CHAPTER 10

GENITOURINARY DISEASES

NEPHROTIC SYNDROME

A clinical complex characterized by profuse proteinuria (>3.5 g/1.73 m^2/24 h), oedema and hypoalbuminaemia. More than 90% of cases of nephrotic syndrome in adults are due to one of these—minimal change disease, membranous glomerulopathy, focal and segmental glomerulosclerosis, membrano-proliferative glomerulonephritis, diabetic nephropathy and amyloidosis.

SALIENT FEATURES

- Periorbital and generalized pitting oedema, transudative pleural effusions, ascites, xanthomata. Hypercoagulability predisposes these individuals to peripheral arterial or venous thrombosis, renal vein thrombosis, and pulmonary embolism.
- Proteinuria of >3-3.5 g/24 h. Renal biopsy is indicated in all adults and children >10 years with nephrotic syndrome for establishing a definitive diagnosis, guiding therapy and estimating prognosis.
- Other associated abnormalities are hyperlipidaemia, lipiduria and hypercoagulability.

Treatment

Nonpharmacological

- Moderate salt restriction, usually 1-2 g/day (no cooking salt) and low cholesterol diet.
- There is no consensus regarding the optimal protein in diet for these patients. High protein diet is not recommended, as it may hasten the progression of renal disease by increasing proteinuria. A protein intake of 0.8-1 g/kg/24 h of mainly first-class proteins is recommended.
- Fluid restriction is not usually required unless the oedema is severe.

Pharmacological

Nonspecific measures.

1. To reduce proteinuria in patients with diabetic nephropathy.

Tab. Captopril 6.25-25 mg/day in 4 divided doses.
Or
Tab. Enalapril 1.25-5 mg/day as a single dose Or Tab. Losartan 25-50 mg/day as single dose.

2. NSAIDs reduce proteinuria in some patients by altering glomerular haemodynamics but benefit must be weighed against risks.
3. Tab. Frusemide 80-250 mg/day in two divided doses (8 AM, 2 PM), depending upon the severity of oedema. The aim is to remove up to 1.0 kg/day of oedematous fluid.
   In addition, if required, Tab. Spironolactone 100 mg once daily may be added.
4. Only in-patients with symptomatic thrombosis, Tab. Warfarin 2-4 mg/day (to titrate the dose to INR of 1.5-2.0).
   Patients may be relatively resistant to heparin.
   Specific. Immunosuppression

Minimal change disease

Tab. Prednisolone 1-1.5 mg/kg/day for 4 weeks; followed by 1 mg/kg/day on alternate day for up to 16-24 weeks, depending upon the time to go into remission. Up to 90% of adults go into remission when Tab. Prednisolone is continued for up to 24 weeks. 50% relapse on withdrawal of steroids. Monitor for presence of symptoms and proteinuria. Treatment of relapse is same unless the patients are resistant to steroids or relapse shortly after withdrawal of steroids (steroid dependent) or relapse occurs more than three times in a year, introduce following second line drugs:

Tab. Cyclophosphamide 2-3 mg/kg/day or Chlorambucil 0.1-0.2 mg/kg/day for 8-12 weeks.

(**Caution**: Adequate hydration must be maintained and monitor for side effects, e.g. cystitis, alopecia, infection, infertility, secondary malignancies).

If patients are resistant to the above cytotoxic drugs (third line) may induce remission in 60-80% of patients:

Tab./Cap Cyclosporin A 5 mg/kg daily in 2 divided doses as maintenance treatment reduced to lowest effective dose according to proteinuria and serum creatinine measurements; discontinue after 3 months, if no response. Monitor these patients for renal functions.

Focal and segmental glomerulosclerosis

Specific treatment—same as above.

Response rate is poor.

Membranous glomerulopathy

Treat underlying disease. If idiopathic, steroids and immunosuppressive treatment have no role. About 40% respond spontaneously; 30-40% remit and relapse spontaneously; 10-20% show progressive decline in GFR over 10-15 years to end stage renal disease (ESRD).

If patient goes into remission in 6 months time, maintenance treatment with low dose prednisolone alternating with Chlorambucil to be given by a specialist.

Membranoproliferative glomerulonephritis

No effective therapy; usually progress to ESRD over 5-10 years.

