GP Handbook

Renal & Genito-Urinary Medicine

(last update 20111020)

ABC IN SEXUALLY TRANSMITTED DISEASES

Common Conditions

- Non-gonococcal urethritis (NGU)
- Non-specific genital infection (NSGI)
- Genital warts
- Gonorrhoea
- Syphilis

General Principles

- Be non-judgmental in dealing with patients suffering from sexually transmitted diseases (STD)
- Important points in history: date of venereal exposure, sexual contacts since then, use of condoms, LMP in women, and behavioural risk assessment
- Physical examination with special attention on concomitant STD
- Laboratory investigations plus HIV and VDRL screening
- Prompt treatment
- Follow-up for re-testing HIV and VDRL at 90 days
- Contact tracing and follow-up for test of cure are textbook recommendations which may prove difficult to practise in the real world. Health education on safe sex is important, but may sound offensive to sex workers.

Investigations

- Discuss with the patient the pros and cons of full laboratory work-up.
- HIV Ab and VDRL are indicated for all patients because both HIV infection and syphilis are serious conditions that can often be asymptomatic.
- Urinary PCR for Chlamydia is indicated practically for every patient because Chlamydial NGU can often be asymptomatic, especially in male.
- Other tests are mainly microbiological, and indicated according to the presented clinical syndrome.
- Do a pregnancy test (blood or urine) in all cases of secondary amenorrhoea.

CHRONIC KIDNEY DISEASE

Chronic Kidney Disease (CKD) is a relatively new term that includes all renal diseases lasting ≥3 months, irrespective of their pathology.

In addition to the development of end-stage renal disease (ESRD), patients with CKD have an increased chance of developing cardiac events such as myocardial infarct and stroke. The cardiovascular complications occur even at the relatively early stage of renal impairment.

Diagnosis

The diagnosis of CKD depends on the following:

- Kidney damage for ≥3 months as shown by the presence of urine abnormalities like proteinuria or red cells in the urine or abnormalities on X-ray, ultrasound or renal biopsy findings, OR
- The detection of renal impairment as evidenced by the impairment of the glomerular filtration rate (GFR) at <60 mL/minute/1.73 m^2 for ≥3 months.

Staging

Stage	Description	GFR (ml/min/1.73m^2)
1	Kidney damage with normal GFR	≥ 90
2	Mildly reduced GFR	60-89
3	Moderately reduced GFR	30-59
4	Severe reduced GFR	15-29
5	Kidney failure	<15 (or dialysis)

GFR is the best measure of renal function and the staging of CKD is based on GFR. Since formal determination of GFR by timed collection of urine or by isotope studies is cumbersome, in clinical practice GFR can be estimated using one of the following equations, both of which have been partially validated in Chinese. They are however not suitable for use in children.

The MDRD equation

MDRD (Modification of Diet in Renal Diseases) was a study to evaluate the influence of diet on renal progression and the formula for calculating the estimated GFR (eGFR) was a 'spin off '. The MDRD equation is based on the age, gender, race and the serum creatinine of the patient. The following link can assist us in calculating the eGFR using this rather complicated equation: http://www.nkdep.nih.gov/professionals/gfr_calculators/idms_con.htm.

The Cockcroft-Gault (CG) equation

This equation is simpler and the calculation can be done by a simple calculator:

Creatinine clearance (mL/minute) = (140 – Age) x weight (kg) / 72 x serum creatinine

Causes

The main causes of CKD in HK are:

- **Diabetes mellitus (DM)**
- **Hypertension (HT)**
- Others: chronic glomerulonephritis, polycystic kidneys disease, analgesic nephropathy and CKD of 'unknown' aetiology

Good control of HT and DM can greatly reduce the progression of CKD. For DM patients, the onset of microalbuminura is an early sign of nephropathy. Angiotensin-converting enzyme inhibitors (ACEI) or angiotensin receptor blockers (ARB) can prevent the development of diabetic nephropathy.

Even for diabetic nephropathy patients with macroalbuminuria (ie proteinuria detectable with dipsticks), using a combination of ACEI and ARB can significantly slow down renal deterioration.

Treatment

The aims of CKD treatment are to delay or arrest the progression of renal deterioration (renal protection) and the prevention of its complications. It is recommended that CKD patients be referred to a nephrologist when the GFR is around 30 mL/minute.

Treatment of HT

HT and renal impairment form a vicious cycle. The rate of renal deterioration is directly proportional to the systolic BP. For patients with CKD, the target BP should be 130/75 mmHg. For patients with DM nephropathy and heavy proteinuria, a target BP of 125/75 mmHg is recommended. ACEI and ARB, either alone or in combination, are shown to have proteinuria lowering effects (via glomerular hyperfiltration) in addition to the BP lowering effect. Recently, the use of low dose aldosterone antagonists, eg spironolactone (Aldactone) was shown to have additional renal protective effects in combination with ACEI/ARB. This combination allows a more complete blockade of the renal-angiotensin-aldosterone system. The drug could cause hyperkalaemia especially in patients with renal impairment and with concurrent administration of ACEI/ARB.

A recent study showed that aliskiren (Rasilez), the first oral direct rennin inhibitor, might have renal protective effects that were independent of its BP-lowering effect in patients with HT, T2DM, and nephropathy who are receiving the recommended renal protective treatment.

Control of calcium, phosphate and parathyroid

In patients with renal failure, the calcium level is low due to impairment of vitamin D metabolism. There is also phosphate retention due to reduced renal excretion. The parathyroid glands are stimulated by the hypocalcaemia causing secondary hyperparathyroidism. Increased phosphate levels cause an increased chance of vascular calcification. Control of the phosphate retention with phosphate binders and the correction of hyper-parathyroidism by vitamin D analogues were shown to be able to reduce the rate of renal deterioration and prevent vascular complications.

