontaneously, with 50% resolution in grade III-V. A period of observation with medical treatment is therefore initially recommended. General advice includes good fluid intake, regular voiding, perineal hygiene, treatment of constipation and use of probiotics. Low dose antibiotic prophylaxis should be given to keep the urine sterile and lower the risk of renal damage until VUR resolves. Anticholinergic drugs are given to treat OAB.

Surgery is indicated in limited cases. Techniques include laparoscopic or open ureteric re-implantation with or without antireflux technic. Endoscopic injection of hyaluronic acid/dextranomer bulking agent (Deflux), which is injected intramurally at the ureteric orifice with 80-90% success rates.

4.1.8. Ectopic ureter

The ureteric orifice is situated either below and medial or above and lateral to the normal anatomical insertion on the trigone of the bladder. Incidence is ~1 in 1900. Female to male ratio is $\geq 3:1$.

The ureteric bud arises from an abnormal position on the mesonephric duct during embryological development. There is a direct correlation between the location of the ectopic ureter and the degree of ipsilateral renal hypoplasia or dysplasia. 80% are associated with a duplicated collecting system. A duplex kidney has an

upper pole and a lower pole units, each with its own renal pelvis and ureter. The two ureters may join to form a single ureter or they may pass down individually to the bladder by complete duplication. In this case, the upper pole ureter always opens onto the bladder below and medial to the lower pole ureter, predisposing to ectopic placement of the ureteric orifice.

Sites of ectopic ureter in females include lateral in the bladder, bladder neck, urethra, vagina, vaginal vestibule, uterus. In male patients sites include lateral in the bladder, posterior urethra, seminal vesicles, ejaculatory duct, vas deferens, epididymis, bladder neck.

Most patients present with an antenatal diagnosis of UHN, which may present as an abdominal mass. Later presentations include acute or recurrent UTIs. When the ureteric opening is below the urethral sphincter girls present with persistent vaginal discharge or false incontinence, despite successful toilet training. In male patients the ureter is always sited above the external urethral sphincter, so boys do not develop incontinence. UTIs may trigger recurrent epididymitis.

US may demonstrate UHN. MRT identifies duplex systems. MCUG assesses VUR in lower pole ureters. Cystourethroscopy can directly identify a ureteric opening in the urethra. DMSA renogram assesses renal function to help plan surgery.

Treatment is mainly expectant if there are no symptoms. Where an ectopic ureter is associated with a poorly functioning renal upper pole or single-system kidney, surgery is an option. This includes open or laparoscopic heminephrectomy or total nephrectomy with excision of the associated ureter. Uretero-pyelostomy and uretero-ureterostomy can be considered in duplex systems where the upper renal pole has reasonable function. Where some function is retained in a single-system kidney, the distal ureter can be resected and re-implanted into the bladder.

4.1.9. Ureterocele

Ureterocele is a cystic dilatation of the distal ureter as it drains into the bladder. Incidence is 1 in 5000-12000. Female to male ratio is 4:1. 80% are associated with the upper pole of a duplex system. Single-system ureteroceles are more commonly found in males and adults. 10% of ureteroceles are bilateral. There is intravesical or orthotopic ureterocele, which is completely confined within the bladder. This ureterocele may be stenotic or non-obstructed. Second type is more common. There is ectopic ureteroceles, if any part extends to the bladder neck or urethra. May be sphincteric (wide orifice, found proximal to the bladder neck within the internal sphincter), sphincterostenotic (stenotic orifice, found proximal to the bladder neck), ceco-ureterocele (ectopic ureterocele that extends into the urethra, but the orifice is within the bladder).

Most patients present with antenatal UHN. Later presentation in infants may be with symptoms of UTIs. Association with ureteric duplication increases the risk of VUR and reflux nephropathy. Ureteroceles can also cause obstruction, which may be identified on antenatal US or present in children with an abdominal mass or pain. A prolapsing ureterocele can present as a vaginal mass in girls.

US shows a thin walled cyst in the bladder often associated with a duplex system. MCUG can identify ureterocele location, size and associated VUR. Cystoscopy may reveal a defect near the trigone. DMSA renogram assesses renal segment function.

There are many treatment options. Endoscopic incision - this is emergency treatment for infected or obstructed ureteroceles. Also indicated for elective management of intravesical ureteroceles. Rarely, these may require further surgery, including ureterocele excision and ureteric re-implantation to preserve renal function and prevent VUR. Uretero-ureterostomy or uretero-pyelostomy (from upper to lower pole unit): option for ectopic ureteroceles associated with a duplex system, with good function in the upper unit and no VUR in the lower. Upper pole partial nephrectomy: option for ectopic ureterocele associated with a duplex system with poor function in the upper unit and no VUR in the lower unit. Upper pole partial nephrectomy, ureterocele excision and ureteric re-implantation: option for ectopic ureterocele associated with a duplex system with poor function in the upper unit and VUR in the lower unit. Nephro-ureterectomy is indicated for significant lower pole reflux with poor function in both renal poles.

4.2. URETHRAL ANOMALIES

4.2.1. Hypospadias

Hypospadias is a congenital deformity where the meatus is sited on the underside of the penis, anywhere from the glans to the perineum. It is often associated with a “hooded” foreskin and chordee, which will lead to ventral curvature of the penile shaft. It occurs in 1 in 250 live male births.

Hypospadias results from incomplete closure of urethral folds on the under-surface of the penis during embryological development. This is related to a defect in production or metabolism of fetal androgens or the number and sensitivity of androgen receptors in the tissues. Chordee is caused by abnormal urethral plate development or an intrinsic abnormality of the corpora cavernosa and the “hooded” foreskin is due to failed fusion of the preputial folds, resulting in a lack of ventral foreskin. Associated anomalies are UDT, inguinal hernia, hydrocele, disorders of sexual development.

Classification:

- Anterior: glandular, coronal and subcoronal;
- Middle: distal penile, midshaft and proximal penile;
- Posterior: penoscrotal, scrotal and perineal;

It is indicated a full clinical examination to establish the diagnosis, assess the penis and urethral plate and detect associated abnormalities needing treatment. Patients with unilateral or bilateral absent testes and hypospadias should undergo chromosomal and endocrine investigation to exclude disorders of sex development. Posterior hypospadias can be associated with other urinary tract malformations.

Surgery is indicated where deformity is severe, interferes with voiding or is predicted to interfere with sexual function. Repair is performed between 6-18 months of age. Local application of testosterone for 1 month preoperative can help increase tissue size. Surgery aims to correct penile curvature, reconstruct a new urethra and bring the new meatus to the tip of the glans using urethroplasty, glanuloplasty and meatoplasty techniques. Some proximal defects may require a 2-stage procedure.

4.2.2. Posterior urethral valves

PUV are derived from an abnormal congenital membrane arising from the verumontanum and attaching obliquely to the anterior urethra, beyond the external urethral sphincter, resulting in lower urinary tract obstruction. Urethral instrumentation or spontaneous partial rupture of the membrane is thought to cause the classical appearance of two valve-like folds in the prostatic urethra. Incidence is 1 in >5000 males.

Most common PUV is diagnosed prenatally. Features include: bilateral UHN, dilated bladder and posterior urethra, thick walled bladder and renal dysplasia. Early diagnosis is associated with poor prognosis. In newborn and infants there are respiratory distress, palpable abdominal mass due to hydronephrotic kidneys or distended bladder, ascites, UTIs, renal impairment. In older children there are recurrent UTIs, poor urinary stream, incomplete bladder emptying, poor growth and incontinence. There is a risk of CRF, VUR and voiding dysfunction.

Associated features: “Pop-off valve syndrome” is seen in 20%. It describes mechanisms by which high urinary tract pressure is dissipated to allow normal renal development. It includes leaking of urine from a small bladder or renal pelvis rupture (urinary ascites), unilateral VUR into a non-functioning kidney and formation of bladder diverticuli.

Patients with PUV have long-term poor renal function, 20% develop ESRD. Bladder dysfunction is common despite treatment of outflow obstruction. This includes OAB, incontinence and bladder underactivity associated with PVR, poor concentration of urine and polyuria. From age 16 years, care should be transferred to an adult urologist or nephrologist. Problems may arise with retrograde ejaculation, impotence and reduced libido due to renal impairment. There are abnormal prostatic or seminal vesicle secretions contributing to reduced fertility.

Assessing of the renal function are performed with MAG3 or DMSA renograms. US may show thickened bladder wall, bilateral UHN and dilated posterior urethra. By MCUG features of PUV include a distended posterior urethra, partially filled anterior urethra, bladder neck hypertrophy, thick walled bladder and diverticuli, incomplete bladder emptying, VUR.

Treatment include prophylactic antibiotics, check serum electrolytes and drain the bladder with a pediatric feeding tube. If there is improvement, cystoscopy and transurethral ablation of valve at 5 and 7 o'clock is recommended. A temporary cutaneous vesicostomy is indicated. Any underlying bladder dysfunction should be diagnosed and treated.

4.3. BLADDER EXSTROPHY AND EPISPADIAS

Exstrophy-epispadias complex describes a spectrum of congenital malformations affecting the abdominal wall, pelvis, GUT and sometimes also the spine and anus. It includes bladder exstrophy and epispadias.

4.3.1. Bladder exstrophy

The most common form, results from defective development of the anterior bladder and lower abdominal walls, resulting in the posterior bladder wall lying ex-

posed on the abdomen. Incidence is 1 in 50 000 live births. Male to female ratio is 5:1. Increased risk in offspring of affected patients and with younger maternal age and increased parity.

Classically described as an embryological malformation causing abnormal over-development of the cloacal membrane, which prevents in-growth of lower abdominal tissues. The cloacal membrane normally perforates to form the urogenital and anal openings, but in exstrophy, premature rupture results in a triangular defect below the umbilicus. The timing of rupture determines the type of resulting defect.

Associated anomalies:

- Bone defects: diastasis of the symphysis pubis due to outward rotation of the pelvic bones along the sacroiliac joints;
- Musculofascial defects: umbilical hernias, inguinal hernias, divarication of rectus abdominis, abnormal pelvic floor, low lying umbilicus;
- Genital defects in male patients: short, broad penis with lateral splaying of the corporal cavernosa, short urethral plate, epispadias, deficiency of dorsal foreskin. Defects in female patients: bifid clitoris, stenotic vaginal orifice, short anteriorly placed vaginal canal, uterine prolapse in adult life;
- Urinary tract defects: exposed bladder plate. Majority suffer from VUR due to lateral displacement of the ureteric orifices;
- GUT defects: anteriorly displaced anus, rectal prolapse, abnormal anal sphincter contributes to incontinence.

Typical features seen on prenatal US include a lower abdominal wall mass, absent bladder filling, low-set umbilicus, small genitalia, abnormal iliac crest widening. Diagnosis can help planning of delivery in a centre with facilities to perform early surgical correction.

Surgery aims to provide a continent reservoir for urine storage, preserve renal function and create functional and cosmetically acceptable external genitalia. Selected cases are suitable for a one-stage complete primary repair of bladder exstrophy involving closure of the bladder plate and epispadias repair.

However, many patients require staged procedures. In newborn pelvic osteotomy (cutting bone to correct deformity) is performed with external fixation and closure of bladder, abdominal wall and posterior urethra. At 6-18 months epispadias repair is indicated. Bladder neck reconstruction and ureteric re-implantation with anti-reflux surgery is performed for 4-5 years patients when there is adequate bladder capacity and children can participate in voiding protocols. Where bladder capacity is too small, bladder augmentation or urinary diversion is required.

4.3.2. Primary epispadias

In epispadias, the urethra opens onto the dorsal surface of the penis, anywhere from the glans, penile shaft or most commonly, the penopubic region. An incomplete urethral sphincter mechanism results in a high risk of incontinence. Epispadias is also associated with dorsal chordee, causing an upward curvature of the penis and with incomplete foreskin dorsally. Epispadias is part of the exstrophy-epispadias complex. Primary epispadias without exstrophy is rare.

Associated anomalies are diastasis of the symphysis pubis results in splaying of the corpora cavernosa and shortening of the penile shaft. Females have a bifid clitoris, poorly developed labia and demonstrate a spectrum of urethral deformities ranging from a patulous urethral orifice to a urethral cleft affecting the entire length of the urethra and sphincter. There is rare abnormality with male:female ratio is 5:1.

Treatment in male patients include urethroplasty with functional and cosmetic reconstruction of the external genitalia with penile lengthening and correction of chordee at 6-18 months. It describes mobilizing the urethra to the ventral aspect of the penis, with advancement of the urethral meatus onto the glans with a meatal advancement glanduloplasty. The corporal bodies are separated and rotated medially above the urethra and re-approximated. From age 4-5 years, when children can be toilet trained, bladder neck reconstruction can be performed, with help of the Youngs-Dees-Leadbetter procedure. This achieves continence and any bladder residuals may then be emptied by urethral catheterization. If this surgery fails, insertion of artificial urinary sphincters or injection of peri-urethral bulking agents may be tried. In female patients surgery involves urethral repair reinforced with pubic fat, along with clitoral reconstruction and bladder neck repair.

4.4. BLADDER ABNORMALITIES

4.4.1. Persistent urachus

Embryologically, the allantois connects the urogenital sinus with the umbilicus. Normally, the allantois is obliterated and is represented by a fibrous cord (urachus) extending from the dome of the bladder to the navel. Incomplete obliteration sometimes occurs. If obliteration is complete except at the superior end, a draining umbilical sinus may be noted. If it becomes infected, the drainage will be purulent. If the inferior end remains open, it will communicate with the bladder, but this does not usually produce symptoms. Rarely, the entire tract remains patent, in which case urine drains constantly from the umbilicus. This is apt to become obvious within a few days of birth. If only the ends of the urachus seal off, a cyst of that body may form and may become quite large, presenting a low midline mass. If the cyst becomes infected, signs of general and local sepsis will develop. Adenocarcinoma may occur in a urachal cyst, particularly at its vesical extremity and tends to invade the tissues beneath the anterior abdominal wall. It may be seen cystoscopically. Stones may develop in a cyst of the urachus. These can be identified on a plain X-ray film. Treatment consists of excision of the urachus, which lies on the peritoneal surface. If adenocarcinoma is present, radical resection is required. Unless other serious congenital anomalies are present, the prognosis is good. The complication of adenocarcinoma offers a poor prognosis.

4.4.2. Contracture of the bladder neck

There is considerable debate about the incidence of congenital narrowing of the bladder neck. Some feel that its presence is a common cause of VUR, vesical diverticula, a hypoactive bladder and OAB associated with enuresis. The diagnosis

is based on endoscopic observation, which is an unreliable method. MCUG has been used to depict such narrowing, but interpretation of the films varies significantly. Empirical treatment after detecting of Qmax is often employed. This consists of TUR or suprapubic bladder neck revision. Making the bladder neck incompetent in young boys may cause later retrograde ejaculation and, therefore, male infertility. Revision of the bladder neck in females may cause urinary incontinence and is never advised. The diagnosis must therefore be made with caution. Genuine functional bladder neck obstruction can be detected only in the presence of already high voiding pressures combined with lower resistance in the external sphincteric segment associated with a low flow rate. This condition is highly suggestive of functional bladder neck obstruction.

4.4.3. Dilated fetal bladder

In the first trimester, the fetal bladder is considered to be dilated if larger than 7 mm on US. If, on subsequent US, the bladder continues to retain urine and shows no evidence of urine cycling, concern regarding obstruction should be raised. If the amniotic fluid does not increase, this may indicate the progression to oligohydramnios. Determination of the sex of the child is important because of the male gender predominance of certain diseases such as PUV. It can be difficult to distinguish in utero if the dilatation is due to obstruction.

Dilatation caused by obstruction

Dilatations of the fetal bladder caused by anatomic obstructions are mostly due to urethral anomalies or external obstruction. Urethral anomalies include congenital urethral strictures, anterior and PUV and urethral atresia. Compression of the bladder outlet region can be due to obstructing pelvic tumors, an anterior sacral myelomeningocele, adilated vagina in a girl with a cloacal anomaly or with rectal anomalies. The observed bladder changes are due to mechanical obstruction and affect bladder development at a critical time point, which can lead to bladder wall hypertrophy and remodeling.

Dilatation in non-obstruction

Affected patients with neurogenic bladder do not demonstrate any sign of obstruction on postnatally performed voiding studies or cystoscopic evaluations, except when urethral atresia is also present. In this case the presentation is similar to PUV patients.

4.4.4. Congenital megacystis

The term megacystis is often used to describe any condition leading to a distended fetal bladder in utero, without referring to the cause of the dilation. Congenital megacystis is defined as a dilated, thin-walled bladder with a wide and poorly developed trigone. The widegaping ureteral orifices are displaced laterally, causing massive VUR. No neurogenic abnormalities are described. Most patients are recognized prenatally and should be placed on prophylactic antibiotics after birth. Correcting the VUR often restores normal voiding dynamics and should be

performed after 6 months of age. Reduction cystoplasty can be performed but is usually unnecessary. Although the bladder is large enough to accommodate the tapered ureters even in a young infant, the operation can be difficult due to the bladder wall's thinness.

4.4.5. Bladder hypoplasia

In order to truly diagnose a fetal bladder on US, the examination has to be repeated after 15 to 20 minutes to rule out that the fetus has not simply emptied the bladder.

The bladder can be hypoplastic due to inadequate filling or storing of urine during fetal life. Although the bladder is formed during fetal development and can be detected on antenatal US throughout pregnancy, it never reaches an adequate capacity. Conditions caused by inadequate bladder outlet resistance: severe epispadias, separation defects, abnormalities of renal development or urine bypassing the bladder by ureteral ectopia can all lead to underdevelopment of the fetal bladder.

4.4.6. Bladder agenesis

Embryologic development of bladder agenesis remains difficult to explain. The division of the cloaca into the urogenital sinus and the anorectum is apparently regular because the hindgut is usually normal. Therefore the defect can be due to either atrophy of the cranial part of the urogenital sinus or a failure to incorporate the mesonephric ducts and ureters into the trigone. The absence of the bladder is often associated with neurologic orthopedic or other urogenital anomalies. The defect is only compatible with life if the ureters drain ectopically into normally developed müllerian structures in the female or in the rectum in males. In surviving infants, the diagnosis can be confirmed by retrograde ureteronephrograms via the ectopic openings. Renal function can be preserved after creation of an ureterosigmoidostomy or external stoma.

4.4.7. Bladder diverticulum

Bladder diverticula are caused by infravesical obstruction or congenital defects. Independent from the cause, all diverticula develop as herniation of bladder mucosa between defects of bladder smooth muscle fibers. The neck of the resulting diverticulum depends on the size of the muscular defect. The true incidence in children is difficult to evaluate because many of the congenital diverticula remain asymptomatic and are probably never detected.

Primary diverticula are seen in smoothwalled bladders, occur isolated with no other diverticula, are intermittent in presentation and happen in children with no infravesical obstruction. Primary diverticula arise as a localized herniation of bladder mucosa through the ureteral hiatus between the intravesical ureter and the roof of the ureteral hiatus. These primary diverticula are also known as congenital diverticula and are most likely caused by a congenitally deficient bladder wall. Congenital diverticula are often found in children with generalized connective tissue diseases. These diverticula can be resected if symptomatic.

Secondary diverticula are found in trabeculated bladders as one of many diverticula in the bladder, are always present and are caused by infravesical obstruction. The resulting increased infravesical pressure forces the bladder mucosa to bulge

between the muscle fibers. These diverticula are usually just one of many “pop-off” mechanisms that can occur throughout the bladder. These diverticula can also be caused by weakening in the bladder muscle by infection or development of a muscular defect after bladder surgery.

4.4.8. Bladder duplication

Duplication of the bladder and urethra can be complete or incomplete. It can occur either in the coronal or sagittal plane. In incomplete duplications, the two bladder halves communicate and are usually drained by a single urethra. In complete duplications, the two bladders are fully separated entities with normal mucosa and a full-thickness musculature wall divided by a peritoneal fold. Although the size and quality of each entity can be different, they are usually supplied with their own ureter and are drained by an individual urethra and external meatus. In rare cases, one bladder can lack a urethra. This leads to ipsilateral renal dysplasia via complete obstruction. Both bladders may possess a sufficient continence mechanism or one side is compromised, causing incontinent episodes. Associated duplication anomalies have been reported. Duplicated vaginas can be connected to a separate unicornuate uterus. Duplicated penises are supplied with an individual urethra. Additional urologic abnormalities such as VUR, renal ectopia or dysplasia are commonly found. Complete preoperative diagnostic evaluations with karyotype, US, IVP, video-urodynamic studies, genitogram and GIT imaging are useful to determine the anatomic situation. VCUG and nuclear renal scans can supply additional information regarding VUR and renal function. Complete understanding of the various anomalies can be difficult. Often the final treatment plan has to be deferred until the time of endoscopic and surgical exploration of the malformation. Initial treatment is directed toward renal preservation and prevention of UTIs by relieving possibly obstructed GUT. Long-term goals include achieving continence and reconstructing the internal and external genitalia. Incomplete duplications may not require surgical procedures if both bladder halves are sufficiently drained by a common urethra. In complete duplications, the two bladders can be combined into one. If both sphincter complexes are competent, the distal urethras are connected. If one is incompetent, the corresponding bladder neck can be closed and the connected urethra excised. Duplicated vaginas are combined in the midline and a vulvoplasty is performed. Due to the rarity of the disease and the large variety of presentations, the surgeries must be individualized and should be performed in centers experienced in complex urogenital reconstruction.

4.5. PENILE ABNORMALITIES

4.5.1. Phimosis

Phimosis is a condition in which the contracted foreskin cannot be retracted over the glans. Chronic infection from poor local hygiene is its most common cause. Most cases occur in uncircumcised males, although excessive skin left after circumcision can become stenotic and cause phimosis. Calculi and SCC may develop under the foreskin. Phimosis can occur at any age. In diabetic older men, chronic

balanoposthitis may lead to phimosis and may be the initial presenting complaint. Children under 2 years of age seldom have true phimosis. Their relatively narrow preputial opening gradually widens and allows for normal retraction of foreskin over the glans. Circumcision for phimosis should be avoided in children requiring general anesthesia, except in cases with recurrent UTIs, the procedure should be postponed until the child reaches an age when local anesthesia can be used. Edema, erythema and tenderness of the prepuce and the presence of purulent discharge usually cause the patient to seek medical attention. The initial infection should be treated with broad-spectrum antimicrobial drugs. By paraphimosis if manual reposition fails, the dorsal foreskin can be slit. Circumcision, if indicated, should be done after the infection is controlled.

4.5.2. Aphallia

Penile agenesis results from failure of development of the genital tubercle. The disorder is rare. The karyotype almost always is 46,XY and the usual appearance is that of a well-developed scrotum with descended testes and an absent penile shaft. The anus is usually displaced anteriorly. The urethra often opens at the anal verge adjacent to a small skin tag or it can open into the rectum. Associated malformations are common. Children with this lesion should be evaluated immediately by a multidisciplinary approach. Testing should include a karyotype and other appropriate studies to determine whether there are associated malformations of the urinary tract or other organ systems. MRT may be beneficial in determining the severity of the defect. Prompt gender assignment is important. Some of these patients have a male gender identity despite reconstruction as a female, presumably because of in-utero or postnatal sex steroid imprinting.

Consequently, the recommendation to perform gender reassignment should be made carefully and only after full evaluation by an ambiguous genitalia assessment team and parental counseling. As a male the patient would potentially be fertile, but currently there is an inability to construct a cosmetically acceptable phallus that would allow normal urinary, sexual and reproductive function. Gender reassignment involves orchiectomy and feminizing genitoplasty in the neonatal period. At a later age, construction of a neovagina is necessary. Urinary tract reconstruction with simultaneous construction of an intestinal neovagina through a posterior sagittal and abdominal approach in patients with penile agenesis has been described.

4.5.3. Diphallia

Duplication of the penis is a rare anomaly and has a range of appearances from a small accessory penis to complete duplication. In some cases, each phallus has only one corporeal body and urethra, whereas others seem to be a variant of twinning, with each phallus having two corpora cavernosa and a urethra. The penises are usually unequal in size and lie side by side. Other associated anomalies are common. Evaluation should include imaging of the entire urinary tract, including a renal US and MCUG. US and MRT can also be done to assess penile development. The etiology has not been delineated. Treatment must be individualized

with consideration of the associated anomalies with the goal of attaining a satisfactory functional and cosmetic result.

4.5.4. Inconspicuous penis

An inconspicuous penis refers to a penis that appears to be small with a normal stretched penile length measured from the pubic symphysis to the tip of the glans and normal diameter of the penile shaft. This condition can be congenital or acquired and is usually of great concern for parents. Several entities are included in this disorder, including buried penis, trapped penis and webbed penis. These conditions must be differentiated from micropenis, in which the penis is abnormally small. When an infant has an inconspicuous penis, prompt evaluation is necessary for proper treatment and the family must be informed as to whether the penis is or is not normal. The stretched penile length should be measured from the pubic symphysis to the tip of the glans. In addition, the diameter of the penile shaft may be measured by palpation.

A buried penis, also referred to as hidden or concealed penis, is a form of inconspicuous penis. A buried penis is a normally developed penis that is hidden away by the suprapubic fat pad. The congenital form of buried penis is believed to be due to the inelasticity of the dartos fascia, which normally allows the penile skin to slide freely on the deep layers of the shaft, with restricted extension of the penis because the penile skin is not anchored to the deep fascia. The acquired form from obesity.

The other acquired form, a trapped penis, results from embedding of the penis in the suprapubic fat pad from scar formation over the glans. This deformity may occur after neonatal circumcision in an infant with significant scrotal swelling due to a hernia or hydrocele or after routine circumcision in an infant with a webbed penis. Also, in some neonates the penile shaft seems to retract naturally into the scrotum and if circumcision is performed in this situation, the skin at the base of the penis may form a cicatrix over the retracted phallus. This condition should be differentiated from a transient buried penis resulting from a large suprapubic fat pad noted in early childhood that resolves with increased age and ambulation. On examination, a buried penis must be differentiated from a micropenis, with the latter not having a normal penile stretched length. The clinician should determine whether the glans can be exposed by retracting the skin covering the glans. If so, it remains the surgeon's judgment whether correction is warranted. However, if the penis is trapped by physiologic phimosis in the uncircumcised or cicatricial scarring in the circumcised penis, this increases the chance of difficulty voiding, maintaining proper hygiene, balanitis, UTIs and psychosocial issues. The treatment options for children with buried penis are based on etiology. Patients with buried penis secondary to obesity should have the underlying condition treated. Referral of the child back to the primary care provider for a weight loss and exercise program is essential, with surgical intervention usually not necessary. Young children with secondary cicatricial scarring after penile surgery can be managed with forceful dilation of the cicatrix with a fine hemostat in the office after the application or injection of analgesia. Another option is the combination of topical betamethasone and manual retraction.

Webbed penis, also known as penoscrotal fusion, is a congenital or acquired condition resulting from the scrotal skin extending onto the ventrum of the penis. The congenital form of a penoscrotal web represents an abnormality of the attachment between the penis and the scrotum, whereas the penis, urethra and remainder of the scrotum are normal. The acquired condition results from circumcision or other penile surgery due to excessive removal of ventral penile skin. Although the penoscrotal web is usually asymptomatic, the cosmetic appearance is often unacceptable.

4.5.5. Micropenis

Micropenis is a normally formed penis that is at least 2.5 SD below the mean size in stretched length for age. The ratio of the length of the penile shaft to its circumference is usually normal, but occasionally the corpora cavernosa are severely hypoplastic. The testes are usually small and frequently cryptorchid, whereas the scrotum is usually fused and often diminutive. Stretched penile length is used because it correlates more closely with erectile length than does the relaxed penile length. The measurements should be compared with standards for penile length. Stretched penile length is determined by measuring the penis from its attachment to the pubic symphysis to the tip of the glans. One must be careful to depress the suprapubic fat pad completely to obtain an accurate measurement, especially in an obese infant or child. In general, the penis of a full-term neonate should be at least 1.9 cm long. One must differentiate buried penis or webbed penis from the micropenis, with the former having a normal penile shaft. Micropenis results from a hormonal abnormality that occurs after 14 weeks of gestation. Differentiation of the male external genitalia is complete by the 12th week of gestation and requires a normal testis producing testosterone, stimulated by maternal hCG. During the second and third trimesters, growth of the penis occurs under the direction of fetal androgen, which is controlled by the secretion of fetal LH. An abnormality in the production or use of testosterone results in a small penis and hypospadias, whereas a true micropenis often seems to be a consequence of a deficiency of gonadotropic hormones. The most common causes of micropenis are hypogonadotropic hypogonadism, hypergonadotropic hypogonadism and idiopathic. Furthermore, micropenis is often associated with major chromosomal defects.

The initial evaluation of a child with micropenis should include a thorough medical history and a karyotype at birth. Accurate measurement of the penile length, palpation of the corporeal bodies and evaluation for cryptorchidism are several important aspects of the physical examination. Consultation with a pediatric endocrinologist is also usually obtained to assist in the determination of the cause of the micropenis and to assess whether other abnormalities are also present. Several issues need to be addressed, including the growth potential of the penis and the etiology of the micropenis. The etiology may be testicular or central. Testicular function may be assessed by measuring serum testosterone levels before and after hCG stimulation. Primary testicular failure produces an absent response and elevated basal concentrations of LH and FSH. In some cases, a GnRH stimulation test is also performed. Anterior pituitary screening tests include serial

measurements of serum glucose, sodium, potassium and serum cortisol concentrations and thyroid function tests. MRT of the head should be done to determine the anatomic integrity of the hypothalamus and the anterior pituitary gland as well as the midline structures of the midbrain. Before extensive evaluation of the hypothalamic pituitary-testicular axis androgen therapy should be administered to determine the end organ response. In general, intramuscular testosterone is given for 3 months. Although prolonged treatment might advance skeletal maturation, short courses of treatment do not affect height. Transdermal testosterone also has been used in these patients. If androgen treatment in a neonate successfully increases the penis so that its size falls within the normal range, the effects at puberty have not been clearly delineated. If the penis does not respond to testosterone, gender reassignment is an option but is controversial.

4.5.6. Penile curvature

Curvature of the penis may occur along the vertical (i.e., ventral or dorsal direction) or horizontal (i.e., lateral direction) plane of the penis. Penile curvature may be congenital or acquired from circumcision, other penile surgery or trauma and has cosmetic significance and future sexual difficulties. Penile curvature is most commonly in the ventral direction, referred to as chordee and is commonly associated with hypospadias. However, chordee may occur without hypospadias and with or without a dorsal hood of prepuce and is commonly associated with a deficiency of the ventral skin. Ventral curvature in boys without hypospadias can generally be corrected by degloving of the penis, excision of fibrous tissue that is usually confined to the region superficial to Buck fascia and development of a Byar flap for penile skin coverage as necessary. Congenital dorsal penile curvature may be an isolated condition with or without asymmetrical penile skin or associated with epispadias and a ventral hood of prepuce. Some individuals may have hypospadias. Surgical repair of this condition without associated urethral anomalies is similar to chordee correction, involving degloving of the penis, excision of fibrous tissue that is usually confined to the region superficial to Buck fascia and development of skin flaps for penile skin coverage as necessary. During correction, one must be careful to avoid injury to the neurovascular bundles. More severe cases involve plication and/or excision of ellipses from the ventral corporeal bodies to correct curvature.

Lateral penile curvature is usually caused by overgrowth or hypoplasia of one corporeal body. Lateral penile curvature may be unrecognized until later in childhood because the penis is normal when flaccid and only recognized as being curved with an erection. Surgical repair of congenital lateral penile curvature involves degloving the penis and performing a plication and/or excision of ellipses from the corporeal bodies from the site of maximum curvature to allow straightening of the penis. Secondary lateral penile curvature follows the same principles as for vertical curvature with degloving of the penis, excision of fibrous tissue that is usually confined to the region superficial to the Buck fascia and development of skin flaps for penile skin coverage as necessary. Intraoperative artificial erection may be necessary.

4.6. TESTICULAR ABNORMALITIES

4.6.1. Cryptorchidism

The testes descend into the scrotum in the third trimester. Failure of testicular descent results in cryptorchidism or congenital UDT. Incidence is 4% at birth for a full-term neonate and unilateral UDT > bilateral. About 80% will spontaneously descend by 6 months. The incidence at 1 year is <2%.

Etiology: abnormal testis or gubernaculum (tissue that guides the testis into the scrotum during development), endocrine abnormalities. Risk factors are pre-term infants, low birth weight or small for gestational age, twins.

Classification:

- Retractable testis: an intermittent active cremasteric reflex causes the testis to retract up and out of the scrotum;
- Ectopic: abnormal testis migration below the external ring of the inguinal canal to perineum, base of penis or femoral areas;
- Incomplete descent: atrophic testis may be intra-abdominal, intra-inguinal or pre-scrotal.

It is indicated full examination to elucidate if testis is palpable and to identify location. If neither testis is palpable, consider chromosome analysis to exclude an androgenized female and endocrine analysis. High LH and FSH with a low testosterone indicates anorchia, confirmed with serum inhibin B. For the impalpable testis, imaging with US inguinal canal may be considered, but most recommend proceeding directly to examination under anaesthetic and diagnostic laparoscopy.

UDT demonstrate degeneration of Sertoli cells, loss of Leydig cells, atrophy and abnormal spermatogenesis, which usually may be irreversible by 2 years old.

Complications:

- Relative risk of cancer is 8-fold higher in UDT. There is a 4% lifelong risk of TC with an intra-abdominal testis. Majority are seminomas. There is a slightly increased risk of cancer in the contra-lateral, normally descended testis;
- Reduced fertility;
- Increased risk of testicular torsion or trauma;
- Increased risk of indirect inguinal hernias due to a patent processus vaginalis.

Orchidopexy is recommended at 6-18 months old, but many operate within the first 12 months. Surgery consists of inguinal exploration, mobilization of spermatic cord, ligation of processus vaginalis and securing the testis into a dartos pouch in the scrotal wall. Risks include rare testicular atrophy. Intra-abdominal testes require a laparoscopic approach to mobilize the testis for orchidopexy as a single or 2-stage (Fowler-Stephens) procedure, involving division of spermatic vessels to provide extra length. The testis then relying on collateral blood flow from the vas. Alternatives include microvascular autotransplantation. Orchidectomy for small intra-abdominal testes should be considered.

5.1. PROSTATE CANCER

Incidence, etiology and risk factors

The diagnosis of PC is increased, probably as a result of screening for both symptomatic and asymptomatic men and the use of more extensive prostatic biopsy protocols. PC is the most commonly diagnosed male cancer. The true prevalence of the disease is hinted at by studies carried out on men who have died of other causes. These have demonstrated histological evidence of PC from 10% of men in their 3rd decade till 70% in their 9th. This leads to the concept of “latent” PC a biologically non-aggressive and slow-growing form of the disease, which may be unnecessarily detected by PSA screening. It is estimated that 3% of men die of PC. Recent trend toward a reduction in PC mortality appears to be due to increased operative treatment of localized disease and, perhaps, early use of hormone therapy for advanced disease and PSA screening programmes.

Growth of PC and also benign prostatic epithelium, is under the promotional influence of testosterone. Removal of androgens by castration largely results in programmed cell death and involution of the prostate. PC is not seen in eunuchs or people with congenital deficiency of 5-AR, which converts testosterone to DHT. Phyto-oestrogens found in foodstuffs used in Asian and Oriental cuisine, have a negative growth effect on PC. This probably explain why these races rarely develop the clinical disease or die of PC. Other dietary inhibitors of PC growth include vitamins E and D, lycopene and selenium.

Age is an important risk factor for development of histological PC and PIN, the disease being rare below 40 years and becoming increasingly common with rising age. However, most PC does not achieve a clinically recognizable stage.

The disease is more common in Western nations and the United States. The disease is rare in Asia and Japan, but US migrants from these countries have increased risk. This suggests that the Western diet may be protective. Black men are at greater risk than Caucasians.

It is reported, that 5-10% of PC are inherited. Hereditary PC tends to occur in <60 years men who have a family history and genetic abnormalities. The risk of a man developing PC is doubled if there is one affected first-degree relative and is 4-fold if there are two relatives.

Prevention

The fact that as many as 10% of men in their 3rd decade have histological PC suggests that there are years of opportunity for preventative strategies. There are many epidemiological and laboratory data supporting dietary interventions, though randomized prospective trials are awaited.

- High fat diets with those rich in saturated fat and omega-6 fatty acids, are linked to increased risk of PC diagnosis;

- Products with phyto-oestrogens including the genistein inhibits PC cell lines;
- Lycopene, which present in tomato products, is considered to reduce risk of PC progression and inhibits cell lines;
- Antioxidant selenium (0.2mg/day) was shown to reduce the risk of developing PC;
- Antioxidant vitamin E was shown to reduce the incidence of PC;
- Vitamins A and D both inhibit growth of prostate cell lines;
- Smoking has recently been shown in population studies to be significantly associated with PC diagnosis;
- No definite link exists between alcohol consumption, vasectomy or sexual activity with PC diagnosis.

Pathology

The most common prostatic malignancy is adenocarcinoma - carcinoma of the acinar or ductal epithelium. The basal cell layer is absent and the basement membrane is breached by the malignant cells which invade into the prostatic fibromuscular stroma. Macroscopically, they tend to be hard and white. In some cases the prostatic urethra, ducts or stroma may be invaded by TCC of the bladder. Prostatic sarcomas rare but may be seen in childhood. Secondary metastases from other sites are rare.

Most (2/3) of adenocarcinomas occur in the peripheral zone of the prostate and most are multifocal. 20% appear to arise from the TZs and 5% from the embryologically distinct central zone. The tumour spreads locally through the poorly formed prostatic capsule into surrounding tissue, at which time it is termed "locally advanced PC". Hence, the disease may involve pelvic organs. Local spread is often along the course of autonomic nerves. The most frequent sites of metastasis are lymph nodes and bone, although lung, liver, testis and brain are involved. Bone metastases are characteristically sclerotic, rarely lytic.

Possible premalignant lesions

There are two premalignant histological lesions: PIN and ASAP. PIN consists of architecturally benign prostatic acini and ducts lined by cytologically atypical cells. The basal cell layer is present, although the basement membrane may be fragmented. PIN was classified into low-grade and high-grade forms, based on the presence of prominent nucleoli. High-grade PIN is believed to be a precursor for intermediate or high-grade PC and its finding in sextant peripheral zone prostate biopsies carries a 30-40% prediction of PC at subsequent biopsy. High-grade PIN is reported in 5-10% of prostate needle biopsies. It does not appear to affect the serum PSA value. Currently, it is recommended that repeat systematic biopsies should be performed if isolated high-grade PIN is reported on needle biopsy or TURP.

ASAP is another histopathological prostatic lesion that pathologists report on needle biopsies as "suspicious for cancer". The acini are small, lined with cytologically abnormal epithelial cells. The columnar cells have prominent nuclei containing nucleoli, while the basal layer may be focally absent. The basement membrane is intact. As with PIN, studies have shown ASAP in needle biopsy pre-

dicts PC at subsequent biopsy in over 40% of cases. Currently, it is recommended that repeat systematic biopsies should be performed if isolated ASAP is reported on needle biopsy or TURP.

Prostate cancer grading

Adenocarcinoma of the prostate is graded using the Gleason system (2005). Microscopically, adenocarcinoma is graded 1 to 5 according to its gland-forming differentiation at relatively low magnification. Since most are multifocal, an allowance is made by adding the two dominant grades to give a sum score between 2 and 10. If only one pattern is observed, the grade is simply doubled. The system is used with needle biopsies, TURP and radical prostatectomy specimens. Gleason scores 2-4 are considered well differentiated, 5-7 are moderately differentiated and 8-10 are poorly differentiated. Among expert pathologists there is good inter-observer reproducibility with Gleason scoring. The importance of the Gleason score is that it correlates well with prognosis. For example, a Gleason 3+3=6 adenocarcinoma carries a worse prognosis than a 3+2=5 cancer of equivalent stage. Moreover, cancers of the same Gleason score have a worse prognosis if the predominant grade is higher. (for example, 4+3=7 is worse than 3+4=7).