(**Caution**: Patients who do not respond to steroids are excellent candidates for renal transplant).

Rapidly progressive glomerulonephritis. Needs aggressive management preferably by a specialist

Inj. Methylprednisolone 1 g/day for 3 days followed by oral prednisolone as above.

Anti-GBM disease needs plasmapheresis.

(For treatment of Nephrotic Syndrome in children see Chapter-19).

References

1. Common Clinical Presentations and Symptoms in Renal Disorders. In: Oxford Textbook of Medicine. Warrell DA, Cox TM, Firth JD, Benz EJ Jr. (eds), 4th edition, Oxford University Press, 2003; pp 3.224-3.234.
2. Glomerular Diseases. In: Harrison's Principles of Internal Medicine. Fauci, Braunwald, Kasper et al (eds), 18th Edition, McGraw Hill Company Inc., New York, 2012; pp; 2334-2366.
3. Proliferative Glomerulonephritis. In: Oxford Textbook of Medicine, Warrell DA, Cox TM, Firth JD, Benz EJ Jr. (eds), 4th edition, Oxford University Press, 2003; pp 3.332-3.333.

ACUTE RENAL FAILURE (ARF)

A significant decline in the renal excretory function, mostly associated with oliguria (<500 ml/day), occurring over hours or days, detected clinically by a rise in plasma concentration of urea and creatinine. Most of the times, ARF is reversible.

SALIENT FEATURES

- The clinical picture is usually dominated by the primary condition, which causes ARF. Manifestations of uraemia like anorexia, nausea, vomiting, muscular cramps and signs of encephalopathy may appear later.
- For purposes of diagnosis and management, ARF is divided into three categories:
  - Pre-renal due to renal hypoperfusion (55%).
  - Renal due to disease which involve renal parenchyma (40%).
  - Post-renal due to diseases causing urinary obstruction.
- Complications of ARF include hyperkalaemia, intravascular volume overload, hyponatraemia, hypocalcaemia, hyperphosphataemia, metabolic acidosis, anaemia, coagulation abnormalities and infections; arrhythmias, pericardial effusion, pulmonary oedema, GI bleeding due to stress ulceration.

Treatment

Identify the causative factors and triggering event and treat accordingly for disease-specific therapy and prevention and management of uraemic complications.

Nutrition: Restrict dietary protein to 0.6 g/kg/day and carbohydrate to 100 g/day.

Prerenal ARF

1. Replacement fluids—tailored according to the composition of lost fluids, e.g. in haemorrhage blood transfusion/packed RBCs (if oliguria despite fluid correction).
   Normal saline (0.9%) in case of burns, pancreatitis, diabetic ketoacidosis.
   Hypotonic saline (0.45%) if increased urinary or GI losses.
   (Fluid intake = 500 ml + urine output + fluid loss from other sources)
2. Management of pulmonary oedema, if present.
3. In patients with cirrhosis complicated by ARF, fluids should be administered slowly and titrated against JVP. Large volume paracentesis should be accompanied by IV albumin.

Intrinsic renal ARF

It should be managed by a specialist. Approach for treatment depends upon the likely cause.

1. Acute glomerulonephritis, vasculitis—glucocorticosteroids, cyclophosphamide, and/or plasmapheresis.
2. Allergic interstitial nephritis—glucocorticoids.
3. Malignant hypertension, toxaemia of pregnancy—aggressive control of blood pressures.

Postrenal ARF

1. Suprapubic catheterization.
2. Referral to a urologist for removal of obstructing lesion.

Other essential measures.

1. Strict intake/output recording.
2. Monitor serum K^+ and acid-base status.
3. Reverse causative renal insult, e.g. restore haemodynamics, eliminate nephrotoxins.
4. Prevention and treatment of complications.
5. Volume overload
   - Restrict salt (1-2 g/day—avoid all table/cooking salt and avoid food rich in sodium like milk) and water.
   - Inj. Frusemide IV dose depending upon extent of overload, usual dose is 40-200 mg/day as bolus or intravenous infusion.
   - Dialysis.