Control of anaemia

Patients with CKD stage 3 and above are usually anaemic. It is now known that some 'uraemic' symptoms such as anorexia, weakness and tiredness are actually anaemic symptoms. Previously renal anaemia had to be treated with blood transfusions, and complications such as infection and iron overload were common. The arrival of erythropoietin revolutionalized the treatment of anaemia. The administration of human recombinant erythropoietin will correct the renal anaemia with relief of the symptoms and improvement in the quality of life.

Other measures

These include control of elevated blood lipids with statins and achievement of good glycaemia control in diabetic nephropathy. Dietary measures such as moderate protein restriction, giving up smoking and reduction of trunkal obesity would also help.

Significance of Urine Protein

The presence of urine protein by dipsticks is a sign of CKD. However, urine dipsticks measure the albumin concentration which is affected by the how concentrated (or diluted) the urine specimen is. A 24-hour urine protein collection gives a reliable and quantitative measurement, but is considered inconvenient by most patients. A simple workaround is to measure the urine albumin and urine creatinine concentration at the same time and express it as a ratio. This cancels out the urine dilution factor. If we express the urine creatinine and the albumin concentration as mg/dL, the albumin/creatinine ratio (urine A/C ratio) will be numerical only. This ratio correlates closely with daily protein excretion in g/1.73 m^2 of body surface area. Thus, a ratio of 6.0 represents daily protein excretion of approximately 6 g/1.73 m^2. Urine A/C ratio is thus simple to use and it useful for the follow-up assessment of the same patient. Another even simpler workaround is to use the ratio of albumin and specific gravity (SG) of the urine.

Early Detection of CKD

In HK, there are > 1000 new kidney failure patients needing dialysis or kidney transplantation every year. The majority of these patients developed end-stage kidney failure because of CKD. As early CKD usually causes no symptoms, a territory-wide screening and detection program for CKD is of great public health importance.

Three most useful screening tests are:

- Routine urinalysis
- Serum creatinine
- MDRD eGFR

CYSTITIS

As in the management of all forms of urinary tract infection, the following are mandatory:

- an MSU for urinalysis and culture (+/- sensitivity tests) and
- a follow-up in 2-3 days when the result of the urine tests become available

Acute Cystitis

Clinical features

- Dysuria, frequency, nocturia, enuresis, incontinence, urethral pain, suprapubic pain, low back pain, hematuria
- Significant fever is unusual
- The onset frequently follows intercourse ("honeymoon cystitis")
- Urinary frequency and urgency can be caused by urinary tract infection (UTI), diuretic use, caffeine, tea, drugs (such as theophylline), interstitial cystitis, vaginitis, pregnancy, pelvic mass…etc.

Causes

- Colonization by faecal flora, usually *Escherichia coli* (75-95%)
- *Staphylococcus saprophyticus* predominantly affect young, sexually active ladies
- Other organisms include Klebsiella (5%), Enterobacter, Proteus, Pseudomonas

Mid-stream urine (MSU) testing – urinalysis and culture

- ***Urine cultures may not be needed in young non-pregnant females with symptoms of simple cystitis.***

- Pyuria - > 5 WBC per high-power field (HPF)
  Pyuria (ie detection of leukocyte esterase in urine) correlates poorly with the definitive diagnosis of cystitis; pyuria may be present in the absence of cystitis and vice versa. Classic symptoms in a patient with previously documented cystitis is about 70% predictive of another cystitis; one can consider treatment even in absence of positive MSU findings.

- Bacteriuria – by microscopy: 2 organisms per HPF; by culture: 10^5 organisms/ml

- Dipstick positive for nitrites +/- protein
  A combination of negative dipstick test for nitrite and leukocyte esterase shows a negative predictive value for UTI of 96.9% and a specificity of 98.7%. It means, in the absence of both urine nitrite and leukocyte esterase activity, urinary tract infection is unlikely.

- Gross or microscopic haematuria

- Culture and sensitivity tests (C/ST) are recommended.
  The traditional cut-off level of significant bacteriuria count of 10^5 colony forming units of bacteria per ml of urine is mainly for diagnosing upper tract. As patients tend to drink more fluid when experiencing cystitis symptoms, this fluid loading may result in reduced urinary bacterial count. Moreover, frequent voiding during cystitis can itself decrease the bacterial count in urine. Therefore, some authors suggest that a lower bacteriuria cut-off level of 10^3 uropathogens, should be adopted for diagnosing cystitis.

Antibiotics

- Simple, uncomplicated cystitis in female patients: 3-5-day course.
- Male patients and complicated cystitis (eg pregnancy, elderly patients, recurrent cystitis, diabetics): 7-10-day course.
- First line: Augmentin 1gm bd or Ofloxacin (Oflon) 200mg bd. The latter is contraindicated in pregnancy (document LMP where appropriate).
- Nitrofurantoin 50-100 mg qid is very effective. Nausea is common. Absorption increased when taken with food.
- If the culture result shows that the organism is resistant to the drug prescribed, a change in antibiotics is indicated only if the patient is still symptomatic at follow-up. Many drugs reach such high levels in the urine that standard sensitivity testing may not reflect the in vivo antibiotic activity.
- Pyuria without bacteriuria should be suggestive of: mycobacterium tuberculosis (TB), or chlamydia infection (in which case a PCR test on urine is indicated).

Urinary analgesics

- Flavoxate (Urispas) 200mg bd is a smooth muscle relaxant. It works by relaxing the detrusor muscle of the urinary bladder, and can therefore be used to relieve urinary incontinence, and reduce the pain, urgency and frequency that occurs in urinary tract infection (including prostatitis).
- Phenazopyridine (Uroprin) is a topical analgesic on the mucosa of the urinary tract. It is used to relieve pain, burning sensation, urgency and frequency. A dosage of 200 mg tds for 2 days is effective in reducing dysuria, but may mask the symptoms even if the organism is resistant to the antibiotic prescribed. Inform the patient that this medication will produce an orange tinge in urine and tears. Warn the patient not to wear contact lenses because they may become discoloured.

Although there have been no important drug interactions reported in association with these urinary analgesics, there are also no well-established indications to prescribe them.