TNM classification of prostate cancer (2009)

As with all cancer, PC staging may be considered clinical or pathological dependent on available data.

T – primary tumor

TX – Primary tumor cannot be assessed

T0 – No evidence of primary tumor

T1 – Clinically inapparent tumor not palpable or visible by imaging

T1a – Tumor incidental histological finding in <5% of tissue resected

T1b – Tumor incidental histological finding in >5% of tissue resected

T1c – Tumor identified by needle biopsy because of elevated PSA

T2 – Tumor confined within the prostate

T2a – Tumor involves one half of one lobe or less

T2b – Tumor involves more than half of one lobe, but not both lobes

T2c – Tumor involves both lobes

T3 – Tumor extends through the prostatic capsule

T3a – Extracapsular extension including microsc. bladder neck involv.

T3b – Tumor invades seminal vesicle(s)

N – Regional lymph nodes

NX – Regional lymph nodes cannot be assessed

N0 – No regional lymph node metastasis

N1 – Regional lymph node metastasis

M – Distant metastasis

MX – Distant metastasis cannot be assessed

M0 – No distant metastasis

M1 – Disant metastasis

M1a – Non-regional lymph node(s)

M1b – Bone(s)

M1c – Other site(s)

Symptoms and signs

Since the widespread use of serum PSA testing, the majority of patients have non-metastatic disease at presentation. Shown below are the possible presentations, grouped by disease stage.

Localized PC (T1-T2)

- Asymptomatic, with elevated serum PSA or pathological DRE;
- LUTS (probably due to coexisting BPH and OAB);
- Hematospermia;
- Hematuria (probably due to coexisting other pathology);
- Perineal discomfort and pain (probably due to coexisting prostatitis);

Locally advanced cancer (T3-T4)

- Asymptomatic, with elevated serum PSA or incidental DRE;
- LUTS;
- Hematospermia;
- Hematuria;
- Perineal discomfort and pain;
- Acute urinary retention;
- Symptoms of renal failure/anuria due to ureteric obstruction;
- Malignant priapism or rectal obstruction (rare).

Metastatic disease (N+, M+)

- Asymptomatic, with elevated serum PSA or incidental DRE;
- Swelling of lower limb due to lymphatic obstruction;
- Anemia, anorexia, weight loss due to toxic effects;
- Bone pain and pathological fracture;
- Neurological symptoms/signs in lower limbs due to spinal cord compression;
- Jaundice due to hepatic metastases;
- Signs of pulmonary metastases;
- Bleeding tendency due to coagulopathy.

Diagnosis

T stage is assessed by DRE, TRUS and MRT. Current imaging limits reliability in detection of local microscopic extraprostatic extension of PC.

Pelvic lymph node dissection is the gold-standard assessment of N stage. MRT or CT scanning may image enlarged nodes and most radiologists report nodes of >8 mm in maximal diameter. However, nodes larger than this often contain no cancer, while micrometastases may be present in normal-sized nodes.

M stage is assessed by physical examination, MRT or isotope bone scan, abdominal and chest CT.

DRE

Since most PC arise in the peripheral part of the prostate, they should be palpable on DRE. An abnormal DRE is defined by asymmetry, a nodule or a fixed craggy mass. ~50% of abnormal DREs are associated with PC, the remainder being BPH, prostatic calcifications or chronic prostatitis. An abnormal DRE in the presence of a normal PSA (2.5-3.0 ng/ml) carries a app. 30% incidence of predicting PC.

PSA

Until the development of commercial serum PSA assays in the late 1980s, the only serum marker for PC was acid phosphatase. This was highly specific for bone metastatic PC, but lacked sensitivity in detecting less advanced disease.

It is reported, that screening of men aged 50-70 years with PSA and DRE and subsequent early detection and treatment, may reduce the significant mortality and morbidity caused by PC. These acceptable and relatively inexpensive tests will detect clinically significant disease before it leaves the prostate. However, because of the low specificity of PSA and the high prevalence of latent PC, many men would suffer unnecessary anxiety, biopsies, over-diagnosis and over-treatment. Added to this, the treatments have morbidity and cost.

Prior to introduction of the PSA screening, most men with newly diagnosed PC had advanced incurable disease. PSA has revolutionized the diagnosis and management of PC, although its use in screening and early detection remains controversial. PSA may have minor (<10 ng/ml), intermediate (10-20 ng/ml) and major (20-100 ng/ml) elevated levels.

In addition to its use as a serum marker for the diagnosis of PC, PSA elevations may help in staging, counselling and monitoring of the patients.

PSA generally increases with advancing stage and tumour volume, although a small proportion of poorly differentiated tumours fail to express PSA. PSA is used, along with clinical T stage and Gleason score, to predict pathological tumour staging and outcome after radical treatments using statistically derived nomograms. >50% of patients have extra-prostatic disease if PSA >10ng/ml. <5% of patients have lymph node metastases and only 1% have bone metastases if PSA <20ng/ml. 66% of patients have lymphatic involvement and 90% have seminal vesicle involvement if PSA >50ng/ml. PSA should be virtually undetectable following radical prostatectomy for organ-confined disease. PSA rise after radical prostatectomy precedes the development of clinical metastatic disease by a mean time of 8 years. PSA falls to within the normal range in 80% of patients with metastatic disease on hormone therapy within 4 months. The PSA rises in a mean time of 18 months after starting hormone therapy, signalling progressing disease. PSA is prostate-specific, but not cancer-specific. Other causes of elevated serum PSA are BPH, UTIs, AUR and catheterization, biopsy, TUR, DRE, ejaculation.

PSA derivatives: are free-to-total ratio, density and velocity. Measurement of the free-to-total (F:T) PSA ratio increases the specificity of total PSA because the ratio is lower in men with PC than in men with BPH. This may be helpful in deciding whether to re-biopsy a patient with previous benign biopsies. An important limitation of this investigation is the instability of free PSA. The serum must be

assayed within 3h or frozen at -20°C , otherwise the free component reduces and a low ratio will be reported.

Consideration may be given to the prostate volume, since large benign prostates are the most common cause of mildly elevated PSA. Serum PSA/prostate volume = PSA density and serum PSA/prostate transition-zone volume = PSA-TZ density.

Short-term variations in serum PSA occur in the presence or absence of cancer, the cause of which may be technical or physiological. Longer term, the PSA tends to rise slowly due to BPH and faster due to PC. This is so-called "PSA velocity". A PSA velocity $>0.75\text{ng/ml}$ per year over at least 18 months in total PSA range 4-10 ng/ml is suggestive of the presence of PC, given that only 5% of men without cancer exhibit such a velocity. A PSA velocity $>20\%$ per year should also prompt the recommendation of a biopsy, although a slower velocity does not exclude the presence of cancer. The use of PSA velocity is an option for the patient who wishes to avoid an initial or repeat prostatic biopsy.

Counselling is mandatory before offering a PSA and DRE to asymptomatic men, particularly to highlight the potential disadvantages of having an abnormal result, since the case for benefit to screening is not currently proven. Only men, who have been appropriately counselled should be tested. All patients should be informed when PSA testing is being considered. Sensitivity is 80%: a false negative result is possible. Specificity is 40-50%: a false positive result is possible. Prostatic biopsy is uncomfortable and carries a $<1\%$ risk of sepsis or significant rectal bleeding, hemospermia or hematuria. Repeat biopsy may be recommended (PIN, ASAP or rising PSA level). Treatment may not be necessary or may not be curative. Treatment-related morbidity could lead to a reduction in quality of life.

TRUS and biopsies

The most common diagnostic modality for PC is currently TRUS with guided biopsies. TRUS provides imaging of the prostate and seminal vesicles using a 7.5 MHz intra-rectal probe. It takes 5 min and is undertaken on an outpatient basis with or without some form of anaesthetic. A DRE precedes insertion of the probe. If biopsies are planned, an antiseptic rectal wall cleansing is also undertaken. Broad-spectrum antimicrobials are given before and after the procedure.

TRUS can image the outline of the prostate, cysts, abscesses and calcifications within the prostate. Hypoechoic and hyperechoic lesions in the peripheral zone may be due to PC or inflammatory conditions, although most PC are isoechoic and are not seen. It is important too that the patient appreciates that negative biopsies do not exclude the possibility of PC and that a positive result will not necessarily result in the recommendation of immediate treatment.

Biopsy protocol

6-8-10-12-18 or more trucut needle biopsies are taken in a systematic fashion, to include any palpable or sonographic target lesion, adding samples from the far lateral peripheral zones. Additional biopsies of each TZ may be taken if a TZ cancer is suspected or if a patient is undergoing repeat biopsies due to a rising PSA. Seminal vesicles biopsies occasionally add staging information if they appear abnormal on imaging.

It is not safe to biopsy a patient, which takes anticoagulant treatment. All such treatments are stopped for 10 days prior. PC may also be diagnosed by TURP histology or clinically in certain circumstances.

Treatment of localized prostate cancer

Watchful waiting

The statement “more men die with PC than because of it” is correct. This is because most PC are slow-growing and the majority of men diagnosed are >70 years, often with competing morbidities. This forms the basis for WW offering some men diagnosed with non-metastatic PC no initial treatment. The risks of developing metastatic disease and of death due to PC after 10-15 years of WW can be considered using published data, according to biopsy grade. Patients with high Gleason scores have poor prognosis.

WW is the best option for patients with localized PC and Gleason score 2-4 disease, Gleason score 5-6 disease and >75 years old, significant comorbidity and life expectancy considered to be <10 years, stage T1a disease with normal PSA. WW should be considered and discussed with all who have Gleason score <7, when small-volume disease is predicted by DRE and the biopsy report.

Most men with localized PC on WW are seen every 6 months for clinical examination and a serum PSA test. If the disease progresses during follow-up, androgen ablation therapy is recommended. Treatment will start when symptoms and signs of advanced disease appeared. However, use of PSA, evidence of benefit with earlier use of hormone therapy and involvement of patient choice, have driven earlier thresholds for treatment. An asymptomatic patient with a rising PSA may choose whether to treat his disease and accept the side-effects or whether to maintain his current quality of life while leaving the disease untreated.

Radical prostatectomy

RP is removing of the entire prostate with the seminal vesicles with lymph nodes dissection. It may be performed by open retropubic, perineal or laparoscopic approaches. Following excision of the prostate, reconstruction of the bladder neck and vesico-urethral anastomosis completes the procedure.

RP is indicated for the treatment of «fit» men with localized PC whose life expectancy >10 years, with curative intent. The patient should consider all available treatment options and the complications of RP prior to proceeding. There may be local guidelines on age and upper PSA cut-off for offering RP, perhaps 70 years and 20 ng/ml respectively.

Technic of the open retropubic procedure is discussed below. The patient is under anaesthetic, catheterized and positioned supine with the middle of the table. Through a lower extraperitoneal midline incision the retropubic space is opened. Obturator fossa lymphadenectomy is undertaken if the PSA >10 ng/ml or the Gleason score >7. Incisions in the endopelvic fascia on either side allow access to the prostatic apex and membranous urethra. Division and haemostatic control of the dorsal vein complex passing under the pubic arch allows access to the membranous urethra, which is divided at the prostatic apex. The prostate is mobilized

retrogradely from apex to base, taking Denonvilliers fascia on its posterior surface. If cavernous nerve sparing is undertaken, the apical and posterior dissection is modified. Denonvilliers fascia is incised at the prostatic base, allowing access to the vasa, which are divided and seminal vesicles, which are excised. The bladder neck is divided, thereby freeing the prostate. The bladder neck is reconstructed to the approximate diameter of the membranous urethra. A sutured vesico-urethral anastomosis is stented by a urethral catheter, typically for 10-14 days. The wound is closed leaving pelvic drains, typically for 48 h. A cystogram is required only if there has been a documented urine leak or other catheter problem.

The nerve-sparing modification aims to reduce the risk of post-operative ED. The surgeon seeks to minimize injury to the cavernosal nerves passing from the autonomic pelvic plexus on either side in the groove between prostate and rectum, during mobilization of the prostate. This should not be attempted in the presence of palpable disease as it may compromise cancer control. The tips of the seminal vesicles may also be spared in cases with low risk of cancer involvement, potentially reducing bleeding and cavernosal nerve injury.

There are general and specific complications of radical prostatectomy. General complications are those of any major surgery: bleeding requiring re-operation and/or transfusion, infection, thromboembolism and cardiac disturbance. These are minimized by attention to hemostasis, prophylactic antimicrobials, pneumatic calf compression, low-dose heparin post-operatively and early mobilization. Chest infection may be prevented by physiotherapy and encouragement of deep breathing, especially in smokers.

Specific complications are perioperative obturator nerve, ureteric or rectal injuries. These should be managed immediately if recognized end-to-end nerve anastomosis, ureteric re-implantation or primary rectal closure with or without a loop colostomy. Postoperative ED affects 70-90% of patients. Spontaneous erections may return up to 3 years post-operatively. Men >65 years or with pre-existing ED are more likely to suffer long term. Most patients will respond to oral PDE5 inhibitors at 6 months, while others require intraurethral or intracavernosal prostaglandin E1 treatments, a vacuum device or a artificial prosthesis implantation. SUI affects 5% of patients beyond 6 months. This is due to injury of the external urethral sphincter during division and haemostatic control of the dorsal vein complex. Predisposing factors include age >65 years and excessive bleeding. Pre-operative teaching of pelvic floor exercises helps to regain continence. Periurethral bulking injections or implantation of an artificial urinary sphincter are occasionally necessary. Incontinence may also develop secondary to bladder neck stenosis or detrusor instability. Bladder neck stenosis affects 5-8% of patients, typically occurs 2-6 months post-operatively, rarely becoming a recurrent problem. Predisposing factors include heavy bleeding, post-operative urinary leak and previous TURP. Patients complain of new voiding difficulties and treatment is by endoscopic bladder neck incision.

Study comparing RP to WW has demonstrated a 50% reduction in death due to PC and a 66% reduction in metastatic progression in the RP group with a mean follow-up of only 6 years. High-grade cancers were excluded from this trial,

though non-randomized data suggest more patients with Gleason 7-10 localized disease survive 10 years following RP than with WW or radiotherapy.

Excellent long-term results are seen in well-selected patients following RP, particularly those with organ-confined disease. Serum PSA is measured a few days after RP, then 6-monthly and it should fall to <0.1 ng/ml. The 10-year PSA progression rate following RP with a serum PSA >0.2 ng/ml is about 30%. Without additional treatment, the time to development of clinical disease after PSA progression averages 8 years. A 20-year clinical disease-free survival of 60% is reported.

Management of biochemical relapse post-RP

The definition of rising PSA is controversial, though most agree >0.2 ng/ml. DRE should be performed. Biopsy of the vesicourethral anastomosis is not widely practised unless there is a palpable abnormality. Studies have shown that MRT and bone scans are rarely helpful in searching for metastatic disease unless the PSA is >7 ng/ml. Current management options include observation, pelvic radiotherapy or hormone therapy.

External beam radiotherapy

Advances in radiotherapy for localized PC have included the advent of linear conformal accelerators and intensity-modulated techniques to minimize toxicity to the rectum and bladder. EBRT is administered with curative intent, often accompanied by 3 months of neoadjuvant hormone therapy in high-risk cases. There is benefit in terms of progression and survival for patients treated with 6 months androgen ablation, in addition to radiotherapy, compared with radiotherapy alone.

Indications are clinically localized PC, life expectancy >5 years. Patients with Gleason score 2-4 disease appear to do as well with WW as with any other treatment with 15-year follow-up. Contraindications are severe LUTS, inflammatory bowel disease, previous pelvic irradiation

Protocol: a 6-week course of daily treatments amounting to a dose of 60-72Gr. Side-effects of such treatment options are transient LUTS and GIT symptoms, hematuria, contracted bladder, pain, ED and the risk of a second solid pelvic malignancy.

Brachytherapy

This is US-guided transperineal implantation of radioactive seeds of I^{125} into the prostate gland. BT is minimally invasive, requires general anaesthesia and is completed in one or two stages. Either way, approximately 150 Gr is delivered and this may be augmented by an EBRT boost. Another approach is to use Iridium¹⁹² wires, left for several hours in situ in a series of applications, either before or after EBRT. The treatment is expensive due to the cost of the consumables.

Indications are: localized T1-2 PC with Gleason <7 , PSA <10 ng/ml, life expectancy >5 years. Contraindications are previous TURP because of incontinence risk, large volume prostate causes difficulty with seed placement, moderate to severe LUTS. Complications are: perineal hematoma, LUTS, urinary retention, incontinence. ED affects up to 50% of patients.

Cryotherapy

This is minimally invasive treatment for localized PC. This is viable alternatives to radical surgery or ERBT and the only current options for salvage treatment of organ-confined recurrent disease following radical radiotherapy.

Transperineal US-guided cryoprobes delivering argon or liquid nitrogen at a temperature of -20 to -40°C. When applied in two cycles of “freezing - thawing”, cellular necrosis occurs. The diameter of the ice-ball is monitored with help of US. Precautions must be taken to protect the urethra, external sphincter and rectal wall, such as warming devices. An anaesthetic is required; this is a day-case procedure which can be repeated.

PSA nadir is usually achieved within 3 months. 1/4-1/2 of men with localized disease achieve a PSA nadir of <0.1ng/ml in 3 months and 96% of men achieve PSA <0.2ng/ml within 6 months. Positive biopsies are observed. Long-term results are awaited.

Complications are: ED, incontinence, LUTS, CPPS, transient penile numbness, recto-urethral fistula (rare).

HIFU

HIFU allows the selective destruction of tissues at depth without damaging intervening structures. Tissue is heated to the point of coagulative necrosis by high-energy US transmitted to the prostate using a transrectal device. The tissue temperature is raised locally at this point over 85°C. With each firing of the probe a “cigar shaped” volume of damage is produced. After one lesion is created, the focus is repositioned in order to create the next lesion with the same heating process. Lesions are placed side by side to create a continuous volume in which the tissue is necrosed. The rectal wall and the surrounding tissues are protected. An anaesthetic is required. This is a day-case procedure which can be repeated. Long-term results are awaited.

Treatment of locally advanced non-metastatic PC (T3-T4 N0M0)

EBRT in combination with hormone therapy has consistently demonstrated better outcomes compared to EBRT alone, which is associated with a low 10-year survival. There are potential advantages in starting hormone therapy prior to EBRT.

Hormone therapy alone is another option in elderly patients or those unwilling to consider ERBT. In this setting, a non - steroidal anti-androgen (e.g. bicalutamide 150 mg) has equivalent efficacy to androgen deprivation by orchidectomy or LH-RH analogue, with potential advantages in terms of side-effects.

WW is also an option for non-metastatic T3 disease in an elderly asymptomatic man who may wish to avoid side- effects of treatment.

Palliative treatment of locally advanced disease

Palliative TURP or medical therapy for LUTS or retention may be necessary. Incontinence can be due to sphincter involvement, though BOO and instability should be considered. Catheter may be required. PNS tubes or ureteric stents are occasionally necessary for ureteric obstruction. Rarely, a colostomy is necessary to bypass a rectal stenosis.

Treatment of advanced prostate cancer

Endocrine therapy

Metastatic disease is the cause of nearly all PC-related death. Currently incurable with 5-year survival is 25% and 10% survive <6 months. The mainstay of treatment is hormone therapy, with cytotoxic chemotherapy in reserve and novel treatments such as growth factor inhibitors, angiogenesis inhibitors, immunotherapy and gene therapy in development. The concept of hormone therapy was established in 1941 when Huggins and Hodges reported favourable responses in PC patients castrated or given oestrogens.

There is hormone dependence of PC. 95% of circulating androgen, mainly testosterone, is produced by the Leydig cells of the testes under the influence of LH. The anterior pituitary LH synthesis, stimulated by LH-RH, produced by the hypothalamus. The remaining 5% of circulating androgen is synthesized by the adrenal cortex from cholesterol, under the influence of pituitary ACTH. Testosterone is metabolized to the more potent DHT, by 1 and 2 types of 5-AR enzymes. DHT binds to the androgen receptor, travels to the cell nucleus and exerts its positive effect on cell growth and division. All prostate epithelial cells are dependent on androgens and fail to grow or undergo apoptosis in their absence. Similarly, most previously untreated PC are dependent on androgens.

Androgen deprivation results in a reduction in PSA and clinical improvement in >70% of PC patients. However, most will still die within 5 years due to the development of androgen-independent growth. This is considered to be due to growth of androgen-independent cell clones. The mean time to disease progression after androgen deprivation is 14 months in men with metastatic disease.

Types of androgen deprivation:

- Surgical castration: bilateral orchidectomy;
- Medical castration: using of the LH-RH agonists, oestrogens - also termed androgen ablation or androgen deprivation;
- Anti-androgens: androgen receptor blockade at target cell;
- MAB: medical or surgical castration plus anti-androgen;
- 5-ARI with finasteride or dutasteride.

Both forms of castration have equivalent efficacy, so patients should be given the choice. Estrogens are no longer used first-line, due to the significant cardiovascular morbidity. Anti-androgens alone are less effective in treating metastatic disease, but equivalent for non-metastatic disease. MAB has a theoretical advantage over castration in blocking the effects of the adrenal androgens, but significant clinical advantages have not been demonstrated. 5ARIs are not licenced for the treatment of PC, but appear to have a role in prevention. Bilateral orchidectomy is a simple procedure, usually carried out under general anaesthesia. Through a midline scrotal incision, both testes may be accessed. The tunica albuginea of each testis is incised and the soft tissue content is removed, after which the capsule is closed. The epididymis is preserved. Serum testosterone falls within 8h to <0.2 nmol/l.

LH-RH agonists developed in the 1980s, giving patients an alternative to bilateral orchidectomy, with which they are clinically equivalent. They are given by

subcutaneous or intramuscular injection, as 3-monthly depots. Examples include goserelin, triptorelin and leuprorelin acetates. If the anterior pituitary is overwhelmed with an analogue of LH-RH, it switches off LH production, although serum testosterone rises in the first 2 weeks due to a surge of LH. This can result in “tumour flare”. To prevent this, cover with anti-androgens is recommended for a week before and two weeks after the first dose of LH-RH agonist.

Side effects of androgen deprivation are: loss of libido and ED, hot flushes and sweats, weight gain, gynaecomastia, anemia, cognitive changes, osteoporosis and pathological fractures.

Anti-androgens are administered as tablets. Examples include bicalutamide (150 mg daily as monotherapy or 50mg daily for MAB, in combination with LH-RH analogues or orchidectomy), flutamide and cyproterone acetate. The first two raise the serum testosterone slightly, so sexual interest and performance should be maintained, although many such patients have pre-existing ED due to the advancing disease. Side-effects include frequent gynaecomastia, breast tenderness and occasional liver dysfunction.

5-ARIs are used by treatment of PC patients. Given that PC starts, in the main, as an androgen-dependent disease, interest in its prevention has also focused on antiandrogens. While non-steroidal antiandrogens would have unacceptable side-effects and cost, the 5-ARIs could be feasible chemoprevention agents. The Prostate Cancer Prevention Trial recruited 18,000 men who had no clinical or biochemical evidence of PC. They were randomized to placebo or finasteride 5mg daily for up to 7 years. The men were offered biopsy if they developed a rising PSA, an abnormality on DRE or at end of study. PC was detected in 24% and 18% of participants in placebo and finasteride arms respectively, suggesting that finasteride reduces the risk of developing PC by 25%. However, Gleason >7 cancers were significantly more frequent in the finasteride arm. While this could be due to the effect of the 5-ARIs on tissue architecture, nobody is rushing to recommend this to their patients without full discussion of the implications.

Monitoring of the endocrine treatment

Typically, patients will have baseline PSA, full blood count, renal and liver function tests, a renal US and a bone scan. The PSA is repeated after 3 months, 6 months and 6-monthly thereafter until it rises. Liver function is checked 3-monthly if anti-androgen monotherapy is used. Renal function should be checked on disease progression and bone imaging if clinically indicated. While PSA is very useful as a marker for response and progression, 15% of patients show clinical progression without PSA rise. This may occur in anaplastic tumours that fail to express PSA. Advice on exercise, diet and treatment of ED is often sought by patients during treatment.

Hormone therapy in the patients with androgen-independent disease

When the PSA rises from its lowest value or if symptomatic progression occurs despite a favorable biochemical response to first-line hormone therapy, the disease has entered its androgen-independent phase. In these circumstances, further

treatment with second-line hormonal therapy is usually considered. Most patients receiving anti-androgen monotherapy respond after switching to androgen ablation orchiectomy or LH-RH analogue. If there is relapse during androgen ablation, 1/4 respond by adding an anti-androgen to establish MAB. If MAB was used from initiation of hormone therapy, withdrawal of the anti-androgen paradoxically elicits a favourable response in 1/4 of patients.

A further rise in PSA may require third-line hormonal therapy such as the addition of oestrogens or corticosteroids.

The prognostic factors for survival with androgen-independent disease are identical to the factors predicting response to hormone therapy, plus time from initiation of hormone therapy to initiation of chemotherapy and visceral metastasis status.

Cytotoxic chemotherapy

Systemic chemotherapy is offered to appropriate patients with androgen-independent metastatic disease. Men with low-volume disease who have failed radical local treatment and hormone therapy are also candidates for chemotherapy. Elderly, frail and infirm patients with significant bone disease, renal impairment, haematological and clotting abnormalities are unsuitable. Correction of renal and bone marrow dysfunction is necessary prior to treatment. Symptom improvements are reported with cytotoxic chemotherapy (mitoxantrone plus prednisolone, prednisolone alone, docetaxel plus prednisolone, estramustine phosphate plus docetaxel). The involvement of the acute pain team, palliative care physicians and nurses is often necessary in the terminal phase of the illness, to optimize quality of life.

5.2. BLADDER CANCER

Epidemiology, etiology and risk factors

Bladder cancer is the second most common urological cancer. This represents 3% of all cancer deaths.

Risk factors:

- Chemical carcinogens due to smoking (30-50%) and exposure to chemical products, found in urine, are the major cause of BC. Cigarette smoke contains the carcinogens 4-aminobiphenyl and 2-naphthylamine. Slow hepatic detoxification and renal excretion of chemical products appear to increase urinary carcinogenic exposure of the urothelium. Smokers have a 2-5 fold risk compared to non-smokers, with respect to development of BC and recurrences. There is a slow (20-year) reduction in risk following cessation of smoking;
- Men are 2.5 times more likely to develop the disease than women, which may be associated with greater urine residuals in the bladder in patients with BPH;
- Age increases risk, most commonly diagnosed in the 8th decade and rare <50 years;
- Black people have a lower incidence than White people, but inexplicably they appear to carry a poorer prognosis;
- Chronic inflammation of bladder mucosa due to bladder stones, long-term catheters and bilharziasis are implicated in the development of SCC of the bladder;
- Occupational exposure to carcinogens, in particular aromatic hydrocarbons like

aniline, is a recognized cause of BC (rubber, dye, textile or leather manufactures; plumbers, painters, drivers). A latent period of 25-45 years exists between exposure and carcinogenesis;

- Drugs: phenacitin and cyclophosphamide;
- Pelvic radiotherapy for other malignancies;
- Hereditary genetic etiology because of many somatic genetic abnormalities have been identified in TCC patients.

Pathology

- Benign tumours of the bladder are rare;
- The vast majority of primary BC are malignant and epithelial in origin and >90% are TCC, which may be single or multifocal. Because 5% of patients will have a synchronous upper tract TCC and metachronous recurrences may develop after several years the urothelial “field-change” theory of polyclonality is favoured over the theory of tumour monoclonality with implantation of the tumor cells.
- 1-7% of BC are SCC most common in areas where schistosomiasis is endemic. SCC is usually solid or ulcerative and muscle-invasive at presentation. SCC in the bladder is associated with chronic inflammation and urothelial squamous metaplasia, rather than CIS. 5% of paraplegics with long-term catheters develop SCC. Smoking is also a risk factor for SCC.
- Adenocarcinoma is rare, usually solid/ulcerative, G3 and carries a poor prognosis. 1/3 originate in the urachus, the remnant of the allantois, located deep to the bladder mucosa in the dome of the bladder. Adenocarcinoma is a long-term complication of bladder exstrophy and bowel implantation into the urinary tract, particularly bladder substitutions and ileal conduits after cystectomy.
- There are also phaeochromocytoma, melanoma, lymphoma and sarcoma arising within the bladder muscle.
- Secondary BC are mostly metastatic adenocarcinoma from GIT, prostate, kidney or ovary.

Tumor Node Metastasis classification of bladder cancer (2009)

T – Primary tumor

TX – Primary tumor cannot be assessed

T0 – No evidence of primary tumor

Ta – Non – invasive papillary carcinoma

Tis - Carcinoma in situ: “flat tumor”

T1 – Tumor invades subepithelial connective tissue

T2 – Tumor invades muscle

T2a – Tumor invades superficial muscle (inner half)

T2b - Tumor invades deep muscle (outer half)

T3 – Tumor invades perivesical tissue

T3a – Microscopically

T3b – Macroscopically (extravesical mass)

T4 – Tumor invades prostate, uterus, vagina, pelvic or abdominal wall

N – Lymph nodes

NX – Regional lymph nodes cannot be assessed

N0 – No regional lymph node metastasis

N1 – Metastasis in a single lymph node in the true pelvis

N2 – Metastasis in multiple lymph nodes in the true pelvis

N3 – Metastasis in common iliac lymph node(s)

M – Distant metastasis

MX – Distant metastasis

M0 – No distant metastasis

M1 – Distant metastasis

Primary TCC is considered clinically as superficial (Ta, T1, CIS) or muscle-invasive (T2-T3).

Flat, high – grade tumours that are confined to the mucosa are classified as CIS, which is a flat, high-grade, non-invasive urothelial carcinoma. It can be missed at cystoscopy or be considered as an inflammatory lesion if it is not biopsied. CIS is often multifocal and can occur in the bladder, but also in the upper urinary tract, prostatic ducts and prostatic urethra.

In 2004, the WHO published a new histological classification of urothelial carcinomas which provides a different patient stratification between individual categories compared to the older 1973 WHO classification. Recently an update of the WHO grading classification was published, but the following guidelines are still based on the 2004 WHO classification.

1973 WHO grading for urothelial papilloma

- Grade 1: well differentiated;
- Grade 2: moderately differentiated;
- Grade 3: poorly differentiated;

2004 WHO grading system for papillary lesions

- Urothelial papilloma (completely benign lesion);
- Papillary urothelial neoplasm of low malignant potential (PUNLMP);
- Low-grade (LG) papillary urothelial carcinoma;
- High-grade (HG) papillary urothelial carcinoma;

Symptoms and signs

- First, early and the most common presenting symptom is painless total hematuria. This may be initial or terminal if the lesion is at the bladder neck or in the prostatic urethra.
- Asymptomatic microscopic hematuria, found on routine urine stick-testing;
- Pain is unusual, even if the patient has obstructed upper tracts, since the obstruction and renal deterioration arise gradually. Pain may be observed by cystitis or muscle invasion;
- LUTS, such as urgency or suprapubic pain. This so-called “malignant cystitis” is typical in patients with CIS and SCC;
- Recurrent UTIs;

- Advanced cases may present with lower-limb swelling due to lymphatic/venous obstruction, bone pain, weight loss, anorexia, confusion and anuria due to bilateral ureteric obstruction;
- Urachal adenocarcinomas may present with a blood or mucus umbilical discharge or a deep subumbilical mass;
- General examination may reveal pallor, indicating anemia due to chronic renal impairment or blood loss;
- Abdominal examination may reveal a suprapubic mass in the case of locally advanced disease;
- DRE and bimanual examination may reveal a mass above or involving the prostate;
- Although the likelihood of diagnosing BC in patients <50 years is low, all patients with these presenting features should be investigated.

Diagnosis

After a UTIs has been excluded or treated, all patients with hematuria require investigation of their upper tracts, bladder and urethra. Usually, renal US and cystoscopy, performed under local anaesthetic, are first-line investigations.

If these fail to find a cause, an IVU, CT and urine cytology are second-line investigations. CT before and after IV contrast is becoming the best investigation of hematuria. It is faster and more sensitive than US or IVU in the detection of renal and ureteric tumours. However, it carries a higher radiation dose and is more expensive. CT also detects some bladder tumours, but may overcall bladder wall hypertrophy as tumour and will miss flat CIS and urethral pathology and it cannot replace cystoscopy. If there is hydronephrosis in association with a bladder tumour, it is likely that the tumour is causing the obstruction to the distal ureter with muscle-invasive disease.

Patients with predominantly filling-type LUTS, suprapubic pain or recurrent UTIs should also have urine cytology and cystoscopy.

False negative cytology is frequent (40-70%) in patients with papillary TCC, but more sensitive (90-100%) in patients with high-grade TCC and CIS. False positive cytology can arise due to UTIs, inflammation, instrumentation and chemotherapy.

If all investigations are normal, consideration should be given to nephrological disorders that may cause hematuria, such as glomerulonephritis. Cross-referral to a nephrologist is advised in patients with persisting microscopic hematuria, especially those with associated proteinuria, casts or hypertension.

Diagnostic TUR of bladder tumor

This provides definitive histological diagnosis and usually undertaken under general or spinal anaesthesia. Bimanual examination is mandatory before and after bladder tumor resection, to assess size, position and mobility. The pathologist should report on the tumor type, grade and stage. In particular, the presence or absence of muscularis propria should be noted, since its absence will preclude reliable T staging. Red patches are biopsied separately, the prostatic urethra is

biopsied if radical reconstructive surgery is under consideration. Care is taken in resecting tumours at the dome, since intraperitoneal bladder perforation may occur, especially in women with thin-walled bladders.

Staging investigations

This usually reserved for patients with biopsy-proven muscle-invasive BC unless clinically indicated, since superficial TCC and CIS disease are rarely associated with metastases. Pelvic CT or MRT may demonstrate extra-vesical tumour extension or iliac lymphadenopathy, reported if >8mm in maximal diameter. Chest X-ray is indicated for suspicion lesions of the lungs. Isotope bone scan is obtained in cases being considered for radical treatment. Open or laparoscopic lymphadenectomy may be indicated in the presence of CT-detected pelvic lymphadenopathy if radical treatment is under consideration.

Treatment of superficial bladder cancer

TUR

This is visually complete resection of bladder wall with tumor and is adequate treatment for 70% of newly presenting patients with Ta/T1 superficial disease. The remaining 30% of patients experience early recurrence, 15% with upstaging. Because of this, it is proposed that all new patients receive adjuvant treatment.

Complications are uncommon, including bleeding, urosepsis, bladder perforation, incomplete resection and urethral stricture. Alternatively, transurethral laser ablation is less likely to cause bleeding but histological sampling would be inadequate.

Most urologists perform review cystoscopy and second TUR at 1 months. If this demonstrates recurrence, 70% will further recur. If not, only 20% will further recur. If the bladder is clear at follow-up, further cystoscopies are performed at 3-6 months and thereafter annually until the patient is no longer fit to undergo treatment. There is no accepted protocol for upper tract surveillance in patients with a history of bladder TCC, although some urologists recommend 2-yearly IVU, US and urine cytology.

Adjuvant intravesical chemotherapy

Intravesical chemotherapy with MMC (40 mg in 50 ml saline) is used for GI-2, Ta or T1 tumours and recurrent multifocal TCC. MMC is an antibiotic chemotherapeutic agent that inhibits DNA synthesis. In experimental studies, it may cause regression of small papillary TCC, so should be cytotoxic for microscopic residual disease post TURBT. It significantly reduces the likelihood of tumor recurrence compared to TUR BT alone, but has never been shown to prevent progression to muscle invasion and has no impact on survival.

It is used either as a single dose within 24 h of first TURBT or weekly for 6 weeks commencing up to 2 weeks post TUR BT. It is administered via a urethral catheter and held in the bladder for 1 h. Other agents include doxorubicin and epirubicin. 15% patients report transient LUTS. Occasionally a rash develops on the genitals or palms of the hands, so treatment must be stopped. Systemic toxicity is rare with MMC.

Adjuvant intravesical BCG

BCG is an attenuated strain of Mycobacterium. It acts as an immune stimulant, upregulating cytokines such as IL-6 and IL-8 in the bladder wall. BCG is given as a 6-week course for G3T1 TCC and for CIS, starting at least 2 weeks post TURBT. It is administered via a urethral catheter, 80 mg in 50 ml saline and retained in the bladder for 1 h. BCG produces complete responses in 60-70% of patients compared to TURBT alone and may delay tumor progression to muscle invasion. 30% do not respond and 30% of responders relapse within 5 years. It is more effective than MMC for adjuvant treatment of some types of BC, but is not often used because of the additional toxicity.

Though less expensive and more effective, BCG is more toxic than intravesical chemotherapy, causing LUTS in nearly all patients and low-grade fever with myalgia in 1/4 cases. Up to 10% of patients develop a high persistent fever, requiring anti-tuberculous therapy for up to 6 months. Granulomatous prostatitis and epididymo-orchitis are rare complications.

Contraindications: immunosuppressed patients, pregnant or lactating women, patients with hematological malignancy, traumatic catheterization.

Cystoscopy too early after BCG can look alarming, due to generalized inflammatory response. Review cystoscopy and biopsy 3 months after BCG may still reveal chronic granulomatous inflammation. The value of maintenance BCG is uncertain, although one study demonstrated a benefit for superficial TCC, excluding CIS, compared with a single 6-week course.

Treatment of muscle-invasive bladder cancer (T2-T3a)

This is a poor type of BC, untreated 5-year survival is only 3%. For example 5-years survival rates by T1 is 90% and by T2-T3 is 60-80%.

Partial cystectomy

This is a good option for well-selected patients with small solitary disease located near the dome and for urachal carcinoma. Morbidity is less than with radical cystectomy. The surgical specimen should be covered with perivesical fat, with a 1.5 cm margin of macroscopically normal bladder around the tumor. There should be no biopsy evidence of CIS elsewhere in the bladder. The bladder must be closed without tension and catheterized for 7-10 days to allow healing. Subsequent review cystoscopies ensure no tumor recurrence.

Radical cystectomy with urinary diversion

This is the most effective primary treatment for muscle-invasive TCC, SCC and adenocarcinoma and can be used as salvage treatment if RT has failed. It is also a treatment for G3T1 TCC and CIS, refractory to BCG treatment. Salvage radical cystectomy is technically a more difficult and slightly more morbid procedure.

The operation steps are described below. Through a midline abdominal transperitoneal approach, the entire bladder is excised along with perivesical vascular pedicles, fat and urachus, plus the prostate or anterior vaginal wall. The anterior urethra is not excised unless there is prior biopsy evidence of tumor at the female

bladder neck or prostatic urethra. The ureters are divided close to the bladder, ensuring their disease-free status by frozen-section histology if necessary and anastomosed into the chosen urinary diversion methods. A bilateral pelvic lymphadenectomy is undertaken at the time.

Major complications affect 1/4 of cystectomy patients. These include peri-operative death (rare), re-operation, bleeding, thromboembolism, urosepsis, wound infection/dehiscence, intestinal obstruction or prolonged ileus (10%), cardio-pulmonary morbidity and rectal injury. ED is likely after cystectomy due to cavernosal nerve injury.

External beam radiotherapy

A good option for treating muscle-invasive (pT2/3/4) TCC in patients who are unfit or unwilling to undergo cystectomy, but who still wish to have the chance of cure. The 5-year survival rates are inferior to those of surgery, but the bladder is preserved and the complications are less significant. Typically, a total dose of 70Gy is administered in 30 fractions over 6 weeks. Higher-grade tumors tend to do less well, perhaps because of the undetected presence of disease outside the field of irradiation. Beyond this, prediction of radiotherapy response remains difficult, relying on follow-up cystoscopy and biopsy. CIS, SCC and adenocarcinoma are poorly sensitive to ERBT.