Hyponatraemia

1. Restrict free water intake (<1 liter/day).
2. Avoid hypotonic IV solutions.

Hyperkalaemia

1. Restrict dietary potassium (K^+) 40 mmol/d (no food containing K^+).
2. Inj. Glucose insulin drip—50 ml of 50% of dextrose with 10 units of plain insulin over 10 min.
   And/Or
   Inj. Sodium bicarbonate 50-100 ml of 4.2% IV 10 min.
   And/Or
   Inj. Calcium gluconate 10 ml of 10% solution over 5 min.
   (More than one step taken, if levels of serum $K^+ > 6.5$)
3. Cation exchange resins, e.g. Sodium or Calcium polystyrene sulphonate 15 g orally 6 hourly.

Metabolic acidosis

1. Restrict dietary protein (0.6 g/kg/day).
2. Inj. Sodium bicarbonate IV to maintain an arterial pH of >7.2.

Hypocalcaemia

1. Tab. Calcium carbonate 1 g/day or
2. IV Calcium gluconate 10% 10-20 ml given over 20 minutes (if tetany).

Hyperphosphataemia

1. Restrict dietary phosphate intake (<800 mg/day).
2. Calcium carbonate as above.

Hyperuricaemia

- Treatment necessary only if uric acid is >10 mg %.
- Tab. Allopurinol 100 mg three times a day

Dialysis is indicated for any of the following:

- Overt uraemia manifesting as encephalopathy, pericarditis, uraemic bleeding.
- Intractable fluid overload.
- Refractory hyperkalaemia.
- Rise in urea >150-180 mg% or creatinine >6-7 mg%.
- Severe acidosis producing circulatory compromise.

Doses of all essential drugs for the underlying disease should be adjusted according to the degree of renal impairment (See Appendix VII).

Prevention

Since there is no specific therapy for ischaemic or nephrotoxic ARF, prevention is very important and includes:

1. Aggressive restoration of intravascular volume in case of losses, e.g. during surgery, trauma, burns, gastroenteritis, etc.
2. Avoid/reduce the dose of nephrotoxic drugs appropriately.
3. Hypovolaemia should be avoided in patients receiving nephrotoxic drugs.

References

1. Acute Kidney Disease. In: Harrison's Principles of Internal Medicine. Fauci, Braunwald, Kasper et al (eds), 18th Edition, McGraw Hill Company Inc., New York, 2012; pp; 2293-2308.
2. Acute Renal Failure. In: Oxford Textbook of Medicine, Warrell DA, Cox TM, Firth JD, Benz EJ Jr. (eds), 4th Edition, Oxford University Press, 2003; pp 3.248-3.262.

CHRONIC RENAL FAILURE (CRF)

An irreversible, substantial and usually gradual loss of renal function leading to a clinical and laboratory syndrome of uraemia. End stage renal disease (ESRD) would result in death without renal replacement therapy. The important underlying causes are diabetes mellitus, hypertension, chronic glomerulonephritis, chronic pyelonephritis, analgesic nephropathy and polycystic disease.

SALIENT FEATURES

- The symptoms of uraemia develop gradually and late. Fatigue, dyspnoea, anorexia, nausea, vomiting, ankle oedema, pruritis, purpura, and neuromuscular disturbances. Nocturia may be present.
- Examination may show the presence of pallor, nail dystrophy, purpura, hypertension, cardiomegaly, CHF, features of pulmonary oedema, pleural effusion and pericarditis with or without effusion.
  Fundus examination may show changes of hypertensive or diabetic retinopathy. The abnormalities in blood urea and creatinine may be detected during evaluation of anaemia.
- Elevated blood urea and creatinine, hypocalcaemia, hyperphosphataemia, hyperkalaemia and a partially compensated metabolic acidosis. Peripheral smear shows a normocytic, normochromic anaemia and urinalysis usually reveals proteinuria and low fixed specific gravity. Presence of shrunken kidneys on ultrasound suggests end-stage renal disease. Kidney biopsy to be done if the kidneys are of normal size. A skeletal survey may show evidence of renal osteodystrophy. In certain diseases like diabetic nephropathy, polycystic kidney disease, kidney size may be normal.