This is unresolved, recurrent, or persistent bladder infection. Under-utilization of MSU examination, coupled with unscrupulous use of phenazopyridine, is thought to contribute to the aetiology of chronic cystitis.

Recurrent Cystitis

When patients present with recurrent episodes of cystitis, more detailed investigations should be performed. Urine cultures during every attack of cystitis are essential for establishing the diagnosis, as well as aiding subsequent management. If recurrent cystitis is caused by the same pathogen, this is highly suggestive of treatment failure or relapsing infection.

Treatment failure can be due to resistant microbial strains, inappropriate antibiotics prescription or poor drug compliance. However, if there is no evidence to suggest treatment failure, the possibility of relapsing infection should be seriously considered.

Relapse is often associated with urinary tract abnormalities including urolithiasis, vesico-ureteric reflux, presence of significant residual urine and bladder diverticulum. If the underlying complicating factors could not be corrected, long-term suppressive antibiotics therapy is needed to help to prevent frequent infections.

Re-infection is diagnosed when patients have repeated positive urine cultures of different micro-organisms. Possible causes include diabetes, poor hygiene, and immuno-compromised states.

There are patients who are labelled as suffering from 'recurrent cystitis' but never have had actual documented positive cultures. These patients should receive further workup. If haematuria is

present, urgent investigation is necessary to rule out serious bladder pathology such as a tumour (the so called 'malignant cystitis') or a bladder stone. Urine for cytology, KUB +/- cystoscopy should also be performed to facilitate subsequent urological management.

Treatment

- Prescribe a full 7-10-day course of antibiotic based on C/ST results.
- Increasing fluid intake and passing water more frequently may help minimizing recurrence.
- If cystitis develops in relationship to sexual intercourse, use Trimethoprim + Sulphamethoxazole (Co-Trimoxazole) tab 1 after coitus may prevent cystitis. Ofloxacin (Oflon) 200mg may also be used. Patients should void immediately after an intercourse.
- The use of a diaphragm for birth control may exacerbate recurrent cystitis secondary to incomplete voiding.
- Vaginal oestrogen cream (0.5-2 gm qd) lowers the incidence of cystitis in postmenopausal women.
- The patient should be instructed to wipe from front to back after a bowel movement to avoid bringing infective organisms toward the urethra.
- Long-term prophylaxis is with Trimethoprim + Sulphamethoxazole (Co-Trimoxazole) tab 1 qd, Nitrofurantoin 50-100 mg qd; an urine acidifier may prove useful in those with recurrent cystitis not related to intercourse.
- Advise the patient to avoid irritating underwear (cotton preferred over synthetic material).

Asymptomatic Bacteriuria

Treat only those who:

- are pregnant
- undergo a urological procedure
- have an indwelling catheter just removed
- have diabetes mellitus
- are children

Asymptomatic bacteriuria is not an indication for treatment with antibiotics in the elderly, since treatment does not affect their clinical outcome.

ERECTILE DYSFUNCTION

Erectile dysfunction is the persistent and consistent or recurrent inability of a man to **attain** and/or **maintain** a penile erection sufficient for satisfactory sexual performance. A minimum duration of three months is generally accepted as definition. With a local prevalence of 9.6%, it is one of the earliest and most useful clinical indicators of cardiovascular risk.

According to an American study, 52% of men above aged 40-70 had some degree of erectile dysfunction and in 10% the loss of erection is complete. In a survey by the Hong Kong Urological Association in 2003, 62% of men aged 40-80 in Hong Kong had erectile dysfunction. Erectile dysfunction is a symptom based on patient"s complaint. The symptom is a starting point for searching for underlying causes and for initiating symptomatic treatment.

The diagnosis of erectile dysfunction should be distinguished from other sexual dysfunctions. Premature ejaculation may actually be more prevalent than erectile dysfunction. Premature ejaculation means ejaculation occurring sooner than desired either before or shortly after penetration, causing distress to one or both partners. Over 90% of premature ejaculation patients have intravaginal ejaculation with latency time of less than 60 seconds.

Categories

Psychogenic (+/- mood disorders)

- Commonly presented as loss of libido and over-inhibition
- Performance anxiety, relationship problems, stress, depression, OCD

Vasculogenic

- Atherosclerosis, trauma, hypertension, DM
- Up to 40% of patients with IHD suffer from erectile dysfunction
- Inadequate arterial flow or impaired veno-occlusion

Drug-induced

- Antihypertensives: beta-blockers, diuretics
- Cigarette smoking
- Alcohol abuse
- Antidepressants and antipsychotics
- Antiandrogens: cyproterone acetate

Neurogenic

- Stroke, pelvic injury, Alzheimer's disease, diabetic neuropathy
- Failure to initiate nerve impulse or interrupted neural transmission

Hormonal

- Hypogonadism, hyperprolactinaemia
- Loss of libido

Others

- Aging
- BPH, DM, IHD, CRF

History

The aim is to define the problem, assess the sexual drive, orgasmic capabilities and overall sexual satisfaction.

- Last successful intercourse
- Relationship with partner
- Presence/rigidity of morning erection
- Drug history
- Mental status
- Situational vs persistent
- Organic causes: eg DM

Examination

- Vascular system: peripheral vascular disease, hypertension
- Neurological system: peripheral neuropathy
- Genitalia: testicular deformities
- Prostate: hypertrophy, cancer
- Blood pressure

Investigations

- Total and free testosterone
- Prolactin
- Blood glucose
- Lipid profile
- PSA

Phosphodiesterase Inhibitors (PDE5-Is)

Preparations

- Viagra (sildenafil): 25mg, 50mg, 100mg – the first available
- Cialis (tadalafil): 10mg, 20mg – the longest-acting
- Levitra (vardenafil): 5mg, 10mg, 20mg – the newest

Side effects

- Common: headache, flushing, dyspepsia, nasal congestion, altered (blus tinge, increase sensitivity to light)
- Rare: acute blindness (nonarteritic anterior ischaemic optic neuropathy, NAION), hypotension

