The incidence and prevalence of renal calculi is increasing.[1,2] The lifetime risk of stone development varies between populations but is about 15% for white men and 6% for white women, with a lifetime recurrence rate of up to 50%.[3] Risk factors include obesity, low fluid intake, and a diet high in protein, refined carbohydrates, and salt.[1] Some conditions can promote calculi formation, including renal tubular acidosis, primary hyperparathyroidism, sarcoidosis, primary hyperoxaluria, inflammatory bowel disease, hyperuricaemic conditions, and cystic fibrosis.[4] Drug-induced calculi can be formed by crystallisation of poorly soluble drugs with a high urinary excretion, or by an effect on calcium oxalate or purine metabolism.[5]

Treatment. Most renal calculi are small, and stones that are less than 5 mm in diameter will usually pass spontaneously.[6-9] Patients may be asymptomatic or may pass small stones with relatively little discomfort, but passage of a larger stone down the ureter can be accompanied by excruciating pain (renal or ureteral colic) requiring analgesia (see Biliary and Renal Colic, p.5). If there is no obstruction, infection, or other complication, conservative treatment is favoured, with the patient being monitored radiographically over several weeks to see if the stone will pass of its own accord.[10] There is some interest in the possible use of drug treatment to ease the spontaneous passage of the stone. Small studies using a calcium-channel blocker (usually nifedipine) or an alpha$_1$-adrenoceptor blocker such as tamsulosin, sometimes with a corticosteroid such as deflazacort, have reported improvements in the rate of stone expulsion and expulsion time, and reductions in analgesic requirements, in patients with uncomplicated lower ureteral stones. A meta-analysis[11] of 9 such studies confirmed the apparent benefit of such treatment; patients had a 65% greater likelihood of spontaneous stone passage than those not given these drugs. Although a suitable randomised controlled study is required to confirm efficacy, such treatment may offer a viable alternative to lithotripsy or uteroscopy.[11] A literature review[12] suggested that daily doses of nifedipine 30 mg, doxazosin 4 mg, tamsulosin 400 micrograms, or terazosin 5 mg given for 28 to 45 days are effective in enhancing expulsion of ureteral stones that are less than 15 mm in diameter.

Where intervention is considered necessary for stone removal the choice of technique depends on the size, composition, and location of the stone. Extracorporeal shock wave lithotripsy is generally favoured, but other procedures such as ureteroscopy or percutaneous nephrolithotomy are used for more complex cases.[7,8,13] Antibacterials may be needed for infection (see Urinary-tract Infections, p.199).

Prevention. In the prevention of recurrence it is important to identify, and where possible correct, any underlying disease process or biochemical or anatomical abnormality. Certain general measures are also appropriate. Patients should drink at least 2 to 3 litres of fluid daily in order to maintain an adequate volume of urine.[1,3,7,14] In hot climates or working environments a higher volume of fluid should be taken.

In preventing the recurrence of *calcium stones*, a balanced diet that is low in protein and salt[1,3,10,15] and high in fibre[1,7] is generally advocated. In the past patients were advised to decrease their calcium intake, but studies have found an inverse relationship between dietary calcium intake and stone formation.[3,7,14,15] Also, because oxalate is bound by calcium in the gut, preventing its absorption, a low calcium intake can increase oxalate absorption and the risk of stone formation. Therefore, a normal level of dietary intake of calcium is now advised[1,3,7,15,16] (an exception to this is in patients with absorptive hypercalciuria type I, a rare condition of intestinal calcium hyperabsorption).[1] However, calcium supplements appear to increase the risk of stone formation and are generally avoided.[3,7,15] If they are used, they should be taken with meals to avoid hypercalciuria.[1,16] Excessive dietary oxalate intake should also be avoided;[3,7,10,15] foods containing large quantities of bioavailable oxalate include spinach, rhubarb, nuts, and cocoa.[15]

Where pharmacological therapy is indicated, choice of treatment depends on the underlying metabolic abnormality and stone composition. Alkaline citrate, usually given as potassium citrate, is commonly used to prevent the recurrence of calcium stones. It acts as a urinary alkaliniser and increases citrate excretion; citrate forms complexes with calcium to reduce urinary saturation of calcium salts and inhibits crystallisation.[2,7,14,16] Potassium citrate is the main treatment option in patients with hypocitraturia and renal tubular acidosis.[1,3,7] In hypercalciuria, a thiazide diuretic or indapamide can also be used to increase distal tubular calcium reabsorption;[1-3,6,7,10,14,17] potassium citrate can also prevent diuretic-induced hypokalaemia in these patients. In the prevention of calcium stones with hyperoxaluria, a restriction of oxalate-rich food and an adequate dietary calcium intake (or calcium supplements taken with meals) are advocated.[6,10,15,16] The use of magnesium has also been suggested[1] although it may be no better than placebo.[3,7] Some patients with primary hyperoxaluria may respond to high doses of pyridoxine.[1,3,7,10,16] In hyperuricosuria, reduced purine intake and allopurinol may be effective.[1,3,7,10]