Treatment

1. Identification and management of associated factors precipitating acute or chronic renal failure, e.g. drugs, hypovolaemia, infections, obstructive uropathy, hypertension, CHF, pregnancy or presence of any life-threatening emergency,

requiring urgent treatment, e.g. hyperkalaemia, pulmonary oedema, metabolic acidosis, uraemic encephalopathy or accelerated hypertension (Treat as mentioned under respective conditions).
2. Identification of specific cause of CRF and their treatment so as to delay the progress of CRF.
3. Modify loading and maintenance doses of drugs that are excreted through renal route.

Nonpharmacological

- Decrease protein intake to 0.6 g/kg/day of high quality protein.
- Phosphate restriction to 1000 g/day to reduce soft tissue calcification (avoid milk, egg, etc.).
- Moderate sodium restriction to 60 mmol/day (low salt during cooking and avoiding foods rich in sodium) to control BP and oedema.
- Potassium restriction, if CRF is moderate to severe (foods rich in K^+ include banana, citrus fruits, coconut water, papaya, etc.)
- Fluid restriction is not generally necessary until late in renal failure.
- Sodium bicarbonate (baking powder) 600 mg 4 times a day, if plasma HCO_3^- is less than 20 mmol/liter.

Pharmacological

Control of hypertension, cardiovascular and pulmonary abnormalities

Target BP is 130/80-85 mmHg and in-patients with proteinuria >1 g/day, target BP is 125/75 mmHg (for details see section on hypertension).

The preferred drugs are:

Tab. Frusemide 40-160 mg per day.

Or

Tab. Amlodipine 5-20 mg per day.

And/Or

Tab. Atenolol 50-100 mg per day (contraindicated if concomitant cardiomyopathy with failure).

In diabetic nephropathy or CRF with proteinuria—ACE inhibitor/angiotensin receptor blocker with or without diuretic are preferred.

Treatment of pericarditis

Uraemic pericarditis is an absolute indication for initiation or intensification of dialysis. Heparin free dialysate should be used.

Treatment of anaemia

1. Look for common aggravating causes of anaemia, e.g. GI blood loss, iron deficiency and chronic infections and treat accordingly. Assess iron status of patient before erythropoietin (EPO) therapy.

2. Iron supplementation to ensure adequate response to EPO. (See section on Anaemia)
3. Inj. EPO subcutaneous 80-120 units/kg/week (divided into 2-3 times a week)

The target Hb should be 10-12 g/dl and optimal rate of correction should be to increase haematocrit by 4-6% over 4-week period.

Treatment of bleeding diathesis

Usually problem arises when a patient of CRF needs to undergo some surgery.

Inj. Vasopressin (DDAVP) 0.3 mcg/kg in 100 ml of saline in 30 min, to be administered before surgery.

Treatment of bone, phosphate and calcium abnormalities and acid base disturbances

1. Phosphate restricted diet.
2. Calcium carbonate – minimum of 1 g/day.
3. Vitamin D_3/Calcitriol – 0.25-2 mcg/day.

Maintain serum calcium at about 10 mg% and phosphate at about 4.5 mg%.

Treatment of hyperuricaemia (gout), if it is symptomatic

Tab. Allopurinol 100-200 mg/day preferably after food, then adjusted according to plasma or urinary uric acid concentration. Management of metabolic acidosis should aim to maintain a near normal value of bicarbonate. Calcium carbonate is usually adequate. If needed, sodium bicarbonate can also be added. For monitoring the progression of renal failure, measure serum creatinine and creatinine clearance. ECG may show evidence of left ventricular hypertrophy (LVH), pericarditis or hyperkalaemia.

Absolute indications for dialysis

Development of complications that cannot be controlled by conservative and pharmacological means, i.e. fluid overload, severe hypertension, pericarditis, refractory hyperkalaemia, severe metabolic acidosis, encephalopathy and progressive neuropathy attributable to uraemia. Renal replacement therapy (RRT) should not be initiated when the patient is totally asymptomatic.

Renal replacement therapy (RRT)

The choice of modality include—haemodialysis, continuous ambulatory peritoneal dialysis or renal transplantation; the choice depends on many factors—their availability, patient's preference and availability of potential donors. Only kidney transplantation offers the potential for nearly complete rehabilitation.

Patient education

- Counselling as most of these patients have varying reactions to illness from anger to depression. Prepare the patient physically and psychologically for renal replacement therapy, when ESRD is inevitable.