Special precautions

- Use the low dose preparations in the elderly, renal failure, hepatic impairment
- Drug interaction: use the lowest possible dosage with concomitant use of P450 inhibitors (eg erythromycin, azole anti-fungals, protease inhibitors, and cimetidine), concomitant use of alpha-blockers

Contraindication

- Nitrates (within 24 hours with Viagra and Levitra, and within 48 hours with Cialis)

Information for patients

- Follow-up is essential
- Viagra and Levitra should be administered about 1 hour prior to sexual stimulation;

Cialis can be taken from 30 minutes to 12 hours prior to sexual stimulation

- Efficacy of Viagra and Levitra may persist up to 4 hours post-dose; efficacy of Cialis may persist up to 36 hours
- Viagra and Levitra should be taken on an empty stomach or after a low fat meal; Cialis doesn't seem to interact with food
- Sexual stimulation is necessary
- Success is often dose dependent (max doses: Viagra 100mg, Levitra 20mg, Cialis 20mg), and results tend to improve after 6-8 attempts

If initial treatment of PDE%-Is fails, ask the patients:

- Where and how did you obtain the medication?
- How many times did you ever take it?
- What's the maximum dose you took?
- Do you know sexual stimulation is needed?
- When did you start to perform intercourse after taking the medication?
- What was the interval between taking the medication and mealtime?
- Did you drink alcohol while taking the medication?
- How was your mood when you take the medication?
- Do you have other health problems?

GENITAL HERPES

Genital herpes is a common, highly infectious venereal disease usually presenting with recurrent outbreaks of blisters or groups of small ulcers (open sores) on and around the genitals in both men and women. Genital herpes is extremely widespread, largely because it is so contagious. Carriers can transmit the disease between outbreaks.

Epidemiology

- 1432 (21 cases per 100,000 population) [2002]
- As many as 80-90% of those infected fail to recognize herpes symptoms or have no symptoms at all.

Diagnosis

- Mainly clinical, although the symptoms and signs associated with HSV-2 can vary greatly.
- HSV infections can be difficult to diagnose between outbreaks.
- Gold standard: viral culture
- Non-specific immunoassays for HSV antibody, which are unable to reliably distinguish between the HSV-1 and -2, offer very little help to clinicians.

Treatment

It is recommended to treat all clinically suspicious cases, even if solid laboratory tests are not available.

First attack and further outbreaks

- Aim: symptomatic and suppressive (no curative treatment available)
- Acyclovir 200mg 5x/day for 5 days has the longest clinical safety record
- Newer anti-viral medications (Famvir and Valtrex), have similar efficacy and an advantage of less frequent dosing.
- The anti-viral therapy should be extended to 10 days if symptoms persist.

Prophylaxis

- Indicated in suppression/prevention of herpes infection in immunosuppressed patients and patients suffering from frequent outbreaks
- Acyclovir 400mg bd regularly
- Therapy should be interrupted periodically at intervals of 6-12 months, in order to observe possible chances in the natural history of the disease.

GENITAL WARTS

Please cross refer to the chapter "Viral Skin Conditions" in the section "Skin".

Epidemiology

- 3245 (48 cases per 100,000 population) [2002]
- Anogential warts are caused by some specific genotypes of human papilloma virus (HPV).

Diagnosis

- CLINICAL.
- Skin biopsy may rarely needed.
- Diagnosis of HPV infection, requiring HPV DNA PCR, is not indicated in routine management of genital warts.

Treatment

- There is no cure of the infection but removal of clinical lesions can be achieved by either surgery or medications.
- Surgical: Excision, CO2 laser vapourization, cryosurgery…etc.
- Medical: Local application of podophyllotoxin (Wartec). Intralesional or systemic alpha interferon injection, intralesional bleomycin injection are reserved for specialist use.

GONORRHOEA & NGU/NSGI

Epidemiology

- Gonorrhoea: 3287 (48 cases per 100,000 population) [2002]
- NGU: 7084 (104 cases per 100,000 population) [2002]
- NSGI: 7066 (104 cases per 100,000 population) [2002]
- 21% of the gonococcal culture isolates were beta-lactamase positive
- Genital discharge is the commonest presentation accounting for more than 3/4 of symptomatic cases in public STD clinics.

Pathogens

- Gonorrhoea: Neisseria gonorrhoeae
- NGU/NSGI: Chlamydia trachomatis, Mycoplasma genitalium, Ureaplasma urealyticum, other non-specific organisms

Clinical Presentation

- Incubation periods for both conditions are usually within 3 weeks of exposure. They varies so greatly as to render them not useful in making diagnosis.
- In clinical practice, treating both conditions together is logical and recommended by WHO.

Investigations

- The gold standard for identifying gonorrhoea is CULTURE. Special transport medium is required. Serological examinations are NOT proper tests for confirmation of current infection.
- Urinary PCR for Chlamydia is useful in diagnosing current infection, and test of cure.
- Since we recommend treating both gonorrhoea and NGU/NSGI together, gonococcal culture may seem unnecessary in our daily practice.

Treatment

- Gonorrhoea: Single dose of ceftriaxone (Broadced) 250mg im, or azithromycin (Zythromax) 1gm PO. A lot of patients feel more reassured with injections.
- NGU/NSGI:
  Single dose of azithromycin (Zithromax) 1gm PO, or
  Multiple doses of doxycycline (Doxymycin) 100mg bd for 2/52, or ofloxacin (Oflon) 200mg bd for 2/52
- In short, a patient presenting with a syndrome of urethritis can be treated with ceftriaxone 250mg im stat plus doxycycline 100mg bd for 2/52, with a single dose of azithromycin 1gm PO stat as an insurance according to the clinical situaion.

HAEMATURIA

Haematuria may be a symptom of conditions ranging from something benign and requiring no treatment, to malignant diseases that demand long-term specialist care. Most of our patients presenting with persistent haematuria (gross or microscopic) are adults who are otherwise apparently healthy, and the most likely cause is **GN (GN)**, of which **IgA nephropathy** is the commonest type of primary GN.