Complications occur in 70% of patients, self-limiting in 90% of cases. These include radiation cystitis and proctitis with diarrhoea and rectal bleeding. These effects usually last few months.

Treatment of locally advanced bladder cancer (pT3b/4)

Many patients treated with primary cystectomy or RT with curative intent will have metastatic disease due to incomplete tumor excision or micrometastases. At this stage, 5-year survival is only 5-10%. There is interest in augmenting primary treatment with help of adjuvant or neoadjuvant RT/chemotherapy in an effort to improve outcomes. Very low or no survival benefit has been demonstrated and it leads to unacceptably high morbidity or has no demonstrable advantages.

Treatment of metastatic bladder cancer

Systemic chemotherapy is routine for patients with unresectable, diffusely metastatic disease. Combination therapy (methotrexate, vinblastine, adriamycin and cisplatin - MVAC) is more effective than single-agent treatment. Gemcitabine has been used alone and in combination with cisplatin. Another new class of agents are taxanes paclitaxel and docetaxel. Long-term disease-free survival is rare. Roles for RT include palliation of metastatic pain and spinal cord compression.

Urinary diversion after cystectomy

Ureterosigmoidostomy

The oldest form of urinary diversion, whereby the ureters drain into the sigmoid colon, either in its native form or following its detubularization and reconstruction into a low-pressure pouch. This diversion requires no appliance (stoma bag, catheter), so remains popular in developing countries. In recreating a "cloaca", the

patient may be prone to upper UTIs with the risk of long-term renal deterioration, metabolic hyperchloraemic acidosis and loose, frequent stools.

Ileal conduit

This was developed in 1950 and remains the most popular form of urinary diversion in EU. 15 cm of subterminal ileum is isolated on its mesentery and the ureters are anastomosed to the proximal end. The distal end is brought out in the right iliac fossa as a stoma. The ileum is anastomosed to gain enteral continuity.

Complications: prolonged ileus, urinary and enteral leak, pyelonephritis, uretero-ileal stricture and stoma problems: skin irritation, stenosis and parastomal hernia.

Patients require stomatherapy support and some find difficulty in adjusting their lifestyle to cope with a stoma-bag. Metabolic complications are uncommon. A jejunal or colonic conduit are also used. The conduit may be brought out in the upper abdomen and patients require careful electrolyte monitoring due to sodium loss and hyperkalaemia.

Continent diversion

The advantage of such a diversion is the absence of an external collection device. A neobladder or pouch is fashioned from 60 cm of detubularized ileum or right hemicolon. The ureters drain into the neobladder, usually through an anti-reflux submucosal tunnel. This may be drained by the patient via a catheterizable stoma, such as the appendix or uterine tube (the "Mitrofanoff principle") brought out in the right iliac fossa. Alternatively, the neobladder may be anastomosed to the patient's urethra so that natural voiding can be established. Patients void by relaxing their external sphincter and performing a Valsalva manoeuvre with abdominal walls straining. This orthotopic neobladder should require no catheter, unless the pouch is too large and fails to empty adequately. In this case, the patient must be prepared to perform CISC.

Popular ileal pouch include Studer operation. The distal 40-44 cm of resected ileum opened along the antimesenteric border with scissors. Spatulated ureters are anastomosed end-to-side with 4/0 running suture on either side of proximal end of afferent tubular ileal limb. Ureters are stented. The 2 medial borders of the U-shaped, opened, distal ileal segment are oversewn with a single-layer continuous suture. The bottom of the U is folded between the 2 ends of the U. Before complete closure of the reservoir, a 8-10 mm hole is cut into the most caudal part of the reservoir. Six sutures are placed between the seromuscular layer of the anastomotic area of the reservoir and the membranous urethra. An 18F urethral catheter is inserted. Before complete closure of the pouch, a cystostomy tube is inserted and brought out suprapubically adjacent to the wound.

Which urinary diversions are chosen comes down to the surgeon's preference. They carry similar complication risks. Previously irradiated bowel can safely be used to form pouches, though complications are more likely.

Complications relating to neobladders include: stone formation, urinary leakage and peritonitis, pelvic abscess, catheterizing difficulties and stomal stenosis,

urinary incontinence and nocturnal enuresis, pouch-ureteric reflux and UTIs, uretero-pouch anastomotic stricture, late neobladder rupture.

Metabolic abnormalities include early fluid and electrolyte imbalances, later, urinary electrolyte absorption may cause hyperchloraemic acidosis and loss of small bowel may result in vitamin B12 deficiency. Metabolic acidosis is less likely in patients with normal renal function. Treatment is with sodium bicarbonate and potassium citrate. Annual B12 monitoring should be undertaken, with supplementation if necessary.

Adenocarcinoma may develop in intestinal conduit (rare), neobladder or sigmoid colon mucosa in the long term, due to the carcinogenic bacterial metabolism of urinary nitrosamines. This tends to occur near to the inflow of urine. It is therefore advisable to perform annual visual surveillance of urinary diversions after 10 years. If the urethra is in situ, annual urethroscopy and cytology is important.

5.3. RENAL PELVIC AND URETERAL CANCERS

TCC accounts for 90% of upper urinary tract tumors. Renal pelvic TCC is uncommon, accounting for 10% of renal tumors and 4% of all TCC. Ureteric TCC is rare, accounting for only 1% of all new cases of TCC. Half are multifocal, 75% located distally, while only 3% are located in the proximal ureter. Risk factors are similar to those of TCC in the BC. Male:female ratio 3:1. Incidence increases with age. Smoking confers a two-fold risk and there are various occupational causes.

Pathology

The tumor usually has a papillary structure, but occasionally solid. It is bilateral in 2-4%. It arises within the renal pelvis, less frequently in one of the calyces or ureter. Histologically, features of TCC are present.

TNM classification 2009 for upper tract urothelial carcinoma

T – Primary tumor

TX – Primary tumor cannot be assessed

T0 – No evidence of primary tumor

Ta – Non-invasive papillary carcinoma

Tis – CIS

T1 – Tumor invades subepithelial connective tissue

T2 – Tumor invades muscle

T3 – Renal pelvis: Tumor invades beyond muscularis into peripelvic fat or renal parenchyma. Ureter: Tumor invades beyond muscularis into periureteric fat

T4 – Tumor invades adjacent organs or through the kidney into perinephric fat

N – Regional lymph nodes

NX – Regional lymph nodes cannot be assessed

N0 – No regional lymph node metastasis

N1 – Metastasis in a single lymph node <2 cm

N2 – Metastasis in a single lymph node >2 cm but <5 cm or multiple lymph nodes, none more than 5cm

N3- Metastasis in a lymph node >5 cm

M – Distant metastasis

M0 – No distant metastasis

M1 – Distant metastasis

Symptoms and signs

- Painless total hematuria;
- “Clot colic”: Loin pain, often caused by clots passing down the ureter;
- Asymptomatic when detected, associated with synchronous bladder TCC;
- At follow-up, ~50% of patients will develop a metachronous bladder TCC and 2% will develop contralateral upper tract TCC.

Diagnosis

US is excellent for detecting the more common renal parenchymal tumors, but not sensitive in detecting tumors of the renal pelvis or ureter. Diagnosis is usually made on urine cytology and IVU or CT, respectively revealing malignant cells and a filling defect in the renal pelvis or ureter. If doubt exists, selective ureteric urine cytology, retrograde pyeloureterography or URS are indicated. If US and cystoscopy are normal during the investigation of hematuria, an IVU or CT is recommended. Staging imaging is obtained by contrast-enhanced abdominal CT, chest X-Ray and isotope bone scan.

Treatment***Nephroureterectomy***

If staging indicates non-metastatic disease in the presence of a normal contralateral kidney, the “gold standard” treatment with curative intent is nephroureterectomy, open or laparoscopic. The open approach uses either a long transperitoneal midline incision or separate loin and iliac fossa incisions. The entire ureter is taken with a cuff of bladder, because of the 50% incidence of subsequent ureteric stump recurrence. Follow-up should include annual cystoscopy, IVU or CT to detect metachronous TCC development.

Percutaneous/ureterorenoscopic resection/ablation

For patients with a single functioning kidney, bilateral disease or those who are unfit, percutaneous or URS resection or ablation of the tumors are the minimally invasive options. Topical chemotherapy with MMC may subsequently be instilled through the nephrostomy or ureteric catheters. This nephron-sparing approach is less likely to be curative than definitive surgery.

Systemic combination chemotherapy for unresectable or metastatic disease using cyclophosphamide, methotrexate and vincristine is associated with a 30% total or partial response at the expense of moderate toxicity. Palliative surgery or arterial embolization may be necessary for troublesome hematuria. Radiotherapy is generally ineffective.

5.4. RENAL TUMORS

5.4.1. Benign renal masses

The most common are simple cysts, present in >50% of >50-year-olds. Rarely symptomatic, treatment by aspiration under US or laparoscopic excision are seldom considered. Most benign renal tumors are rare. The two most clinically important are oncocytoma and AML.

Oncocytoma

This is uncommon, accounting for 3-7% of renal tumors. Male:female ratio is 2:1. They occur simultaneously with RCC in 7-32% of cases.

Oncocytomas are spherical, capsulated, brown/tan colour, mean size 4-6 cm. Half contain a central scar. They may be multifocal and bilateral and extend into perinephric fat. Histologically, they comprise aggregates of eosinophilic cells, packed with mitochondria. Mitoses are rare and they are considered benign, not known to metastasize. There is often loss of the Y chromosome.

Oncocytomas often present as an incidental finding or with loin pain or hematuria. Oncocytoma cannot often be distinguished radiologically from RCCs and may co-exist with RCC. Rarely, they exhibit a “spoke-wheel’s” pattern on CT scanning, caused by stellate central scar. Percutaneous biopsy is not recommended since it often leads to continuing uncertainty about the diagnosis. Radical or partial nephrectomy is indicated, as for RCC. No follow-up is necessary.

Angiomyolipoma

80% of these benign clonal neoplasms (hamartomas) occur sporadically, mostly middle-aged females. 20% are in association with TS - an autosomal dominant syndrome characterized by mental retardation, epilepsy, adenoma sebaceum and other hamartomas. 50% of TS patients develop AMLs. Mean age 30 years, 66% female, frequently multifocal and bilateral.

AML is composed of blood vessels, smooth muscle and fat. They are always considered benign, although extrarenal AMLs have been reported in venous system and hilar lymph nodes. Macroscopically, it looks like a well-circumscribed lump of fat. Solitary AMLs are more frequently found in the right kidney.

AMLs frequently present as incidental findings (>50%) on US or CT scans. They may present with flank pain, palpable mass or painless hematuria. Massive and life-threatening retroperitoneal bleeding occurs in up to 10% of cases.

US reflects from fat, hence a characteristic bright echo pattern. This does not cast an “acoustic shadow” beyond, helping to distinguish an AML from a calculus. CT shows fatty tumor as low-density is low in most of AMLs. If the proportion of fat is low, a definite diagnosis can not be made. Measurement of the diameter is relevant to treatment.

Many patients with AML >4 cm are symptomatic compared with only 1/4 with smaller tumors. Therefore, asymptomatic AMLs can be followed with serial US. While those bleeding or >4cm should be treated with renal resection or by embolization. Emergency nephrectomy or selective renal artery embolization may

be life-saving. In patients with TS, in whom multiple bilateral lesions are present, conservative treatment should be attempted.

5.4.2. Renal cell carcinoma

RCC - is the most common renal tumor, accounting for 85% of renal malignancies and 2% of all cancer deaths. RCC is the most lethal of all urological tumors, app. 40% of patients dying of the condition. Incidence has increased since the 1980s when US was introduced to clinical practice. It occurs in common sporadic and rare hereditary forms.

Etiology

Males are affected twice as commonly as females and peak incidence of sporadic RCC is 6th-8th decade.

Risk factors:

- Urban dwelling;
- Tobacco chewing, smoking cigarettes, pipe or cigars;
- Renal failure and hemodialysis;
- Obesity and hypertension;
- Asbestos exposure;
- The analgesic phenacitin abuse;
- Renal injury;
- Nutrition with fatty products consumption is considered important. Asian migrants to Western countries are at increased risk.
- Vitamins A, C, E and fruit/vegetable consumption are protective;
- 50% of individuals have genetic predisposition with autosomal dominant VHL syndrome characterized by pheochromocytoma, renal and pancreatic cysts and cerebellar hemangioblastoma. They develop RCC, often bilateral and multifocal. VHL syndrome occurs due to loss of both copies of a tumor suppressor gene. This results in upregulation of vascular endothelial growth factor, the most prominent angiogenic factor in RCC, explaining why some RCCs are highly vascular.

Pathology

RCC is adenocarcinoma of the renal cortex, believed to arise from proximal convoluted tubule. Usually tan coloured and solid, 7-20% are multifocal, 10-20% contain calcification and 10-25% contain cysts. Rarely grossly infiltrative, they are usually circumscribed by a pseudocapsule of compressed tissue.

Histological classification

- Conventional: arise from the proximal tubule, highly vascular, cells clear or granular;
- Papillary: papillary, tubular and solid variants. 40% multifocal, small incidental tumors could equate with "benign adenoma";
- Chromophobe: arises from the cortical portion of the collecting duct, possess a perinuclear halo of microvesicles;

- Collecting duct carcinoma: rare tumors in young patients with poor prognosis;
- Medullary cell: rare; arises from calyceal epithelium.
- The term “sarcomatoid” is used to describe an infiltrative, poorly differentiated variant of any type.

TNM classification system (2009)

T – Primary tumor

T0 – Primary tumor cannot be assessed

T1 – Tumour <7 cm, limited to the kidney

T1a – Tumor <4 cm, limited to the kidney

T1b – Tumor >4 cm but <7 cm in greatest dimension

T2 – Tumour >7 cm, limited to the kidney

T2a – Tumor >7 cm but <10 cm

T2b – Tumor >10 cm, limited to the kidney

T3 – Tumor extends into major veins or perinephric tissues but not into the ipsilateral adrenal gland or beyond Gerota’s fascia

T3a – Tumor grossly extends into the renal vein or invades perirenal and/or renal sinus fat (peripelvic), but not beyond Gerota’s fascia

T3b – Tumor grossly extends into the vena cava below the diaphragm

T3c – Tumor grossly extends into vena cava above the diaphragm or invades the wall of the vena cava

T4 – Tumor invades beyond Gerota’s fascia (including contiguous extension into the ipsilateral adrenal gland)

N – Regional lymph nodes

NX – Regional lymph nodes cannot be assessed

N0 – No regional lymph node metastasis

N1 – Regional lymph node metastasis

M – Distant metastasis

MX – Distant metastasis

M0 – No distant metastasis

M1 – Distant metastasis

Grading

is performed by the Fuhrman system (1 = well-differentiated; 2 = moderately differentiated; 3 and 4 = poorly differentiated) based on nuclear size, outline and nucleoli.

Symptoms and signs

More than 50% of RCCs are now detected incidentally on abdominal US carried out to investigate vague or unrelated symptoms. Thus, the stage at diagnosis of RCC is lower than it was in the pre-US era.

Of the symptomatic RCCs diagnosed, 50% of patients present with hematuria, 40% with loin pain, 30% of patients notice a mass and 25% have symptoms or signs of metastatic disease (night sweats, fever, fatigue, weight loss, hemoptysis). Less than

10% patients exhibit the classic triad: hematuria, pain and mass. Less common presenting features include acute varicocele due to obstruction of the testicular vein by tumour within the left renal vein and lower limb edema due to venous obstruction.

Paraneoplastic syndromes arise due to ectopic hormone secretion by the tumour. May be anemia due to hematuria and chronic disease. Polycythemia arises due to ectopic secretion of erythropoetin. Hypertension may be observed due to ectopic secretion of renin and renal artery compression. Hypoglycaemia is detected due to ectopic secretion of insulin, Cushing's syndrome due to ectopic secretion of ACTH, hypercalcaemia due to ectopic secretion of parathyroid hormone-like substance. Gynaecomastia, amenorrhoea and reduced libido may be observed due to ectopic secretion of gonadotrophins. Stauffer's syndrome (hepatic dysfunction, fever, anorexia) occur in 10-40% of patients. These may be associated with any disease stage.

Diagnosis

Full blood count may reveal polycythemia, anemia or high ESR. Serum Cr, BUN and electrolytes, calcium and liver function tests are essential.

Staging chest CT and bone scan will follow. Any suggestion of renal or IVC involvement on CT may be further investigated with MRT.

Angiography may be helpful in planning partial nephrectomy or surgery for abnormal kidneys. Contralateral kidney function is assessed by uptake and excretion of CT contrast, serum Cr measurement and an isotope renogram.

Abdominal US is first-line investigation for a patient with loin pain or a suspected renal mass. The size resolution for renal masses is 1.5 cm, exhibiting variable echo patterns. US may also detect renal cysts with smooth-walled, round or oval, without internal echoes and complete transmission with a strong acoustic shadow posteriorly. If the cyst has a solid intracystic element, septations, an irregular or calcified wall, further imaging with CT is indicated.

If a renal mass is detected, a thin slice CT scan before and after contrast is the most important investigation. In general, any solid enhancing renal mass is considered a RCC until proven otherwise. Even relatively avascular renal carcinomas enhance by 10-25 HU. Occasionally, an isodense but enhancing area of kidney is demonstrated ("pseudotumour") and may correspond to a harmless hypertrophied cortical column of Bertini or dysmorphic segment. Lymphadenopathy >2 cm is invariably indicative of metastases.

Bosniak developed the following radiological classification of renal cysts:

1. Uncomplicated, simple and benign, no follow-up if asymptomatic;
2. Minimally complicated, septa, calcification, hyperdense, benign but require radiological follow-up;
3. Complicated, irregular margin, thickened septa, thick irregular calcification, indeterminate, surgical exploration may be indicated;
4. Large, irregular cyst margins with solid components internally, cystic renal carcinoma until proved otherwise, surgery required.

MRT may be used for imaging the IVC, locally advanced disease, CRF or for allergic patients. Renal arteriography may be helpful to delineate the number and position of renal arteries in preparation for nephron-sparing surgery.

Treatment of localized renal cancer

Surgery is the good option for treatment for RCC. Increases in diagnosis of smaller early-stage RCC and the concept of cytoreductive surgery for advanced disease has impacted on surgical treatment strategies of the disease.

Open radical nephrectomy

This remains the gold standard treatment of localized RCC. The aim is to excise the kidney with Gerota's fascia, perhaps with ipsilateral adrenal gland and regional nodes, removing all tumour with adequate surgical margins. Surgical approach is transperitoneal with good access to hilar vessels or thoraco - abdominal for very large or T3c tumours. Following renal mobilization, the ureter is divided. Ligation and division of the renal artery or arteries should ideally take place prior to ligation and division of the renal vein to prevent vascular swelling of the kidney.

Excision of hilar or para-aortic/para-caval lymph nodes will improve pathological tumour staging. Lymph node involvement in RCC is a poor prognostic factor. Incidence ranges from 6% in T1-2 tumours, to 46% in T3a, to 62-66% in higher stage disease. Lymphadenectomy at time of nephrectomy will add prognostic information, especially if there is obvious lymphadenopathy, but therapeutic benefit remains unclear. Formal lymphadenectomy adds time and increases blood loss, while nodes are clear in about 95% of cases.

Complications include mortality up to 2% from bleeding or embolism of tumour thrombus and maybe bowel, pancreatic, splenic or pleural injuries.

Laparoscopic approach

Well accepted for treating benign disease, this approach appears suitable for T1 RCCs. Approaches are either transperitoneal or retroperitoneal. The kidney is removed whole or morselated in a bag through an iliac incision. Advantages over open surgery include less pain, reduced hospital stay and quicker return to normal activity. Morbidity is reported in 10-40% of cases. 5-year disease-specific survival may be >90% for T1 tumours.

Partial nephrectomy

Laparoscopic or open nephron-sparing surgery is the best option for multifocal, bilateral tumours, particularly if the patient has VHL syndrome or single functioning kidney. It has become acceptable to treat small tumours, even with a normal contralateral kidney, unless the tumour is close to the pelvicalyceal system. Arteriography or 3D CT reconstructions are helpful to the surgeon.

Open transperitoneal or loin approaches are used. Laparoscopic partial nephrectomy may be performed. The renal artery is clamped and the kidney packed with crushed ice. Generally, results are comparable with open surgery.

Specific complications include failure of complete excision of the tumour(s) leading to local recurrence and urinary leak from the collecting system. Some patients develop acute renal failure. Local recurrence is more common after partial nephrectomy, where it can be treated by a further partial or total nephrectomy.

Post-operative follow-up

This aims to detect local or distant recurrence to permit additional treatment if indicated. After partial nephrectomy, concern will also focus on recurrence in the remnant kidney. Typically, stage-dependent 6-monthly clinical assessment and annual CT imaging of chest and abdomen for many years.

5-year survival by organ-confined T1 is 90-100%, T2 is 60-95%, T3 is 50-80%, N+ is 5-30%, by distant metastasis is 5-30%.

Alternatives to surgery:

- Observation: small solid, well-marginated renal masses may be safely followed with repeat scans in elderly or unfit patients. Growth is slow and metastasis rare.
- Cryosurgery is performed using intra-operative US by open, percutaneous or laparoscopic routes. This is a nephron-sparing treatment option.
- HIFU is extra-corporeal minimally invasive and highly accurate treatment is under evaluation.

Treatment of the locally advanced RCC

Disease involving the IVC, right atrium, liver, bowel or posterior abdominal wall demands special surgical skills. In appropriate patients, an aggressive surgical approach will be needed to achieve negative margins. Pre- or postoperative ERBT or immunotherapy are used as adjuvant treatment.

Treatment of the metastatic RCC

~25-30% of patients with RCC exhibit metastatic disease at presentation and 20-30% progress subsequently to this stage following nephrectomy. The prognosis is poor. Nephrectomy is undertaken to relieve local symptoms of pain or hematuria. If inoperable, arterial embolization can be helpful. A median survival benefit of 10-12 months for patients with good performance status treated with cytoreductive nephrectomy prior to immunotherapy with interferons was reported.

Metastectomy may be of benefit to the 1.5-3% of patients who develop a solitary metastases following nephrectomy. Resection of solitary metastases is an option for a few patients, usually a few months after nephrectomy, thereby ensuring the lesion remains solitary.

Hormone therapy and chemotherapy have little role in RCC. Radiotherapy useful for palliation of metastatic lesions in bone and brain and in combination with surgery for spinal cord compression. The first cytokines to be used therapeutically, to activate anti-tumour immune response, were interferons and, subsequently, interleukin-2. Randomized studies in the 1990-s demonstrated modest response rates (10-20%) after systemic immunotherapy using these cytokines alone and in combination. Toxicity could be severe. Responses were more likely in patients with good performance status, prior nephrectomy and small-volume metastatic burden. The current first-line treatment of metastatic RCC is single-agent immunotherapy preceded by nephrectomy in selected patients.

As discussed earlier, most RCCs are highly angiogenic, so should be a good therapeutic target for angiogenesis inhibitors.

5.5. TESTICULAR CANCER

Primary TC is the most common solid cancer in men aged 20–45. Constituting 1–2% of all male cancers, the lifetime risk of developing TC is 1 in 500. It is also considered the most curable cancer. Bilateral testicular cancer occurs in 1–5% of cases.

Etiology and risk factors

- The most common affected age group is 20–45 years, with germ cell tumours. Rarely, infants and boys below 10 years develop yolk sac tumours and 50% men >60 years with TC have lymphoma.
- White:black peoples ratio is 3:1;
- 10% of TC occur in UDT. The risk increases by 5–18 times compared to men with normally descended testes. Because of ultrastructural changes are present in these testes by age 3 years, earlier orchidopexy does not completely eliminate the risk of developing TC. 5–10% of patients with a UDT will develop malignancy in the normally descended contralateral testis.
- IGCN synonymous with CIS. 50% of cases develop invasive germ cell TC within 5 years. Risk factors include cryptorchidism, extra-gonadal germ cell tumour, previous or contralateral TC, atrophic contralateral testis, 45XO karyotype and infertility.
- Patients infected with the HIV virus are developing TC more frequently;
- Genetic factors may play a role;
- Maternal estrogen ingestion during pregnancy increases the risk of cryptorchidism and TC in the male;
- Traumatic and post-orchitis atrophy may be implicated as risk factors for TC.

Pathology

90% of TC are malignant GCT are divided into seminomatous and non-seminomatous GCTs for clinical purposes. Seminoma appears pale and homogeneous. NSGCTs are heterogeneous and sometimes contain cartilage or hair.

WHO histopathological classification of testicular tumours

Germ cell tumours

Seminoma

Spermatocytic, classical and anaplastic subtypes

Non-seminomatous GCT

Teratoma:

Differentiated/mature

Intermediate/immature

Undifferentiated/malignant

Yolk sac tumour

Choriocarcinoma

Mixed NSGCT

Mixed GCT

Other tumours

- Epidermoid cyst (benign)
- Adenomatoid tumour
- Adenocarcinoma of the rete testis
- Carcinoid
- Lymphoma
- Metastatic, from another site

Sex cord stromal tumours

- Leydig cell
- Sertoli cell
- Mixed or unclassified

Mixed germ cell/sex cord tumours

The right testis is affected slightly more commonly than the left. Synchronous bilateral TC occurs in 2% of cases. TC spreads into the epididymis, spermatic cord and, rarely, the scrotal wall. Lymphatic spread occurs initially to the para-aortic nodes. Involvement of the epididymis, spermatic cord or scrotum may lead to pelvic and inguinal node metastasis. Blood-borne metastasis to the lungs, liver and bones may be observed.

TC is staged using various classifications, most recently the TNM (2009) system. T stage is pathological, N stage involves imaging and M stage involves physical examination, imaging and biochemical investigations. An additional S category is appended for serum tumour markers.

TNM classification for testicular cancer (2009)***pT – Primary tumor***

- pTX – Primary tumour cannot be assessed
- pT0 – No evidence of primary tumour
- pTis – IGCN
- 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 sperm. cord with or without vascular/lymphatic invasion
- pT4 – Tumour invades scrotum with or without vascular/lymphatic invasion

N – Regional lymph nodes

- NX – Regional lymph nodes cannot be assessed
- N0 – No regional lymph node metastasis
- N1 – Metastasis with a lymph node/s <2 cm
- N2 – Metastasis with a lymph node/s >2 but <5 cm
- N3 – Metastasis with a lymph node/s >5 cm

M – Distant metastasis

MX – Distant metastasis cannot be assessed

M0 – No distant metastasis

M1 – Distant metastasis

M1a - Non-regional lymph nodes/or lung

M1b – Other sites

S – Serum tumor markers levels

SX – Serum marker studies not available or not performed

S0 – Serum marker study levels within normal limits

S1-S2-S3: Pathological levels of LDH, hCG, AFP

Symptoms and signs

Testicular self-examination is indicated for young men. Most patients present with a scrotal lump, usually painless or slightly aching. There are patients with metastatic disease. This may be due to patient factors (fear, self-neglect, ignorance) or earlier misdiagnosis. Occasionally acute scrotal pain may occur, due to intratumoural hemorrhage, causing diagnostic confusion. The lump may have been noted by the patient, sometimes after minor trauma or by his partner. Symptoms suggestive of advanced disease include weight loss, lumps in the neck, chest symptoms and bone pain.

Examination of the genitalia should be carried out in a warm room with the patient relaxed. Using careful bimanual palpation, the normal side is first examined, followed by the abnormal side. This will reveal a hard, non-tender, irregular, non-transilluminable mass in the testis or replacing the testis. Care should be taken to assess the epididymis, spermatic cord and overlying scrotal wall, which may be normal or involved. Rarely, a secondary hydrocele may be present. General examination may reveal cachexia, supraclavicular lymphadenopathy, chest signs, hepatomegaly, lower limb edema or abdominal mass all suggestive of metastatic disease. May be gynaecomastia due to endocrine manifestations of some tumours.

Differential diagnosis include testicular torsion, epididymo-orchitis, hydrocele, epididymal cyst, hernia, hematoma.

Diagnosis

US will confirm that the palpable lesion is within the testis, distorting its normally regular outline and internal echo pattern. Any hypoechoic area within the tunica albuginea should be regarded with suspicion. It may distinguish a primary from a secondary hydrocele. US may also be used to identify impalpable lesions as small as 1-2 mm tumour in a patient presenting with systemic symptoms and signs or an incidental finding.

Abdominal and chest CT scans are usually obtained for staging purposes if the diagnosis of TC is confirmed.

Tumour markers

Serum tumour markers are measured prior to any treatment of TC. GCTs may express and secrete into the blood measurable proteins. These tumour markers are useful in diagnosis, staging, prognosis and monitoring of response to treatment.

AFP is expressed by trophoblastic elements within 50-70% of teratomas and yolk sac tumours. With respect to seminoma, the presence of elevated serum AFP strongly suggests a non-seminomatous element. Serum half-life is 3-5 days. Normal level is <10 ng/ml.

HCG is expressed syncytiotrophoblastic elements of choriocarcinomas (100%), teratomas (40%) and seminomas (10%). Serum half-life is 24-36h. Normal level is <5 mIU/ml.

LDH is cellular enzyme, elevated in serum for various causes, therefore less specific. It is elevated in 10-20% of seminomas, correlating with tumour burden and is most useful in monitoring treatment response in advanced seminoma.

These markers are measured at presentation, 1-2 weeks after radical orchidectomy and during follow-up to assess response to treatment and residual disease.

Normal markers prior to orchidectomy do not exclude metastatic disease. Normalization of markers post orchidectomy cannot be equated with absence of disease. Persistent elevations of markers post-orchidectomy may occur with liver dysfunction and hypogonadotrophism, but usually indicate metastatic disease.

Treatment

Radical orchiectomy

The final investigation and the primary treatment for all TC. This involves excision of the testis, epididymis and cord through a groin incision. The cord is clamped, transfixed and divided near the internal inguinal ring before the testis is manipulated into the wound, preventing inadvertent metastasis. A silicone prosthesis may be inserted at the time or at a later date. Fertility prophylaxis by freezing sperm should be offered to patients without a normal contralateral testis. Contralateral testis biopsy should be considered in patients at high risk for IGCN.

Treatment of non-seminomatous germ cell tumours

Following radical orchidectomy and formal staging, the patient is normally managed by the oncologist. Urologist may be asked to perform RPLND in selected cases. In the presence of elevated AFP, a seminoma would be managed as for teratoma. Combination chemotherapy, introduced in the 1980s, revolutionized the treatment of metastatic testicular teratoma.

In patients with non-metastatic disease (T1-4N0M0S0) are performed surveillance or chemotherapy (bleomycin, etoposide, cisplatin) depending on risk factors for relapse.

In patients with metastatic disease and good prognosis, chemotherapy (bleomycin, etoposide, cisplatin) is indicated. RPLND is performed for residual or recurrent mass. Salvage chemotherapy is indicated if histology confirms tumour.

In patients with metastatic disease, intermediate and poor prognosis, chemotherapy (bleomycin, etoposide, cisplatin) is indicated. RPLND for residual or recurrent mass. Salvage chemotherapy is indicated if histology confirms tumour.

In most countries RPLND remains the gold standard staging investigation following radical orchidectomy. RPLND is usually the first and only evidence of extra-gonadal metastasis of teratoma. Sometimes RPLND is used only to remove

or de-bulk residual mass post chemotherapy. RPLND may remove viable tumour in 10-30% of patients, taking para-aortic nodes up to the origin of the superior mesenteric artery and down to the iliac bifurcation.

Complications: 1% mortality and 25% morbidity includes lymphocele, pancreatitis, ileus and ejaculatory failure. Modified techniques reduce the risk of ejaculatory disturbance, by taking nodes on the unaffected side only down to the inferior mesenteric artery.

Treatment of seminoma and IGCN

Of all seminomas, 75% are confined to the testis at presentation and are cured by radical orchidectomy. 10-15% of patients harbour regional node metastasis and 5-10% have more advanced disease. Following radical orchidectomy and formal staging, the patient is managed by the oncologist. Treatment and follow-up depends largely on disease stage according to presence of metastases and size of nodal disease.

In patients with non-metastatic disease (T1N0M0) risk of subsequent para-aortic node relapse is 20%. Adjuvant RT 20Gy in 10 fractions reduces risk to 1%. RT includes para-aortic nodes. Early results of a randomized MRC study comparing one cycle of carboplatin with radiotherapy suggest equivalence. In patients with metastatic disease chemotherapy and RT are indicated.

5.6. PENILE NEOPLASMS

5.6.1. Viral-related and premalignant lesions

Viral - related lesions

- Condyloma acuminatum: also known as genital warts, related to HPV infection. Soft, usually multiple benign lesions on the glans, prepuce, shaft, genitalia or perineum. A biopsy is worthwhile prior to topical treatment with podophyllin. 5% have urethral involvement, which may require diathermy. HPV infection (types 16,18,21) is potentially carcinogenic and condylomata have been associated with penile SCC.
- Bowenoid papulosis: a condition resembling CIS, but with a benign course. Multiple papules appear on the penile skin or flat glanular lesion. These should be biopsied. HPV is the suspected cause.
- Kaposi's sarcoma is reticulo-endothelial tumour has become the second most common malignant PC. It presents as a raised, painful, bleeding violaceous papule or as a bluish ulcer with local edema. It is slow-growing, solitary or diffuse. It occurs in immunocompromised men.

Premalignant cutaneous lesions

Some histologically benign lesions are recognized to have malignant potential or occur in close association with SCC of the penis.

- Cutaneous horn: rare, solid skin overgrowth, extreme hyperkeratosis, the base may be malignant;

- Pseudoepitheliomatous micaceous and keratotic balanitis: unusual hyperkeratotic growths on the glans. Require excision, histological examination and follow-up, as they may recur.
- Balanitis xerotica obliterans: also known as lichen sclerosus et atrophicus. This is a common sclerosing condition of glans and prepuce. It occurs at all ages and most commonly presents as phimosis. The meatus and fossa navicularis may be affected, causing obstructed and spraying voiding. The histological diagnosis is usually made after circumcision, with epithelial atrophy, loss of rete pegs and collagenization of the dermis.
- Leukoplakia: solitary or multiple whiteish glanular plaques that usually involve the meatus. Leukoplakia is associated with in situ SCC, follow-up is required.
- Erythroplasia of Queyrat: also known as CIS of the glans, prepuce or penile shaft. A red, velvety, circumscribed painless lesion, though it may ulcerate resulting in discharge and pain. Histology reveals hyperplastic mucosal cells with malignant features.
- Bowen's disease: this is CIS of the remainder of the keratinizing genital or perineal skin.
- Buschke - Lewenstein tumour: also known as verrucous carcinoma or giant condyloma acuminatum, this is an aggressive locally invasive tumour of the glans. Metastasis is rare. Urethral erosion and fistulation may occur.

A chronic red or pale lesion on the glans or prepuce is a cause for concern. Note should be made of its colour, size and surface features. Early review following steroid, antibacterial or antifungal creams is recommended. If persistent, biopsy and excision are advised.

5.6.2. Penile cancer

SCC is the most common PC, accounting for 95% of penile malignancies. Others include Kaposi's sarcoma and, rarely, basal cell carcinoma, melanoma, sarcoma, Paget's disease. PC is rare, representing 1% of male cancers, most occurring in elderly men.

Risk factors

- PC incidence rises during the 6th decade and peaks in the 8th decade. It is unusual <40 years, but has been reported in children.
- Many patients with penile SCC are reported about a pre-existing penile lesion and phimosis. PC is rare in men circumcised at a young age and it is non-existent in Israel. It is thought that chronic irritation with smegma and balanitis is contributory.
- HPV infection are suggested, especially with types 16, 18 and 21.
- Smoking.

Pathology

Believed to be preceded by CIS, SCC starts as a slow-growing papillary, flat or ulcerative lesion on the glans, prepuce, coronal sulcus or shaft. It grows locally beneath the foreskin before invading the corpora cavernosa, urethra and, eventually, the perineum, pelvis and prostate. Metastasis is initially to the superficial then

deep inguinal and, subsequently, iliac and obturator lymph nodes. Skin necrosis, ulceration and infection of the inguinal lymph nodes may lead to sepsis or hemorrhage from the femoral vessels. Metastasis to lungs and liver are rare.

SCC exhibits keratinization, epithelial pearl formation and mitoses. Grading is low, intermediate or high and correlates with prognosis.

TNM classification for penile carcinoma (2009)

T – Primary Tumour

TX – Primary tumour cannot be assessed

T0 – No evidence of primary tumour

Tis – CIS

Ta – Non-invasive carcinoma

T1 – Tumour invades subepithelial connective tissue

T1a – Tumour invades subepithelial connective tissue without lymphovascular invasion and is not poorly differentiated or undifferentiated

T1b – Tumor invades subepithelial connective tissue with lymphovascular invasion or is poorly differentiated or undifferentiated

T2 – Tumour invades corpus spongiosum and/or corpora cavernosa

T3 – Tumour invades urethra

T4 – Tumour invades other adjacent structures

N – Regional Lymph Nodes

NX – Regional lymph nodes cannot be assessed

N0 – No palpable or visibly enlarged inguinal lymph nodes

N1 – Palpable mobile unilateral inguinal lymph node

N2 – Palpable mobile multiple unilateral or bilateral inguinal lymph nodes

N3 – Fixed inguinal nodal mass or pelvic lymphadenopathy, unilateral or bilateral

M – Distant Metastasis

M0 – No distant metastasis

M1 – Distant metastasis

Symptoms and signs

Most common phimosis is present. A hard, painless lump on the glans penis is visible or palpable. Many patients delay presentation due to embarrassment, personal neglect, fear or ignorance. A bloody discharge may be confused with hematuria. Rarely, a groin mass or urinary retention are presenting symptoms.

Examination reveals a solid non-tender mass or ulcer beneath or involving the foreskin. There is usually evidence of local infection. In more advanced disease, prepuce, glans, shaft, scrotum and even perineum are replaced by tumour. The inguinal lymph nodes may be enlarged, fixed or even ulcerate overlying skin.

Diagnosis

A biopsy is indicated. Chest radiology, pelvic and abdominal CT scan, serum calcium and liver function tests are usually obtained.

Treatment

The primary tumour

The first-line treatment of PC, regardless of the inguinal node status, is surgery. Circumcision is appropriate for preputial lesions, but may be local recurrences, if the excision margin is positive. Organ-preserving wide excision of glanular lesions with skin graft glanular reconstruction may be suitable for smaller G1-2 Ta-T1 tumours, giving good cosmetic and functional results.

For G3T1 and more advanced tumours, partial or total penile amputation is required, depending on the extent of the tumour. Partial amputation is preferable, provided a 2 cm margin of palpably normal shaft can be obtained. The patient must be prepared for poor cosmetic and functional results: inability to have sexual intercourse and need to sit to void urine. Total amputation involves excision of the scrotum and its contents, with formation of a perineal urethrostomy. The most common complication is urethral stenosis. RT remains an alternative, but disadvantages include radio-resistance. Tissue necrosis and damage leading to urethral stricture, fistula and pain. Patients with M1 disease are offered palliative surgery.

Alternatives to surgery include laser or cryoablation, brachytherapy, photodynamic therapy or topical 5-fluorouracil.

Lymphadenectomy

Six weeks of broad-spectrum antimicrobials are given after the primary tumour has been removed. Nodes become clinically insignificant in 50% of patients, who may then be followed-up.

For those with persistent inguinal lymphadenopathy, in the absence of demonstrable pelvic or metastatic disease, bilateral inguinal lymphadenectomy should be considered, since 5-year survival is 80%. Even if lymphadenopathy is unilateral, >50% will have contralateral metastases. However, this is major surgery with a high morbidity including lymphedema, thromboembolism and wound breakdown, so it is not suitable for elderly or unfit men.

RT and chemotherapy are alternative or adjuvant treatments for metastatic nodal disease in unfit, elderly or inoperable patients. 5-year survival 25%. Rarely, lymphadenopathy ulcerates the skin, may encase the femoral vessels and invade the deeper musculature.