References

1. Chronic Kidney Disease. In: Harrison's Principles of Internal Medicine. Fauci, Braunwald, Kasper et al (eds), 18th Edition, McGraw Hill Company Inc., New York, 2012; pp. 2308-2321.
2. Chronic Renal Failure. In: Oxford Textbook of Medicine, Warrell DA, Cox TM, Firth JD, Benz EJ Jr. (eds), 4th Edition, Oxford University Press, 2003; pp. 3.263-3.278.

URINARY TRACT INFECTIONS (UTI)

UTI is defined as an infection of any part of the urinary tract. UTIs are common bacterial infections managed in general practice, particularly in sexually active women except in first year of life and in elderly. UTIs predominantly affect females.

SALIENT FEATURES

- Lower UTI includes infections of the urethra and bladder and can present with pain and burning during micturition, frequency of micturition, urgency, dysuria, pyuria or sometimes even haematuria. Fever is usually absent in lower UTI. Acute cystitis may present with suprapubic pain or discomfort.
- Upper UTI includes infections of the kidneys and ureters. The symptoms usually develop rapidly, sometimes within a few hours. In addition to symptoms of lower UTI, these patients may have high fever, chills, rigours and pain in the loins, nausea and vomiting.
- Sometimes UTIs may be asymptomatic, and are detected accidentally when the urine is tested. Asymptomatic infections are more common in pregnant women and the elderly. Untreated, asymptomatic bacteriuria in pregnancy can progress to upper UTI which can further lead to premature delivery and poor foetal outcome.
- Urine—microscopic exam >10 pus cells/HPF and on culture bacterial growth, i.e. >105/mm^3 is diagnostic. In asymptomatic patients, two consecutive urine specimens should be examined and >105/mm^3 bacteria of a single species should be demonstrable in both specimens before therapy is instituted. The presence of bacteriuria of any degree in suprapubic aspirates or >102/mm^3 in urine obtained by catheterization indicates infection.

Collection of urine sample. Collection of urine sample for culture should be from the midstream and should be preceded by adequate cleaning of external genitalia avoiding any antiseptic washes. Patients with recurrent UTIs should undergo ultrasonography of the genitourinary tract and micturating cystourethrogram to detect underlying structural or functional abnormality.

Treatment

General principles

- Except in acute uncomplicated cystitis in women, diagnosis must be confirmed before treatment is begun and antimicrobial sensitivity should direct the therapy.
- Identify the predisposing factors and correct, if possible.
- Relief of clinical symptoms does not always mean bacteriologic cure.
- Each course of treatment should be defined as failure or cure on the basis of symptoms and eradication of bacteria.
- Uncomplicated lower UTIs generally respond to short courses of therapy while upper UTIs and complicated lower UTIs require longer treatment.
- Recurrences more than two weeks after cessation of therapy nearly always represent reinfection.
- Community acquired infections particularly the first infections are usually due to more antibiotic sensitive strains.
- In hospitalized patients, those requiring instrumentation and having recurrent infections, antibiotic resistant strains are the more likely causes of UTI.

Nonpharmacological

Plenty of oral fluids.

Pharmacological

If symptoms are severe, antibiotics may be started empirically, after sending the urine samples. If symptoms are not severe, the antibiotics can be started as suggested by the culture and sensitivity report.

1. The specific treatment regimen is shown in the Table 10.1.
2. Alkalinizing agents may be used with certain antibiotics like cotrimoxazole to prevent precipitation of crystals.
3. Tab. Pyridium up to 2 tablets 3 times a day for the first 2-3 days as a urinary analgesic to relieve dysuria.