Three Key Questions

- Is the haematuria transient or persistent?
- Are there any clues from the history or physical examination that suggest a particular diagnosis?
- Does the haematuria originate from a glomerular or an extra-glomerular source?

History

Other common primary glomerular diseases are thin-basement-membrane disease (benign familial haematuria) and hereditary nephritis (when there is a positive family history of renal failure). Polycystic kidney disease can also run in families and should be considered when there is a family history of renal failure. Occasionally nephritis can be the primary presentation of SLE in women. Systemic enquiry revealing arthralgia, alopecia, spontaneous abortion or sun sensitivity is suggestive of SLE. A recent upper respiratory infection suggests either IgA nephropathy or post-infectious GN (less common nowadays). Concurrent pyuria and dysuria point towards urinary tract infection. A history of unilateral loin or groin pain could indicate ureteric obstruction with a stone or blood clot.

Examination

Abdominal examination may reveal palpable enlarged kidneys in polycystic kidney disease, but is usually unremarkable in GN. Loin tenderness may indicate urinary stones. Signs of advanced renal failure are usually obvious, and associated findings for SLE should be actively looked for.

Investigation

All patients with gross haematuria warrant a thorough investigation, because ~25% of cases are due to urological cancers. Complete urological evaluation includes history and physical examination, laboratory analysis (blood and urine tests) and radiological imaging (USG, IVU or CT) of the upper urinary tract followed by cystoscopy.

Identification of glomeruli as the source of bleeding is important as further work-up for serious urological diseases is unnecessary in glomerular bleeding.

Urinary evidence of glomerular bleeding

- red cell casts (essentially pathognomonic)
- dysmorphic RBCs
- proteinuria of greater than 500mg/day

The absence of these findings does not exclude glomerular disease. On the other hand, the presence

of blood clots in the urine makes haematuria unlikely to be glomerular in origin. Transient haematuria due to fever, trauma or exercise is not uncommon. We should, therefore, confirm the presence of persistent haematuria by repeating urinalysis (macro- and micro-) on separate occasions. We should avoid performing urine tests in women from a couple of days before to 7 days after the end of menstruation.

The presence of crystals on urine microscopy, eg urate crystals, is suggestive of renal stones as the cause of haematuria. Urine samples should also be sent for bacterial culture and antibiotic sensitivity tests. Sterile pyuria means renal tuberculosis until proven otherwise. Since urological malignancies are uncommon in patients below the age of 50, urine cytology and cystoscopy are probably not necessary in them. In lupus nephritis, serum complement levels (C3 and C4) may be lowered, and, ANA and Anti-dsDNA may be raised. Serum IgA level (approximately 50%) may be raised in IgA nephropathy. HBsAg is positive in HBV-related GN.

Imaging techniques such as renal ultrasound, IVU and CT are usually unremarkable in GN but are useful to detect renal stones, polycystic kidneys, and renal cell carcinoma.

Renal biopsy
This should be considered when GN is suspected and significant proteinuria and/or renal impairment. Renal biopsy is not necessary when there is only isolated haematuria where IgA nephropathy and thin-basement-membrane disease are the most likely causes.

Microscopic Haematuria

Always consider contamination – presence of epithelial cells or bacteria.

Dipstick testing
A positive dipstick is simply a colour change resulted from oxidation of a test-strip reagent; it does not confirm the presence of RBCs.

False positives: haemoglobinuria, myoglobinuria, concentrated urine, dehydration, presence of oxidizing agents (eg bleaching powder).

Asymptomatic patients who have a positive dipstick test and negative microscopic urinalysis can be described as having **dipstick pseudohaematuria**.

When to investigate?
- proteinuria
- renal insufficiency
- red cell casts in urine
- dysmorphic RBCs in urine

Patients < 40 years of age with asymptomatic microscopic haematuria and no risk factors of urological diseases can be managed conservatively.

Follow-Up

As haematuria can precede the diagnosis of bladder cancer by years, follow-up becomes important in high-risk patients (eg > 40 years old, smokers, environmental/occupational exposures to paint components, polycyclic aromatic hydrocarbons (PAHs), diesel exhausts, and aromatic amines).

Consideration should be given to repeating urinalysis and voided urine cytology at 6, 12 and 36 months.

SYPHILIS

Epidemiology

- 1061 (16 cases per 100,000 population), of which 241 were either primary or secondary syphilis [2002]

Serology

- False-negatives can appear for up to 3 months after infection. False-positives also occur.
- Screening test: VDRL (false positives in viral infection, autoimmune diseases…)
- Confirmatory tests: FTA-ABS or TPHA. In practice, both of these tests are ordered in case of a positive VDRL.

Medications

Procaine penicillin (NOT AVAILABLR IN HK STARTING 2011)
The gold standard for treatment of syphilis is consecutive daily intramuscular injections with procaine penicillin. The dosage and duration of treatment are determined by the clinical presentation. e.g. chancre, secondary mucocutaneous manifestations, neurosyphilis, etc. If no clinical staging is possible (as is usually the case), serological staging (eg RPR or VDRL titres) determines the treatment regime.

Benzathine penicillin (NOT AVAILABLR IN HK STARTING 2011)
Benzathine penicillin as a single IM injection will adequately treat primary and secondary syphilis, or sero-positive syphilis with a VDRL or RPR titre of 1:16 or higher. This same dose can be given to sexual contacts of the above groups as epidemiological treatment. As benzathine penicillin DOES NOT cross the blood brain barrier it is only suitable for use in treating latent syphilis (VDRL or RPR titre< 8) if the CSF is normal. Benzathine penicillin DOES cross the placenta and is therefore suitable for treating pregnant women with early syphilis.

Alternative medications
Tetracycline, erythromycin, and ceftriaxone have shown antitreponemal activity in clinical trials. When penicillin was still available, they were used only in patients allergic to penicillin. According to the 2010 CDC STD treatment guidelines, a course of ceftriaxone is effective for treating early syphilis, although the optimal dose and duration (10- or 14- days) have not been established.