Prophylactic lymphadenectomy is currently practised for tumours exhibiting vascular invasion, high grade or stages T2-4, without evidence of benefit. It is argued that the risk of metastatic disease with palpably normal groins is greater than 20% and delayed lymphadenectomy could reduce the chance of cure. 20-30% of patients with inguinal metastases will also have pelvic node involvement.

Metastatic disease is treated using single-agent or combination chemotherapy: cisplatin, bleomycin or methotrexate. Responses are partial and short-lived.

5.7. URETHRAL CANCER

Primary urethral cancer is rare, occurring in elderly patients.

Female:male ratio is 4:1.

Risk factors

Urethral stricture and STD are implicated. Direct spread from tumour in the bladder or prostate is more common.

Pathology

75% are SCC, occurring in the anterior urethra. 15% are TCC, occurring in the posterior/prostatic urethra. 8% are adenocarcinoma. The remainder include sarcoma and melanoma. Urethral cancer metastasises to the pelvic lymph nodes from the posterior urethra and to the inguinal nodes from the anterior urethra in 50% of patients.

TNM classification for urethral cancer (7th edition)***T – Primary Tumour***

TX – Primary tumour cannot be assessed

Tis – CIS

T0 – No evidence of primary tumour

Ta – Non-invasive papillary carcinoma

T1 – Tumour invades subepithelial connective tissue

T2 – Tumour invades any of the following structures: corpus spongiosum, prostate, peri-urethral muscle

T3 – Tumour invades any of the following structures: corpus cavernosum, invasion beyond prostatic capsule, anterior vaginal wall, bladder neck

T4 – Tumour invades other adjacent organs

N – Regional Lymph nodes

NX – Regional lymph nodes cannot be assessed

N0 – No regional lymph-node metastasis

N1 – Metastasis in a single lymph node <2 cm

N2 – Metastasis in a single lymph node >2 cm or in multiple nodes

M – Distant Metastasis

MX – Distant metastasis cannot be assessed

M0 – No distant metastasis

M1 – Distant metastasis

Symptoms and signs

- Initial or terminal hematuria or a bloody urethral discharge;
- LUTS;
- Perineal pain;
- Periurethral abscess or urethro-cutaneous fistula;
- Past history of STD or stricture disease;
- Examination may reveal a hard palpable mass at the female urethral meatus or along the course of the male anterior urethra. Inguinal lymphadenopathy, chest signs and hepatomegaly may suggest metastatic disease.

Diagnosis

Cysto-urethroscopy, biopsy and bimanual examination under anaesthesia will obtain a diagnosis and local clinical staging. Chest X-Ray and abdomino-pelvic CT scans will enable distant staging.

Treatment

For localized anterior urethral cancer, surgery or EBRT are the options. Male patients would require perineal urethrostomy. Post-operative incontinence due to disruption of the external sphincter mechanism is minimal unless the bladder neck is involved, but the patient would need to sit to void. For posterior/prostatic urethral cancer, cystoprostatourethrectomy should be considered for fit men. Anterior pelvic exenteration (excision of the pelvic lymph nodes, bladder, urethra, uterus, ovaries and part of the vagina) should be considered for women. In the absence of distant metastases, inguinal lymphadenectomy is performed if nodes are palpable. For locally advanced disease, a combination of preoperative RT and surgery is recommended. For metastatic disease, chemotherapy is the only option.

6.1. RENAL INJURIES

The kidneys are located retroperitoneally, surrounded by peri-renal fat, the vertebral column and spinal muscles, the lower ribs and abdominal contents. They are therefore relatively protected from injuries and a considerable degree of force is usually required to injure them. Injuries of spleen, liver and mesentery of bowel are therefore common.

Children's kidneys are said to be more prone to injury in children because of the relatively greater size of the kidneys in children, the smaller protective muscle mass and cushion of peri-renal fat and the more pliable rib cage.

Classification

There are two categories: blunt and penetrating. Proportion depends on whether urban or non-urban community. Experience from large series shows that 95% of blunt injuries can be managed conservatively, whereas most of stab and gunshot wounds require exploration.

Blunt injures

Rapid deceleration or acceleration frequently causes renal pedicle injuries. Most common cause are motor vehicle accidents: pedestrian hit by a car, direct blow. Direct falls onto the flank or sporting injuries can lead to significant renal injuries.

Penetrating injuries

Stab or gunshot injuries to the flank, lower chest and anterior abdominal area may inflict renal injuries. 1/2 of patients with penetrating trauma and hematuria have grade III, IV or V renal injuries. Penetrating injuries anterior to the anterior axillary line are more likely to injure the renal vessels and renal pelvis, compared with injuries posterior to this line where less serious parenchymal injuries are more likely. There are iatrogenic injuries due to PCNL.

Staging of the renal injuries

Using CT, renal injuries can be staged according to the AAST Organ Injury Severity Scale. Higher injury severity scales are associated with poorer prognosis.

- Grade I Contusion or subcapsular hematoma with no parenchymal laceration;
- Grade II <1 cm deep parenchymal laceration of cortex, no extravasation of urine (i.e. collecting system intact);
- Grade III >1 cm deep parenchymal laceration of cortex, no extravasation of urine;
- Grade IV Parenchymal laceration involving cortex, medulla and collecting system or renal artery/vein injury with contained hemorrhage;
- Grade V Completely shattered kidney or avulsion of renal hilum.

Diagnosis

There are 2 types of patients: hemodynamically stable and unstable (SBP < 90 mmHg recorded at any time since the injury). While significant renal injury is more likely with macroscopic hematuria, in some cases of severe renal injury hematuria may be absent. Thus the relationship between the presence, absence and degree of hematuria and the severity of trauma is not absolute. In blunt trauma macroscopic hematuria predicts the likelihood of significant renal injury. Conversely, in penetrating trauma, hematuria may be absent in severe IV-V type renal injuries.

History is taken for nature of trauma (blunt, penetrating). Examination: pulse rate, SBP, respiratory rate, location of entry and exit wounds, flank bruising, rib fractures.

Hemodynamic instability may preclude standard imaging such as CT, the patient having to be taken to the operating theatre immediately to control the bleeding. In this situation, an on-table IVU is indicated if a retroperitoneal hematoma is found and/or a renal injury is found which is likely to require nephrectomy. A single shot abdominal X-ray, taken 10 min after contrast administration (2 ml/kg), can establish the presence/absence of a renal injury and the presence of a normally functioning contralateral kidney where the ipsilateral kidney injury is likely to necessitate a nephrectomy.

The IVU has been replaced by contrast enhanced CT scan as the imaging study of choice in patients with suspected renal trauma. Compared with IVU, it provides clearer definition of the injury, allowing injuries to the parenchyma and collecting system to be more accurately graded. An arterial-venous phase scan is done within minutes of contrast injection, followed by a repeat scan 10-20 min after contrast administration to allow time for contrast to reach collecting system.

Imaging is designed to grade injury, to document presence and function of contralateral kidney, to detect associated injuries and pre-existing renal pathology in affected kidney.

Indications for CT:

- Macroscopic hematuria;
- Penetrating chest and abdominal wounds;
- Microscopic hematuria in a hypotensive patient;
- A history of a fall from a height, high speed motor vehicle accident. Falls from even a low height can cause serious renal injury in the absence of shock and of hematuria;

On contrast enhanced CT look for:

- Depth of parenchymal laceration;
- Parenchymal enhancement;
- Presence of urine extravasation;
- Presence, size and position of retroperitoneal hematoma;
- Presence of injuries to adjacent organs (bowel, spleen, liver, pancrea...);
- Presence of a normal contralateral kidney.

While US can establish the presence of two kidneys and identify blood flow in the renal vessels with power Doppler, it cannot accurately identify parenchymal tears, collecting system injuries or extravasation of urine until a later stage when a urine collection occurs.

Treatment

Most blunt and many penetrating renal injuries can be managed non-operatively.

If SBP since injury has always been >90 mmHg, no history of acceleration or deceleration and hematuria is present, there is Grade I injury.

Cardiovascularly stable patient with macroscopic hematuria, having Grade II-III injury admits for bed rest, observation, antibiotics and NSAID's treatment, until the macroscopic hematuria, if present, resolves.

Indications for surgical exploration:

- The patient develops shock which does not respond to resuscitation with fluids and/or blood transfusion;
- The hemoglobin decreases <80 ;
- There is urinary extravasation;
- There are associated bowel or pancreatic injuries;
- Expanding and pulsatile peri-renal hematoma;

The finding of an expanding and/or pulsatile retroperitoneal hematoma at laparotomy will often indicate a renal pedicle injury and nephrectomy may be required to stop further hemorrhage. Controversy surrounds the correct management of the finding at laparotomy of a non-expanding, non-pulsatile retroperitoneal hematoma. Most can be left alone, because of exploration, which increases the chances of kidney loss. In these cases bleeding can be controlled only by nephrectomy. This is a disaster if the contralateral kidney is absent or damaged.

If patient has Grade IV injury, this is an indication for exploration or drainage (JJ- stent or PNS). Sometimes these injuries will heal spontaneously. Operation is indicated if there are associated bowel or pancreatic injuries. In these situations the renal repair should be well drained and omentum interposed between the kidney and bowel or pancreas.

Renal imaging is repeated if the patient develops a peritonitis or a fever, since these signs may indicate the development of a urinoma which can be drained percutaneously. Renal exploration is required for a persistent leak and fistula formation.

Exploration is usually required for patients with Grade V injury with devitalized segments of kidney and urinary extravasation.

Technique of renal exploration

Midline incision allows exposure of renal pedicle, so allowing early control of the renal artery and vein and inspection for injury to other organs.

Lift the small bowel upwards to allow access to the retroperitoneum. Incise the peritoneum over the aorta, above the inferior mesenteric artery. A large perirenal hematoma may obscure the correct site for this incision. If this is the case, look for the inferior mesenteric vein and make your incision medial to this. Once on the aorta, the inferior vena cava may be exposed, then the renal veins and the

renal arteries. Pass slings around all of these vessels. Expose the kidney by lifting the colon off of the retroperitoneum. Bleeding may be reduced by applying pressure to the vessels via the slings. Control bleeding vessels within the kidney and close any defects in the collecting system with 4/0 vicryl or monocryl sutures. If your sutures cut out, place a strip of Surgicel over the site of bleeding, place your sutures through the capsule on either side of this and tie them over the Surgicel. This will stop them from cutting through the friable renal parenchyma.

Complications

Arteriovenous fistulae can sometimes occur following renal injuries. Arteriography with embolization can be used to stop the bleeding in these cases. The “second-stage” bleeding usually occurs over a longer time of injury, rather than as acute hemorrhage causing shock.

Excess renin excretion occurs following renal ischaemia from renal artery injury or thrombosis or renal compression by hematoma or fibrosis. This can lead to hypertension months or years after renal injury.

6.2. URETERIC INJURIES

External injuries are registered due to road traffic accidents and fall from a height. Penetrating injuries may be observed by knife or gunshot wounds. Iatrogenic injuries are detected during pelvic or abdominal surgery (hysterectomy, colectomy, aneurysm repair, URS). The ureter may be divided, ligated or angulated by a suture. A segment may be excised or damaged by diathermy.

Symptoms and signs of ureteric injuries

- Urine peritonitis due to urine collection within the peritoneal cavity;
- Prolonged post-operative fever
- Urosepsis;
- Persistent drainage of fluid from drains, the abdominal wound or the vagina. Cr estimation of this fluid is indicated (Cr level higher than that of serum).
- Renal colic if the ureter has been ligated;
- Retroperitoneal mass, representing as a urinoma;
- The pathology report on the organ that has been removed may note the presence of a segment of ureter.

Diagnosis

IVU or CT can be used to determine the presence of a ureteric injury. If doubt remains, retrograde ureterography should be done.

The iatrogenic injury may be suspected at the time of surgery, but injury may not become apparent until some days or weeks post-operatively.

Intra-operative diagnosis

For ureteric contusions and perforations seen at the time of URS, JJ-stent is inserted. During abdominal or pelvic surgery direct inspection of the ureter - a good way of inspecting the ureter for injury, but requires exposure of a considerable length of ureter to establish that it has not been injured. Lower ureteric exposure

is more difficult than upper ureteric. Extravasation after injection of methylene blue into the ureter to look for leakage of dye from a more distant section of ureter. On-table retrograde ureterography - a very accurate method of establishing the presence or absence of a ureteric injury. Both ureters can easily be examined.

Post-operative diagnosis

The diagnosis is usually apparent in the first few days following surgery, but it may be delayed by weeks, months or years. Symptoms and signs are UHN, flank pain and post-hysterectomy false incontinence. A continuous leak of urine from vagina suggests a ureterovaginal fistula. IVU and/or retrograde ureterogram are indicated. US may demonstrate UHN, but hydronephrosis may be absent when urine is leaking from a transected ureter into the retroperitoneum, peritoneal cavity or vagina. The IVU usually shows an obstructed ureter or occasionally a contrast leak from the site of injury.

Treatment

Generally, the best time to repair the ureter is as soon as the injury has been diagnosed. Delay definitive ureteric repair when there is evidence of active infection and urinoma at the site of proposed ureteric repair.

A PNS should be placed, i.v. antibiotics given and ureteric repair delayed until the patient is afebrile.

Surgical repair should be delayed when the injury was diagnosed between day 7 and day 14 after ureteric injury, the time when maximal edema and inflammation at the site of repair was believed to occur. However, favourable outcomes have been demonstrated after early repair.

The options of treatment depend on whether the injury is recognized immediately, level of injury and other associated problems.

The options are:

- Open JJ-stent for 3-6 weeks if there is injury recognized immediately;
- Primary closure of partial transection of the ureter with open JJ-stent;
- Direct end-to-end anastomosis if a tension-free anastomosis is possible;
- Re-implantation of the ureter into the bladder (ureteroneocystostomy) either using Boari flap;
- Replacement of the ureter with ileum where the segment of damaged ureter is very long (rare option);
- Permanent cutaneous ureterostomy (rare option).

General principles of ureteric repair:

- The ends of the ureter should be debrided and spatulated, so that the edges to be anastomosed are bleeding freely and to allow a wide anastomosis to be done;
- The anastomosis should be tension free;
- A JJ-stent should be placed across the repair;
- Watertight closure;
- Use 4/0 absorbable suture material;
- A drain should be placed around the site of anastomosis.

6.3. BLADDER AND URETERIC INJURIES ASSOCIATED WITH PELVIC FRACTURES

Pelvic fractures are observed usually due to run-over or crush injuries, where massive force is applied to the pelvis. Associated head, chest, intraabdominal, pelvic and genital injuries are common and these injuries plus the massive blood loss from pelvic veins and arteries account for the substantial mortality after pelvic fractures.

Bladder injuries associated with pelvic fractures

~10% of male and 5% of female pelvic fractures are associated with a bladder injuries. Fracture type leading to bladder injury is usually an antero-posterior pelvic compression fracture i.e. “open book” pelvic fracture. 60% of bladder ruptures are extra-peritoneal, 30% intraperitoneal and 10% combined extraperitoneal and intraperitoneal.

Urethral injuries associated with pelvic fractures

The membranous urethra is injured with roughly the same frequency as the bladder in subjects who sustain a pelvic fracture, occurring in 5-15% of such cases. Most posterior urethral injuries occur in association with pelvic fractures.

Combined bladder and posterior urethral injuries following pelvic fractures

1/3 of patients with a traumatic bladder rupture have injuries to other urinary structures, most commonly the urethra. 10-20% of patients with a pelvic fracture and bladder rupture also have a posterior urethral rupture.

There are stable, where the fracture can withstand normal physiologic forces and unstable fractures, where the fracture cannot withstand normal physiologic forces.

Instability suggests a greater degree of trauma to the pelvis and increases the likelihood of serious associated injuries. In addition, fixation of an unstable fracture reduces blood loss, mortality, hospital stay, leg length discrepancy and long-term disability. It makes nursing care easier and reduces analgesic consumption.

Stability can be defined according to the Tile classification system of pelvic ring fractures:

- Type A stable: A1 - fracture of pelvis not involving the pelvic ring and A2 - minimal displacement of pelvic ring with no instability;
- “Open book” pelvic fracture (B1) caused by anteroposterior compression. A dramatic rise in pelvic volume stretches vessels, nerves and organs. This is horizontally unstable pelvic fracture.
- “Closed book” pelvic fracture (B2 or B3) caused by a lateral compression force to the pelvis. The pubic rami fracture and overlap and the ilium and sacral wings may be fractured. Nerves and vessels are not stretched, but the urethra is more likely to be damaged by scissors like action of overlapping pubic rami. This is horizontally unstable pelvic fracture.
- Vertically and horizontally unstable pelvic fracture (C1,C2,C3), where vessels and nerves can be damaged by stretching.

6.4. BLADDER INJURIES

Risk factors

Risk factors are pelvic fracture, rapid acceleration/deceleration injuries with full bladder, iatrogenic bladder injuries by gynecologists, TUR, cystolitholapaxy, penetrating trauma to the lower abdomen or back, caesarian section, spontaneous rupture after bladder augmentation.

Types of perforation

- Intraperitoneal perforation, where the peritoneum overlying the bladder is breached allowing urine to escape into the peritoneal cavity;
- Extraperitoneal perforation, where the peritoneum is intact and urine escapes into the space around the bladder with pelvic urinoma formation.

The classic symptoms and signs

- Difficulty or inability in passing urine;
- Suprapubic pain and tenderness if patient has extraperitoneal injury;
- Macrohematuria in patient with catheter;
- Abdominal distension and absent bowel sounds in patient with urine peritonitis due to intraperitoneal injury.

Diagnosis

During endoscopic urological operations the diagnosis is usually obvious on visual inspection alone. A dark hole is seen in the bladder and loops of bowel may be seen on the other side. No further diagnostic tests are required.

Abdominal/pelvic CT detects presence/absence of associated pelvic and abdominal organ injury.

In pelvic fracture patients, if there is no blood present at the meatus, a gentle attempt at urethral catheterization may be made to do a retrograde cystogram, assess integrity of the bladder and detects signs of extraperitoneal or intraperitoneal bladder rupture.

Retrograde or CT cystography

The bladder must be adequately distended with a contrast. With inadequate distension a clot, omentum or small bowel may block the perforation, which may not therefore be diagnosed. At least 350–400 ml of contrast is used in an adult. Images are obtained before and after the contrast agent has been completely drained from the bladder (a post-drainage film). A whisper of contrast from a posterior perforation may be obscured by a bladder distended with contrast. In extraperitoneal perforations extravasation of contrast is limited to the immediate area surrounding the bladder. In intraperitoneal perforations, loops of bowel may be outlined by the contrast.

Treatment

Extraperitoneal bladder injuries are treated with a urethral catheter for ~2–3 weeks followed by a cystogram to confirm the perforation has healed.

Indications for surgical repair of extraperitoneal bladder perforation:

- If the bladder is opened to place a suprapubic catheter for a urethral injury;
- A bone protruding into the bladder on CT;
- Associated rectal, vaginal or ureteral perforations;
- Where the patient is undergoing open fixation of a pelvic fracture, the bladder can be simultaneously repaired.

Intraperitoneal bladder injuries usually repaired surgically to prevent complications from urine peritonitis.

6.5. URETHRAL INJURIES

6.5.1. Posterior urethral injuries in males

Mechanisms

- External, blunt: pelvic fracture, road traffic accidents, falls from a height, crush injury;
- External, penetrating: gunshot or stab wounds;
- Internal, iatrogenic: endoscopic surgery or radical prostatectomy;
- Internal, self-inflicted: foreign bodies inserted into urethra.

Symptoms and signs

Blood at meatus in 1/2 of patients. Next will be AUR and urinoma formation in pelvic cavity. In patients with partial injury may be hematuria. Perineal or scrotal bruising and edema may be observed by patients with urethral injury.

“High riding” prostate is palpated. The prostate and bladder become detached from the membranous urethra and are pushed upwards by the expanding pelvic urohematoma. The “high riding” prostate is said to be a classic sign of posterior urethral rupture. Traditional teaching states that a DRE should be done in cases of pelvic trauma to determine prostatic position. The pelvic hematoma may make it impossible to feel the prostate, so the patient may be thought to have a “high riding” prostate when, in fact, it is in a normal position. Conversely, what may be thought to be a normal prostate in a normal position may actually be the palpable pelvic hematoma. In pelvic fracture, a DRE is done not to identify a “high riding” prostate, but rather to establish the presence of an associated rectal injury, where there is blood seen on the examining finger. However, rectal injury can still occur in the absence of rectal blood.

Diagnosis

Retrograde urethrography

This investigation detects urethral injury. Urethral injury is suspected in all pelvic fracture patients, where the pubic rami have been disrupted and there is blood at the meatus.

Rules of retrograde urethrogram are presented below. This is aseptic technique. Position the patient at an oblique angle. Bottom leg flexed at the hip and knee. A 12-14 Ch catheter is placed in the fossa navicularis of the penis 1-2 cm from the external meatus, with the catheter balloon with 2 ml of water or with a pe-

nile clamp applied to prevent contrast spilling out of the urethra and to hold the catheter in place. Continuous X-Ray imaging is done as contrast is instilled until the entire length of the urethra is demonstrated. Remember, as the membranous urethra passes through the pelvic floor, there is a normal narrowing and similarly the prostatic urethra is narrower than the bulbar urethra.

Treatment

Immediate open repair of posterior urethral injuries is not recommended and associated with a high incidence of urethral strictures and subsequent re-stenosis after stricture repair, incontinence and impotence. The surrounding hematoma and tissue swelling makes it difficult to identify structures and to mobilize the two ends of the urethra to allow tension-free anastomosis. Immediate repair over urethral catheter is indicated where there is an only open wound.

One gentle attempt is performed to place a urethral catheter in suspected urethral disruption. If any resistance is encountered, a retrograde urethrogram is indicated. If there is a urethral rupture, insert a suprapubic catheter via a formal open approach, to allow inspection of the bladder and repair of bladder injury.

Placement of the suprapubic catheter via an open approach is generally better than a percutaneous approach, because it allows inspection of the bladder for associated injuries which may require repair, but also because the catheter may inadvertently be placed into the large pelvic hematoma which always accompanies such fractures. In this case suprapubic can act as a potential source of infection of the pelvic hematoma, which can lead to life-threatening urosepsis.

In the majority of male posterior urethral injuries, treatment should be deferred for 3 months to allow the edema and hematoma to completely resolve. As this occurs, the two distracted ends of the urethra come closer together, thereby reducing the amount of mobilization. Most such injuries can be repaired by an anastomotic urethroplasty. Optical urethrotomy using an endoscopic knife or laser, via a cystoscope inserted into the urethra is performed rare and has little benefit.

Management of combined urethral and bladder injuries associated with pelvic fractures:

- If a urethral catheter can be passed and a cystogram shows an extraperitoneal bladder rupture, a catheter will be in place until the bladder has healed (2-3 weeks).
- If a urethral catheter cannot be passed, because of a complete urethral rupture, a open cystostomy should be performed to allow inspection of the bladder and repair if the bladder has been injured.

6.5.2. Anterior urethral injuries in males

Mechanisms

- External, blunt: straddle injury by forceful contact of perineum with bicycle cross-bar. Most common bulbar urethra being crushed against pubic bone. Also may be kick to perineum and/or penile fracture.
- External, penetrating: gunshot and stab wounds;
- Internal, iatrogenic: inflated catheter balloon, endoscopic surgery, penile surgery.
- Internal, self-inflicted: foreign bodies inserted into urethra.

Symptoms and signs

The patient usually presents with difficulty in passing urine and frank hematuria in the context of a straddle injury. Blood may be present at the end of the penis and a hematoma around the site of the rupture.

If the deep layer of the superficial fascia of the penis (Buck's fascia) has been ruptured, urine and blood track into the scrotum causing swelling and a "butterfly wing" pattern of bruising, reflecting the anatomical attachments of Colles fascia.

Extravasation of urine can create a collection of urine around the urethra. This urinoma generates an inflammation, with subsequent stricture formation. Superadded infection can lead to abscess formation, which may burst onto the surface of the skin leading to a urethrocutaneous fistula. More rarely, Fournier's gangrene supervenes.

Diagnosis

Retrograde urethrography delineates the extent of urethral injury.

Treatment

Urinary diversion with urethral or suprapubic catheter prevents further extravasation of urine and antibiotics may reduce the likelihood of superadded infection.

If there is anterior urethral contusion, but no extravasation of contrast on retrograde urethrogram a small urethral catheter (12 Ch) is inserted for 1 week.

Partial rupture of anterior urethra

This is leak of contrast from urethra with retrograde flow into bladder. Most can be managed by a period of suprapubic or urethral catheterization and heal without stricture formation. Primary closure can be difficult because of edema and of hematoma at site of injury. A broad spectrum antibiotics are used to prevent infection of extravasated urine and blood. If a voiding cystogram 2 weeks later confirms urethral healing, suprapubic catheter is removed. If contrast still extravasates, leave it in place a little longer.

Suprapubic catheterization is preferred over urethral catheterization. If the bladder cannot be palpated, such that a suprapubic catheter cannot safely be inserted, then open suprapubic cystostomy is performed.

Complete rupture of anterior urethra

This is diagnosed, if there is lack of contrast from urethra on retrograde urethrogram, no filling of the posterior urethra or bladder. The urethra may either be immediately repaired or a suprapubic catheter can be placed with delayed repair.

Penetrating partial and complete anterior urethral injuries

Immediate surgical repair of anterior urethral injuries is only done in the context of penile fracture or where there is an open wound. If there is knife or gunshot wound, primary repair is recommended. Suprapubic diversion and subsequent repair may be indicated.

6.5.3. Urethral injuries in females

Rare, because the female urethra is short and its attachments to the pubic bone are weak, such that it is less prone to tearing during pubic bone fracture. When

they do occur, such injuries are usually associated with rectal or vaginal injuries. In developing countries, prolonged labour can cause ischaemic injury to the urethra and bladder neck, leading to urethrovaginal or vesicovaginal fistula formation.

6.6. TESTICULAR INJURIES

Mechanisms

There are blunt or penetrating injuries. Most in civilian practice are blunt, a blow forcing the testicle against the pubis or the thigh. Bleeding occurs into the parenchyma of the testis and if sufficient force is applied, the tunica albuginea of the testis is ruptured, allowing extrusion of seminiferous tubules and hematocele formation. Penetrating injuries occur as a consequence of gunshot and knife wounds and from bomb blasts. Associated limb, perineal, pelvic, abdominal and chest wounds may occur.

Symptoms and signs

Where bleeding is confined by the tunica vaginalis, a hematocele is present. Intratesticular hemorrhage and bleeding beneath the parietal layer of tunica vaginalis will cause the testis to enlarge slightly. The testis may be under great pressure as a consequence of the intra-testicular hemorrhage confined by the tunica vaginalis. This can lead to ischaemia, necrosis and atrophy of the testis.

Severe pain is common, as are nausea and vomiting. If the testis is surrounded by hematoma it will not be palpable. If it is possible to palpate the testis, it is usually very tender. The resulting scrotal hematoma can be very large and the bruising and swelling so caused may spread into the inguinal region and lower abdomen.

Testicular ultrasound in cases of blunt trauma

A normal parenchymal echo pattern suggests there is no significant testicular injury. Hypoechoic areas within the testis, indicating intraparenchymal hemorrhage, suggests testicular rupture. US will show hematocele.

Treatment

If patient has testicular rupture, exploration allows evacuation of the hematoma, excision of extruded seminiferous tubules and repair of the tear in the tunica albuginea. If patient has penetrating trauma, exploration allows repair to damaged structure.

6.7. PENILE INJURIES

6.7.1. Penile amputation

Blood loss can be severe. The shocked patient is resuscitated and cross-match of blood is performed. The penis is placed in a wet swab inside a plastic bag, which is then inserted inside another bag containing ice. It can survive for 24 hours.

By knife and gunshot wounds associated injuries are common. Most injuries, other than minor ones, should undergo primary repair. Debris is removed from wound, necrotic tissues are debrided and repair as for penile fractures is performed.

Surgical reimplantation of amputated penis

By penile amputation the urethra is repaired first, over a catheter, to provide a stable base for subsequent neurovascular repair. The tunica albuginea of the corpora is closed with 4/0 absorbable suture. The dorsal artery of the penis is anastomosed with 11/0 nylon, then the dorsal vein with 9/0 nylon to provide venous drainage and, finally, the dorsal penile nerve with 10/0 nylon.

6.7.2. Penile fracture

This is rupture of the tunica albuginea of the erect penis. May be rupture of one or both corpora cavernosa \pm rupture of corpus spongiosum with rupture of the urethra. The tunica albuginea is 2 mm thick in the flaccid penis. It thins during erection and is therefore vulnerable to rupture if the penis is forcibly bent during vigorous sexual intercourse.

Symptoms and signs

The patient usually reports a sudden “snapping” or “popping” sound and/or sensation, with sudden penile pain and detumescence of the erection.

The penis is swollen and bruised, sometimes resembling an aubergine. If Buck’s fascia has ruptured, bruising extends onto the lower abdominal wall and into the perineum and scrotum. A tender, palpable defect may be felt over the site of the tear in the tunica albuginea. If the urethra is damaged, there may be blood at the meatus, hematuria and pain on voiding or urinary retention. Retrograde urethrogram is performed in such cases.

Treatment

Surgical repair is indicated due to lower complication rate e.g. reduced penile deformity, less chance of penile scar tissue and prolonged penile pain.

Surgical repair of penile fracture

The fracture site is exposed by degloving the penis via a circumcising incision around the subcoronal sulcus. A degloving incision allows better exposure of the urethra for associated urethral injuries and excellent exposure of both corpora cavernosa so that an unexpected bilateral injury can be repaired easily. Defect is closed in the tunica with absorbable sutures or by non - absorbable sutures. A urethral catheter is used for 1-2 days. Urethral rupture is repaired with a spatulated single or two-layer urethral anastomosis with a urethral catheter for 3 weeks. In postoperative period conservative treatment is used: application of cold compresses to the penis, analgesics and NSAIDs, abstinence from sexual activity for 6-8 weeks to allow healing.

7.1. ACUTE URINARY RETENTION

7.1.1. Acute urinary retention in male

This is painful inability to void, with relief of pain following drainage of the bladder by catheterization. Central to the diagnosis is the presence of a large volume of urine, which when drained by catheterization, leads to resolution of the pain. What represents “large” has not been strictly defined, but volumes of 500-800 ml are typical. Volumes <500 ml should lead one to question the diagnosis. Volumes >800 ml may be defined as acute-on-chronic retention.

Four broad mechanisms can lead to urinary retention:

- Increased urethral resistance (BOO);
- Low bladder pressure (i.e. impaired bladder contractility);
- Interruption of sensory or motor innervation of bladder;
- Central failure of coordination of bladder contraction with external sphincter relaxation.

Common causes in men:

- BPH;
- Prostatic cancer;
- Urethral stricture;
- Prostatic abscess.

Urinary retention in men is either spontaneous or precipitated by an event. Precipitated retention is less likely to recur once the event which caused it has been removed. Spontaneous retention is more likely to recur after TWC and therefore to require definitive treatment. Precipitating events include anaesthetic and other drugs (anticholinergics, sympathomimetic agents), non-prostatic abdominal or perineal surgery, immobility following surgical procedures, alcohol abuse.

Causes in either sex:

- Blood clots retention;
- Post-operative retention;
- Radical pelvic surgery damaging pelvic parasympathetic plexus;
- Pelvic fracture rupturing urethra;
- Neurogenic bladder (multiple sclerosis, transverse myelitis, diabetic cystopathy)
- Spinal cord injuries (prolapsed discs, trauma, benign or metastatic tumours)

Causes in women:

- Pelvic prolapse (cystocele, rectocele);
- Urethral stricture;
- Urethral diverticulum;
- Pelvic masses (e.g. ovarian masses).

Treatment

Urethral catheterization

Urethral catheterization is performed to relieve pain. Suprapubic catheterization is indicated if urethral route not possible. The volume drained is recorded. This confirms the diagnosis, determines subsequent management and provides prognostic information with regard to outcome from this treatment. TWC is indicated. Urethral catheter for 3 days is inserted and alpha – blockers are used. Precipitated retention often does not recur. Spontaneous retention often does. 50% with spontaneous retention will experience a second episode of retention within the next week or so and 70% within the next year. $Q_{max} < 5\text{ml/s}$ and low voiding detrusor pressure predict subsequent retention. Thus, while most will require TUR or open operation, a substantial minority will get away without needing surgery. If there is success with TWC prostate shrinking drugs are used several months later. 5 ARIs are indicated for BPH patients. LHRH agonists are used in those with malignant prostates. If patient has CRF suprapubic catheter for several months is indicated. Most patients will require second operation (TUR or open prostatectomy).

Indications:

- Relief of urinary retention;
- Prevention of urinary retention in the postoperative period;
- Post-operative monitoring of urine output;
- Prevention of damage to the bladder during caesarian section;
- Bladder drainage following surgery to the bladder, prostate or urethra.

Technique is described below. Usually a 16-20Ch catheter is used, with a 10 ml balloon. For longer catheterization periods a silastic catheter is used to limit tissue reaction, thereby reducing risk of a catheter-induced urethral stricture. If there is clot retention, a 3 way catheter (22-24Ch or greater) is used to allow evacuation of clots and bladder irrigation to prevent subsequent catheter blockage. One gloved hand holds penis or separates labia to allow cleansing of urethral meatus. Sterile cleaning solution to prepare skin around meatus is used. Lubricant jelly is applied to urethra. Traditionally this contains local anaesthetic (e.g. 2% lignocaine), sterile glycerin and antiseptic which takes between 3-5 min to work. In male, gel is injected towards posterior urethra, while squeezing meatus to prevent it from coming back out of meatus. The catheter is inserted using another sterile hand, until flow of urine to confirm it is in bladder. Failure of urine flow may indicate that the catheter balloon is in the urethra. Intra-urethral inflation of balloon can rupture urethra. If no urine flows attempt aspiration of urine using a 50 ml bladder syringe. Absence of urine flow indicates either catheter is not in the bladder or there is anyria. If the catheter will not pass into the bladder and you are sure that the patient is in retention, proceed with suprapubic catheterization.

Suprapubic catheterization

Indications:

- Failed urethral catheterization in urinary retention;
- Preferred site for long-term catheters.

Contraindications:

- Patients with clot retention, the cause of which may be an underlying bladder cancer;
- Patients with lower midline incisions (bowel may be fixed to the deep aspect of the scar, leading to the potential for bowel perforation);
- Pelvic fractures, where the catheter may inadvertently enter the large pelvic hematoma which always accompanies severe pelvic fracture. This can lead to infection of the hematoma and the resulting urosepsis can be fatal. Failure to pass a urethral catheter in a patient with a pelvic fracture usually indicates a urethral rupture confirmed by urethrography and is an indication for formal open, suprapubic cystotomy.

Technique is described below. Prior to insertion of trocar, be sure to confirm the diagnosis by abdominal examination. Palpation and percussion of lower abdomen are performed to confirm bladder is distended. US confirms diagnosis and US guided catheterization may be sensible. Wide-bore trocar is used. The catheter is inserted about 2 finger-breadths above the pubis symphysis. A few ml of local anaesthetic is instilled into skin of intended puncture site and down to rectus sheath. Location of bladder by aspiration of urine from bladder is confirmed. A 1cm incision with a sharp blade through the skin is performed. Hold trocar handle in your right hand and steady needle end with your left hand. This hand helps prevent insertion too deeply. As soon as urine issues from the trocar, withdraw the latter, holding the attached sheath in place. Push the catheter in as far as it will go. Balloon is inflated. The sides of the sheath are removed.

7.1.2. Bladder outlet obstruction and retention in women

It may be symptom-free and present with LUTS or as AUR. The causes are related to obstruction of the urethra (urethral stricture, compression by a prolapsing pelvic organs, post-surgery for stress incontinence) or have a neurological basis (injury to sacral cord or parasympathetic plexus, degenerative neurological disease e.g. MS, diabetic cystopathy).

Women have a higher Q_{max}, for a given voided volume, than do men. Women with BOO have lower Q_{max} than those without BOO.

By BOO in women the cause is treated. Where this it is not possible (because of a neurological cause), the options are:

- In woman CISC either until normal voiding function recovers or permanently if it does not;
- Indwelling catheter (preferably suprapubic rather than urethral);
- Mitrofanoff catheterizable stoma.

Where urethral CISC is technically difficult, a catheterizable stoma can be constructed between the anterior abdominal wall and the bladder, using the appendix, Fallopiian tube or a narrowed section of small intestine as a so called Mitrofanoff procedure.

It is simply a new urethra which has an abdominal location, rather than a perineal one and is therefore easier to access for CISC.

7.2. TORSION OF THE TESTIS AND TESTICULAR APPENDAGES

A testicular torsion is a twist of the spermatic cord resulting in strangulation of the blood supply to the testis and epididymis. Testicular torsion occurs most frequently between the ages 13-15 years of age, but any age group may be affected.

Symptoms and signs

Sudden onset of severe pain in the hemiscrotum, sometimes waking the patient from sleep. It may radiate to the groin, loin or epigastrium. There is sometimes a history of minor trauma to the testis. Some patients report previous episodes with spontaneous resolution of the pain. The testis is usually slightly swollen and very tender to touch. It may be “high-riding” and lying at a higher than normal position in the testis and may be in a horizontal position due to twisting of the cord.

Differential diagnosis and investigations

Epididymo-orchitis, torsion of a testicular appendage and testicular injuries are most common cases of “acute scrotum” syndrom. Colour doppler US with detection of reduced arterial blood flow in the testicular artery can be used to diagnose testicular torsion, but in many hospitals this test are not readily available and the diagnosis is based on symptoms and signs.

Emergent surgical management

Scrotal exploration should be undertaken as a matter of urgency. >6 hours of delay in relieving the twisted testis results in permanent ischaemic damage to the testis causing atrophy, loss of hormone and sperm production and, as the testis undergoes necrosis and the blood - testis barrier breaks down, an autoimmune reaction against the contralateral testicular tissue. Both testes are fixed since the “bell-clapper” abnormality which predisposes to torsion can occur bilaterally.

Torsion of testicular appendages

The appendix of testis (hydatid of Morgagni a remnant of the Mullerian duct) and the appendix of epididymis (a remnant of a cranial mesonephric tubule of the Wolffian duct) can undergo torsion causing pain that mimicks a testicular torsion. At scrotal exploration they are easily removed with scissors or a diathermy probe.

7.3. PARAPHIMOSIS

This is emergent situation, where the foreskin is retracted from over the glans of the penis, becomes edematous and cannot then be pulled back over the glans into its normal anatomical position. It occurs most commonly in teenagers or young men and also in elderly men, who have had the foreskin retracted during catheterization, but where it has not been returned to its normal position. Paraphimosis is usually painful. The foreskin is edematous and a small area of ulceration of the foreskin may have developed.

Treatment

The “iced-glove” method: topical lignocaine gel is applied to the glans and foreskin for 5 min. The penis is invaginated into the thumb of the glove and the edematous

paraphimosis is compressed. Squeeze the edema fluid out of the foreskin. This may reduce the swelling and allow reduction of the foreskin. Foreskin is returned to its normal position.

The Dundee technique is described below. A ring block is applied to the base of the penis using a 26G needle and 10-20 ml of 0.5% plain bupivacaine. Children usually require general anaesthesia. The skin of the foreskin and the glans is cleaned with cleaning solution. Using a 25G needle make approximately 20 punctures into the edematous foreskin. Squeeze the edema fluid out of the foreskin and return to its normal position. Approximately 1/3 of patients subsequently will require circumcision for an underlying phimosis.

If this fails, the traditional surgical treatment is a dorsal slit under general anaesthetic or ring block. A longitudinal incision is made in the tight band of constricting tissue and the foreskin pulled back over the glans. The incision is closed transversely to lengthen the circumference of the foreskin and prevent recurrences.