Table 10.1. Treatment regimen for bacterial urinary tract infections

Condition	Characteristic pathogens	Mitigating circumstance	Recommended empirical treatment
Acute uncomplicated cystitis in women	*E.coli*, *S. saprophyticus P. mirabillis*, *K. pneumoniae*	None	3-day regimen: Oral TMP- SMZ 160/800 mg BD, TMP 100 mg BD, Norfloxacin 400 mg BD, Ofloxacin 200 mg BD, Ciprofloxacin 500 mg BD
		Diabetes, symptoms for <7 days, recent UTI use of diaphragm age <65	Consider 7-day regimen: Oral TMP-SMZ, TMP Quinolone

Condition	Characteristic pathogens	Mitigating circumstance	Recommended empirical treatment
		Pregnancy	Consider 7-day regimen: Oral Amoxicillin 250 mg TDS, Cefpodoxime 100 mg BD
Acute uncomplicated pyelonephritis in women	*E. coli*, *S. mirabillis*, *S. saprophyticus*	Mild to moderate illness-outpatient therapy	Oral Ciprofloxacin 500 mg BD, Ofloxacin 400 mg BD, Amoxicillin 500 mg TDS, Cefpodoxime 100 mg BD
		Severe illness-hospitalization required	Parenteral Ciprofloxacin 200-400 mg BD, Ofloxacin 1 mg/kg TDS, Ampicillin 1g QID, Ceftriaxone 1-2 g/d for 14 days.
Complicated UTI in men and women	*E. coli*, *Proteus*, *Klebsiella*, *Pseudomonas Staphylococci*	Mild to moderate illness-outpatients therapy	Oral Quinolone for 10-14 days (Doses as above)
		Severe illness or possible hospitalization required	Parenteral, Ampicillin and Gentamicin, Quinolone, Ceftriaxone (Doses as above) until defervescence.

TMP - Trimethoprim, SMZ - Sulfamethoxazole

Prophylaxis

Antibiotics for prevention are recommended to women who have two or more episodes of infection within 6 months or three or more infections within one year. The recommended antimicrobials include daily or thrice weekly administration of a single dose of Trimethoprim-sulfamethoxazole (TMP-SMZ) (80/400 mg), TMP alone (100 mg) or Nitrofurantoin (560 mg). Prophylaxis should be initiated only after bacteriuria has been eradicated with a full dose treatment regimen. Same regimen can be used as a single dose after sexual intercourse in women in whom episodes of symptomatic UTIs are related to sexual intercourse. Frequent urine cultures are essential during this period.

Suppressive antibiotics

Indicated in patients with repeated infections with an underlying cause, till the underlying cause is removed or controlled, e.g. infants and children with vesico-ureteric reflux till 3-5 years of age and elderly requiring prolonged catheterization. The recommended drugs are same as above.

Note: See also UTIs in paediatric section.

Treatment of specific cases

UTIs in pregnancy. Asymptomatic bacteriuria in pregnancy must be treated appropriately.

(**Caution**: Cotrimoxazole and fluoroquinolones are not recommended during pregnancy).

UTIs in elderly. Treatment is not recommended for asymptomatic infections among the elderly, particularly men.

UTIs in catheterized patients. Need for treatment and optimal type and duration of treatment for such patients with asymptomatic bacteriuria have not been established.

Removal of catheter with a short course of antibiotic may be appropriate.

If catheter cannot be removed, bacteriuria should be ignored unless patient is symptomatic or at high risk of developing bacteriuria.

Follow-up

Patient should be re-evaluated within 3-5 days for relief of symptoms and urine microscopic examination and culture examination should be repeated. In upper UTIs, fever and other symptoms normally subside within 2-3 days after starting the treatment. If symptoms do not subside within 5 days, underlying abnormalities like obstruction to the urinary tract, stones or collection of pus should be looked for. If the infection relapses after an initial treatment for 14 days, a six-week treatment is recommended.

Patient education

- To drink plenty of water, at least 10 glasses per day.
- Not to control the urge to pass urine. To empty the bladder completely and very often.
- To empty the bladder after sexual intercourse.
- Both the partners to clean the genitalia before and after sexual intercourse.
- Avoid diaphragm with spermicide as a contraceptive.
- Wipe from front to back during eblution.

For treatment of UTI in children, see Chapter 19.

References

1. Urinary Tract Infections. In: Oxford Textbook of Medicine. Warrell DA, Cox TM, Firth JD, Benz EJ Jr. (eds), 4th edition, Oxford University Press, 2003; pp. 3.420-3.434.
2. Urinary Tract Infections, Pyelonephritis and Prostatits. In: Harrison's Principles of Internal Medicine. Fauci, Braunwald, Kasper et al (eds), 18th Edition, McGraw Hill Company Inc., New York, 2012; pp. 2387-2395.