The above guidelines also cite the effectiveness of azithromycin in treating early syphilis. Its use in men who have sex with men (MSM) or pregnant women is contraindicated. A 2010 study by Hook et al showed a single dose of azithromycin (2 gm PO) to be equivalent to benzathine penicillin G (2.4 million units IM) in patients with early syphilis without HIV.

Treatment Regimes

For penicillin, 50mg = 80,000 IU (Injectable penicillin not available in HK starting 2011)

Early syphilis - primary, secondary and early latent (<2 years duration)

- procaine penicillin 1gm IM QD x 10 days (Not available in HK starting 2011)

- benzathine penicillin 1.8gm IM stat (Not available in HK starting 2011)
- ceftriaxone 250mg IM x 14 days
- azithromycin 2gm PO stat
- doxycycline 100mg PO TDS x 21 days
- amoxycillin 3.0gm PO BD for 14 days (with 1gm probenocid PO QD)

Latent syphilis (> 2 years duration)

- procaine penicillin 1gm IM QD x 15 days (Not available in HK starting 2011)
- benzathine penicillin 1.8gm IM weekly for 3 weeks (Not available in HK starting 2011)
- ceftriaxone 250mg IM x 14 days

Neurosyphilis (or where CSF examination not performed)

- benzyl penicillin 2-4 gm IV Q4H x 10 days (Not available in HK starting 2011)
- procaine penicillin 1gm IM QD x 21 days (Not available in HK starting 2011).
- doxycycline 100mg PO TDS x 21 days.

Congenital syphilis

- Refer

HIV patients

- Refer.

URETHRAL DISCHARGE

General Information

A urethral discharge means the appearance of yellow pus, or muco-pus at the urethra at the tip of the penis or at the vagina. It should not be confused with the clear discharge of lubricating mucus from the urethra in the male following sexual excitement. A yellow discharge appearing a few days after a venereal exposure is almost certainly a sign of an STD.

Urethritis is classified as either gonococcal urethritis (GCU) if caused by *Neisseria gonorrhoeae*, or non-gonococcal urethritis (NGU) if caused by other organisms. *Chlamydia trachomatis* or *Ureaplasma urealyticum* are the most frequent causes of NGU, which occurs more frequently than gonococcal urethritis worldwide. Although the clinical spectrum of gonococcal urethritis and non-gonococcal urethritis differ, there is often so much overlap that any differentiation cannot be based reliably on clinical features alone.

Laboratory Tests

Urethral discharge
Urethral discharge for Gram stain, routine culture, gonococcal smear and culture - urethral milking may be needed to collect a good specimen.

Urine

- First voided 10ml of urine for chlamydia PCR. The patient should not pass urine for at least 2 hours before testing. Clinical studies have shown that PCR detects about 15% more chlamydial infections than does culture with a specificity >99%. In addition, the test is able to utilize bloody specimens which are not compatible with culture.

- MSU for routine culture and sensitivity tests. Some laboratories including Bright Growth Medical Laboratory perform a routine Gram stain on all urine specimens for culture. Check with the receiving laboratory if necessary.

- Urine PCR for gonorrhoea is only indicated where the patient is an asymptomatic contact of a known gonorrhoea case.

Blood
Screening for HIV and VDRL - document on the notes if the patient does not consent to such blood tests. There is no useful serological test for gonorrhoea. The previous GCFT (gonococcal complement fixation test) is obsolete. The HSV-II antibody test may give rise to confusing results, especially in patients with a known history of herpes simplex type I infections, and is not recommended.

Treatment

In settings where laboratory tests are refused by the patient (which is not uncommon), or are unavailable on site, treatment of presumptive urethritis is justified in symptomatic men. In these cases treatment should be given to cover both gonococcal and non-gonococcal urethritis.

Gonococcal urethritis

- Ceftriaxone (Broadced) 250mg im single dose, OR
- Azithromycin (Zithromax) 2gm PO single dose (ie 8 cap of Zithromax 250mg)

Chlamydial urethritis

- Doxycycline (Doxymycin) 100mg bd PO for 1 week, OR
- Ofloxacin (Oflon) 200mg bd PO for 1 week, OR
- Ciprofloxacin (Ciproxin) 500mg bd PO for 1 week, OR
- Azithromycin (Zithromax) 1gm PO single dose (ie 4 cap of Zithromax 250mg), OR Erythromycin 500mg bd for 14 days (mainly in pregnancy)

Prolonged treatment (eg for 2 weeks) may be necessary in cases with complications like epidydymo-orchitis or other concomitant infections. Although a single dose of Zithromax 2gm PO may seem to be the best treatment covering both gonococcal and chlamydial urethritis, it is seldom used alone, because most patients feel insecure with single dose treatment. In fact, quite many of them actually see injections as the mainstay of treatment for any STD.

Presumptive urethritis
Taking into considerations factors like patient's expectation, variation in absorption, risk of concomitant infections, and compliance, our latest recommendation for treatment of presumptive urethritis is:-

(1) Broadced 250mg im single dose, AND
(2) Zithromax 2gm PO single dose (ie 8 capsules of Zithromax 250mg), AND
(3) Doxymycin 100mg bd PO for 1 week, OR Ciprofloxacin 500mg bd PO for 1 week

URINARY STONES

Background

Acute passage of a kidney stone from the renal pelvis through the ureter gives rise to pain at times so excruciating that it has been likened to the discomfort of childbirth.

Most calculi arise in the kidney when urine becomes supersaturated with a salt that is capable of forming solid crystals. Symptoms arise as these calculi become impacted within the ureter as they pass toward the urinary bladder.

About 10% of the population will have at least one episode of urinary stone in their lifetime. An epidemiological study on renal calculi in the Chinese population revealed that the prevalence rate was 8% and 5% in men and women respectively. Moreover, up to 50% of patients would have a recurrence within 10 years after their initial stone or stones were cleared. The male-to-female ratio is approximately 3:1. Peak onset of symptomatic nephrolithiasis is in the 3rd and 4th decades of life.