7.4. MALIGNANT URETERIC OBSTRUCTION

Locally advanced PC, bladder or ureteric cancer may cause unilateral or bilateral ureteric obstruction. Locally advanced non - urological malignancies (cervical cancer, rectal cancer, lymphoma) can also obstruct the ureters.

Unilateral obstruction is often asymptomatic. An incidental US finding that requires no specific treatment in the presence of a normal contralateral kidney. Occasionally, loin pain and systemic symptoms may develop due to infection of the obstructed upper urinary tract. In this circumstance, drainage by PNS or stenting is required.

Bilateral ureteric obstruction is a urological emergency. The patient presents with symptoms and signs of renal failure and has anuria.

Renal US will demonstrate bilateral UHN and an empty bladder. CT urography will confirm the presence of dilated ureters down to a mass at the bladder base.

Treatment

After treating any life-threatening hyperkalaemia, options include bilateral PNS or ureteric stenting. A clotting screen is required prior to nephrostomy insertion. Insertion of retrograde ureteric stents in this setting is usually unsuccessful because tumour involving the trigone obscures the location of the ureteric orifices. More successful is antegrade ureteric stenting following PNS tube insertion. The full-length double-J silicone or polyurethane ureteric stents require periodic changes to prevent calcification or blockage.

Such emergent situations as renal colic, hematuria and anyria are discussed in other chapters.

Definitions

UTI is defined as the inflammatory response of the urothelium and tissue to bacterial invasion. This inflammatory response causes many symptoms, depending on what organ is inflamed (urethritis, cystitis, prostatitis, pyelonephritis...) or there is urosepsis with/without septic shock. The strict requirement for $>10^5$ bacteria/ml of urine is no longer required to make a diagnosis of UTI. In symptomatic patients many clinicians will now make a diagnosis of UTI with bacterial counts of $>10^2$ /ml. The low counts are due to irritation and frequent voiding caused by the infection and also represent the slow doubling time of acteria in urine.

An uncomplicated UTI is one occurring in a patient with a structurally and functionally normal urinary tract. The majority of such patients are women who respond quickly to a short course of antibiotics.

A complicated UTI is one occurring in the presence of an underlying anatomical or functional abnormality: functional problem causing incomplete bladder emptying (BOO), urinary stone disease, fistulas. Most UTIs in men occur in association with a structural or functional abnormality and are therefore defined as complicated UTIs. Complicated UTIs take longer to respond to antibiotic treatment than uncomplicated UTIs and they need removing of the underlying anatomical or structural abnormality.

Bacteriuria is the presence of bacteria in the urine. Bacteriuria may be asymptomatic or symptomatic. Bacteriuria without pyuria indicates the presence of bacterial colonization of the urine, rather than the presence of active infection. Active implies an inflammatory response to bacterial invasion of the urothelium. Risk factors for bacteriuria: female sex, increasing age, low oestrogen states, pregnancy, DM, previous UTIs, indwelling catheters, stone disease, genitourinary malformation and obstruction.

Pyuria is the presence of WBC in the urine, implying an inflammatory response of the urothelium to bacterial infection or, in the absence of bacteriuria, some other pathology such as CIS, TB infection, bladder stones or other inflammatory conditions.

Isolated UTI: an interval of at least 6 months between infections.

Recurrent UTI: >2 infections in 6 months or 3 within 12 months. Recurrent UTI may be due to reinfection with infection by a different bacteria or bacterial persistence with infection by the same organism originating from a focus within the urinary tract. Bacterial persistence is caused by the presence of bacteria within struvite calculi, within a chronically infected prostate, within an obstructed or atrophic infected kidney, occurs as a result of a vesicovaginal fistula or urethral diverticulum.

Etiology and microbiology

Most UTIs are bacterial and are caused by faecal-derived bacteria which are facultative anaerobes, and can grow under both anaerobic and non-anaerobic conditions.

The most common cause by uncomplicated UTIs is *Escherichia coli* (*E. coli*), a gram-negative bacillus, which accounts for 85% of community acquired and 50% of hospital acquired infection. Other common causative organisms include *Staphylococcus saprophyticus* and *Streptococcus faecalis* (gram-positive), *Neisseria* (gram-negative cocci).

By complicated UTI *E. coli* is responsible for up to 50% of cases. Other causes include *Streptococcus faecalis*, *Staph. aureus*, *Staph. epidermidis* (gram positive).

Nosocomial infections are: gram-negative Enterobacteria (*Escherichia*, *Klebsiella*, *Proteus*), *Pseudomonas aeruginosa*.

Anaerobic infections of the bladder and kidney are uncommon. Anaerobes are normal commensals of the perineum, vagina and distal urethra. However, infections of the urinary system which produce pus (e.g. scrotal, prostatic or perinephric abscesses) are often caused by anaerobic organisms (e.g. *Bacteroides* species such as *Bacteroides fragilis*, *Fusobacterium* species, anaerobic cocci and *Clostridium perfringens*).

Other etiological factors:

- *Mycobacterium* (*M. tuberculosis* acid-fast, aerobic, gram-positive);
- *Chlamydia trachomatis*;
- *Candida albicans*;
- *Mycoplasma*: *Mycoplasma* species and *Ureaplasma urealyticum*, which cause UTIs in patients with indwelling catheters and STD.

Route of infection

The vast majority of UTIs result from infection *ascending retrogradely* up the urethra. The bacteria, derived from the large bowel, colonize the perineum, vagina and distal urethra. They ascend easily along the female urethra to the bladder causing cystitis and from the bladder they may ascend, via the ureters, to involve the kidneys. Presence of VUR will encourage ascending infection, as will any process that impairs ureteric peristalsis (e.g. ureteric obstruction, microorganisms, pregnancy). Infection which ascends to involve the kidneys is also more likely where the infecting organism has factors increasing bacterial virulence - pili or fimbriae, which allow binding of bacteria to the surface of epithelial cells. There are many other factors of bacteria to avoid host defense mechanisms (toxins, enzymes).

Haematogenous route of infection is uncommon, but is seen with *Staph. aureus*, *Candida* and TB.

Infection via *lymphatics* is seen rarely in inflammatory bowel disease and retroperitoneal abscess.

Host defences

Factors which protect against UTIs are:

- Mechanical flushing effect of urine through the urinary tract;
- A mucopolysaccharide coating of bladder (Tamm - Horsfall protein) helps prevent bacterial attachment;
- Low urine pH and high osmolarity reduces bacterial growth;
- Urinary immunoglobulin (IgA) inhibits bacterial adherence.

8.1. CYSTITIS

This is infection and/or inflammation of the bladder. Cystitis may be also due to pelvic radiotherapy as a radiation cystitis. Bladder capacity by radiation cystitis is reduced and multiple areas of mucosal telangiectasia are seen cystoscopically. Inflammation of the bladder may be as a drug-induced cystitis. Haemorrhagic cystitis may be as consequence of viral (Herpes zoster) infection.

Symptoms

Symptoms are: frequent voiding of small volumes, dysuria (urethral burning on voiding), urgency, cloudy urine, suprapubic pain or discomfort, hematuria.

Diagnosis

Urinanalysis

Leukocyte esterase activity detects the presence of WBS in the urine with help of dipstick. Leukocyte esterase is produced by neutrophils and causes a colour change in a chromogen salt on the dipstick. Remember, there are many causes for pyuria and therefore a positive leukocyte esterase test occurring in the absence of bacteria on urine microscopy. This is so-called sterile pyuria and it occurs with TB infection, urinary stone disease, glomerulonephritis, interstitial cystitis, CIS. Thus, the leukocyte esterase dipstick test may be truly positive, in the absence of infection.

Nitrite testing

Nitrites are not normally found in urine and their presence suggests the possibility of bacteriuria. Many species of gram-negative bacteria can convert nitrates to nitrites and these are detected in urine by a reaction with the reagents on the dipstick. The specificity of the nitrite dipstick for detecting bacteriuria is >90%. Less accurate test may be in urine containing fewer than 10^5 organisms/ml. So, if the nitrite dipstick test is positive, the patient probably has a UTI, but a negative test often occurs in the presence of infection.

Cloudy urine which is positive for WBCs on dipstick and is nitrite positive is very likely to be infected.

If this is a first episode of cystitis in an otherwise healthy individual, no further investigations are required. However, further investigations are required if:

- The patient develops symptoms and signs of upper tract infection (loin pain, malaise, fever) and therefore acute pyelonephritis, a pyonephrosis or perinephric abscess is suspected;
- Recurrent UTIs develop;
- The patient is pregnant;
- Unusual infecting organism (e.g. *Proteus*), suggesting the possibility of an infection stone or NSI

These further investigations will include a renal US in pregnant women and KUB X-ray or CT.

Treatment

The aim is to eliminate bacteria from the urine. Empirical treatment involves the administration of antibiotics according to the clinical presentation and most likely causative organism, before culture sensitivities are available. Once urine or blood culture results are available, antimicrobial therapy should be adjusted according to bacterial sensitivities. Men are often affected by complicated UTI and may require imaging and longer treatments. Underlying abnormality should be corrected if feasible: extraction of infected calculus, removal of catheter, PNS of an infected or obstructed kidney.

There is one big problem: bacterial resistance to drug therapy. Organisms susceptible to concentrations of an antibiotic in the urine (or serum) after the recommended clinical dosing are termed “sensitive” and those that do not respond are “resistant”.

Recommended antimicrobial therapy in acute uncomplicated cystitis in premenopausal women (EAU 2014)

Antibiotics → Daily dose → Duration of therapy

- Fosfomycin trometamol 3 g SD 1 day;
- Nitrofurantoin 50 mg q6h 7 days;

Alternatives

- Ciprofloxacin 250 mg bid 3 days;
- Levofloxacin 250 mg qd 3 days;
- Norfloxacin 400 mg bid 3 days;
- Ofloxacin 200 mg bid 3 days;

If local resistance pattern is known (E. coli resistance <20%)

- Trimethoprim-sulphamethoxazole 160/800mg bid 3 days;
- Trimethoprim 200 mg bid 5 days.

8.2. URETHRITIS

This is inflammation of the urethra. Urethritis in men is a STD, which presents with dysuria and urethral discharge.

GU is caused by the gram-negative diplococcus *Neisseria gonorrhoea*. Diagnosis is on cultures from urethral swab. Treatment involves a single dose of III- IV generation of cephalosporin (ceftriaxone or cefotaxime) or course of ciprofloxacin. Sexual contacts must be informed and treated.

NGU is mainly caused by *Chlamydia trachomatis* and *Mycoplasma*. Acute NGU is treated with a single dose of azithromycin, 7-10 days of doxycycline or macrolides. Transmission to females results in increased risk of pelvic inflammatory disease, abdominal pain, ectopic pregnancy, infertility and perinatal infection. If NGU caused by *Trichomonas vaginalis* metronidazole is used.

Urethral syndrome

This is a condition of uncertain etiology that only affects women. It manifests as dysuria, frequency and urgency without evidence of infection, although some cases improve with antibiotics.

8.3. RECURRENT URINARY TRACT INFECTION

Recurrent UTI is defined as >2 UTIs in 6 months or 3 within 12 months. It may be due to reinfection with infection by a different bacteria or bacterial persistence with infection by the same organism originating from the urinary tract

Re-infections

Usually occur after a prolonged interval from the previous infection and are often caused by a different organism than the previous infecting bacterium.

Women with reinfection do not usually have an underlying functional or anatomical abnormality. Re-infections in women are associated with increased vaginal mucosal receptivity for uropathogens and ascending colonization of faecal flora from the perineum.

Men with re-infection may have underlying BOO, which makes them more likely to develop a repeat infection, but between UTIs their urine is sterile. A urethrogram, US, cystoscopy, bladder US for PVR and, in some cases, urodynamics may be helpful in establishing the potential causes.

Bacterial persistence

Bacterial persistence usually leads to frequent recurrence of infection within days or weeks and the infecting organism is usually the same organism as that causing the previous UTIs.

Presence of bacteria within a site in the urinary tract leads to repeated episodes of UTIs. Such sites include kidney stones, chronic bacterial prostatitis, bacteria within an obstructed or atrophic infected kidney, bacteria gaining access to the urinary tract via a fistula, bacteria within a urethral diverticulum.

As stated above, both men and women with bacterial persistence usually have an underlying functional or anatomical abnormality and they can potentially be cured of their recurrent UTIs, if this abnormality can be identified and corrected.

Management of women with recurrent UTIs due to re-infection

Most urologists will arrange a series of screening tests (KUB X-ray, renal US, cystoscopy) to double check there is no potential source of bacterial persistence.

In the absence of finding an underlying functional or anatomic abnormality, these patients cannot be cured of their tendency to recurrent UTIs, but they can be managed in one of the following ways:

- Avoidance of spermicides used with the diaphragm or on condoms. Spermicides reduce vaginal colonization with lactobacilli and may enhance *E. coli* adherence to urothelial cells. Alternative form of contraception is recommended.
- Lack of estrogen in post-menopausal women causes loss of vaginal lactobacilli and increased colonization by *E.coli*. Estrogen replacement can result in recolonization of the vagina with lactobacilli and eliminate colonization with bacterial uropathogens.
- Low-dose antibiotic prophylaxis. Oral antimicrobial therapy causes resistant strains in the faecal flora and subsequent resistant UTIs. However, trimethoprim, nitrofurantoin, low-dose cephalexin and the fluoroquinolones have a

minimal adverse effects on the faecal and vaginal flora. Prophylactic therapy requires only a small dose of an antimicrobial agent, generally given at bedtime for 6 to 12 months. Symptomatic reinfection during prophylactic therapy is managed with a full therapeutic dose with the same prophylactic antibiotic or another antibiotic. Prophylaxis can then be restarted. Symptomatic reinfection immediately after cessation of prophylactic therapy is managed by restarting nightly prophylaxis.

- Sexual intercourse has been established as an important risk factor for acute cystitis in women and women who use the diaphragm have a significantly greater risk of UTI than women who use other contraceptive methods. Post-intercourse therapy with antimicrobials such as nitrofurantoin or trimethoprim, taken as a single dose, effectively reduces the incidence of reinfection.
- Self-start therapy. Women keep a home supply of an antibiotic (e.g. trimethoprim, nitrofurantoin, a fluoroquinolone) and start treatment when they develop symptoms suggestive of UTIs.

Management of men and women with recurrent UTIs due to bacterial persistence

Investigations for identifying the potential causes of bacterial persistence:

- KUB X-ray to detect radio-opaque renal calculi;
- Renal US to detect hydronephrosis and renal calculi;
- Determination of PVR by bladder US;
- IVU or CT where a stone is suspected, but not identified on plain X-ray or US;
- Cystoscopy to identify possible causes of recurrent UTIs such as bladder stones, an underlying bladder cancer, urethral or bladder neck stricture or fistula.

Treatment of bacterial persistence depends on the functional or anatomical abnormality which is identified as the cause. If a stone is identified, this should be removed and if there is obstruction, this should be corrected.

8.4. PYELONEPHRITIS

8.4.1. Acute pyelonephritis

There are many risk factors: VUR, urinary tract obstruction, stone disease, neurogenic bladder, DM, congenital malformations, pregnancy, indwelling catheters.

A clinical diagnosis based on the presence of fever, flank pain and tenderness, often with an elevated WBC count. It may affect one or both kidneys. There are usually accompanying LUTS suggestive of a lower UTI responsible for the ascending infection which resulted in the subsequent acute pyelonephritis. Nausea and vomiting are common. Differential diagnosis includes “acute abdomen” syndrome.

Pathogenesis and microbiology

Initially, there is infiltration of neutrophils and bacteria in the parenchyma. Later changes include the formation of inflammatory bands extending from renal papilla to cortex and small cortical abscesses. 80% of infections are secondary to *E. coli*. Other infecting organisms: *Streptococcus faecalis*, *Klebsiella*, *Proteus* and *Pseudomonas*.

Urine culture will be positive for bacterial growth, but the bacterial count may not necessarily be $>10^5$ cfu/ml of urine. Thus, if a diagnosis of acute pyelonephritis is suspected from the symptoms of fever and flank pain, but there are $<10^5$ cfu/ml of urine, this case is treated as acute pyelonephritis.

Diagnosis and treatment

- For those patients who have a fever but are not systemically unwell, outpatient management is reasonable. Culture the urine and start oral antibiotics according to local antibiotic policy, which will be based on the likely infecting organisms and their likely antibiotic sensitivity.
- If the patient is systemically unwell, culture urine and blood, start i.v. fluids and antibiotics, again selecting the antibiotic according to local antibiotic policy.
- A KUB X-ray and renal US are used, to see if there is an underlying upper tract abnormalities such a ureteric stone or hydronephrosis.
- If the patient does not respond within 3 days to this regimen of appropriate i.v. antibiotics, CT is performed. The lack of response to treatment suggests the possibility of a pyonephrosis or a perinephric abscess. The CT may demonstrate an obstructing ureteric calculus that may have been missed on the KUB X-ray and may show a perinephric abscess. A pyonephrosis should be drained by insertion of a PNS tube. A perinephric abscess should also be drained by insertion of a drain percutaneously.
- If the patient responds to i.v. antibiotics, these are changed to an oral antibiotics of appropriate sensitivity when they become afebrile and continue this for approximately 10-14 days.

Recommended initial empirical antimicrobial therapy in acute uncomplicated pyelonephritis in premenopausal women

1. Oral therapy in mild and moderate cases:

Antibiotics → Daily dose → Duration of therapy

- Ciprofloxacin 500-750 mg bid 7-10 days;
- Levofloxacin 250-500 mg qd 7-10 days;
- Levofloxacin 750 mg qd 5 days;

Alternatives

- Cefixime 400 mg qd 10 days;
- Amoxiclav 0.5/0.125 g tid 14 days;

2. Initial parenteral therapy in severe cases:

After improvement, the patient can be switched to an oral regimen using one of the above-mentioned antibacterials to complete the 1-2-week course of therapy.

Antibiotics → Daily dose

- Ciprofloxacin 400 mg bid;
- Levofloxacin 250-500 mg qd;
- Levofloxacin 750 mg qd;

Alternatives:

- Cefotaxime 2 g tid;
- Ceftriaxone 1-2 g qd;

- Ceftazidime 1-2 g tid;
- Cefepime 1-2 g bid;
- Amoxiclav 1.2 g tid;
- Piperacillin/tazobactam 2.5-4.5 g tid;
- Gentamicin 5 mg/kg qd;
- Amikacin 15 mg/kg qd;
- Ertapenem 1 g qd;
- Imipenem/cilastatin 0.5/0.5 g tid;
- Meropenem 1 g tid;
- Doripenem 0.5 g tid.

8.4.2. Emphysematous pyelonephritis

A rare, severe form of acute pyelonephritis caused by gas-forming organisms. It is characterized by fever and abdominal pain, with radiographic evidence of gas within and around the kidney on plain X-Ray or CT. It usually occurs in DM patients and in many cases is precipitated by urinary obstruction. The high glucose levels of the poorly controlled diabetic provides an ideal environment for fermentation by Enterobacteria, carbon dioxide being produced during this process.

It presents as a severe acute pyelonephritis, which fails to respond within 2-3 days with conventional treatment in the form of i.v. antibiotics. Commonly caused by *E.coli*, less frequently *Klebsiella* and *Proteus*. On KUB X-ray a crescent or kidney-shaped distribution of gas may be seen around the kidney. Renal US often demonstrates focal echoes, indicating gas within the kidney. Intra-renal gas is seen on CT scan.

Patients with emphysematous pyelonephritis are usually very unwell and mortality is high. In selected cases, it can be managed conservatively, by i.v. antibiotics and fluids, drainage and careful control of diabetes. In those where urosepsis is poorly controlled, emergency nephrectomy is required.

8.4.3. Purulent forms of pyelonephritis

Pyonephrosis

This is an infected hydronephrosis. Pus accumulates within the renal pelvis and calyces. The causes are essentially those of hydronephrosis, where infection has supervened.

Patients with pyonephrosis are usually very unwell, with a high fever, flank pain and tenderness. Again, patients with this combination of symptoms and signs will usually be investigated by a renal US, where the diagnosis of a pyonephrosis is usually obvious. Treatment consists of PNS with i.v. antibiotics and fluids. By loss of function nephrectomy is indicated.

Perinephric abscess

Perinephric abscess develops as a consequence of extension of infection outside the parenchyma of the kidney in acute pyelonephritis or from hematogenous spread of infection from a distant site. The abscess develops within Gerota's fascia.

These patients are often diabetic and associated conditions such as an obstructing ureteric calculus may be the precipitating event leading to development of the perinephric abscess.

Failure of acute pyelonephritis to respond to i.v. antibiotics within a few days arouses the suspicion that there is an accumulation of pus in or around the kidney or obstruction with infection.

Imaging studies, such as US and more especially CT will establish the diagnosis and allow radiographically controlled percutaneous drainage of the abscess. If the pus collection is large, formal open surgical drainage under general anaesthetic will provide more effective drainage.

Maintaining a degree of suspicion in all cases of presumed acute pyelonephritis is the single most important thing in allowing an early diagnosis of complicated renal infection, such as a pyonephrosis, perinephric and kidney abscess or emphysematous pyelonephritis. If the patient is very unwell, diabetic or has a history suggestive of stones, they may have something more than just a simple acute pyelonephritis. Specifically ask about a history of sudden onset of severe flank pain a few days earlier, suggesting the possibility that a stone passed into the ureter, with later infection supervening. Arranging a KUB X-ray and renal US in all patients with suspected renal infection, which will demonstrate the presence of hydronephrosis, pus or stones.

Clinical indicators suggesting a more complex form of renal infection are length of symptoms prior to treatment and time taken to respond to treatment. Most patients with uncomplicated acute pyelonephritis have been symptomatic for <5 days. Most patients with a perinephric abscess have been symptomatic for >5 days prior to hospitalization. Patients with acute pyelonephritis became afebrile within 4-5 days of treatment with an appropriate antibiotic, whereas those with perinephric abscesses remain pyrexial.

8.4.4. Chronic pyelonephritis

It can be a radiological or pathological diagnosis (renal scarring) or description. The scarring can be due to previous infection or it can occur from the long-term effects of VUR. A child with VUR, particularly where there is reflux of infected urine, will develop reflux nephropathy, which if bilateral may cause CRF. An adult may also develop radiological and pathological features of chronic pyelonephritis, due to the presence of VUR or obstruction combined with high bladder pressures, again particularly where the urine is infected. This was a common occurrence in male patients with neurogenic bladder before the advent of effective treatments for this condition.

The scars are closely related to a deformed renal calyx. Distortion and dilatation of the calyces is due to scarring of the renal pyramids. These scars typically affect the upper and lower poles of the kidneys, because these sites are more prone to intrarenal reflux. The cortex and medulla in the region of a scar is thin.

The kidney may be so scarred that it becomes small and atrophic. Scars can be seen on a renal US, an IVU, renal isotope scan or a CT.

8.5. FOURNIER'S GANGRENE

A necrotizing fasciitis of the genitalia and perineum, causing necrosis and subsequent gangrene of infected tissues. Culture of infected tissue reveals a combination of aerobic (*E. coli*, enterococcus, *Klebsiella*) and anaerobic organisms (*Bacteroides*, *Clostridium*, microaerophilic streptococci), which are believed to grow in a synergistic fashion. Conditions which predispose to the development of Fournier's gangrene include DM, local trauma to the genitalia and perineum (e.g. zipper injuries to the foreskin, periurethral extravasation of urine following traumatic instrumentation of the urethra) and surgical procedures such as circumcision.

Symptoms

A previously well patient may become systemically unwell over a very short time following a seemingly trivial injury to the external genitalia. A fever is usually present, they may have marked pain in the affected tissues and the developing urosepsis may alter their mental state. The genitalia and perineum are edematous and on palpation of the affected area, tenderness and crepitus may be present indicating the presence of subcutaneous gas produced by gas-forming organisms. As the infection advances, bullae appear in the skin and, within a matter of hours, areas of necrosis may develop which spread to involve adjacent tissues. The condition advances very rapidly.

Diagnosis

The diagnosis is a clinical one and is based on awareness of the condition and a low index of suspicion.

Treatment

While i.v. access is obtained, blood taken for culture, i.v. fluids started and oxygen administered, broad spectrum antibiotics are given to cover both gram-positive and negative aerobes and anaerobes (e.g. ampicillin, gentamicin and metronidazole or clindamycin). Make arrangements to transfer the patient to the operating room as quickly as possible so that debridement of necrotic tissue can be carried out. Extensive areas of tissue may have to be removed, but it is unusual for the testes or deeper penile tissues to be involved and these can usually be spared. A suprapubic catheter is inserted to divert urine and allow monitoring of urine output.

Where facilities allow, consider treatment with hyperbaric oxygen therapy. There is some evidence that this may be beneficial. Repeated debridements to remove residual necrotic tissue are not infrequently required. Mortality is in the order of 20-30%.

8.6. EPIDIDYMITIS AND ORCHITIS

This is an inflammatory condition of the epididymis, often involving the testis and caused by bacterial infection. It has an acute onset and a clinical course lasting <6 weeks. It presents with pain, swelling and tenderness of the epididymis. It should be distinguished from chronic epididymitis where there is longstanding pain in the epididymis, but usually no swelling.

Infection ascends from the urethra or bladder. In men aged <35 years, the infective organism is usually *N. gonorrhoeae*, *C. trachomatis*. In children and older men, the infective organisms are usually coliforms. *Mycobacterium tuberculosis* is a rarer cause of the epididymis.

Differential diagnosis

Torsion of the testicle is the main differential diagnosis. A preceding history of symptoms suggestive of urethritis or urinary infection, LUTS suggest that epididymitis is the cause of the scrotal pain, but these symptoms may not always be present in epididymitis. In epididymitis pain, tenderness and swelling may be confined to the epididymis, whereas in torsion, the pain and swelling are localized to the testis. However, there may be overlap in these physical signs.

Where doubt exists, exploration is the safest option. Though radionuclide scanning can differentiate between a torsion and epididymitis, this is not available in many hospitals. Colour doppler US, which provides a visual image of blood flow, can differentiate between a torsion and epididymitis, but its sensitivity for diagnosing torsion is only 80%. These 20% have torsion but normal findings on doppler US of the testis. Again, if in doubt, scrotum is explored.

Treatment

This consists of antibiotics, bed rest and analgesia. Where *C. trachomatis* is a possible infecting organism, a 10-14 day course of doxycycline 100 mg twice daily is prescribed. If gonorrhoeae is confirmed on a gram stain of the urethral discharge and on culture, ciprofloxacin or ceftriaxon is used. For non-STD related epididymitis, antibiotics are prescribed empirically (until culture results are available) according to local microbiology department advice. Fluoroquinolones, cephalosporins and aminoglycosides are used for empirical treatment (2-4 weeks).

Complications of acute epididymitis: abscess formation, infarction of the testis, chronic pain and infertility.

Chronic epididymitis

is diagnosed in patients with long-term pain in the epididymis and testicle. It can result from recurrent episodes of acute epididymitis. Clinically, the epididymis is thickened and may be tender. Treatment is with the appropriate antibiotics and NSAIDs or epididymectomy in severe cases.

Orchitis

is inflammation of the testis, although it often occurs with epididymitis (epididymo-orchitis). Causes include mumps, *M. tuberculosis*, syphilis, autoimmune processes as a granulomatous orchitis. The testis is swollen and tense, with edema of connective tissues and inflammatory cell infiltration. The underlying cause is treated.

Mumps orchitis occurs in 30% of infected post-pubertal males. It manifests 3-4 days after the onset of parotitis and can result in tubular atrophy. 10-30% of cases are bilateral and are associated with infertility.

8.7. PROSTATITIS

This is infection and/or inflammation of the prostate. Overall prevalence in men is 5-11%. Age groups at increased risk are 20-50 and >70 years old.

Etiology and pathogenesis

The tissues surrounding the prostatic acini become infiltrated with lymphocytes. The most common infective agents are gram-negative Enterbacteriaceae (*Escherichia coli*, *Pseudomonas aeruginosa*, *Klebsiella*, *Serratia*, *Enterobacter aerogenes*). 5-10% of infections are caused by gram - positive bacteria (*Staphylococcus aureus* and *saprophyticus*, *Streptococcus faecalis*). The etiology of inflammatory and non-inflammatory forms of prostatitis is not well understood.

Risk factors: UTI and intraprostatic ductal reflux, urethral catheters, transurethral surgery, prostatic stones, which can provide a nidus of infection for chronic prostatitis, venous and secretory stasis.

Classification of prostatitis

- I. Acute bacterial prostatitis;
- II. Chronic bacterial prostatitis;
- III. Chronic pelvic pain syndrome;
- IIIA Inflammatory CPPS: WBC in EPS, VB3 or semen. Where cultures are negative, increased leucocytes per HPF (>10) favor a diagnosis of inflammatory CPPS;
- IIIB Non-inflammatory CPPS (prostatodynia): no WBC in EPS, VB3 or semen;
- IV. Asymptomatic inflammatory prostatitis (histological prostatitis or male infertility cases).

Diagnosis

- Segmented urine cultures localize bacteria and WBC to a specific part of the urinary tract with (EPS) or without (VB3) prostatic massage.

VB1 - first 10 mls of urine voided. Positive culture and WBC indicates urethritis or prostatitis.

VB2 - midstream urine. Positive culture and WBC indicates cystitis.

VB3 - first 10 mls of urine voided following prostatic massage. Positive culture indicates prostatitis.

EPS - positive culture indicates prostatitis.

- NIH-CPSI questionnaire (National Institute of Health Chronic Prostatitis Symptom Index). This scores 3 main symptom areas: pain (location, frequency, severity), voiding (LUTS) and impact on quality of life.

Acute bacterial prostatitis

ABP is infection of the prostate associated with lower UTIs and generalized urosepsis. *E. coli* is the most common cause. *Pseudomonas*, *Serratia*, *Klebsiella* and enterococci are less common causes.

Acute onset of fevers, chills, nausea and vomiting, perineal and suprapubic pain, LUTS. Signs of systemic toxicity (fever, tachycardia, hypotension) may be present. Suprapubic tenderness and a palpable bladder will be present if there is AUR. On DRE the prostate is extremely tender.

Treatment includes an oral fluoroquinolone (ciprofloxacin 500mg bd) for 2-4 weeks. For a patient who is systemically unwell, i.v. antibiotics (aminoglycosides, fluoroquinolones and/or 3rd generation cephalosporins). NSAIDs are used for pain relief. Catheterization or suprapubic catheter are used for relief of retention. Traditional teaching was that a suprapubic catheter should be inserted to avoid the potential obstruction of prostatic urethral ducts by a urethral catheter. However, in-and-out catheterization or short periods with an indwelling catheter probably does no harm and is certainly an easier way of relieving retention than suprapubic catheterization.

Prostatic abscess

Failure to respond to this treatment regimen with persistent symptoms and fever while on antibiotic therapy suggests the development of a prostatic abscess. A TRUS or CT scan is the best way of diagnosing a prostatic abscess. This may be drained by a TUR.

Chronic bacterial prostatitis

History of recurrent UTIs. Chronic episodes of pain and voiding dysfunction may be a feature. DRE may show a tender, enlarged and boggy prostate. Treatment as for acute bacterial prostatitis.

Chronic pelvic pain syndrome

Both inflammatory (IIIA) and non-inflammatory (IIIB) types present with >3 month history of localized pain (perineal, suprapubic, penile, groin or external genitalia) or pain with ejaculation, There are LUTS and ED. Symptoms can recur over time and severely affect patient's quality of life.

Treatment options for inflammatory and non-inflammatory CPPS are not fully understood. NSAIDs and alfa – blockers are used. Alfa – blockers acts on prostate and bladder neck alfa -receptors, causing smooth muscle relaxation, improved urinary flow and reduced intraprostatic ductal reflux. Sometimes patients need antibiotics, biofeedback and psychological support.

Asymptomatic inflammatory prostatitis

Incidental histological diagnosis of prostatic inflammation from prostate tissue taken for other indications (i.e. biopsy for raised PSA) or male infertility. Treatment options: oral fluoroquinolone, alpha-blockers, NSAIDs as a suppositories, physiotherapy, phytotherapy.

8.8. INTERSTITIAL CYSTITIS

IC is a refractory bladder disorder of unknown etiology. Predominantly affects females. Patients suffer from chronic urinary frequency, nocturia, urgency and bladder/suprapubic pain, in the absence of any obvious cause.

Possible contributing factors:

- Studies have demonstrated increased mast cells in bladder smooth muscle. Activated mast cells release histamine, which can cause symptoms and fibrosis in tissues;
- Defective bladder epithelium: an abnormal GAG layer may allow urine to leak past the luminal surface, causing inflammation in muscle layers;
- Neurogenic mechanisms: abnormal activation of sensory nerves causes release of neuropeptides, resulting in neurogenic inflammation;
- Reflex sympathetic dystrophy of the bladder due to excessive sympathetic activity;
- Urinary toxins or allergens;
- Bladder autoimmune response.

Diagnosis

A higher prevalence of allergies, irritable bowel syndrome, fibromyalgia, focal vulvitis and Segren's syndrome has been reported in IC.

History, pelvic examination, DRE, urinalysis and culture are mandatory. IC symptom index questionnaire, voiding diaries and urodynamics are useful.

Diagnostic studies:

- Cystoscopy: 10% of patients will have pink ulceration of bladder mucosa. This is Hunner's ulcer. Under anaesthesia, the bladder should be distended twice (to 80-100 cm H₂O for 1-2 min) and then inspected for diffuse glomerulations (>10 per quadrant in 3/4 bladder quadrants). Bladder biopsy is only indicated to rule out other pathologies. Bladder filling causes pain and reproduces symptoms.
- Intravesical KCl challenge In 75% of IC patients, installation of KCl into the bladder will provoke pain and symptoms.

Exclusion criteria:

- Bladder capacity >350 ml, measured by cystometry;
- Lack of urgency with a 150 ml injection in cystometry;
- Uninhibited contractions during cystometry;
- <9 months from onset;
- Absence of nocturia;
- Symptoms improved by antibiotics, anticholinergics or antispasmodics;
- Daytime voids <8;
- Bacterial cystitis or prostatitis within 3 months;
- Bladder or ureteral calculi;
- Genital herpes;
- Uterine, cervical, vaginal or urethral cancer;
- Urethral diverticulum;
- Cyclophosphamide- or drug-induced cystitis;
- Tuberculous cystitis;
- Radiation cystitis;
- Bladder tumour;
- Vaginitis;
- <18 years old.

Treatment

- Tricyclics have anticholinergic, antihistamine and sedative effects;
- Pentosan polysulphate (Elmiron) is an anti-inflammatory synthetic GAG analogue;
- Long-term analgesia with NSAIDs or paracetamol;
- Opiates may be prescribed and monitored via pain clinics;
- Repeated intravesical drug installation of dimethyl sulphoxide (DMSO) ± local anaesthetic (Lidocain), GAG analogues (pentosan polysulphate and hyaluronic acid), BCG, capsaicin, resiniferotoxin;
- Transcutaneous electrical nerve stimulation (TENS) and neuromodulation;
- TUR, laser coagulation or diathermy of Hunner's ulcers;
- Bladder hydrodistention;
- Bladder aufmentation should be considered after failed conservative treatments;
- As a last option surgery urinary diversion ± cystectomy may be required.

8.9. UROSEPSIS

Bacteraemia is the presence of pathogenic organisms in the blood stream. In the hospital setting, the most common causes are the presence of or manipulation of indwelling urinary catheters, urinary tract endoscopic surgery and urinary tract obstruction. Diabetic patients, patients in ICUs and patients on chemotherapy and steroids are more prone to urosepsis. From a urological perspective, the clinical scenario is usually a post-operative patient or patients with obstruction or purulent forms of UTIs. Consider the possibility of a non-urological source of sepsis (e.g. pneumonia).

Causative organisms in urosepsis: *E. coli*, *Streptococcus faecalis*, *Staphylococci*, *Pseudomonas aeruginosa*, *Klebsiella* and *Proteus mirabilis*.

Sepsis is the clinical syndrome caused by bacterial infection of the blood, confirmed or most common not confirmed by positive blood cultures for a specific organism and accompanied by a systemic response to the infection known as SIRS.

SIRS is defined by at least two of the following:

- Fever ($>38^{\circ}\text{C}$) or hypothermia ($<36^{\circ}\text{C}$);
- Tachycardia (>90 beats/min);
- Tachypnoea (respiratory >20 /min or $\text{PaCO}_2 < 4.3$ kPa or a requirement for mechanical ventilation);
- WBC count >12000 cells/ mm^3 , <4000 cells/ mm^3 or 10% immature forms.

Septicemia is often accompanied by endotoxemia. This is the presence of circulating bacterial endotoxins.

Severe sepsis is a state of altered organ perfusion or evidence of dysfunction of one or more organs, with at least one of the following: hypoxemia, lactic acidosis, oliguria or altered mental status.

Septic shock is severe sepsis with hypotension, hypoperfusion and organ dysfunction. It results from gram-positive bacterial toxins or gram-negative endotoxins which trigger release of cytokines, vascular mediators and platelets, resulting in vasodilatation, which manifest as hypotension and DIC.

Diagnosis

- Urine culture: gram-stain may aid in deciding which antibiotic to use;
- Full blood count. The WBC count is usually elevated. The platelet count may be low. This is a possible indication of impending DIC.
- Coagulation screen is important if surgical or radiological drainage of the source of infection is necessary;
- Urea and electrolytes as a baseline determination of renal function;
- Arterial blood gases to identify hypoxia and the presence of metabolic acidosis;
- Blood cultures;
- Thorax X-Ray for pneumonia, atelectasis and effusions;
- Depending on the clinical situation, a renal US may be helpful to demonstrate hydronephrosis or pyonephrosis and CT urography may be used to establish the presence or absence of a ureteric stone.

Treatment

The principles of management include early recognition, resuscitation, localization of the source of sepsis, early and appropriate antibiotic administration and removal of the primary source of sepsis.

- A (Airway), B (Breathing), C (Circulation);
- 100% oxygen via a face-mask;
- Establish i.v. access with a wide-bore i.v. cannula;
- I.v. crystalloid (e.g. normal saline or colloid);
- Catheterize to monitor urine output;
- If there is septic shock, the patient needs to be transferred to ICU. Inotropic support may be needed. Steroids may be used as adjunctive therapy in gram-negative infections. Naloxone may help revert endotoxic shock.
- Treat the underlying cause. Drain any obstruction and remove any foreign body. If there is a stone obstructing the ureter, JJ-stent or PNS tube is inserted to relieve the obstruction. Send any urine specimens obtained for microscopy and culture.
- Empirical antibiotic treatment. This is blind use of antibiotics based on an educated guess of the most likely pathogen that has caused the urosepsis. Gram-negative aerobic rods are common causes of urosepsis (e.g. *E. coli*, *Klebsiella*, *Citrobacter*, *Proteus* and *Serratia*). The enterococci (gram-positive aerobic non-haemolytic streptococci) may sometimes cause urosepsis. In urinary tract operations involving the bowel, anaerobic bacteria may be the cause of urosepsis and in wound infections, staphylococci (e.g. *Staph. aureus* and *Staph. epidermidis*) are the usual cause.
- Antibiotic therapy should be adjusted later when cultures are available;

Recommendations for antibacterial therapy of urosepsis

- A IIIrd-generation cephalosporins (e.g. i.v. cefotaxime or ceftriaxone). These are active against gram-negative bacteria, but have less activity against gram-positive bacteria. Ceftazidime also has activity against *Pseudomonas aeruginosa*.
- Fluoroquinolones are an alternative to cephalosporins. They exhibit good activity against enterobacteria and *P. aeruginosa*, but less activity against staph-

ylcocci and enterococci. GIT absorption of ciprofloxacin is good, so oral administration is as effective as i.v.;

- Use metronidazole if there is a potential anaerobic source of sepsis;
- Aminoglycosides are used in conjunction with other antibiotics. It has a relatively narrow therapeutic spectrum against gram-negative organisms. Close monitoring of therapeutic levels and renal function is important. It has good activity against enterobacteria and *Pseudomonas*, with poor activity against streptococci and anaerobes and, therefore, should ideally be combined with beta-lactam antibiotics or ciprofloxacin.
- If no clinical response to the above antibiotics, consider a combination of piperacillin/tazobactam, which is active against enterobacteria, enterococci and *Pseudomonas*.
- If there is clinical improvement, i.v. treatment should continue for at least 48–72 h and then be changed to oral medication. Make appropriate adjustments when sensitivity results are available from urine cultures.