Prevention of *uric acid stones* is based on adequate fluid intake, a low purine diet, and urinary alkalinisation with potassium citrate. Allopurinol may be used if there are high levels of urate.[1-3,6,7] Acetazolamide has been used short term.[6]

Struvite stones are caused by urease-producing bacteria. Antibacterials are used, and may be required long term, with urinary acidification using ammonium chloride[7] or methionine.[1,7] Dietary phosphate restriction may also be appropriate for patients with phosphate excretion of more than 35 mmol/day.[1] Acetohydroxamic acid, an inhibitor of bacterial urease, may be used as an adjunct in selected cases of severe infection,[7] but its use has been limited by adverse effects.[3,10]

Cystine stones are associated with cystinuria (p.1459) and are prevented by alkalinisation of the urine and a high fluid intake (3 to 4 litres daily).[2,3,6,7] Penicillamine may be used as a chelating agent.[3,6,10] Ascorbic acid, tiopronin,[1,7] and captopril[7] have also been suggested.

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Renal colic

For the treatment of urological pain see Biliary and Renal Colic, p.5.

Renal failure

For discussions of acute and chronic renal failure and their management, see p.1672.

Sexually transmitted diseases

For discussion of sexually transmitted diseases and their treatment see p.191.

Syndrome of inappropriate ADH secretion

In some patients secretion of antidiuretic hormone (ADH; vasopressin) occurs despite hypotonicity of the extracellular fluid and normal or raised fluid volume, and such patients are said to have the syndrome of inappropriate ADH secretion (SIADH). With severe water excess, the resultant hyponatraemia may result in symptoms ranging from lassitude or headache to profound neurological symptoms such as confusion, convulsions, or coma. Some patients may experience inappropriate thirst as well as ADH secretion, thus exacerbating their condition. For a discussion of sodium homoeostasis and dilutional hyponatraemia, see p.1670.

Conditions that can precipitate SIADH include CNS disorders, infections such as encephalitis and meningitis, head trauma, porphyria, or pulmonary diseases such as tuberculosis and pneumonia. ADH may also be secreted ectopically from malignancies, most commonly from small-cell bronchial carcinoma. SIADH may also be drug-induced; drugs associated with the condition include carbamazepine, chlorpropamide, cytotoxic drugs such as cyclophosphamide and the vinca alkaloids, oxytocin, some antipsychotics, tricyclic antidepressants, and SSRIs.

Diagnosis of SIADH is initially prompted by the presence of hyponatraemia and corresponding plasma hypo-osmolality with or without neurological symptoms. Hypervolaemia, persistent excess sodium excretion, lack of oedema, and normality of both renal and adrenal function are confirmatory.

Mild water excess is frequently asymptomatic and may not require specific therapy, but patients with SIADH often have a more severe disorder and treatment is best aimed at the underlying cause. If such treatment is not possible or if symptoms persist, water restriction may be considered. However, fluid restriction is unpleasant, particularly for patients who retain inappropriate thirst, and may not be tolerable. In these patients demeclocycline may be given to antagonise the effect of ADH on the renal tubules. Lithium has been given as an alternative but has a high frequency of adverse effects, and phenytoin has been used occasionally to inhibit pituitary ADH secretion. Diuretics such as furosemide (used with oral sodium chloride) have also been tried in an attempt to optimise diuresis while retaining sodium. In patients with life-threatening severe acute water intoxication (see Hyponatraemia, p.1670), treatment initially involves cautious improvement of the profound hyponatraemia by intravenous infusion of hypertonic (usually 3%) or isotonic sodium chloride, often with furosemide or another loop diuretic to avoid volume expansion. Drugs that act directly in the renal tubules as vasopressin V_2 receptor antagonists are under investigation.

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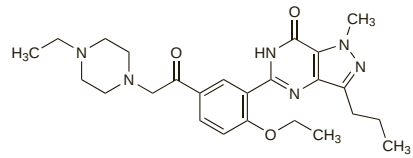
Urinary-tract infections

The treatment of urinary-tract infections is discussed on p.199.

Acetildenafil

Hongdenafil. 5-{2-Ethoxy-5-[2-(4-ethylpiperazine-1-yl)-acetyl]-phenyl}-1-methyl-3-*n*-propyl-1,6-dihydro-7*H*-pyrazolo[4,3-*d*]-pyrimidin-7-one.

$C_{25}H_{34}N_6O_3$ = 466.6.



Profile

Acetildenafil is an analogue of sildenafil (p.2193) that has been used in various preparations or dietary supplements and illegally promoted in some countries for the management of erectile dysfunction. Other analogues of sildenafil detected in similar products include homosildenafil and hydroxyhomosildenafil.