Beware of the patient > 60 years with an apparent first kidney stone. Consider the possibility of a symptomatic abdominal aortic aneurysm, and rule out this possibility before pursuing the diagnosis of nephrolithiasis. Use bedside ultrasonography if the patient's condition is potentially unstable. CT scan is a reasonable alternative in the patient in stable condition.

Nephrolithiasis in children is rare. In September 2008, there were media reports saying that melamine* was found in some infant formulae produced in China, causing kidney stones and even fatal cases of kidney failure in infants. Fortunately none of the melamine contaminated infant formulae including are found to be available in HK via normal import channels.

** Melamine (also known as tripolycyanamide) is an industrial chemical used for the production of melamine resins. It is the same chemical involved in a massive pet food recall in the US in 2007. It is not supposed to be added to any food ingredients, but unscrupulous suppliers in China sometimes mix it in to make foodstuffs appear to be high in protein. Melamine is nitrogen rich, and standard tests for protein in bulk food ingredients measure levels of nitrogen.*

Melamine has low acute toxicity when taken orally. However, chronic excessive exposure to melamine has been found to cause urinary stones in experimental animals. Compared to adults, infants are more susceptible to the damage caused by melamine because they weigh much less, and milk is their major food.

History

Most calculi originate within the kidney and proceed distally, creating various degrees of urinary obstruction as they become lodged in narrow areas, including the ureteropelvic junction, pelvic brim, and ureterovesical junction. Location and quality of pain are related to position of the stone within the urinary tract. Severity of pain is related to the degree of obstruction, presence of ureteric spasm, and presence of any associated infection.

- Stones obstructing the ureteropelvic junction may present with mild-to-severe deep flank pain without radiation to the groin.
- Stones impacted within the ureter cause abrupt, severe, colicky pain in the flank and radiating to the genital area. Nausea and vomiting is common.
- Stones lodged at the ureterovesical junction also may cause irritative voiding symptoms, such as urinary frequency and dysuria.
- Calculi that have entered the bladder are usually asymptomatic and are passed relatively easily during urination.

Physical Examination

The classic patient with renal colic is writhing in pain, pacing about, and unable to lie still, in contrast to a patient with peritoneal irritation, who remains motionless to minimize discomfort.

Fever is not part of the presentation of uncomplicated nephrolithiasis. If present, suspect infected hydronephrosis, pyonephrosis, or perinephric abscess.

A common finding in ureterolithiasis is flank tenderness to palpation or percussion due to dilation and spasm of the ureter from transient obstruction as the stone passes from the kidney to the bladder.

Aetiology

There are 4 basic chemical types of renal calculi.

Calcium stones (75%)
Calcium oxalate, calcium phosphate, and calcium urate are associated with the following disorders:

- Hyperparathyroidism - treated surgically or with orthophosphates if the patient is not a surgical candidate
- Increased gut absorption of calcium - the most common identifiable cause of hypercalciuria, treated with calcium binders or thiazides plus potassium citrate
- Renal calcium leak - treated with thiazide diuretics
- Renal phosphate leak - treated with oral phosphate supplements
- Hyperuricosuria - treated with allopurinol, low purine diet, or alkalinizing agents such as potassium citrate
- Hyperoxaluria - treated with dietary modification, oxalate binders, vitamin B-6, or orthophosphates
- Hypocitraturia - treated with potassium citrate
- Hypomagnesuria - treated with magnesium supplements

Struvite (magnesium ammonium phosphate) stones (15%)
Struvite stones are associated with chronic UTI with gram-negative rods capable of splitting urea into ammonium, which combines with phosphate and magnesium.

- Usual organisms include Proteus, Pseudomonas, and Klebsiella species. *E coli* is not capable of splitting urea and, therefore, is not associated with struvite stones.
- UTI does not resolve until the stone is removed entirely.
- Urine pH is typically > 7.

Uric acid stones (6%)
These are associated with urine pH < 5.5, high purine intake (eg offals, legumes, fish, meat extracts, gravies), or malignancy (ie rapid cell turnover). ~ 25% of patients with uric acid stones have gout.

Cystine stones (2%)
Cystine stones arise because of an intrinsic metabolic defect resulting in failure of renal tubular reabsorption of cystine, ornithine, lysine, and arginine. Urine becomes supersaturated with cystine with resultant crystal deposition. These are treated with low-methionine diet (unpleasant), binders such as penicillamine or a-mercaptopropionylglycine, large urinary volumes, or alkalinizing agents.

Drug-induced stone disease
A number of medications or their metabolites can precipitate in urine causing stone formation. These include indinavir; atazanavir; guaifenesin; triamterene; silicate (overuse of antacids containing magnesium silicate); and sulfa drugs including sulfasalazine, sulfadiazine, acetylsulfamethoxazole,

acetylsulfasoxazole, and acetylsulfaguanidine.

Investigations

Urinalysis
One retrospective study found that 67% of patients with ureterolithiasis had > 5 RBC per high power field (hpf). In addition, 95% have haematuria if screened with microscopy plus urine dipstick testing (degree of haematuria NOT predictive of stone size or likelihood of passage).

Pyuria (> 5 WBC/hpf on a centrifuged specimen) in a patient with ureterolithiasis should prompt a careful search for signs of infected hydronephrosis. Obtain a complete blood count (CBC), creatinine, and urine culture. Treatment with antibiotics is indicated in patients with ureterolithiasis and pyuria. Review the patient within 24 hours, or admit the patient to hospital if the patient has any signs of infected hydronephrosis (fever, elevated WBC count, elevated creatinine).

A urine pH > 7 suggests presence of urea-splitting organisms, such as Proteus, Pseudomonas, or Klebsiella species, and struvite stones; a urine pH < 5 suggests uric acid stones.

KUB
Multiple studies show that KUB has low (40-50%) sensitivity and specificity for diagnosing ureterolithiasis. It is more useful at follow-up.

NB Most stones will appear larger on KUB radiograph than on CT, with CT-based measurement of maximum stone dimension approximately 12% smaller compared with a KUB-based measurement.