8.10. UTIS AND PREGNANCY

Pregnancy does not alter the incidence of UTI, which remains at 4% for women of reproductive age. However, physiological and anatomical changes associated with pregnancy alter the course of infection, causing an increased risk of recurrent UTIs and progression to acute pyelonephritis up to 1/4 cases. A common causative organism of gestational pyelonephritis is *E.coli*.

Risk factors:

- Renal size is enlarged, secondary to increased interstitial volume and distended renal vasculature;
- RPF increases early in the 1st trimester;
- GFR increases by 50%, related to an increased cardiac output;
- Renal function and biochemical parameters are affected by changes in RPF and GFR. Cr clearance increases and serum levels of Cr, urea and urate fall in normal pregnancy. Raised GFR causes an increased glucose load at the renal tubules and results in glucose excretion (glycosuria) in most pregnancies. Urine output increases.
- Plasma renin activity is increased 10-fold and levels of angiotensinogen and angiotensin are increased 5-fold. Osmotic thresholds for ADH and thirst decrease.
- Serum bicarbonate is reduced. Increased progesterone stimulates the respiratory centre resulting in reduced PCO₂;
- Bladder displacement occurs due to the enlarging uterus. The bladder becomes hyperaemic and raised oestrogen levels cause hyperplasia of muscle and connective tissues.
- LUTS: urinary frequency (>8 voids during the day) and nocturia (>1 void at night) increases over the duration of gestation. Urgency and urge incontinence also increase secondary to pressure effects from the enlarging uterus.
- Previous history of recurrent UTIs and pre-existing VUR;
- Physiological changes in pregnancy include hydronephrosis with decreased ureteral

peristalsis causing urinary stasis. Up to 75% of pyelonephritis occurs in the 3rd trimester, when these changes are most prominent. Hydronephrosis develops from week 6 to week 10 of gestation. By week 28 of gestation, 90% of pregnant women have hydronephrosis. It has usually resolved within 2 months of birth. It is due to a combination of the smooth muscle relaxant effect of progesterone and to mechanical obstruction from the enlarging fetus and uterus, which compress the ureter.

- UTI increases the risk of pre-term delivery, low fetal birth weight and maternal anemia.

Diagnosis

MSU should be obtained at the first antenatal visit and sent for urinalysis and culture to look for bacteria, protein and blood. A second MSU investigation is recommended at later visits (week 16) to examine for bacteria, protein and glucose.

The hydronephrosis of pregnancy poses diagnostic difficulties in women presenting with flank pain thought to be due to a renal or ureteric stone. Renal US is often used as the initial imaging technique in those presenting with flank pain. In the non-pregnant patient, the presence of hydronephrosis is taken as surrogate evidence of ureteric obstruction. Because hydronephrosis is a normal finding in the majority of pregnancies, its presence cannot be taken as a sign of a possible ureteric stone. US is an unreliable way of diagnosing the presence of stones in pregnant women.

Treatment

All proven episodes of UTIs should be treated (asymptomatic bacteriuria or symptomatic UTIs), guided by urine culture sensitivities. Antibiotics which are safe to use during pregnancy include amoxicillin/clavulonic acid and cephalosporins. Nitrofurantoin may be used in 1st and 2nd trimesters only. Repeat urine cultures after treatment to check bacteria have been eliminated. Acute pyelonephritis requires hospital admission for i.v. antibiotics until afebrile, followed by oral antibiotics for 14 days and repeated cultures for the duration of pregnancy.

Antibiotics to avoid in pregnancy: tetracyclines (fetal malformation, maternal hepatotoxicity, dental discolouration), fluoroquinolones (arthropathy), trimethoprim (folate antagonist), aminoglycosides (auditory or vestibular nerve damage), sulphonamides (neonatal hemolysis, methemoglobinemia), nitrofurantoin (maternal or neonatal hemolysis).

Acute renal failure is a common problem in the current time. Prospective studies have demonstrated that 2% to 5% of all patients admitted to a general medical/surgical hospital unit will develop ARF. In the ICUs after cardiovascular or abdominal vascular surgery, the incidence may be >20%. ARF is defined as a rapid reduction in renal function characterized by progressive azotemia and creatinemia, which may or may not be accompanied by oliguria. This abrupt decline in renal function occurs over the course of hours to days and results in the failure to excrete nitrogenous wastes from the plasma or to maintain normal volume and electrolyte homeostasis. The ARF can be diagnosed with certainty when the patient's prior renal function is known and the reduction in renal function is documented.

Classification of acute renal failure

Clinically, it is very useful to separate the causes of ARF into three major categories: prerenal, renal and postrenal. Assigning a patient to one of the three categories usually requires a combination of clinical, laboratory evaluations and imaging studies of the GUT. The importance of differentiating the major causes of ARF must be stressed, because the initial evaluation and management are tailored to the particular cause.

9.1. PRERENAL ARF

Etiology of prerenal ARF

Volume depletion:

- Surgical: hemorrhage, shock;
- GIT losses: vomiting, diarrhea, fistulas;
- Renal: overdiuresis, salt-wasting disorders;

Cardiac causes with primary decrease in cardiac output:

- Acute disorders: myocardial infarction, arrhythmias, malignant hypertension, tamponade, endocarditis;
- Chronic disorders: valvular diseases, chronic cardiomyopathy (ischemic heart disease, hypertensive heart disease);

Redistribution of extracellular fluid

- Hypoalbuminemic states: nephrotic syndrome, advanced liver disease, malnutrition;
- Diseases: peritonitis, burns, crush injury;
- Peripheral vasodilatation: sepsis, antihypertensive agents;
- Renal artery stenosis (bilateral).

Prerenal ARF is caused by transient renal hypoperfusion that may induce a fall in GFR and produce urinary sodium avidity. The hallmark of prerenal ARF is its reversibility with treatment of the underlying cause and the lack of structural damage to the kidney. The "gold standard" is the response to appropriate fluid

repletion: return of renal function to the previous baseline within 24 to 72 hours is usually considered to represent prerenal disease.

Under normal circumstances, the kidney can maintain normal RBF and GFR down to perfusion pressures of approximately 60 mm Hg. The phenomenon of autoregulation requires a complex interaction of physiologic factors to maintain RBF and GFR. In some hospitalized patients with disordered autoregulation, a reduction in RBF and GFR may occur with modest or even no discernable fall in SBP. In the setting of decreased renal perfusion, angiotensin II and vasodilatory prostaglandins play an important role in maintaining glomerular hydrostatic pressure and GFR.

Prerenal ARF may be encountered in both the volume-depleted and volume-overloaded patient. True volume depletion may result from renal or extrarenal losses that result in systemic hypotension and renal hypoperfusion. In the volume-overloaded patient, with edematous states such as cirrhosis and congestive heart failure, prerenal ARF may occur because the kidney perceives that the vascular tree is underfilled (i.e., “ineffective arterial blood volume”). This results in renal hypoperfusion. Prerenal ARF may also occur owing to high-grade bilateral renal artery stenosis or in states of renal hypoperfusion due to redistribution of extracellular fluid with peripheral vasodilation as seen with sepsis.

The pathophysiology of prerenal ARF relates to the reduction in RBF. Renal hypoperfusion stimulates both the sympathetic nervous system and renin-angiotensin system to cause renal vasoconstriction and sodium avidity. Furthermore, hypotension is a powerful stimulus to the release of antidiuretic hormone, which mediates water reabsorption. Hence, urine production is characterized by low volume, decreased concentration of urinary sodium, increased urinary excretion of Cr and a high urine osmolality. Microscopy of the urinary sediment is usually bland.

Therapy for prerenal ARF is directed at optimizing volume status with isotonic fluids. In patients with the edematous disorders who have prerenal ARF, special efforts are directed at treating the underlying disease states (i.e., heart failure, cirrhosis) and optimizing systemic hemodynamics and renal perfusion.

9.2. POSTRENAL ARF

Obstruction of the urinary tract may cause ARF. To be the cause of ARF, urinary tract obstruction must involve the outflow tract of both kidneys, unless preexisting renal dysfunction is present, in which case the obstruction may involve only a single kidney. Patients with acute urinary tract obstruction may present with hematuria, flank or abdominal pain or signs of uremia. Lesions that may cause obstruction can be either intrinsic (stones) or extrinsic (periureteral metastatic disease or retroperitoneal fibrosis) to the GUT. Although anuria suggests complete obstruction, partial obstruction may exist in the presence of adequate urinary output.

If urinary tract obstruction is a diagnostic consideration, the renal US is indicated in confirming the diagnosis of UHN or hydronephrosis. Renal radionuclide studies or retrograde pyelography may be helpful in this circumstance.

Iatrogenic causes should additionally be considered. Urinary extravasation or fistula formation are signs of iatrogenic injuries and can be confirmed with help of excretory urography or retrograde ureterography. Other ways to confirm urinary

extravasation during the time of operation are by i.v. administration of a vital dye excreted by the kidneys (e.g., indigo carmine or methylene blue).

Obstruction represents a potentially reversible cause of ARF. Any drainage device such as a urethral catheter, ureteral stent or PNS tube should be inserted for treatment of postrenal ARF.

9.3. RENAL ARF

The major causes of ARF due to renal disease include acute glomerulonephritis, acute interstitial nephritis and acute tubular necrosis.

Acute Glomerulonephritis

The presence of proteinuria, hematuria and RBC casts is pathognomonic of AGN. The importance of the urinalysis in the evaluation of patients with ARF cannot be overemphasized and the physician must develop skill and expertise in interpreting the microscopic findings.

Acute Interstitial Nephritis

The diagnosis of ARF secondary to AIN may be suggested by the urinalysis findings of sterile pyuria, WBC casts and eosinophiluria. AIN is most often induced by drug therapy, although infections may also be responsible. Most common causes of AIN are: NSAIDs, penicillins and cephalosporins, rifampicin, furosemide, thiazide-type diuretics, trimethoprim-sulfamethoxazole, cimetidine, allopurinol, ciprofloxacin, 5-aminosalicylates.

The major histologic changes are interstitial edema and marked interstitial infiltrate of T lymphocytes and monocytes. Eosinophilic plasma cells and polymorphonuclear cells may also be detected.

The clinical presentation, although variable, usually involves an abnormal urine sediment, fever and a rising serum Cr value associated with the administration of the offending drug. Rash is seen in about 25% of cases. Eosinophilia and eosinophiluria are present in more than 75% of cases, with the exception of AIN due to NSAIDs, in which fever, rash and eosinophilia are typically absent. Proteinuria with most drugs is usually modest, with less than 0.5-1 g/day. The development of AIN is not dose dependent and recurrence can occur with second exposures to the same or related drug. The onset of AIN may occur from 3-5 days to several weeks after drug therapy. The diagnosis is usually suspected in the ARF patient with characteristic urinary sediment abnormalities and a history of an offending drug therapy. The diagnosis is confirmed only by renal biopsy.

Initial therapy consists of discontinuing the offending drug with the expectation that renal function will begin to improve in 3 to 7 days. There is some experimental and suggestive clinical evidence that corticosteroid and/or cytotoxic therapy may be beneficial to hasten recovery of renal function and reduce interstitial fibrosis.

Acute tubular necrosis

The majority of all hospital-acquired ARF is secondary to ATN. Renal hypoperfusion and renal ischemia are the most common causes of ATN, although nephrotoxins from various agents are being recognized with increasing frequency.

Endogenous nephrotoxic products:

- Pigment nephropathy (myoglobin, hemoglobin, methemoglobin);
- Intrarenal crystal deposition (uric acid, calcium, oxalate);
- Tumor-specific syndromes (tumor lysis syndrome, myeloma kidney);

Exogenous nephrotoxins:

- Antibiotics (aminoglycosides, co-trimoxazole, amphotericin B, polymyxin, colistin, vancomycin, acyclovir);
- Anesthetic agents and analgesics;
- Contrast media;
- Antiulcer drugs;
- Diuretics;
- Chemotherapeutic and immunosuppressive agents;
- NSAIDs;
- HIV Protease inhibitors;
- Organic solvents;
- Heavy metals;
- Poisons (mushrooms, snake bites, bacterial toxins)
- Chemicals (aniline, hexol, cresol, chlorates, potassium bromated);
- Other drugs (dextran, EDTA, radiation).

A patient who develops ATN while receiving medications should have each medication reviewed for the possibility of nephrotoxicity.

Stages and symptoms

After the inciting incident (Ist phase), the oligoanuric IInd phase usually begins less than 24 hours and may last for 1 to 3 weeks. Urine volume averages 150 to 300 mL/day and may be absent. The IInd phase may be prolonged in the elderly. During this phase, the clinician must be alert for the expected complications, with special emphasis on metabolic consequences, gastrointestinal bleeding and infection.

The diuretic (polyuric) IIIrd phase is characterized by a progressive increase in urine volume, a harbinger of renal recovery. However, the serum Cr may continue to rise for another 24 to 48 hours before it reaches a plateau and falls. Severe polyuria during this phase is seen less frequently now. Careful management during this phase is crucial, because up to 25% of deaths with ARF may occur in this phase, usually related to fluid and electrolyte abnormalities, as well as infection. Finally, the recovery IVth phase ensues. Renal function returns to near baseline, but abnormalities of urinary concentration and dilution may persist for weeks or months.

Uremic signs and symptoms:

- Gastrointestinal: nausea, vomiting, upper gastrointestinal bleeding;
- Neurologic: mental status changes, encephalopathy, coma, peripheral neuropathy;
- Cardiac: pericarditis, uremic cardiomyopathy;
- Pulmonary: pleuritis;
- Hematologic: bleeding, anemia;
- Immunologic: impaired granulocyte and lymphocyte function.

Complications:

- Fluid overload: hypertension, edema, acute pulmonary edema;
- Electrolyte disturbances: hyperkalemia, hyponatremia, hypermagnesemia, hyperphosphatemia, hypocalcemia or hypercalcemia, hyperuricemia, metabolic acidosis.

Differential diagnosis of acute renal failure

Distinguishing between prerenal, renal and postrenal causes of ARF may be complex. A thorough history and physical examination to assess volume status, cardiovascular hemodynamics, potential nephrotoxins and evidence of systemic disease should be undertaken in ARF patients. All interventions and drug therapies surrounding an ARF event should be outlined. Therefore, it is critical to know the level of preexisting renal function. One should identify the presence of risk factors and diseases known to be associated with ARF.

On examination, the vital signs and hemodynamic parameters should be assessed. Hypotension, particularly orthostatic hypotension, suggests volume depletion and prerenal ARF. Hypertension with advanced CRF can be an indicator of volume overload, suggesting the need for diuretics or dialysis. A patient's weight is helpful information and its daily measurement is important in the diagnosis and management of ARF. After major urologic procedures (e.g., cystectomy, nephrectomy, transplantation), measurement of the central venous pressure or pulmonary artery wedge pressure is the most accurate method to assess volume status. Other clinical parameters that correlate with volume status include neck vein distention, lung rales and peripheral edema.

The urine output may be a clue to the diagnosis of ARF. The presence of marked oligoanuria suggests urinary tract obstruction, renovascular occlusion or cortical necrosis. In contrast, nonoliguric ARF is being recognized with increased frequency and careful monitoring of serum Cr levels in patients at risk is of paramount importance.

Examination of the urinalysis results is fundamental to the evaluation of the patient with ARF. The simple urinalysis may distinguish the cause of ARF among the various possibilities. For example, proteinuria, hematuria and RBC casts are pathognomonic of AGN. The classic sediment of ATN includes pigmented granular casts and renal tubular epithelial cells, which may be seen in nearly 80% of cases of oliguric ARF. Normal urinalysis will be by prerenal and postrenal ARF. Eosinophils may be seen by AIN.

For diagnosis of ARF there are a variety of imaging modalities. The most widely used is renal US. This noninvasive and readily available study is fairly sensitive for the identification of hydronephrosis. Duplex US of the renal artery is useful for the identification of renal artery stenosis or thrombosis. The absence of a Doppler signal from the artery is a noninvasive sign to confirm renal artery thrombosis. Another common imaging study in ARF is the abdominal plain radiograph to identify the presence or location of renal calculi or both. Additionally, the abdominal plain radiograph is particularly helpful to discern the proper position of the stents and drains. The radionuclide renal scan is a useful imaging study in selected clinical circumstances. The renal scan is a simple way to evaluate for renal flow in situations in which renal artery thrombosis is a serious consideration, such as after

partial nephrectomy or renal transplantation. It is especially useful when there is renal insufficiency that prohibits the use of iodinated contrast media.

Radiocontrast studies (IVP, CT, angiography) are of limited value during ARF because of their ability to worsen renal insufficiency. Angiography is used to confirm renal artery thrombosis, stenosis or dissection. Studies such as an IVP yield poor-quality images in azotemic patients, owing to the inability to adequately excrete contrast agent.

Treatment of ARF

Conservative treatment

Fluid balance:

- Carefully monitor intake/output and weights;
- Restrict fluids;

Electrolytes and acid-base balance:

- Prevent and treat hyperkalemia;
- Avoid hyponatremia;
- Keep serum bicarbonate >15 mEq/L;
- Minimize hyperphosphatemia;
- Treat hypocalcemia only if symptomatic or if i.v. bicarbonate is required;

Uremia and Nutrition:

- Administer protein (1.0–1.8 g/kg/day) and maintain caloric intake, consider forms of nutritional support;
- Keep carbohydrate intake at least 100 g/day to minimize ketosis and endogenous protein catabolism;

Drugs:

- Diuretics, dopamine and calcium channel blockers;
- Stop magnesium-containing medications;
- Adjust dosage of all other medications for renal failure.

Management of ARF is based on its cause. When ARF is identified as prerenal, correction of the precipitating factors and restoration of renal perfusion usually lead to its resolution. Nephrotoxic drugs should be eliminated when clinically appropriate. Maintaining normal volume status is essential. In the postoperative setting, this implies judicious replacement of crystalloid, colloid and blood with close monitoring of the central venous pressure. The management of postrenal ARF will depend on its etiology. Any obstruction needs appropriate drainage and urinary extravasation needs to be controlled.

The management of ATN focuses on the prevention of complications and providing a treatment options that will lead to renal recovery. During the initial evaluation it is imperative to search for reversible causes, such as volume depletion and obstruction. During the initial stages, a trial of parenteral hydration with isotonic fluids may correct ARF secondary to prerenal causes. Thereafter, fluid status should be monitored. In a patient with oliguria, special attention must be given to avoiding excessive hydration that might precipitate the need for dialysis. Consideration may be given to using pharmacologic intervention to convert the patient from an oliguric to a nonoliguric

state. Increases in urinary volume make it easier to treat problems of volume overload, hyperkalemia and metabolic acidosis. The morbidity, need for dialysis and mortality lower in the nonoliguric patients.

Once the clinical diagnosis of ATN is made, conservative treatment is in order. This would include attempts to minimize further renal parenchymal injury, ensure provision of nutrition, maintain the metabolic balance and promote recovery of renal function. Pharmacologic intervention have the goal to convert oliguric ATN to nonoliguric ATN.

It is suggested that patients who respond to mannitol, furosemide or dopamine with an increased urine output have better outcomes than nonresponders. Both loop diuretics and mannitol administration have been proved to minimize the degree of renal injury if given at the time of the ischemic insult. Diuretics are capable of inducing a diuresis to wash out obstructive debris and casts. It is reasonable to give a trial of a loop diuretic in escalating doses and if the patient does not respond, the drug should not be readministered because large doses of loop diuretics may be ototoxic and the large infusion volume may cause pulmonary edema. Mannitol, an osmotic diuretic, theoretically ameliorates ARF by flushing intratubular casts, increasing RBF, increasing urine flow, reducing hypoxic cell swelling, protecting mitochondrial function and scavenging free radicals. Mannitol use continues to be promoted prophylactically or within a short time after an ischemic or nephrotoxic insult in certain high-risk patient groups. Dopamine has selective renal vasodilator properties that cause natriuresis and increased urine output. Low-dose "renal-dose" dopamine activates dopamine-1 receptors, which induce renal vasodilation and increased RBF.

Calcium channel blockers inhibit voltage-gated calcium entry into cells and are reported to reverse vascular constriction, increase GFR and improve renal plasma flow. The clinical benefit of calcium channel blockers most widely studied has been the effect on graft function in renal transplant recipients.

Adequate nutrition is important for the recovery of the critically ill patient with ARF. Preexisting or hospital-acquired malnutrition is an important factor contributing to high mortality seen in patients with ARF. ARF not only affects water, electrolyte and acid-base metabolism but also induces specific alterations in protein and amino acid, carbohydrate and lipid metabolism. The metabolic alterations in ARF patients are determined not only by acute loss of renal function but also by the underlying disease process (i.e., sepsis, trauma or multiple-organ failure) and by the type and intensity of renal replacement therapy. Nutritional therapy in patients with ARF may be beneficial in promoting recovery. Caloric intake should be maintained and carbohydrate intake should be at least 100 g/day to minimize ketosis and endogenous protein catabolism. A moderate protein intake of about 1.0 to 1.8 g/kg/day may be required to maintain positive nitrogen balance. Higher protein intakes of up to 2.5 g/kg/day have been needed to improve nitrogen balance in critically ill ARF patients on continuous dialysis, although no survival advantage was noted. Hence, it should be stressed that a low-protein intake (<0.5 g/kg/day) may be unnecessary and protein intake should not be severely restricted in ARF to limit the need for dialysis. In terms of types of amino acids utilized, diet or solutions including

both essential and nonessential amino acids in standard proportions is recommended. Dietary phosphorus, potassium and sodium chloride may be restricted. In the critically ill patient, nutritional support via total parenteral nutrition or enteral feedings should be considered. Prior studies demonstrate that provision of adequate nutrition to the ARF population may improve survival. Patients with ARF are candidates to develop significant electrolyte abnormalities such as hyperkalemia, metabolic acidosis, hyperphosphatemia and hypocalcemia. These problems may be minimized by the prophylactic institution of a low-potassium diet accompanied by fluid restriction and oral phosphate binders.

Hyperkalemia is the most common and most dangerous electrolyte abnormality in the ARF setting. If the serum potassium level exceeds 6.0 mEq/L, an electrocardiogram should be performed with subsequent therapy based on the findings. With hyperkalemia, the earliest changes demonstrate peaked T waves with subsequent broadening of the PR interval and eventual QRS broadening, which may mature into a sine wave form. Stabilizing the membrane of the cardiac conduction system may be accomplished with i.v. calcium salts, which have an immediate effect and a rather short duration of action. Shifting potassium into cells may be accomplished by a combination of i.v. glucose and insulin or i.v. sodium bicarbonate. Elimination of potassium from the body in a patient with ARF may be accomplished via the GIT with a cationic binding resin. If severe hyperkalemia exists, dialysis may be required.

Dialysis

Despite adequate medical therapy, dialysis may be required for patients with severe ARF. The indications for the initiation of dialysis include:

- Volume overload;
- Severe hyperkalemia;
- Severe metabolic acidosis;
- Pericarditis, selected poisonings;
- Uremic symptomatology.

HD is the standard dialytic modality for hemodynamically stable patients with ARF. To perform acute HD, access to the circulation is required and usually involves placement of a venous catheter in the jugular, subclavian or femoral vein. Blood is transported by a blood pump to the dialyzer, where it comes into close proximity with the dialysate solution across a semipermeable membrane. Contact of the blood with dialysate allows the removal of solutes by the process of diffusion, driven by a concentration gradient from blood to dialysate. Fluid may also be removed by the process of ultrafiltration driven by a pressure gradient across the dialyzer.

PD permits the removal of solutes and fluid by using the peritoneal membrane as the dialyzer. This process does not require access to the circulation and is generally less stressful hemodynamically than standard HD. For this procedure, dialysate is instilled into the peritoneal space via a catheter, which is percutaneously placed. Fluid is allowed to dwell for a period of time and is then removed, taking with it uremic solutes by diffusion, as well as accomplishing ultrafiltration of fluid from an osmotic pressure gradient induced by high concentrations of glucose in the dialysate.

The diagnosis of CKD implies a persistent abnormality in GFR with a wide spectrum of causes. It is recommended that “chronic kidney disease” should be defined as sustained kidney damage greater than 3 months resulting in a GFR <60 mL/min/1.73 m². After an initial kidney insult, if the acute injury does not completely resolve, a continuing diminishing of functional nephrons occurs over time. The renal failure consists of 4 stages, associated with specific clinical and biochemical abnormalities. Small changes in the SCr measurement correlate with significant alterations in the GFR when renal function is > 60 mL/min. This is especially true in CKD as the GFR decreases to levels <30 mL/min. Although an initial disease may decrease an individual’s renal reserve, biochemical abnormalities are uncommon before the “renal insufficiency” stage. Once severe “renal failure” occurs, clinical symptoms become more common. The rate of progression throughout the delineated stages depends on many factors.

When kidney function is minimally impaired, physiologic adaptation is complete. As the GFR falls usually below 20% of normal, progressive anorexia with nausea, salt retention, acidosis, anemia, muscle fatigue and worsening blood pressure control may occur. Structurally, after the GFR in humans falls below 1/2 of normal, a relentless progressive loss of function ensues even when the initial disease becomes inactive.

The clinical course of progressive renal disease moves through several different phases, which include: decreased renal reserve, renal insufficiency, renal failure, uremia.

Etiology

There are a number of diseases involve the kidney and can lead to progressive renal insufficiency. Progressive deterioration in renal function can occur in tubulointerstitial disease, hematopoietic disease, ureteral obstructions, VUR, BPH, vascular disease (hypertension, atheroemboli), metabolic disease (cystinosis, oxalosis, uric acid nephropathy, hypercalcemia), toxic injuries (analgesic, NSADs, chemotherapy, lead, lithium), cystic disease (ADPKD, medullary cystic disease), glomerular diseases (glomerulonephritis, IgA nephropathy), systemic diseases (DM, systemic lupus erythematosus, systemic sclerosis, systemic vasculitis).

Urologic diseases can result in CKD. Urinary stone disease, obstructive uropathy involving the ureter, bladder or urethra can lead to progressive CRF. Undetected PUJO and PUVs are the most common types of congenital causes for progressive CRF. The percentage of ESRD population attributable to reflux nephropathy and nonreflux nephropathy has increased. VUR may result in CKD from renal scarring. VUR may be either unilateral or bilateral and progression to CRF is related to the severity of reflux.

Diagnosis

Once the GFR decreases to <60 mL/min for 3 months or more, patients are classified as having CKD. The adjusted relative risk from a population survey adjusted for age, proteinuria, hematuria and hypertension found that changes in GFR occurred at a cutoff SCr clearance value of 1.2-1.4 mg/dL. Other measurements that complement the SCr value may give a better index to the underlying, predicted GFR. Cr clearance, Cr clearance plus urea clearance divided by 2, GFR measurements - all provide information on the level of renal dysfunction. The Cockcroft-Gault formula [$\text{Cr clearance} = (140 - \text{age}) \times \text{weight} \times (0.85 \text{ if female})$] divided by $72 \times \text{plasma Cr}$] is widely used throughout the world to estimate RRF.

Most forms of CKD gradually and inevitably progress to ESRD over a 2-10 years, depending on the underlying renal lesion responsible for the CKD, combined with patient-specific factors. Staging and the approach to treatment of CKD depend on the assessment of GFR (function assessment), level of proteinuria and clinical comorbidities.

Function Assessment

The SCr level is widely used as an index of RRF, the measured value is affected by factors other than the GFR. At any given GFR the SCr concentration is significantly higher in men than in women and in blacks than in whites. The mean of the Cr and the urea clearance is a more accurate estimate of the GFR than either is separately.

Radiographic Assessment

The radiographic assessment of CKD patients should take into account the impact of contrast on RRF. Contrast material can induce worsening of underlying renal disease to the point of requiring RRT. All patients with abnormal SCr greater than 2 mg/dL should be considered for alternative diagnostic testing and prophylactic preventive strategies to avoid worsening renal function. Specific measures may help lower the risk for ARF in patients with CKD undergoing radiographic assessment. These include volume expansion, hydration with i.v. administration of sodium chloride 0.9%, sodium bicarbonate solution, infusion of mannitol, loop diuretics, calcium antagonists, theophylline, dopamine.

Urinalysis

The urine sediment examination is helpful in detection of CKD and the identification of the type of kidney disease. Cells can originate from the kidney or from other sites within the urinary tract. The presence of a RBC cast strongly suggests glomerulonephritis especially if the RBCs are dysmorphic. Urinary eosinophils are usually associated with allergic tubular interstitial nephritis. If the urinalysis is negative, despite the patient's having apparent CKD, a second specimen should be examined at another time.

Increased excretion of albumin is a sensitive marker for CKD attributable to DM, glomerular disease, interstitial disease and hypertension. It is recommended screening assessment using proteinuria measurement to detect CKD. Traditionally the cut-off value indicating a urinary albumin excretion >30 mg/24 hr has been 3 mg/L.

Kidney biopsy

A US-guided renal biopsy is not usually performed to evaluate asymptomatic hematuria but is warranted if the GFR is <60 mL/min and the urinalysis is abnormal. The structural severity of glomerular injury and the immunopathologic category of disease are helpful in predicting renal outcome.

Conservative treatment

Regardless of the disease, once a critical number of nephrons is destroyed, a steady decline in GFR occurs as the progressive loss in viable nephrons occurs. Well-designed renal assessment and management programs are feasible and can be systematically applied to large numbers of CKD patients to decrease the rate of progression. The list are: lifestyle modifications, blood pressure control, glycemic control, reduction of proteinuria, protein restriction, lipid control, avoidance of nephrotoxins, correction of anemia, optimization of calcium-phosphorus product, correction of acidosis and maintenance of fluid balance.

Optimal renal care begins with the early detection of CRF. It means screening high-risk patients with serum Cr >1.2 mg/dl. Next will be initiation of interventions that delay progression (using of ACE inhibitors to control blood pressure, blood sugar target of HbA1C less than 7%, glucose before meals of 80 to 120 mg/dl, hyperlipidemia control, protein restriction), prevent uremic complications (malnutrition, abnormal body composition, osteodystrophy, anemia, edema, acidosis), modification of comorbidities (DM, vascular, pulmonary and cardiac disease) and preparation of the patients for RRT (referral to nephrologist for evaluation, dialysis) to optimize patient survival.

Various pharmacologic trials comparing different medications have shown that patients with better blood pressure control have significantly slower rates of deteriorating kidney function. Clinical trials have suggested that reducing mean arterial pressure to 125/75 mm Hg provides more optimal renal function stability in patients with diabetes and proteinuria, compared with mean arterial pressure targets of 140/90 mm Hg. Aggressive blood pressure control should also be a goal for patients on dialysis. Angiotensin II is critical in causing progressive renal disease by both hemodynamic and nonhemodynamic mechanisms. Blockade of the renin-angiotensin system contributes to preservation of renal function by decreasing glomerular pressure and proteinuria. Because proteinuria plays a sentinel role in renal scarring, a reduction in proteinuria correlates with slowing of disease progression. For optimal control of blood pressure a combination regimen that includes a diuretic and ACE inhibitors is essential.

Protein restriction can ameliorate many symptoms of CRF and prevent its progression. However, without regular dietary consultation, patients on a low-protein diet may experience a decrease in protein intake and deterioration of several nutritional parameters. A number of different diets have been used to help slow the progression of CKD. The overall dietary requirement in CKD is approximately 0.6 g of protein/kg/day.

Decreased GFR is associated with complications in most organ systems. The most important complications include high blood pressure, anemia, malnutri-

tion, bone disease, neuropathy and alterations in quality of life. As the patient moves from stage to higher stages, additional comorbidities are more likely to develop. Atherosclerotic risk factors are frequently present in CKD. Patients at high risk for cardiovascular events warranting lipid-lowering therapy and close cardiovascular screening. Both statin and fibric acid derivatives have proven effective, although individual differences mandate periodic monitoring of fasting lipid levels and liver function tests. Cigarette smoking is universally recognized as an independent risk factor for cardiovascular disease and should be discouraged with this disease. If GFR <60 ml/min there is a higher prevalence of abnormalities of bone metabolism. Treatment of calcium-phosphorus abnormalities or reduction in the use of calcium-based phosphate binders reduces the risk of cardiovascular disease outcomes. Obese patients are associated with increasing risks for a variety of cardiovascular complications and with higher all-cause mortality. Weight reduction is an important lifestyle modification for overweight patients. There are associations between anemia and adverse cardiovascular outcomes in CKD patients. The treatment goal should be to achieve hemoglobin of ~12 g/dl with erythropoetin.

Treatment of the patients with end-stage renal disease

Multiple different RRTs are available for treatment of ESRD patients. The most commonly utilized RRTs are HD, PD and renal transplantation. HD is the predominant form of therapy for adults with ESRD. Transplantation, however, is the predominant mode of care for patients younger than 20 years. ESRD patients are treated also with chronic PD. A desire for self-care, a long distance from a HD unit, difficulties with HD therapy, serious cardiac disease, DM and small stature are characteristics of patients especially suited for PD. Unsuitable characteristics of patients for chronic PD are considered to be obesity, hernias, poor hygiene, inflammatory bowel disease and obliterated peritoneal space. Outcome comparison suggests that renal transplantation is still the best overall treatment for ESRD patients, despite advances in dialytic options. Therefore, patients who reach ESRD should undergo transplantation as soon as possible, once on dialysis. The estimated number of patients starting renal replacement therapy each year for ESRD is elevated. The increase in living renal donation has been further facilitated by the widespread adoption of minimally invasive donor nephrectomy techniques, the increased use of living, biologically unrelated renal donors and the development of protocols for transplantation across alloantibody barriers, including ABO blood group incompatibility.

The purposes of RRT are to prolong and to maintain the quality of life. Permanent renal failure in adults is commonly defined as an irreversible glomerular filtration rate <10 mL/min or a serum Cr level of greater than 8 mg/dL. A reasonable goal for ESRD treatment programs is the transplantation of all patients in whom the risk is equal to or less than that of remaining on maintenance dialysis. Renal transplantation is the preferred method of therapy for most patients with ESRD because it is more cost effective and allows a return to a more normal lifestyle than maintenance dialysis does. Data indicate that survival after renal transplantation is significantly better than that of patients treated with dialysis.

The survival of kidney grafts has steadily improved and those for the current era are quite remarkable. Kidney transplant 5 year survival rates for HLA-identical sibling is 80-87%, for one-haplotype sibling is 75-81%, for spouse is 78%, for other biologically unrelated is 70-78%, for deceased is 60-66%, for standard criteria is 60-70%, for expanded criteria is 40-52%.

Indications for RRT:

- Anuria or extreme oliguria (urine output < 50 mL/12 hr);
- Hyperkalemia ($K > 6.5$ mmol/l);
- Severe acidemia ($pH < 7.1$);
- Azotemia (urea > 30 mmol/l);
- Clinically significant organ edema;
- Uremic encephalopathy, pericarditis, neuropathy/myopathy;
- Severe dysnatremia ($Na > 160$ or < 115 mmol/l).

Selection and preparation of kidney transplant recipients

The pretransplantation evaluation is a multidisciplinary process that is performed well in advance of the renal transplantation operation and immunosuppression. The purposes of the evaluation are generally considered to be to diagnose the primary renal disease and its risk of recurrence in the kidney graft and to rule out active invasive infection.

The process of evaluating the transplantation candidate is initiated by identifying the presence or absence of the risk factors. Candidates with a history of substance abuse must have unannounced drug screens with negative results before continuing the process. Candidates with morbid obesity must demonstrate weight reduction before continuing the process because of the risks associated with renal transplantation in obese patients. Candidates considered to be at risk for noncompliance must demonstrate contract satisfaction. Cigarette smoking increases the risks of surgery, post-transplantation malignancy, cardiovascular disease and renal allograft loss. It must be stopped before transplantation in patients who already have clinical evidence of vasculopathy or cardiopulmonary disease. Compliance issues are extremely important in the long-term management of kidney transplant recipients. Transplantation candidates with chemical dependency need to have an objectively documented drug- or alcohol-free period of at least 6 months before transplantation.

It is recommended that patients >50 years or with a history of coronary artery disease, cardiac symptoms or insulin-dependent DM undergo stress cardiac testing with further diagnosis and treatment of significant cardiac disease.

Patients with focal segmental glomerulosclerosis, hemolytic-uremic syndrome, primary oxalosis, renal amyloidosis, cystinosis should be counseled about the significant probability of disease recurrence and the risk of secondary graft failure. DM and IgA nephropathy are examples of diseases that commonly recur in the transplanted kidney but rarely result in graft failure. ADPKD, renal dysplasia and Alport's syndrome without antiglomerular basement membrane antibodies are examples of renal diseases that do not recur in the transplanted kidney.

Infections must be detected and treated before transplantation or prevented with immunizations. Potential sources of dental sepsis must be treated. Dialysis access sites must be clear of infection. Pulmonary infections or tuberculin skin test conversions require treatment before immunosuppression. Reasonable indications for pretransplantation cholecystectomy are considered to be symptomatic cholecystitis, multiple small gallstones and polyps. Segmental colectomy is reasonable for patients with recurrent diverticulitis because of the morbidity and mortality of bowel perforation in the immunosuppressed kidney transplant recipient. Diabetic foot ulcers must be healed before transplantation and UTIs should be inactive at the time of engraftment. Serologic testing for CMV is important because this disease is a major cause of morbidity in immunosuppressed patients. Patients with herpes simplex virus need antiviral therapy during intense immunosuppression. Recipient HIV infection has been considered to be a contraindication to renal transplantation. The treatment of chronic active hepatitis B and C is evolving and patients with active hepatitis C infection may benefit from antiviral therapy before transplantation. Corticosteroids enhance viral replication and these infections should be inactive at the time of transplantation. Unless the patient is pro-

tected by antibody development after infection or prior immunizations, the following immunizations are given to transplantation candidates: hepatitis A, hepatitis B, pneumococcus, diphtheria, tetanus, pertussis, polio, varicella, measles, mumps and rubella.

To reduce the risk of cancer recurrence, a waiting time of 2 to 5 cancer-free years from the time of the last cancer treatment is recommended for patients who have had invasive malignancies. Shorter intervals from cancer treatment to transplantation are generally accepted for patients who have had low-grade, noninvasive cancers.

Heart disease is the predominant cause of death after renal transplantation and it is common for kidney transplantation candidates with a history of cardiac disease, cerebrovascular disease or DM or who are older than 50 years to undergo a cardiac evaluation. Further testing and treatment are based on the results of a screening evaluation. Cerebrovascular disease, peptic ulcer disease and significant pulmonary disease must be detected and treated.

Evaluations of the vascular system and the urinary tract are necessary to identify problems that need to be corrected before transplantation or addressed at the time of transplantation. Patients with symptoms and signs of lower extremity arterial disease or a history of abdominal or pelvic vascular surgery need to undergo a diagnostic evaluation to be certain that revascularization of a kidney graft is possible. If significant arteriosclerosis or venous disease is detected, it may be necessary to perform angiography to select alternative sites, such as the aorta or splenic artery, for renal revascularization or to plan corrective vascular surgery before renal transplantation.

Thrombosis is a significant cause of kidney transplant loss. Renal transplantation patients at risk for graft thrombosis are those with previous vascular problems. A decision can be made about intermediate- or long-term anticoagulation with low-molecular-weight heparin or warfarin.

The purposes of the urologic evaluation are to determine the suitability of the urinary bladder or its substitute for urinary tract reconstruction and to determine the necessity for removal of the native kidneys before or at the time of renal transplantation. Patients need the urologic evaluation and treatment before or after transplantation if there is a history for urologic disease, abnormalities and operations on the urinary tract.

Indications for nephrectomy:

- Renal stones not cleared by minimally invasive techniques;
- Solid renal tumors;
- Polycystic kidneys that are symptomatic, have been infected or have tumors;
- Significant not controlled proteinuria;
- Recurrent pyelonephritis;
- Nephroslerosis or terminal hydronephrosis.

Pretransplantation nephrectomy is usually performed 6 weeks before transplantation or active wait-listing for deceased donor renal transplantation to allow wound healing and the detection and treatment of surgical complications. It is common to perform kidney removal at the time of renal transplantation in children. It is common to do preliminary nephrectomies in adults.

Donor selection and preparation

The basic criteria for a renal donor are an absence of renal disease, active infection and an of transmissible malignancy. Whether the kidney is removed from a living donor or a deceased donor, the surgical goals are to minimize warm ischemia time, to preserve renal vessels and to preserve ureteral blood supply. In the deceased donor, it is also necessary to obtain histocompatibility specimens.

Living Donor

On the basis of the preoperative evaluation, one must be able to assure the living donor of nearly normal renal function after unilateral nephrectomy. On evaluation, if one of the potential donor's kidneys is better than the other, the better kidney is left with the donor.

A living renal donor is considered to be unsuitable when one of the following is present: significant renal disease, mental dysfunction, high risk of perioperative mortality or morbidity and significant transmissible disease. ABO incompatibility and a positive crossmatch between donor lymphocytes and recipient serum were usually considered to be contraindications to directed living renal donation. Serologic testing is performed for HIV, hepatitis, CMV infection and syphilis. DM is excluded in the donor. Abdominal US can be performed to exclude donors with significant renal abnormalities and to detect incidental intra-abdominal abnormalities. 3D CT angiography followed by plain X-Ray of the abdomen has been widely accepted because it satisfactorily excludes stone disease, demonstrates renal and vascular anatomy and defines the urinary collecting system.

The mortality of kidney donation has been estimated to be 0.02%, the risk of a potentially life-threatening or permanently debilitating complication has been estimated to be 0.23%. The short- and long-term risks of living donor nephrectomy are generally considered to be low enough and the probability of successful graft outcome high enough, to make the risks acceptable for fully informed donors.

Live donor nephrectomy can be performed either as an open or laparoscopically assisted procedure. Laparoscopic donor nephrectomy has become the preferred technique for live donor nephrectomy. The kidney is then taken in an ice bath into the recipient's operating room or cold-stored until the time of transplantation.

5-year graft survival for living biologically unrelated donor kidney transplants is better compared with primary deceased kidney transplants.

Deceased Donor

The criteria for an ideal deceased kidney donor are normal renal function, no hypertension requiring treatment, no DM, no malignancy other than a primary brain tumor or treated superficial skin cancer, no generalized viral or bacterial infection, acceptable urinalysis, age between 6 and 50 years and negative assays for STD, hepatitis, HIV and human T-lymphoproliferative virus. Exceptions are made in an effort to expand the donor pool, resulting in the adoption of the "expanded criteria donor". ECDs are defined as donors >50 years old with any two of the following risk factors: cerebrovascular death, hypertension and serum Cr level >1.5 mg/dl. ECD kidney transplant survival rates and those from donors younger than

the age of 6 years and older than the age of 50 years are significantly inferior to those from ideal deceased donor kidney transplants.

The initial goals of resuscitation of the brain-dead deceased donor are SBP of 90 mm Hg or mean arterial pressure of 60 mm Hg and urinary output exceeding 0.5 mL/kg/hr. Monitoring of central venous pressure, capillary wedge pressure or pulmonary artery pressure is helpful for managing fluid administration. Serum electrolyte levels are checked every 2 to 4 hours. In some cases dopamine or dobutamine can be infused without causing renal vasospasm. If intravascular volume expansion and vasopressors are unsuccessful in promoting a diuresis, furosemide, 1 mg/kg, with or without mannitol, 0.5 to 1 g/kg, can be infused. Because hypothermia can cause cardiac irritability and coagulopathy, the head can be wrapped, i.v. fluids can be warmed and the body can be placed on a warming blanket. Tissue typing and crossmatching can be performed on a peripheral blood sample or groin lymph nodes before organ retrieval. The deceased donor is maintained in the operating room by the anesthesiology team to ensure ventilation and circulatory support and to administer drugs such as diuretics, heparin and α -adrenergic blocking agents.

The principles of deceased donor organ retrieval are adequate exposure, control of the vessels above and below the organs to be removed, initiation of preservation in situ, the removal of the organs, separation of the organs, completion of preservation, removal of histocompatibility specimens, removal of iliac vessels for vascular reconstruction of pancreas and liver grafts and organ packaging. The kidneys are the last transplantable organs to be removed. A total midline incision with splitting of sternum and diaphragm exposes all transplantable organs in the chest and abdomen. For multiple abdominal organ retrieval, the aorta is controlled above the celiac axis. The IVC is controlled above the liver. The aorta and IVC are controlled below the renal vessels, heparin is administered to the donor and the great vessels are cannulated. The proximal aorta is occluded, the IVC is vented into the chest or through the distal IVC cannula and in-situ flushing with an ice-cold preservation solution is performed through the aortic cannula. The gastrocolic ligament is divided, the small bowel mesentery is divided along with the superior mesenteric artery and vein and the small bowel is divided at the ligament of Treitz. The esophagus is divided and, with further dissection, the en bloc specimen consisting of the liver, stomach, spleen, pancreas, both kidneys, aorta and IVC is removed. The specimen is placed down in a pan of slush and is separated.

Kidney preservation and preparation

Warm ischemic injury of organs for transplantation is caused due to failure of oxidative phosphorylation and cell death due to ATP depletion. ATP is required for the function of the cellular sodium-potassium pump. When the sodium-potassium pump is impaired, sodium chloride and water passively diffuse into the cells, resulting in cellular swelling and the “no-reflow” phenomenon after renal revascularization. Lysosomal enzymes are activated and this results in cell death. During reperfusion, hypoxanthine is oxidized to xanthine with the formation of free radical scavengers that cause further cell damage.

Cellular energy requirements are significantly reduced by hypothermia. This is done by surface cooling, hypothermic pulsatile perfusion or flushing with an ice-cold solution followed by cold storage. Making the flush solution slightly hyperosmolar with impermeant solutes helps prevent endothelial cell swelling. When the sodium-potassium pump is impaired, there is passive transfer of ions across the cell membrane. If the electrolyte composition of the flush solution is nearly the same as that inside the cell, electrolyte balance will be maintained. Calcium channel blockers, xanthine oxidase inhibitors, free-radical scavengers, vasoprotective agents and lysosome stabilizers such as methylprednisolone have all been used to reduce ischemic injury.

The basic methods of kidney preservation are pulsatile machine perfusion with a protein-based solution or hypothermic flushing followed by simple cold storage. In current time after demonstration that the two methods provided equivalent results, simple cold storage became more widely used for human kidney preservation. The commonly used solutions (UW solution or Euro-Collins) minimizes cellular swelling.

A kidney graft removed from a living renal donor by an open technique requires little preparation by the kidney transplant recipient team because most of the preparation has been done in situ by the donor team. Because of the presence of significant amounts of perirenal fat, stapled vessels and retraction of the renal vein into the renal hilum, significantly more bench work is required for kidneys removed laparoscopically. It is needed prompt identification of the renal artery and vein, removal of the staple lines and rapid flushing of the kidney with ice-cold preservation solution is the initial priority, followed by the final dissection. For a deceased donor kidney, the short right renal vein can be extended with a variety of techniques that use the inferior vena cava or donor external iliac vein. The left kidney may be preferred because of its longer renal vein. There are techniques for the management of multiple renal arteries from deceased and living donors.

Recipient operation

Just before surgery a prophylactic antibiotic is administered and continued postoperatively until the results of cultures are known. Immunosuppression is started just before or during surgery in the deceased kidney graft recipient. After the induction of anesthesia and the placement of central venous catheter, the genitalia and skin are prepared and a Foley catheter is placed in the bladder. The bladder is filled before the ureteroneocystostomy. A self-retaining ring retractor attached to the operating table that has been flexed and rotated toward the surgeon allows the operation to be performed by a surgeon and one assistant. Most common kidney is transplanted into right iliac fossa. Placement of the kidney on the right side will allow access to a wider choice of arteries and veins for vascular reconstruction. In men, the spermatic cord is preserved and in women, the round ligament is divided. The recipient's target blood vessels are dissected. Lymphatic vessels are divided between ligatures to prevent the development of postoperative lymphocele. Before temporary vascular occlusion, heparin, is commonly given i.v. to the recipient. During the vascular anastomosis, an infusion of mannitol and fluids are begun to act as a free-radical scavenger and as an osmotic diuretic. The addition of an albu-

min infusion has been found to be helpful in promoting early renal function in the deceased donor kidney transplant. The renal artery is usually anastomosed to the end of the internal iliac artery or to the side of the external or common iliac artery. The renal vein, with or without an extension, is usually anastomosed end to side to the external iliac vein or to the junction of the external and common iliac veins. Furosemide is commonly infused just before release of the vascular clamps. Urinary tract reconstruction is usually by antireflux ureteroneocystostomy, of which there are several techniques. Double-pigtail ureteral stents are used. The routine use of a ureteral stent for all cases has been shown to reduce the incidence of ureteral complications. Stent is left in place for several weeks. The uncomplicated renal transplantation can be closed by a variety of running or interrupted suture techniques with retroperitoneal drain. A closed suction drain is recommended in the subcutaneous tissue of an obese patient.

Renal allograft rejection

There are two histocompatibility systems of greatest importance in renal transplantation: the ABO blood group and the MHC. Most common the donor and recipient must be ABO compatible because A and B substances are present on endothelial cells and most individuals have antibodies to the RBC antigens they lack. The MHC antigens are glycoproteins on the cell membrane. They are encoded by MHC genes on the short arm of chromosome 6. Autosomal class I antigens are known as the HLA-A, HLA-B and HLA-C antigens and they are present on nearly all nucleated cells. They are detected by tissue typing T lymphocytes, usually with a DNA polymerase chain reaction amplification technique. HLA-DR, HLA-DQ and HLA-DP antigens are class II antigens present on B lymphocytes, activated T lymphocytes, monocytes, macrophages, dendritic cells and some endothelial cells. HLA-DR antigens are detected by tissue typing B lymphocytes. Testing for HLA-DQ and HLA-DP antigens is not routinely done. Recipient circulating cytotoxic antibodies against the MHC antigens of a specific donor are detected by pretransplantation crossmatching techniques and a positive complement-dependent T-cell lymphocytotoxicity crossmatch is considered to be a contraindication to renal transplantation when the serum used is recently obtained from the transplantation candidate. Protocols have been developed to use kidney transplants when the recipient has a positive crossmatch to the donor and the crossmatch is rendered negative by plasmapheresis and immunoglobulin administration to permit an otherwise prohibited transplant to take place.

Because of inheritance patterns of the HLA antigens, each potential kidney graft recipient is a “half-match,” or haploidentical, with his or her parents and children and has a 0.25 probability of HLA identity, a 0.50 probability of haploidentity and a 0.25 probability of a total HLA mismatch with a sibling. Within the past 5 years, the influence of histocompatibility matching on graft survival has decreased in the presence of more effective and less toxic immunosuppressive regimens.

Incompatibility with MHC antigens on donor tissue stimulates the very complex immune response.

Classification of Rejection

Hyperacute rejection occurs immediately after renal revascularization. It is an irreversible process mediated by preformed circulating cytotoxic antibodies that develop after pregnancy, blood transfusions or an earlier failed transplantation. It is very rare when the microlymphocytotoxicity crossmatch between recipient serum and donor lymphocytes is negative.

Accelerated rejection is mediated by humoral and cellular components of the immune response. It occurs within days to weeks and often does not respond to antirejection therapy.

Acute rejection can occur any time after transplantation. The symptoms of acute kidney transplant rejection are those of "the flu," accompanied by pain over an enlarged kidney graft, hypertension, decreased urinary output, fluid retention, increased serum Cr levels and radioisotope renography indicating decreased renal blood flow, glomerular filtration and tubular function. Acute pyelonephritis must be ruled out by urinalysis and, subsequently, negative urine culture. Needle biopsy of the kidney graft is the standard to confirm the diagnosis of acute rejection. The typical histologic findings of acute renal allograft rejection are mononuclear cellular infiltration, tubulitis and vasculitis.

Chronic rejection is characterized by a gradual decline in renal function associated with interstitial fibrosis, vascular changes and minimal mononuclear cell infiltration. A positive B-cell crossmatch or a positive flow crossmatch against donor B or T cells is considered by some to be predictive of chronic rejection and poorer long-term graft survival.

Immunosuppression

Immunosuppressive drug regimens commonly include a corticosteroid in combination with other drugs such as cyclosporine or tacrolimus (calcineurin inhibitors), azathioprine or mycophenolate mofetil (purine antagonists) and sometimes antilymphocyte antibody preparations. Triple maintenance immunosuppression with prednisone, cyclosporine or tacrolimus and azathioprine or mycophenolate mofetil is common. Corticosteroid therapy (reduce transcription of cytokine genes) is usually started at high doses and then rapidly tapered during the first few weeks after engraftment. Cyclosporine and tacrolimus have similar mechanisms of action (inhibit calcineurin and interleukin-2 production), effectiveness and cost, but slightly different side effect profiles and they are not used together. A determination of cyclosporine or tacrolimus blood levels is helpful when toxicity or insufficient immunosuppression is suspected. Azathioprine and mycophenolate mofetil have similar mechanisms of action (inhibit purine synthesis), but mycophenolate mofetil is more effective, more toxic and more expensive.

Urinary incontinence is the complaint of any involuntary leakage of urine. It results from a failure to store urine during the filling phase of the bladder due to abnormality of bladder smooth muscle or the urethral sphincter.

Urine loss is either urethral or extra-urethral or secondary to anatomical abnormalities including ectopic ureters, rectovesical or vesicovaginal fistulae is defined as a false UI.

Overflow incontinence is leakage of urine when the bladder is abnormally distended with large residual volumes. Typically, men present with chronic urinary retention and dribbling incontinence. This can lead to back pressure on the kidneys and CRF.

Nocturnal enuresis describes any involuntary loss of urine during sleep. The prevalence in adults is 0.5%. Childhood enuresis can be further classified into primary types (never been dry for longer than a 6-month period) or secondary (the re-emergence of bed wetting after a period of being dry for at least 6-12 months).

Risk factors

- Gender (female > males) and genetic predisposition;
- Neurological disorders (spinal cord injury, stroke, MS, Parkinson's disease), radical pelvic radiotherapy) and estrogen deficiency for UUI;
- Anatomical disorders (vesicovaginal and uretero-vaginal fistulas, ectopic ureter, urethral injuries) for false UI;
- Childbirth, weakness in collagen tissue, pelvic and prostate surgery (radical hysterectomy, radical prostatectomy, TURP) leading to injury of sphincter in the case of SUI.

Diagnosis of UI

History

LUTS and triggers for incontinence (cough, sneezing, exercise, position, urgency), frequency and severity of symptoms are discussed. Risk factors are established (see above). A validated patient completed questionnaire may be helpful.

Physical examination

A pelvic examination is performed in the supine with a Sim's speculum. The patient is asked to cough or strain and inspection for vaginal wall prolapse (cystocele, rectocele, enterocele) is performed. Uterine or perineal descent and urinary leakage during the stress test are detected. Urethral hypermobility is assessed with this test. A lubricated cotton-tipped applicator is introduced through the urethra to bladder neck level. Hypermobility is defined as a resting or straining angle of >30 from horizontal.

The abdomen is examined for a palpable bladder, indicating urinary retention. A neurological examination should include assessment of anal tone and reflex, perineal sensation and lower limb function.

Bladder diaries: the frequency and volume of urine, incontinent episodes, pad usage, fluid intake and degree of urgency are recorded. Alternatively, pads can be weighed to estimate urine loss (pad testing).

Urinalysis can exclude UTIs. Blood tests, X-Ray imaging and cystoscopy are indicated for persistent or severe symptoms, bladder pain and voiding difficulties.

Uroflowmetry measures the velocity of voided urine. A low rate indicates BOO or reduced bladder contractility. PVR is also useful (<50ml is normal; >200ml is abnormal; 50-200ml requires clinical correlation). Urodynamic investigations are also performed.

12.1. STRESS URINARY INCONTINENCE

SUI is involuntary urinary leakage on effort, exertion, sneezing or coughing, due to hypermobility of the bladder and urethra and/or ISD.

Urethral hypermobility is due to a weakness of pelvic floor support causing a rotational descent of the bladder neck and proximal urethra during increases in intra-abdominal pressure. If the urethra opens concomitantly, there will be urinary leaking.

ISD describes an intrinsic malfunction of the sphincter, regardless of its anatomical position, which is responsible for type III SUI. Causes include inadequate urethral compression (previous urethral surgery, ageing, menopause, radical pelvic surgery, anterior spinal artery syndrome) or deficient urethral support (pelvic floor weakness, childbirth, pelvic surgery, menopause).

Classification

- Type I - leakage that occurs during stress with <2cm descent of the bladder base below the upper border of the symphysis pubis.
- Type II - leakage on stress accompanied by marked bladder base descent (>2cm) that occurs only during stress (IIa) or is permanently present (IIb).
- Type III - bladder neck and proximal urethra are already open at rest with or without descent. Also known as ISD.

In males, the urethral sphincter may be damaged after prostatic or pelvic surgery (TURP; prostatectomy).

Treatment of SUI

The injection of bulking materials

This treatment option is used to increase outlet resistance. Indications are SUI I-II type secondary to demonstrable ISD with normal bladder muscle function. Contraindications are UTI, untreated bladder dysfunction, bladder neck stenosis.

Suburethral injections are given by a transurethral route using a cystoscope and injection needle. Requires either a local block or a general anaesthetic, with full antibiotic cover. In men, the injection should be proximal to external sphincter to avoid sphincter spasm or in the proximal membranous urethra beside verumontanum. In women, a periurethral technique can also be used, with endoscopic or US guidance. In women, 2 injections are recommended. In men 3 or 4 circumferential injections are administered, with the aim of achieving urethral muscosal apposition and closure of the lumen. Overall success rate ~50-70%.

Complications are urinary urgency, urinary retention (which may need drainage), hematuria, cystitis, granuloma formation. Often, repeat treatments are needed.

Retropubic suspension procedures

Surgery is considered after conservative methods have failed. These procedures are used to treat female SUI caused by urethral hypermobility. The aim of surgery is to elevate and fix the bladder neck and proximal urethra in a retropubic position, to support the bladder neck and regain continence. These procedures are contraindicated in the presence of significant ISD. All operations done via a Pfannenstiel or lower midline abdominal incision to approach the bladder neck and develop the retropubic space. Better results are seen in patients with pure SUI and primary repair.

By Marshall – Marchetti - Krantz procedure sutures are placed either side of the urethra around the level of the bladder neck and then tied to the hyaline cartilage of the pubic symphysis. Short-term success is about 90%, but declines over time.

Burch colposuspension requires good vaginal mobility, to allow vaginal wall to be elevated and attached to the lateral pelvic wall where the formation of adhesions over time secures its position. Paravaginal fascia is exposed and approximated to the iliopectineal (Cooper's) ligament of the superior pubic rami. Initial success rates are 90%. Better long-term results compared to other retropubic repairs. A laparoscopic approach can also be performed, but long-term results have proven to be poor.

By vagino-obturator shelf/paravaginal repair sutures are placed by the vaginal wall and paravaginal fascia and then passed through the obturator fascia to attach to part of the parietal pelvic fascia below the tendinous arch. Cure rates are up to 85%.

Complications are osteitis pubis, may be urinary retention and OAB.

Sling procedures are mainly used for female SUI associated with poor urethral function (type III or ISD) or when previous surgical procedures have failed. Also used for incontinence due to urethral damage in male patients. It is essential that urethral and bladder function is evaluated prior to surgical repair.

At present time synthetic monofilament polypropylene such as TVT or TOT are used most common. The TVT is a popular procedure as it is less invasive, it can be inserted under local anaesthetic as a day case and it has few complications. The tape has long trocars on each end, which are inserted either side of the urethra through a vaginal approach (TVT) or trocars are inserted through obturator membranes (TOT). They perforate soft tissues and are pushed out onto the lower abdominal wall. Once the tape is positioned loosely behind the mid-urethra, its covering is removed and the ends cut flush to the abdomen. Both techniques use cystoscopy to assist prevention of bladder perforation during sling placement. Post-operatively, patients may temporarily require CISC until PVR are <100ml.

Overall, long-term cure rates for slings are 80%, with improvement seen in 90%. Complication rates are voiding disorders (urinary retention, de novo OAB), may be vaginal, urethral and bladder erosions. Sometimes bowel, bladder perforation and pelvic bleeding are detected.

The artificial urinary sphincter

AUS consists of an inflatable cuff placed via a lower abdominal incision around the bladder neck in both men or women or the bulbar urethra in men, a pressure-regulating balloon placed extraperitoneally and an activating pump placed in the scrotum or labia majora. The cuff provides a constant pressure to compress the urethra. To void, the pump is squeezed, which transfers fluid to the reservoir balloon, thereby deflating the cuff. The cuff then automatically refills within 3 minutes. Voiding takes place in the interval taken for the cuff to refill.

Indications are incontinence III type secondary to ISD in patients with normal bladder capacity and compliance. It is used for sphincter damage due to prostatectomy, TUR, pelvic radiotherapy, pelvic fracture and following urethral reconstruction. In women it is used after other treatments for incontinence have failed. It can be used for neuropathic sphincter weakness if the incontinence is not due to OAB. If there is combined bladder overactivity and sphincter weakness, treat the bladder first with help of anticholinergics, intravesical botulinum injections and augmentation. In some cases this will be enough to achieve continence. If incontinence persists, proceed with AUS at a later date.

Patients should undergo urodynamics, cystoscopy and upper tract imaging to evaluate voiding function and identify anatomical abnormalities that might affect the efficacy of the sphincter. Good manual dexterity is required to manipulate the pump and perform CISC if needed. The patient must also have sufficient cognitive function to operate the sphincter themselves, several times daily.

Complications are recurrent incontinence secondary to urethral atrophy underneath the cuff, mechanical failure, urethral erosion, OAB or reduced compliance causing reflux, hydronephrosis and renal failure. Recurrent incontinence is investigated by cystoscopy to exclude erosion, X-Ray is used to determine leaks from the system and urodynamics to detect high bladder pressures. Primary implant infection rates are 1-3%. With infection or erosion, entire device is removed and wait 3-6 months before reinsertion. Hematoma, late urinary retention may signify obstruction from urethral stricture or bladder neck contracture.

AUS can function well for many years. Overall long-term success with continued continence and no device malfunction is 80%. Revision rates are about 20%

12.2. URGE URINARY INCONTINENCE

UI is involuntary urine leakage accompanied by or immediately preceded by a sudden, strong desire to void. It is a component of the OAB. OAB is a syndrome which includes urgency, with or without urge incontinence, frequency and nocturia. The symptoms are usually caused by OAB, but can be due to other forms of voiding dysfunction. This diagnosis is common for the population >40 years old.

The underlying etiology for UI can only be absolutely determined by urodynamic studies. Detrusor overactivity is a urodynamic observation characterized by involuntary bladder muscle contractions during the filling phase of the bladder, which may be spontaneous or provoked and can consequently cause UI. The underlying cause may be neurogenic, where there is a relevant neurological condition or idiopathic, where there is no defined cause.

Low bladder compliance is characterized by a decreased volume to pressure relationship, where there is a high increase in bladder pressure during filling due to alterations in elastic properties of the bladder wall or changes in muscle tone (neurogenic bladder or microcyst).

Treatment of OAB

Conservative treatment

Any underlying cause is treated: urethral obstruction, bladder stones, spinal disease or tumor. TUR for BPH can provide symptomatic relief in >2/3 of patients. Treatment of SUI component includes pelvic floor exercises, biofeedback and high-frequency electrical stimulation, which strengthens the pelvic floor and sphincter by increasing tone through sacral neural feedback systems. Behavioural modification involves modifying fluid intake, avoiding stimulants (caffeine, alcohol) and bladder training for urgency. This is delay micturition for increasing periods of time by inhibiting the desire to void.

Anticholinergic drugs act to inhibit bladder contractions and increase capacity (oxybutynin, tolterodine, trospium, solifenacin). Oxybutynin also exerts a direct muscle effect and can be administered intravesically in patients performing intermittent catheterization (5 mg in 30 ml normal saline 8 hourly after emptying the bladder). Contraindication is closed angle glaucoma. Side-effects are dry mouth, constipation, blurred vision.

Tricyclic antidepressants exert a direct relaxant effect on bladder muscle as well as producing sympathomimetic and central effects.

Desmopressin is a synthetic vasopressin analogue which acts as an antidiuretic. It is used intranasally to alleviate nocturia in adults.

Baclofen is a GABA receptor agonist, which is used orally or via intrathecal pump in patients with bladder dysfunction and limb spasticity.

Botulinum toxin A injection therapy acts by inhibiting calcium-mediated release of acetylcholine at the neuromuscular junction, reducing muscle contractility. It is used predominantly for neuropathic bladder dysfunction, but increasingly is being used for failed medical therapy of the OAB in non-neuropaths. It is injected directly into detrusor muscle under cystoscopic guidance with help of flexible or rigid cystoscopy under regional or general anaesthetic at 20-30 random sites, excluding the trigone. Repeat treatments are required with 6-12 months between injections and CISC may be needed to empty residuals. Side-effects lasting a week or so can occur.

Neuromodulation involves electrical stimulation of the bladder's nerve supply to suppress reflexes responsible for involuntary bladder muscle contraction. The "Interstim" device stimulates the S3 afferent nerve which then inhibits detrusor activity at the level of the sacral spinal cord. An initial percutaneous nerve evaluation is performed, followed by surgical implantation of permanent electrode leads into the S3 foramen, with a pulse generator which is programmed externally.

Surgery of the OAB

The aim is to increase functional bladder capacity, decrease maximal detrusor pressure and protect the upper urinary tract.

Auto-augmentation may be used. Detrusor muscle is excised from the dome of bladder, leaving the underlying bladder endothelium intact. A large epithelial bulge is created which augments bladder capacity.

Augmentation ileocystoplasty relieves intractable frequency, urge and UUI in 90% of patients. The bladder dome is cut open (bivalved) and a detubularized segment of ileum is anastomosed, creating a larger bladder volume.

Conduit diversion may be indicated as a non-continent urinary outlet. Typically, both ureters are anastomosed and connected to a short ileal pouch, which is brought out cutaneously as a stoma.

12.3. MIXED INCONTINENCE

This is involuntary urinary leakage associated with urgency and also with exertion, effort, sneezing or coughing. 30-50% of women with SUI also have symptoms of frequency, urgency or UUI. Underlying etiologies and evaluation remain the same as for SUI and UUI.

Risk factors for women include frequent and severe childbirth, ageing, estrogen withdrawal, previous pelvic surgery and obesity. There also appears to be an intrinsic loss of urethral strength, often associated with urethral hypermobility. In men, damage occurs to the external sphincter from pelvic fractures, after prostatectomy or TUR. Neurological disorders also cause sphincter weakness.

This mixed UI patient group needs further investigation to rule out pathologies such as BC, stones and interstitial cystitis. Voiding records and urodynamic studies are most useful. Female examinations are stress test, pelvic organ prolapse investigation. In male patients a palpable bladder and penile abnormalities are examined. Imaging (prostate size, flow rate, PVR) are indicated.

When SUI appears to be the predominant symptom, initially start with conservative methods and then review. Behavioural and pelvic floor exercises with vaginal weights (Kegel's exercises) are important and can improve symptoms in 1/3 of women with mild SUI. When no success with conservative treatment of SUI, surgical repair can alleviate remaining symptoms. Surgical procedures for SUI in women include colposuspension, vagino - obturator shelf procedure, slings for bladder neck support and tension- free vaginal tape (TVT or TOT). Urethral bulking agents and artificial urinary sphincters can be used in both sexes. Pelvic organ prolapse is corrected with a pessary or surgery.

In mixed UI electrostimulation is used to reduce OAB, which can alleviate the urge and UUI component. However, if UUI is the most marked symptom, surgery will be less helpful and behavioural therapy with pharmacotherapy for UUI should be used first for minimally 3 months.

12.4. POST-PROSTATECTOMY INCONTINENCE

This type of incontinence is diagnosed slightly <1% after TUR and 0.5% after BPH-ectomy. Results after RP are variable up to 40% suffer from mild UI, but this usually improves over 12-18 months post-surgery, severe UI persisting in 2-10%.

Risk-factors are increasing age, pre-existing bladder dysfunction, previous radiotherapy, prior TURP, advanced stage of disease and surgical technique. Earlier

recovery of continence after RP is achieved using a perineal approach, nerve-sparing techniques, sphincter and bladder neck preserving procedures.

The proximal sphincter mechanism is removed at prostatectomy and TUR. Post-prostatectomy continence therefore requires a functioning distal urethral sphincter mechanism and low bladder pressure during bladder filling. Nerve-sparing RP produces better continence rates. The main cause of post-radical prostatectomy incontinence is sphincter dysfunction. A substantial proportion of men also have OAB before prostatectomy and this may remain so after prostatectomy.

History detects stress-induced leakage. Cough, standing from a sitting position suggests sphincter dysfunction. There is leakage on coughing. PVR volume measurement on US is used to exclude retention with overflow. Urodynamic studies allow determination of OAB and sphincter function. Cystoscopy allows identification of strictures.

12 months for spontaneous improvement is needed unless incontinence is severe. Pelvic floor exercises, insertion of urethral bulking agents, bulbourethral sling to compress the urethra are treatment options. AUS insertion is usually deferred until 1 year post-prostatectomy and is the most effective long-term treatment.

If OAB exists, conservative treatment includes behavioural therapy, pelvic floor exercises and anticholinergic medication. Surgery for intractable cases includes augmentation cystoplasty or urinary diversion. Catherization may be considered in the older patient.

12.5. ENURESIS

Enuresis is any involuntary loss of urine in the absence of any demonstrable abnormality of the urinary tract. It may occur at an inappropriate time or social setting, during the day, night or diurnally. Nocturnal enuresis describes loss of urine occurring during sleep. Monosymptomatic nocturnal enuresis is a term used to describe bedwetting in children with no daytime urinary symptoms to suggest an underlying voiding disorder.

Nocturnal enuresis is estimated to affect up to 15% of 5-years olds and 10% of 7-year old children. There is 15% spontaneous resolution of symptoms per year. The prevalence in adults is ~0.5%. There are primary nocturnal enuresis (never been dry for more than a 6-month period) and secondary (the re-emergence of bed wetting after a period of being dry for at least 6 months).

Risk factors

- An abnormal decrease in ADH levels at night causes increased urine production;
- Altered sleep/arousal mechanism with impaired “arousal from sleep” response to a full bladder;
- Reduced nocturnal functional bladder capacity;
- OAB during sleep;
- Familial predisposition, psychological factors and UTIs are also considered to contribute to nocturnal enuresis.

The aim of the evaluation is to establish the underlying pathophysiological factors to guide treatment. In the patients with enuresis it is helpful to discuss about

the frequency of episodes, daytime symptoms, new or recurrent problems, family history, symptoms of UTIs, bowel problems and psychosocial history. Abdomen is examined for palpable bladder. Neurological exam include investigation of the perineal sensation, anocutaneous reflex and lower limb sensation. The spine is inspected for sacral agenesis. The voiding diary is investigated to assess for nocturnal polyuria and functional bladder capacity. Urinalysis is used to assess for infection, the presence of glucose (DM) or protein (UTIs, renal disease).

Treatment

- Reassurance and counselling with motivational techniques to improve child's self-esteem;
- Bladder training: regular daytime toileting, emptying the bladder before bed, avoiding bladder stimulants (i.e. blackcurrant drinks, caffeine), reduced fluid intake in the hours before sleep;
- Conditioning therapy: an enuretic alarm is connected to the child's underwear, which is triggered with the first few drops of urine, waking the child from sleep with 60-70% successful response;
- Synthetic analogue of ADH (desmopressin) given intranasally or orally just before bedtime to exert an antidiuretic response in the patients with nicturia and normal bladder function;
- Imipramine, a tricyclic antidepressant with anticholinergic and antispasmodic properties;
- Patients with OAB benefit most from a combination of options: enuretic alarm, bladder training and anticholinergic drugs (oxybutynin, trospium chloride, solifenacin) with/without desmopressin.

Infertility is failure of conception after at least 12 months of unprotected intercourse. The chance of a normal couple conceiving is estimated at 20-25% per month, 75% by 6 months and 85-90% at 1 year.

It is estimated that up to 50% of infertility is due to male factors. Defects of the spermatozoa will lead to failure of fertilization of the normal ovum due to defective sperm development, function or inadequate numbers.

There may be abnormalities of morphology (teratozoospermia), motility (asthenozoospermia), low sperm numbers (oligozoospermia) or absent sperm (azoospermia).

Male reproductive physiology

Hypothalamic – pituitary - testicular axis

The hypothalamus secretes LHRH, which causes pulsatile release of anterior pituitary gonadotrophins, called FSH and LH, which act on the testis. FSH stimulates the seminiferous tubules to produce spermatozoa. LH acts on Leydig cells to produce testosterone. It promotes development of the male reproductive system and secondary sexual characteristics. Steroidogenesis is stimulated by a cAMP-protein kinase C mechanism, which converts cholesterol to pregnenolone. Further steps in the biosynthesis pathway produce intermediary substances (dehydroepiandrosterone and androstenedione) prior to producing testosterone. In the blood, testosterone is attached to SHBG and albumin. At androgen-responsive target tissues, testosterone is converted into a potent androgen, DHT, by intracellular 5-AR.

Spermatogenesis and conception

Seminiferous tubules are lined with Sertoli cells, which surround developing germ cells (spermatogonium) and provide nutrients and stimulating factors, as well as secreting androgen-binding factor and inhibin. Germ cells divide to form primary spermatocytes. These undergo a first meiotic division to create secondary spermatocytes with 46 chromosomes, followed by a second meiotic division to form spermatids with 23 chromosomes. Finally, these differentiate into spermatozoa. This process with transport of spermatozoa takes app. 70 days. Spermatozoa that are not released are reabsorbed by phagocytosis. Mature spermatozoa have a head, middle piece and tail. The head is composed of a nucleus covered by an acrosome cap, containing vesicles filled with lytic enzymes. The middle piece contains mitochondria and contractile filaments, which extend into the tail to aid motility. After deposition at the cervix, sperm penetrate cervical mucus and travel through the uterus to the site of fertilization in the fallopian tube, during which time they undergo functional maturation (capacitation). Sperm start to penetrate the oocyte and bind to the zona pellucida. The activation phase is initiated, triggering hyperactivated motility and the acrosomal reaction, leading to enzyme release, penetration into the cytoplasm of the oocyte, fusion and fertilization.

Etiology

- Idiopathic/genetic (?) (25-70%);
- Varicocele (40%);
- UTIs;
- Cryptorchidism;
- Functional disorders: immunological infertility (sperm antibodies), head or tail defects, Kartagener's syndrome (immotile cilia), dyskinetic cilia syndrome;
- Erectile or ejaculatory problems;
- Testicular injuries: orchitis, testicular torsion, trauma, radiotherapy;
- Endocrine disorders: Kallmann's syndrome (isolated gonadotrophin deficiency causing hypogonadism), hyperprolactinemia, hyper- or hypothyroidism, hyperostrogenia, anabolic steroids abuse, congenital adrenal hyperplasia;
- Genetic disorders: Klinefelter's syndrome (47XXY), XX male, XYY syndrome, presence of AZF factor;
- Male genital tract obstruction: congenital absence of vas deferens, epididymal obstruction or infection, Mullerian prostatic cysts, groin or scrotal surgery;
- Systemic disease: renal failure, liver cirrhosis;
- Drugs: chemotherapy, sulphasalazine;
- Environmental factors: alcohol, smoking, toxic substances, hot baths.

Diagnosis

- Sexual history: duration of problem, frequency and timing of intercourse, previous successful conceptions, previous birth control, erectile or ejaculatory dysfunction;
- Endocrinological status: age at puberty, history of cryptorchidism, gynaecomastia, hypogonadism;
- Medical and surgical anamnesis: detailed assessment for risk factors, recent febrile illness, post-pubertal mumps orchitis, varicocele, testicular torsion, trauma, tumour, STD, genitourinary surgery, radiotherapy, respiratory diseases associated with ciliary dysfunction, DM;
- Drugs and environmental: previous drug consumption, exposure to substances which impair spermatogenesis or erectile function, alcohol abuse, smoking habits, hot baths.

Examination

A full assessment of all systems is performed, with attention to general appearance (signs of hypogonadism, gynaecomastia). Urogenital examination should include assessment of the penis, measurement of testicular consistency, tenderness and volume with a Prader orchidometer (normal >15ml), palpate epididymis (tenderness, swelling) and spermatic cord (vas deferens present or absent, varicocele), DRE of the prostate.

Semen analysis 2-3 specimens over several weeks, collected after 3-4 days of sexual abstinence. Specimens are delivered to the laboratory within 1h. Ejaculate volume, liquefaction time and pH are noted. Microscopy techniques measure sperm concentration, total numbers, morphology and motility. The mixed agglutination reaction (MAR test) is used to detect antisperm antibodies. The presence of leucocytes (>1x10⁶/ml of semen) suggests infection and cultures should be requested.

Semen analysis: normal parameters (WHO 1999, 2010)

Semen volume	>1,5-2.0ml
pH	7.2-7.8
Time to liquefy	<60 min
Total sperm count	>40 x 10 ⁶ /ejaculate
Sperm concentration	>15-20 x 10 ⁶ /ml
Sperm motility	>32-50% with progressive motility (A+B) >25% grade A
Sperm morphology	>4-14% normal forms (Kruger)
Viability	>75% viable sperm
White blood cells	<1 x 10 ⁶ WBC/ml
MAR test	<10% with adherent particles

Screening of STD, investigations of urethral discharges and prostatic secretions, bacteriological exam of ejaculate are performed.

Hormone measurement for serum FSH, LH and testosterone, prolactin, estradiol, inhibin B levels are indicated. In cases of isolated low testosterone level, it is recommended to test free testosterone levels. Raised prolactin is associated with sexual dysfunction and may indicate pituitary disease.

Chromosome analysis is indicated for clinical suspicion of an abnormality (azoospermia or severe oligospermia, small atrophic testes with high FSH level). Detecting of AZF and CFTR mutations are used for patients with azoospermia.

Testicular biopsy is performed for azoospermic patients, to differentiate between non-obstructive and obstructive causes. It is also used for sperm retrieval.

Functional sperm tests

- Post coital (in vivo) test: cervical mucus is taken just before ovulation and within 8 hours of intercourse and microscopy performed. Normal results shows >10 sperm per HPF, the majority demonstrating progressive motility. Abnormal results indicate inappropriate timing of the test, cervical mucus antisperm antibodies, abnormal semen, inappropriately performed coitus.
- Sperm penetration (in vitro) test: a sample of semen is placed directly onto pre-ovulatory cervical mucus on a slide and the penetrative ability of spermatozoa is observed.
- Sperm-cervical mucus (in vitro) test: a specimen of semen (control) and one mixed with cervical mucus are placed separately on a slide and observed for 30 minutes. More than 25% exhibiting jerking movements in the mixed sample (but not the control) is a positive test for antisperm antibodies.

Imaging

- Scrotal US scan is used to confirm a varicocele and testicular abnormalities;
- TRUS is indicated for low ejaculate volumes, to investigate seminal vesicle obstruction (>1.5 cm width) or absence and ejaculatory duct obstruction (>2.3 mm);
- Vasography: Vas deferens is punctured at the level of the scrotum and injected with contrast. A normal test shows the passage of contrast along the vas deferens, seminal vesicles, ejaculatory duct and into the bladder, which rules out obstruction.