Ultrasonography (USG)
This radiation-free and contrast-free investigation is useful in pregnant patients.

Non-contrast computerized tomography (NCCT)
NCCT has a sensitivity of 95-100% and superior specificity and accuracy compared with IVU, and has become the gold standard in diagnosing urinary stones.

Other advantages of NCCT include rapid (< 5 min) acquisition time, avoidance of intravenous contrast, and potential for diagnosis of other pathologies including AAA, pancreatitis, appendicitis, ovarian disorders, diverticular disease, and biliary tract disorders.

NCCT however gives no information on renal function or the degree of urinary obstruction.

IVU
Prior to the advent of NCCT, IVU was the test of choice in diagnosing ureterolithiasis. It is widely available and fairly inexpensive but less sensitive than NCCT.

Disadvantages include radiation exposure and risk of nephrotoxicity or anaphylactoid reaction to contrast agent. IVU is relatively contraindicated in pregnant or dehydrated patients or if serum creatinine level > 180 µmol/L. IVU is contraindicated in patients with a history of contrast-induced anaphylaxis. False-negative results usually occur with stones located at the ureterovesical junction.

Management

Emergency care
Patients with severe renal colic should be hospitalized immediately. Intravenous access should be obtained to facilitate delivery of analgesics and antiemetics.

The pain of renal colic is mediated by prostaglandin E2. NSAIDs inhibit formation of this mediator, and its parenteral preparation* has been proven in multiple studies to be as effective as narcotic analgesics, with fewer adverse effects. NSAIDs may however cause gastrointestinal bleeding, heart failure and renal impairment.

Narcotics are titratable and fast-acting, but more likely to cause nausea and vomiting.

** COX-1: Ketorolac (Toradol); COX-2: Parecoxib (Dynastat)*

When to consult a urologist?
Refer immediately in case of ureterolithiasis with proximal UTI. Infected hydronephrosis is a true urologic emergency and requires urgent hospital admission, intravenous antibiotics, and immediate drainage of the infected hydronephrosis via percutaneous nephrostomy or ureteral stent placement.

Urologic consultation is also indicated in patients with renal failure, a renal transplant, a solitary functioning kidney, and a history of prior stones that required invasive intervention.

A stone < 4 mm has an 80% chance of spontaneous passage; this falls to 20% for stones > 8 mm.

Medical expulsive theray
Although up to two-thirds of ureteric stones will pass out spontaneously within 4 weeks from symptom onset, the interval between symptom onset and stone passage is highly variable.

A trial of medical expulsive therapy may be considered for patients with lower ureteric stones. A 2- to 4-week course of alpha blockers (eg tamsulosin, terazosin, and doxazosin) or calcium channel blockers (eg nifedipine) may shorten stone passage time and increase stone expulsion rate. The mechanism of action is thought to be related to their inhibition on the ureteric smooth muscle spasm. Medical expulsive therapy is especially useful for distal ureteric stones of moderate size (5 - 10mm). Stones < 5mm can usually pass out spontaneously within four weeks even without any intervention.

Extracorporeal shock wave lithotripsy (ESWL) utilizes an underwater energy wave focused on the stone to shatter it into passable fragments. Approximately 70% of stones can be treated with ESWL alone. This technique is especially suitable for stones that are < 2 cm and lodged in the upper or middle calyx. Anaesthesia or sedation is required. ESWL is contraindicated in pregnancy, untreatable bleeding disorders, patients weighing > 300 lb, tightly impacted or cystine stones, or in cases of ureteric obstruction distal to the stone.

Ureteroscopy is especially suitable for removal of stones that are 1-2 cm, lodged in the lower calyx or below, cystine stones, and high attenuation ("hard") stones. Stones < 5 mm in diameter generally are retrieved using a stone basket, whereas tightly impacted stones or those > 5 mm are manipulated proximally for ESWL or are fragmented using an endoscopic direct-contact fragmentation device.

Percutaneous nephrolithotomy involves entering the renal pelvis percutaneously using the Seldinger technique after ultrasonography or fluoroscopic localization. Renal calyces, pelvis, and proximal ureter can be examined and stones extracted with or without prior fragmentation. This technique is especially useful for stones > 2 cm. A percutaneous nephrostomy can be used as an emergency procedure to relieve obstruction in a high-risk patient in whom other treatments are not feasible.

Outpatient Care
Patients who do not require admission can be symptomatically treated, investigated without delay, and reviewed in 2 days. Patients should be told to report fever, uncontrolled pain, or vomiting immediately.

As stone analysis will help to direct dietary advice and prophylactic measures, any stone passed should be sent for chemical analysis whenever feasible.

Patients with recurrent ureterolithiasis should undergo a thorough metabolic evaluation. A stone chemical analysis together with serum and appropriate 24-hour urine metabolic tests* can identify the aetiology in > 95% of patients. Most common findings are hypercalciuria, hyperuricosuria, hyperoxaluria, hypocitraturia, and low urinary volume.

** urinary volume, pH, specific gravity, calcium, citrate, magnesium, oxalate, phosphate, and uric acid.*

Prevention

The general advice is to have at least 2 litres of urine passed every day or at least have sufficient fluid intake to maintain clear coloured urine. Dietary calcium restriction has now been shown to be ineffective. Oxalate food should only be restricted when and if taken in excess. Reduced salt and animal protein intake is always advisable.

Prospective studies suggest that daily consumption of citrus fruits, coffee, tea, beer, or wine decreases risk of stone formation, while daily consumption of soft drinks (eg cola), apple or grapefruit juice increases risk of stone formation.

Prognosis

- ~ 80% of ureteric stones pass spontaneously without hospitalization or invasive intervention.
- ~ 20% of patients require hospitalization due to dehydration, continued pain or vomiting, or inability to pass the stone spontaneously.
- Recurrence rates are 14%, 35%, and 52% at 1, 5, and 10 years, respectively.
- Risk of recurrence can be reduced drastically by specific medical therapy based on analysis of the stone and serum and urine metabolic profiles.