Oligozoospermia

Defined as a sperm concentration <15-20 million/ml of ejaculate.

Etiology

- Varicocele;
- Genetic causes;
- Androgen deficiency;
- Testicular cancer or lymphoma;
- Drug and toxin exposure;
- Cryptorchidism.

It is often associated with abnormalities of morphology and motility. The combined disorder is called oligoasthenoteratozoospermia (OAT) syndrome.

If sperm counts <5 million/ml (severe form) this requires hormone investigation, including FSH and testosterone. Severe oligospermia is associated with seminiferous tubular failure, small soft testes and high FSH.

Treatment

Correct the underlying cause. Idiopathic cases may respond to empirical medical therapy or require assisted reproductive techniques.

Azoospermia

Defined as an absence of sperm in the ejaculate fluid.

Etiology

- Obstructive: absent or obstructed vas deferens; epididymal or ejaculatory duct obstruction (related to infection, iatrogenic injury, cystic fibrosis);
- Non-obstructive: hypogonadism (Kallmann's syndrome, pituitary tumour), abnormalities of spermatogenesis (chromosomal anomalies, toxins, idiopathic, varicocele, orchitis, testicular torsion).

Diagnosis

- Hormone assay (raised FSH indicates non-obstructive cause, normal FSH with normal testes indicates increased likelihood of obstruction);
- Chromosomal analysis may be used to exclude Klinefelter's syndrome in patients presenting with azoospermia, small soft testes, gynaecomastia, high FSH/LH and low testosterone;
- Testicular biopsy is performed to assess if normal sperm maturation is occurring and for sperm retrieval for later IVF.
- TRUS assesses absence or blockage of vas deferens and ejaculatory duct obstruction. Cystic fibrosis may be observed in patients with vas deferens defects.

Treatment for azoospermia

- Bilateral absence of vas deferens: MESA or consider donor insemination.
- Primary testicular failure with testicular atrophy: TESE or in vitro fertilization (IVF).
- Obstructive cause with normal testis: epididymovasostomy or vasovasostomy or IVF.

Treatment options for male factor infertility

- General: modification of life style factors (reduce alcohol consumption, avoid smoking and hot baths);
- Medical treatment: correct any reversible causative factors;
- ED is treated with oral, intracavernosal drugs, vacuum devices or prostheses;
- Ejaculatory failure may respond to sympathomimetic drugs (desipramine) or electroejaculation (used in spinal cord injury), where an electrical stimulus is delivered via a rectal probe to the postganglionic sympathetic nerves that innervate the prostate and seminal vesicles;
- Antisperm antibodies: assisted conception methods are usually required.

Hormonal causes

- Hypogonadotropic hypogonadism may respond to HCG 2000IU subcutaneously 3 times a week, which stimulates an increase in testosterone and testicular size. If the patient remains azoospermic after 6 months of treatment, recombinant FSH is added. Alternatively, pulsatile LHRH can be administered subcutaneously via a minipump.
- Hypergonadotropic hypergonadism: testosterone deficiency requires testosterone replacement therapy;
- Hyperprolactinaemia is treated with dopamine agonists;
- Anti-estrogens (clomiphene citrate or tamoxifen) are often used empirically to increase LHRH, which stimulates endogenous gonadotrophin secretion.

Surgical treatment by genital tract obstruction

- Epididymal obstruction can be overcome by microsurgical anastomosis between the epididymal tubule and vas (epididymovasovasostomy);
- Vas deferens obstruction is treated by microsurgical reanastomosis of ends of the vas and is used for vasectomy reversal;
- Ejaculatory duct obstruction requires transurethral resection of the ducts;
- Varicocele: repaired by open/laparoscopic surgical ligation or embolization.

Assisted reproductive techniques

Sperm extraction used for obstructive azoospermia. Sperm are removed directly from the epididymis by MESA or by PESA. If these methods fail, TESE or TESA may be tried. Spermatozoa are used as a “fresh” or undergo cryopreservation until required. Later, they are separated from seminal fluid by dilution and centrifuge methods with further selection of motile sperm and normal forms using Percoll gradient techniques and used for assisted conception. By IUI following ovarian stimulation, separated spermatozoa are injected across catheter directly into the uterus. By IVF controlled ovarian stimulation produces oocytes which are then retrieved under transvaginal US-guidance. Oocytes and sperm are placed in a Petri dish for fertilization to occur. Embryos are transferred to the uterine cavity. Pregnancy rates are 15-20% per cycle. By ICSI a single spermatozoon is injected directly into the oocyte cytoplasm. Pregnancy rates are 15-22% per cycle.

This is the persistent (during 3 months) inability to achieve or maintain a penile erection sufficient for sexual intercourse.

Mechanism of erection

Neuroendocrine signals from the brain, created by audiovisual or tactile stimuli, activate the autonomic nuclei of the spinal erection centre (T11-L2 and S2-S4). Signals are relayed via the cavernosal nerve to the erectile tissue of the corpora cavernosa with help of NO and PGE1 activating smooth muscle relaxation and induce the veno-occlusive mechanism. This triggers increased arterial blood flow into sinusoidal spaces secondary to arterial and arteriolar dilatation, relaxation of cavernosal smooth muscle and opening of the vascular space. The result is expansion of the sinusoidal spaces against the tunica albuginea, which compresses the subtunical venous plexuses, decreasing venous outflow. Maximal stretching of the tunica albuginea acts to compress the emissary veins which lie within its inner circular and outer longitudinal layers, reducing venous flow even further. Rising intracavernosal pressure and contraction of the ischiocavernosus muscles produces a rigid erection. Following orgasm and ejaculation, vasoconstriction (due to increased sympathetic activity and many secondary messengers) produces detumescence.

Phases of erection

- Flaccid phase (0) - cavernosal smooth muscle contracted, sinusoids empty, minimal arterial flow;
- Latent (filling) phase (I) - increased pudendal artery flow, penile elongation;
- Tumescence phase (II) - rising intracavernosal pressure, forming of the erection;
- Full erection phase (III) - increased cavernosal pressure causes penis to become fully erect;
- Rigid erection phase (IV) - further increases in pressure + ischiocavernosal muscle contraction;
- Detumescence (V) - following ejaculation, sympathetic discharge resumes, there is smooth muscle contraction and vasoconstriction, reduced arterial flow, blood is expelled from sinusoidal spaces.

Etiology

ED is generally divided into psychogenic and organic causes, although it is often multifactorial.

Causes of erectile dysfunction

- Psychological (depression, anxiety, relationship difficulties, stress);
- Arteriogenic factors: hyperlipidaemia and hypercholesterolemia, hypertension, smoking, DM, peripheral vascular disease;
- Venogenic: impairment of veno-occlusive mechanism (due to anatomical or degenerative changes), spinal cord injury, penile trauma;
- Iatrogenic: pelvic surgery, prostatectomy;

- Endocrine: hypogonadism, hyperprolactinaemia, hypo and hyperthyroidism, DM;
- Neurological: multiple sclerosis, parkinson's disease, multi-system atrophy, tumours, spina bifida, syringomyelia, pelvic surgery or radiotherapy, peripheral neuropathy (DM, alcohol-related);
- Drug-induced (antihypertensives, anti-arrhythmics, antidepressants, anti-androgens, statins);
- Other: CRF, cirrhosis, prostatitis, peyronie's disease.

Diagnosis

History

- Sexual: onset of ED (sudden or gradual), duration of problem, presence of erections (nocturnal, early morning, spontaneous), ability to maintain erections (early collapse, not fully rigid), loss of libido, relationship issues (frequency of intercourse and sexual desire, relationship problems);
- Medical and surgical: hypertension, cardiac disease, peripheral vascular disease, DM, endocrine or neurological disorders, pelvic surgery, radiotherapy, trauma with damaging innervation and blood supply to the pelvis and penis;
- Drugs: enquire about current medications and ED treatments already tried, smoking, alcohol consumption.

An organic cause is more likely with gradual onset, unless associated with an acute obvious cause such as surgery, loss of spontaneous erections, intact libido and ejaculatory function, existing medical risk factors and older age groups. The IIEF scale can be used to quantify severity.

Examination

Full physical examination (CNS, abdomen, neurological), DRE to assess prostate and external genitalia assessment to document phimosis and Peyronie's disease. Confirm presence, size and location of testicles. The bulbocavernosus reflex can be performed to test integrity of spinal segments S2-S4 (squeezing the glans causes anal sphincter and bulbocavernosal muscle contraction).

Investigation

- Blood tests: fasting glucose, PSA, serum testosterone, SHBG, LH/FSH, prolactin, thyroid function test, fasting lipid profile;
- Nocturnal penile tumescence testing: rigiscan device contains 2 rings which are placed around base and distal penile shaft to measure tumescence and number, duration and rigidity of nocturnal erections;
- Colour Doppler US measures arterial peak systolic and end diastolic velocities, pre and post intracavernosal injection of PGE1;
- Cavernosometry: intracavernosal injection of vasoactive drug followed by saline infusion, the rate of which is proportional to the degree of any venous leaking;
- Cavernosography: imaging and measurement of blood flow of the penis after intracavernosal injection of contrast and induction of artificial erection, which used to identify venous leaks;
- Penile arteriography.

Treatment

Psychosexual therapy

Aims to understand and address underlying psychological issues and provides information and treatment in the form of sex education, instruction on improving partner communication skills, cognitive therapy and behavioural therapy with programmed re-learning of couple's sexual relationship.

Oral medication

PDE-5 inhibitors: sildenafil (Viagra), tadalafil (Cialis), vardenafil (Levitra). PDE5 inhibitors enhance cavernosal smooth muscle relaxation and erection by blocking the breakdown of cGMP. Sexual stimulus is still required to initiate events. Side-effects are eadache, flushing, visual disturbance. Contraindications are nitrates, recent myocardial infarction, recent stroke, hypotension, unstable angina.

Dopamine receptor agonist is apomorphine (Uprima). This drug is administered sublingually and acts centrally on dopaminergic receptors in the paraventricular nucleus of the hypothalamus to enhance and co-ordinate the effect of sexual stimuli. Adverse effects: nausea, headache, dizziness.

Androgen replacement therapy

Testosterone replacement is indicated for hypogonadism. It is available in oral, intramuscular, pellet, patch and gel forms. In older men, it is recommended that PSA is checked before and during treatment.

Intracavernosal therapy

Alprostadil/Caverjet (synthetic PGE1), papaverine (smooth muscle relaxant), phentolamine. Training of technique and first dose is given by health professional. Needle is inserted at right angles into the corpus cavernosum on the lateral aspects of mid-penile shaft. Adverse effects are pain, priapism, hematoma.

Vacuum erection device

It contains 3 components: vacuum chamber, pump and constriction band. The penis is placed in the chamber and the vacuum created by the pump increases blood flow to the corpora cavernosa to induce an erection. The constriction band is placed onto the base of the penis to retain blood in the corpora and maintain rigidity. Adverse effects are penile coldness and bruising.

Penile prosthesis

Semi-rigid, malleable and inflatable penile prostheses are available for surgical implantation into the corpora to provide penile rigidity and sufficient erectile size for sexual intercourse. Side-effects are mechanical failure, erosions, infections.

Tuberculosis of the GUT is caused by *Mycobacterium tuberculosis*. Urinary TB is a disease of young adults and is a little more common in males than in females.

Etiopathogenesis

Mycobacterium tuberculosis reaches the genitourinary organs by the hematogenous route from the lungs. The primary site is often not symptomatic or apparent. The kidney and possibly the prostate are the primary sites of tuberculous infection in the GUT.

The primary granulomatous lesion forms in the lung. It consists of a central area of caseation surrounded by epithelioid and Langhans' giant cells, accompanied by caseous lesions in the regional lymph nodes. There is early spread of bacilli via the bloodstream to the GUT, but immunity rapidly develops and the infection remains quiescent. Acute diffuse systemic dissemination of tubercle bacilli can result in symptomatic miliary TB.

Reactivation of infection is so called post primary TB, which triggered by immune compromise. When a shower of tubercle bacilli hits the renal cortex, the microorganisms may be destroyed by normal tissue resistance and this is commonly seen in autopsies of persons who have died of TB. Only scars are found in the kidneys. However, if enough bacteria of sufficient virulence become lodged in the kidney and are not overcome, a clinical infection is established. TB of the kidney progresses slowly during 15-20 years. As a rule, there is no renal pain and little or no clinical disturbance of any type until the lesion has involved the calyces or the pelvis, at which time pus and organisms may be discharged into the urine. Symptoms of cystitis are manifested. The infection then proceeds to the pelvic mucosa and the ureter. This may lead to stricture and obstruction with hydronephrosis. As the disease progresses, a caseous breakdown of tissue occurs until the entire kidney is replaced by cheesy material. Calcium may be laid down in the reparative process. The ureter undergoes fibrosis and tends to be shortened and therefore straightened. This change leads to a "golfhole" ureteral orifice, typical of an incompetent valve. Vesical irritability develops as an early clinical manifestation of the disease as the bladder is bathed by infected material. Tubercles in the field of involved ureteral orifice finally coalesce and ulcerate with bleeding. With severe involvement, the bladder becomes fibrosed and contracted. This leads to marked frequency. VUR or stenosis and, therefore, UHN may develop. The passage of infected urine through the prostatic urethra ultimately leads to invasion of the prostate and one or both seminal vesicles. There is no local pain. On occasion, the primary hematogenous lesion in the GUT is in the prostate. Prostatic infection can ascend to the bladder and descend to the epididymis. Because this is a slow process, there is usually no pain. If the epididymal infection is extensive and an abscess forms, it may rupture through the scrotal skin, thus establishing a permanent sinus or it may extend into the testicle.

Symptoms and signs

Tuberculosis of the GUT may be present in the following situations:

- Chronic cystitis that not respond to adequate therapy;
- Sterile pyuria;
- Macro or microhematuria;
- Presence of enlarged epididymis with a beaded or thickened vas;
- A chronic draining scrotal sinus;
- Induration or nodulation of the prostate and thickening of one or both seminal vesicles especially in a young man;
- A history of present or past TB elsewhere in the body;
- Presence of tubercle bacilli in the urine by culture or positive PCR.

The extent of the infection is determined by:

- The palpable findings in the epididymis, vasa, prostate and seminal vesicles;
- Specific renal and ureteral lesions as revealed by imaging;
- Involvement of the bladder as seen through the cystoscope;
- The degree of renal damage as measured by loss of function.

There are no classic symptoms of renal TB. Generalized malaise, fatigability, low-grade but persistent fever and night sweats are some of the non-specific complaints. Even vesical irritability may be absent, in which case only proper collection and examination of the urine will afford the diagnosis. Active TB elsewhere in the body is found in less than half of patients with GUT. Because of the slow progression of the disease, the affected kidney is usually completely asymptomatic. On occasion, however, there may be a dull ache in the flank. The passage of a blood clot, secondary calculi or a mass of debris may cause renal and ureteral colic. Rarely, the presenting symptom may be a painless mass in the abdomen. Perinephric abscess may cause an enlarging mass in the flank. A plain film of the abdomen shows obliteration of the renal and psoas shadows. US and CT scans may be more helpful. Renal stones may develop if secondary nonspecific infection is present. Uremia is the end stage if both kidneys are involved.

The earliest symptoms of renal TB may arise from secondary vesical involvement. These include burning, frequency and nocturia. Hematuria is occasionally found and is of either renal or vesical origin. At times, particularly in a late stage of the disease, the vesical irritability may become extreme. If ulceration occurs, suprapubic pain may be noted when the bladder becomes full. When severely damaged, the bladder wall becomes fibrosed and contracted. Stenosis of the ureters or VUR occurs, causing hydronephrotic atrophy. Scarring with stricture formation is one of the typical lesions of TB and most commonly affects the juxtavesical portion of the ureter. Complete ureteral obstruction may cause complete nonfunction of the kidney.

TB of the prostate and seminal vesicles usually causes no symptoms. Prostate and seminal vesicles may be normal to palpation. Ordinarily, however, the TB prostate shows areas of induration, even nodulation. The involved seminal vesicle is usually indurated, enlarged and fixed. The first clue to the presence of TB infection of these organs is the onset of a TB epididymitis. TB of the epididymis usually presents as a painless or only mildly painful swelling. A thickened, non-

tender or only slightly tender epididymis may be discovered. The vas deferens often is thickened and beaded. In the more advanced stages, the epididymis cannot be differentiated from the testis on palpation. This may mean that the testis has been directly invaded by the epididymal abscess. Hydrocele occasionally accompanies TB epididymitis. The idiopathic hydrocele should be tapped so that underlying pathologic changes, if present, can be evaluated (epididymitis, testicular tumor). An abscess may drain spontaneously through the scrotal wall. A chronic draining sinus should be regarded as TB until proved otherwise. In rare cases, the onset is quite acute and may simulate an acute nonspecific epididymitis. If epididymitis is present, the ipsilateral seminal vesicle usually shows changes as well. The ducts of the involved epididymis become occluded. If this is bilateral, sterility results. Abscess of the epididymis may rupture into the testis, through the scrotal wall or both.

Signs of extragenital TB may be found (lungs, bones, lymph nodes, tonsils, intestines). Involvement of the penis and urethra is rare.

Diagnosis

Urinalysis

Persistent pyuria without organisms on culture means TB until proved otherwise. Acid-fast stains done on the concentrated sediment from a 24-hour specimen are positive in at least 2/3 of cases. However, this must be corroborated by a positive culture. If clinical response to adequate treatment of bacterial infection fails and pyuria persists, TB must be ruled out by bacteriologic and imaging.

Cultures for tubercle bacilli from the first morning urine are positive in a very high percentage of cases of TB infection. If positive, sensitivity tests should be ordered. In the face of strong presumptive evidence of TB, negative cultures should be repeated. Three to five first morning voided specimens are needed. It can also be infected with tubercle bacilli or it may become hydronephrotic from fibrosis of the bladder wall or VUR. If TB is suspected, the tuberculin test should be performed. A positive test, particularly in an adult, is hardly diagnostic, but a negative test in an otherwise healthy patient speaks against a diagnosis of TB.

Imaging

A plain X-Ray of the abdomen may show enlargement of one kidney or obliteration of the renal and psoas shadows due to perinephric abscess. Punctate calcification in the renal parenchyma may be due to TB. Renal stones are found in 10% of cases. Calcification of the ureter may be noted, but this is rare. IVP can be diagnostic if the lesion is moderately advanced. The typical changes include:

- A “moth-eaten” appearance of the involved ulcerated calyces;
- Obliteration of calyces;
- Dilatation of the calyces due to ureteral fibrosis;
- Abscess cavities;
- Single or multiple ureteral strictures;
- Absence of function of the kidney.

US and CT also show the calcifications, renal contractions and scars, ureteral and calyceal strictures suggestive of genitourinary TB. US has the advantage of low

cost and low invasiveness. Contrast CT is highly sensitive for calcifications and the characteristic anatomic changes.

Cystoscopic study is indicated even when the offending organism has been found in the urine and IVP show the typical renal lesion. This study clearly demonstrates the extent of the disease. Cystoscopy may reveal the typical tubercles or ulcers of TB. Biopsy can be done if necessary. Severe contracture of the bladder may be noted. A cystogram may reveal VUR.

Treatment

The primary treatment is medical therapy. Surgical excision of an infected organ, when indicated, is an adjunct to overall therapy.

If patient has renal TB, a strict medical regimen should be instituted. A combination of drugs is usually desirable. The following drugs are effective in combination: isoniazid, rifampin, ethambutol, streptomycin, pyrazinamide. It is preferable to begin treatment with a combination of isoniazid, rifampin and ethambutol. It is recommended 2 or 3 months of intensive triple drug therapy daily followed by 3 months of continuation therapy with isoniazid and rifampin two or three times per week. If resistance to one of these drugs develops, one of the others listed should be chosen as a replacement.

TB of the bladder always secondary to renal or prostatic TB. It tends to heal promptly when definitive treatment for the "primary" genitourinary infection is given. Vesical ulcers that fail to respond to this regimen may require transurethral electrocoagulation. Should extreme contracture of the bladder develop, it may be necessary to divert the urine from the bladder or perform augmentation cystoplasty after subtotal cystectomy (ileocystoplasty, ileocecocystoplasty, sigmoidocystoplasty) to increase bladder capacity.

In patients with TB of the epididymis, the prostate is always involved and usually the kidney as well. Only rarely does the epididymal infection break through into the testis. Treatment is medical. If after months of treatment an abscess or a draining sinus exists, epididymectomy is indicated.

Although a few urologists advocate removal of the entire prostate and the vesicles when they become involved by TB, the majority opinion is that only medical therapy is indicated. Control can be checked by culture of the semen for bacilli.

Perinephric abscess usually occurs when the kidney is destroyed, but this is rare. The abscess must be drained and nephrectomy should be done either then or later to prevent development of a chronic draining sinus. Prolonged antimicrobial therapy is indicated. If ureteral stricture develops on the involved side, ureteral dilatations are indicated. The severely involved bladder may cause incompetence of the ureterovesical junction on the uninvolved side. Ureteroneocystostomy cannot be done in such a bladder. Some form of urinary diversion may be required.

16.1. SCHISTOSOMIASIS (BILHARZIASIS)

Etiopathogenesis

Schistosomiasis, caused by a blood fluke, is a disease of warm climates. In its 3 forms (*Schistosoma mansoni*, *Schistosoma japonicum*, *Schistosoma hematobium*) it affects about 350 million people. Schistosomiasis is on the increase in endemic areas because of the construction of modern irrigation systems that provide favorable conditions for the intermediate host, a freshwater snail. This disease principally affects the urogenital system, especially the bladder, ureters, seminal vesicles and the male urethra and prostate gland. Infection with *S. mansoni* and *S. japonicum* mainly involves the colon.

Humans are infected when they come in contact with larva-infested water in canals, ditches or irrigation fields during swimming, bathing or farming procedures. Forktailed larvae, the cercariae, lose their tails as they penetrate deep under the skin. They are then termed schistosomules. They cause allergic skin reactions that are more intense in people infected for the first time. These schistosomules enter the general circulation through the lymphatics and the peripheral veins and reach the lungs. If the infection is massive, they may cause pneumonitis. They pass through the pulmonary circulation, to the left side of the heart and to the general circulation. The worms that reach the vesicoprostatic plexus of veins survive and mature, whereas those that go to other areas die.

The adult *S. hematobium* worm, a digenetic trematode, lives in the prostatovesical plexus of veins. The male is about 10×1 mm in size, is folded upon itself and carries the long, slim 20×0.25 mm female in its “schist,” or gynecophoric canal. In the smallest peripheral venules, the female leaves the male and partially penetrates the venule to lay her eggs in the subepithelial layer of the affected viscus, usually in the form of clusters that form tubercles. The ova are seen only rarely within the venules. They are almost always in the subepithelial or interstitial tissues. The female returns to the male, which carries her to other areas to repeat the process. The living ova, by a process of histolysis and helped by contraction of the detrusor muscle, penetrate the overlying urothelium, pass into the cavity of the bladder and are extruded with the urine. If these ova reach fresh water, they hatch and the contained larvae—ciliated miracidia - find a specific freshwater snail that they penetrate. There they form sporocysts that ultimately form the cercariae, which leave the snail hosts and pass into fresh water to repeat their life cycle in the human host.

The fresh ova excite little tissue reaction when they leave the human host promptly through the urothelium. The contents of the ova trapped in the tissues and the death of the organisms cause a severe local reaction, with infiltration of round cells, monocytes, eosinophils and giant cells that form tubercles, nodules and polyps. These are later replaced by fibrous tissue that causes contraction of different parts of the bladder and strictures of the ureter. Fibrosis and massive de-

posits of eggs in subepithelial tissues interfere with the blood supply of the area and cause chronic bilharzial ulcerations. Epithelial metaplasia is common and SCC is a frequent sequela. Secondary infection of the urinary tract is a common complication and is difficult to overcome. The trapped dead ova become impregnated with calcium salts and form sheets of subepithelial calcified layers in the ureter, bladder and seminal vesicles.

Symptoms and signs

Penetration of the skin by the cercariae causes allergic reactions, with cutaneous hyperemia and itching that are more intense in people infected for the first time. During the stage of generalization or invasion, the patient complains of symptoms such as malaise, fatigue, lowgrade fever, excessive sweating, headache and backache. When the ova are laid in the bladder wall and begin to be extruded, the patient complains of terminal, slightly painful hematuria that is occasionally profuse. This may remain the only complaint for a long time until complications set in, when vesical symptoms become exaggerated and progressive. Increasing frequency, suprapubic and back pain, urethralgia, profuse hematuria and pyuria are likely to occur, with secondary UTIs, ulceration or malignancy. Renal pain may be due to ureteral stricture, VUR or secondary stones obstructing the ureter. Fever, rigor, toxemia and uremia are manifestations of renal involvement.

In early uncomplicated cases, there are essentially no clinical findings. Later, a fibrosed, pitted, bilharzial glans penis, a urethral stricture or fistula or a perineal fibrous mass may be found. A suprapubic bladder mass or a renal swelling may be felt abdominally. DRE may reveal a fibrosed prostate, an enlarged seminal vesicle or a thickened bladder walls.

Diagnosis

Urinalysis usually reveals the terminal-spined dead or living ova, blood and pus cells and bacteria. SCC cells may be seen. The hemogram usually shows leukocytosis with eosinophilia and hypochromic normocytic anemia. Serum Cr and BUN measurements may demonstrate some degree of CRF. A variety of immunologic methods have been used to confirm the diagnosis of schistosomiasis. Positive immunologic tests indicate previous exposure but not whether schistosomiasis is currently present. The cercariae, schistosomules, adult worms and eggs are all potentially antigenic. Adult worms, however, acquire host antigen on their integument that circumvents the immunologic forces of the host. Antibody production may be manifested as hypergammaglobulinemia.

A plain X-Ray of the abdomen may show enlarged hydronephrotic kidney or large tumor in the bladder area. Calcifications or stones may be noted in the kidney, ureter or bladder. Linear calcification may be seen in the ureteral and bladder walls. Punctate calcification of the ureter and a honeycombed calcification of the seminal vesicle may be obvious. IVP may show either normal or diminished renal function and varying degrees of pathology of the upper urinary tracts. These changes include hydronephrosis, dilated and tortuous ureters, ureteral strictures or a small contracted bladder having a capacity of only a few milliliters. Gross irreg-

ular defects of the bladder wall may represent cancer. Abdominal and pelvic CT is replacing IVP as the initial imaging of choice. Retrograde urethrography may reveal a bilharzial urethral stricture. Cystograms often reveal VUR, particularly if the bladder is contracted.

Cystoscopy may show fresh conglomerate, grayish tubercles surrounded by a halo of hyperemia, old calcified yellowish tubercles, sandy patches of mucous membrane and a lusterless ground-glass mucosa that lacks the normal vascular pattern. Other obvious lesions include bilharzial polyps, chronic ulcers on the dome that bleed when the bladder is deflated, vesical stones, malignant lesions, stenosed or patulous ureteric orifices and a distorted, asymmetric trigone. All are signs of schistosomal infection.

Bilharzial cystitis is unmistakable in endemic areas. The presence of schistosomal ova in the urine, together with radiographic and cystoscopic findings, usually confirms the diagnosis. Nonspecific cystitis usually responds to medical treatment unless there is a complicating factor. Tuberculous cystitis may mimic bilharzial cystitis. The detection of tubercle bacilli, together with the radiographic picture, is confirmatory, but TB may occur in a bilharzial bladder. Vesical calculi and malignancy should be diagnosed by thorough urologic examination, although both conditions are common in association with bilharzial bladder. Complications of schistosomiasis are the result of fibrosis, which may be extreme and causes contraction of the bladder neck as well as of the bladder itself. It also causes strictures of the urethra and ureter that are usually bilateral. VUR is a frequent sequela. Secondary persistent infection and stone formation usually complicate the picture still further. SCC of the bladder is common.

Treatment

Praziquantel, metrifonate and oxamniquine are the drugs of choice in treating schistosomiasis. These drugs do not have the serious side effects associated with the older drugs. Cure rates are 70-95%. Niridazole, a nitrothiazole derivative, is effective in treating *S. mansoni* and *S. hematobium* infections. It may be tried against *S. japonicum* infections. Side effects may include nausea, vomiting, anorexia, headache, T-wave depression and temporary suppression of spermatogenesis. Antibiotics or urinary antiseptics are needed to overcome or control secondary infection. Supportive treatment in the form of iron, vitamins and a high-calorie diet is indicated in selected cases.

Surgical treatment may be needed sometimes. Juxtavesical ureteral strictures require resection of the stenotic segment with ureteroneocystostomy. If the ureter is not long enough to reimplant, a tube of bladder may be fashioned, turned cephalad and anastomosed to the ureter. VUR requires a suitable surgical repair. A contracted bladder neck may need TUR. A chronic "weeping" bilharzial bladder ulcer necessitates partial cystectomy. The contracted bladder is treated by enterocystoplasty with placing a segment of bowel as a patch on the bladder. This procedure, which significantly increases vesical capacity, is remarkably effective in lessening the severity of symptoms associated with contracted bladder. SCC requires total cystectomy with urinary diversion if the lesion is deemed operable. Unfortunately, late diagnosis is common.

16.2. FILARIASIS

Filariasis is endemic in the countries bordering the Mediterranean, in south China and Japan, the West Indies and the South Pacific islands.

Etiopathogenesis

Wuchereria bancrofti is a threadlike nematode about 0.5 cm or more in length that lives in the human lymphatics. In the lymphatics, the female gives off microfilariae, which are found in the peripheral blood, particularly at night. The intermediate host is a mosquito, which bites an infected person and becomes infected with microfilariae, which develop into larvae. These are in turn transferred to another human, in whom they reach maturity. Mating occurs and microfilariae are again produced. The adult nematode in the human host invades and obstructs the lymphatics. This leads to lymphangitis and lymphadenitis. In long-standing cases, the lymphatic vessels become thickened and fibrous and there is a marked reticuloendothelial reaction.

Symptoms and signs

In mild cases, the patient suffers recurrent lymphadenitis and lymphangitis with fever and malaise. Not infrequently, inflammation of the epididymis, testis, scrotum and spermatic cord occurs. These structures then become edematous, boggy and at times, tender. Hydrocele is common. In advanced cases with many exposures, obstruction of major lymph channels may cause chyluria and elephantiasis. Varying degrees of painless elephantiasis of the scrotum and extremities develop as obstruction to lymphatics progresses. Lymphadenopathy is common.

Diagnosis

Chylous urine may look normal if minimal amounts of fat are present, but in an advanced case or following a fatty meal, it is milky. On standing, the urine forms layers: the top layer is fatty, the middle layer is pinkish and the lower layer is clear. In the presence of chyluria, large amounts of protein are to be expected. Hypoproteinemia is found and the albumin-globulin ratio is reversed. Both WBC and RBC are found. Marked eosinophilia is the rule in the early stages. Microfilariae may be demonstrated in the blood, which should be drawn at night. The adult worm may be found by biopsy. When filariae cannot be found, an indirect hemagglutination titer of 1/128 and a bentonite flocculation titer of 1/5 in combination are considered diagnostic. Following a fatty meal, endoscopy to observe the efflux of milky urine from the ureteral orifices may differentiate between unilateral and bilateral cases. Retrograde urography and lymphangiography may reveal the renolymphatic connections in patients with chyluria.

Treatment

Diethylcarbamazine (Hetrazan) is the drug of choice, but it is toxic. This drug kills the microfilariae but not the adult worms. Several courses of the drug may be necessary. Antibiotics may be necessary to control secondary infection.

Prompt removal of recently infected patients from the endemic area almost always results in regression of the symptoms and signs in early cases.

Elephantiasis of the external genitalia may require surgical excision.

Mild cases require no therapy. Spontaneous cure occurs in 50% of cases. If nutrition is impaired, the lymphatic channels may be sealed off by irrigating the renal pelvis with 2% silver nitrate solution. Should this fail, renal decapsulation and resection of the renal lymphatics should be performed. This can now be performed laparoscopically with diminished morbidity.

16.3. ECHINOCOCCOSIS (HYDATID DISEASE)

Hydatid disease is common in Australia, South America, Africa, Asia and Europe. Livestock are the intermediate hosts. Canines, especially dogs, are the final hosts.

Etiopathogenesis

The adult tapeworm, which is *Echinococcus granulosus*, inhabits the intestinal tracts of carnivorous animals. Its eggs pass out with the feces and may be ingested by such animals as sheep, cattle, pigs and occasionally humans. Larvae from these eggs pass through the intestinal wall of the various intermediate hosts and are disseminated throughout the body. In humans, the liver is principally involved, but about 3% of infected humans develop echinococcosis of the kidney. If a cyst of the liver should rupture into the peritoneal cavity, the scoleces may directly invade the retrovesical tissues, thus leading to the development of cysts in this area.

Symptoms, signs and diagnosis

If renal hydatid disease is closed and not communicating with the pelvis, there may be no symptoms until a mass is found. With communicating disease, there may be symptoms of cystitis and renal colic may occur as cysts are passed from the kidney. X-Ray films may show calcification in the wall of the cyst and IVP often reveal changes typical of a space-occupying lesion. The cystic nature of the lesion may be demonstrated on US and CT scans. Calcification in the cyst wall may be noted. Scintillation scanning or angiography can also suggest the presence of a cyst. Serologic tests that should be done include immunoelectrophoresis and indirect hemagglutination. The Casoni intracutaneous procedure is unreliable. Retroperitoneal and perivesical cysts may cause symptoms of cystitis or AUR may develop secondary to pressure. The presence of a suprapubic mass may be the only finding. It may rupture into the bladder and cause hydatiduria, which establishes the diagnosis.

Treatment

Nephrectomy is generally the treatment of choice for renal hydatid disease. Aspiration of the cyst is dangerous. Leakage or rupture may occur. Retroperitoneal cysts are best treated by marsupialization and curettage.

17.1. VARICOCELE

A varicocele is defined as dilated and tortuous veins within the pampiniform plexus of scrotal veins most common on the left side. It is the most surgically correctable cause of male subfertility. The varicocele is a disease of puberty and is only rarely detected in boys <10 years of age. Found in 15% of men in the general population, 20-40% of males presenting with primary infertility and 45-80% of men with secondary infertility. Bilateral varicoceles are uncommon in healthy men (<10%) but are palpated in up to 20% of subfertile men.

Pathogenesis

Several anatomic features contribute to the predominance of left-sided varicoceles. The left internal spermatic vein is longer than the right. In addition, it usually joins the left renal vein at right angles. The right internal spermatic vein has a more oblique insertion into the IVC. This particular anatomy in the standing man may cause higher venous pressures to be transmitted to the left scrotal veins and result in retrograde reflux of blood into the pampiniform plexus. Varicoceles are associated with testicular atrophy and varicocele correction can reverse atrophy in adolescents. There is indisputable evidence that the varicocele affects semen quality. A classic semen analysis pattern has been attributed to varicoceles in which low sperm count and motility is found in conjunction with abnormal sperm morphology. The finding of semen abnormalities constitutes the main indication for varicocele surgery in infertile men. Precisely how a varicocele exerts an effect on the testicle remains unclear. Several theories have been postulated. It is likely that a combination of effects results in infertility. Pituitary-gonadal hormonal dysfunction, internal spermatic vein reflux of renal or adrenal metabolites and an increase in hydrostatic pressure associated with venous reflux are also postulated effects of a varicocele. The most intriguing theory of how varicoceles affect testis function invokes an inhibition of spermatogenesis through the reflux of warm corporeal blood around the testis, with disruption of the normal countercurrent heat exchange balance and elevation of intratesticular temperature. Although most men with varicoceles are fertile, but the association of varicoceles with infertility is well established.

Symptoms and signs

Possible clinical manifestations of a varicocele:

- Inguinal, scrotal or testicular pain;
- Testis damage: fibrosis with impaired spermatogenesis, testicular atrophy;
- Infertility: the classic semen abnormalities include decreased motility, low sperm count and increased abnormal forms.

Examination of the scrotum with the patient in the supine and upright positions and while he performs a Valsalva maneuver in the standing position: a varicocele

feels like a “bag of worms “ and should become more prominent when the patient is standing or performing a Valsalva.

- Grade I is small, not grossly visible and palpated only during Valsalva;
- Grade II is moderate size, not grossly visible, but easily palpable in the standing position;
- Grade III is large and grossly visible.

Scrotal Doppler US is diagnostic, when venous diameter >3.5 mm with reflux of the blood.

Semen analysis: varicoceles are associated with low or absent sperm counts, reduced sperm motility and abnormal morphology, either alone or in combination.

Treatment

Several treatment modalities, both surgical and nonsurgical, are available for varicoceles. These include incisional ligation of the veins through the retroperitoneal, inguinal or subinguinal approaches, percutaneous embolization and laparoscopy. The common goal of all treatments is to eliminate the retrograde reflux of venous blood through the internal spermatic veins. Treatments can be compared in terms of expected success rates (semen improvement and pregnancy), cost and outcomes (pain pills, return to work or other activity) and their relative merits can be analyzed.

If watchful waiting is chosen, a pregnancy rate of 16% can be expected. If IVF is chosen, a pregnancy rate of 35% can be expected. An overall complication rate of 1% is associated with the incisional approach, compared with a 4% complication rate for laparoscopy and 10-15% for radiologic occlusion. A significant problem with the radiologic approach is technical failure, meaning the inability to access and occlude the spermatic vein. After varicocele repair in an infertile male, perform semen analysis every three months until either one year has passed or pregnancy occurs.

17.2. HYDROCELE

A hydrocele is an abnormal quantity of peritoneal fluid between the parietal and visceral layers of the tunica vaginalis, the double layer of peritoneum surrounding the testis and which was the processus vaginalis in the foetus. Normally the processus vaginalis becomes obliterated along its entire length, apart from where it surrounds the testis where a potential space remains between the parietal and visceral layers. The adult hydrocele is caused by excessive fluid secretion by the visceral tunica albuginea without adequate reabsorption of this fluid by the parietal peritoneum around the testis.

Pathogenesis

May be primary or secondary. Primary hydroceles develop slowly over the course of years and there is no precipitating event such as epididymo-orchitis or trauma and the underlying testis appears normal on US. Secondary hydroceles may be due to infection, tumor, trauma and represent an effusion between the layers of the tunica vaginalis, analogous to a pleural or peritoneal effusion. In filariasis, obstruction of the lymphatics of the spermatic cord give rise to the hydrocele.

Hydrocele formation is the most common complication reported after nonmicroscopic varicocelectomy with an average incidence of about 7%. Analysis of the protein concentration of hydrocele fluid indicates that hydrocele formation after varicocelectomy is due to lymphatic obstruction. At least half of postvaricocelectomy hydroceles grow to a size large enough to warrant surgical excision due to the discomfort and growth of the hydrocele to a large size. The effect of hydrocele formation on sperm function and fertility is uncertain. The development of a large hydrocele creates an abnormal insulating layer that surrounds the testis. Use of magnification to identify and preserve lymphatics can virtually eliminate the risk of hydrocele formation after varicocelectomy. The management of postvaricocelectomy hydrocele is identical to that for other forms of hydrocele.

Symptoms and signs

Usually painless, unless the underlying testicular disease is painful. A hydrocele has a smooth surface and it is difficult or impossible to feel the testis which is surrounded by the tense, fluid collection. The superior margin can be palpated. It is possible to transilluminate a hydrocele. The light from a torch applied on one side can be seen on the other side of the hydrocele.

Treatment

Men diagnosed with hydroceles, where there is suspicion for concomitant malignancy, should undergo high-resolution scrotal US. If malignancy is suspected, an inguinal approach should be used to allow control of the spermatic cord in preparation for radical orchiectomy. If this approach is taken and no malignancy is encountered, the testis can be spared and the hydrocele can be repaired by one of the techniques.



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