Great Ormond Street Hospital for Children
NHS Trust

Renal Physiology & Pathophysiology in ITU

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Updated: Christine Pierce March 2007

Associated clinical guidelines/protocols:
1. Oliguria/acute renal failure
2. Management of hyponatremia
3. Management of hyperkalemia
4. GOSH renal transplant protocol (attached – please do not circulate widely as this is from renal team and only available to nephro-urology trainees). Relevant sections are the anaesthetic/operation check list, the immediate post-operative management and immunosuppression.
5. GOSH hypertension protocol (renal unit)

Fundamental Knowledge:
List of topics relevant to PIC that will have been covered in membership examinations.
They will not be repeated here.

Physiology & anatomy:
- Gross anatomy & microanatomy of the glomerulus and tubules.
- Understand physiology of renal circulation
- Effects of ADH, atrial natriuretic hormone, parathyroid hormone
- Glomerular filtration and plasma clearance; tubular function & urine formation
- Regulation of fluid, electrolyte & acid-base balance
- Assessment of renal function
- Biochemical changes with age
- Endocrine functions of kidney

Pathophysiology:
- Definitions of renal failure, oliguria and anuria; polyuria;
- Understand causes of acute failure: pre-renal, renal & obstructive.
- Acute tubular necrosis vs acute cortical necrosis:
- Methods of preventing renal failure
- Investigation of impaired renal function;
- Knowledge of nephrotoxic drugs and monitoring; adjustment of drug doses in renal impairment/failure

Investigations:
- Urinanalysis
- Renal ultrasound
- Radionucleotide studies.
- Cystoscopy

Information for Year 1 ITU Training (basic):

> **Year 1 ITU curriculum**
> **Pathophysiology**:
> - Definitions of renal failure
> - Understand causes of acute failure: pre-renal, renal & obstructive.
> - Acute tubular necrosis vs acute cortical necrosis:
> - Methods of preventing renal failure
> - Knowledge of nephrotoxic drugs & monitoring; adjustment of doses.
>
> **ITU Management of clinical conditions:**
> - Acute renal failure: diagnosis and investigation
> - Electrolyte abnormalities: hyponatraemia, hypernatraemia, hyperkalaemia, hypo- & hyper phosphataemia, hypo- & hyper calcaemia.
> - HUS

Physiology and pathophysiology

Definitions of renal failure

- The kidneys constitute <0.5% of body weight but blood flow to the kidneys equals to 25% of cardiac output. 90% of renal blood flow is directed to the renal cortex
- Autoregulation maintains RBF and GFR relatively constant over a range of mean arterial and renal perfusion pressures from 80 – 160 mmHg. However significant decreases in BP will result in activation of the sympathetic nervous system and release of norepinephrine, epinephrine and angiotensin. This causes intense vasoconstriction of renal arterioles, resulting in decreased RBF and GFR, and may progress to renal failure if untreated.
- Little is known about autoregulation of renal blood flow in infants and neonates but they are likely to have a lower and narrower range of autoregulation. There is also decreased blood flow to the outer cortex in the neonate with less developed outer glomeruli and tubules. Therefore neonates are more vulnerable to renal dysfunction due to hypoperfusion at systemic BPs only slightly lower than the normal range.
- Glomerular ultrafiltrate is normally devoid of cellular elements and contains very little protein. Presence of cells or protein in the urine indicate kidney disease.
- GFR is estimated by measurement of creatinine clearance, as creatinine is produced at relatively constant rate, proportional to the muscle mass, and not reabsorbed
- The composition and volume of the urine is determined by the processes of selective reabsorption of solutes and water, and secretion of solutes by the nephron.
- Sodium and water reabsorption is regulated by various hormones (angiotensin, aldosterone, ADH and ANP), the sympathetic nervous system and Starling forces. This maintains osmolality and circulatory volume within a narrow range.
- The kidneys maintain acid-base balance by excretion of non-volatile acids and reabsorption of HCO_3. The kidneys respond to respiratory acid-base disorders over several hours to days. However the pulmonary response to metabolic acid-base disorders occurs in a matter of minutes.

Causes of acute failure: pre-renal, renal & obstructive.

Acute renal failure
Acute renal failure (ARF) is defined as urine output of <1 ml/kg/h or a 50% increase above baseline creatinine. ARF is seen in 10% of critically ill children because the kidneys are susceptible to hypovolaemia and hypotension (see physiology above). Hence the kidneys are usually one of the first organs to be affected, but usually the last to recover.

The cause of ARF in ICU is often multifactorial and is associated with significant mortality. Consider congenital renal disease and perinatal events with ARF in neonates.

Causes of ARF
1. **Pre-renal**
   This is the commonest cause of renal failure in children. This is caused by decreased renal perfusion due to a fall in cardiac output, extracellular fluid loss (e.g. shock or dehydration) or decreased intravascular volume during rapid "third space" accumulation (e.g. peritonitis). Renal function is impaired but renal parenchyma is preserved, hence this form of renal failure is rapidly reversed with fluid therapy.
2. **Intra-renal (intrinsic**)
   This is due to acute tubular necrosis (ATN) as well as other glomerular and vascular causes. Causes of ATN include nephrotoxic drugs and severe unrelieved pre-renal oliguria. Pre-existing renal disease and hypertension are significant predisposing factors.
3. **Post-renal (obstructive)**
   This is caused by obstruction to the flow of urine at upper tract or bladder outlet level. Examples of this include severe rhabdomyolysis causing myoglobinuria, and the presence of posterior urethral valves in male children. The parenchymal damage correlates with the duration, degree and site of obstruction, as well as the presence or absence of infection.

Early recognition and treatment of pre-renal failure by adequate volume resuscitation and maintenance of an adequate renal perfusion pressure will prevent progression to acute tubular necrosis. Fluid overload at the end of resuscitation may have a worse outcome [1], hence the larger volumes required when using crystalloids instead of colloids may be detrimental.

"Renal dose" dopamine is not effective in increasing renal perfusion [2], but there is evidence that "renal dose" norepinephrine may be beneficial in increasing myocardial performance, mean urine output and creatinine clearance in animals [3].

Acute tubular necrosis vs acute cortical necrosis:
Investigations to help differentiate the cause of ARF

1. Urinalysis

   Normal in pre and post renal cause of failure
   Abundant cells, casts and protein suggest renal pathology
   - Granular and epithelial cell casts suggest acute tubular necrosis
   - White cell or eosiniphilic casts suggest acute interstitial nephritis
   - Red cell casts and proteinuria suggest acute glomerulonephritis or vasculitis

	Pre-renal	**Renal**
Sediment	Normal	Cells & casts
Specific gravity	High >1.020	Fixed 1.010
Sodium	Low <20	High >40
U/P urea	High 20	Low 10
U/P creatinine	High 40	Low 10
U/P osmolality	High 2.1	Low 1.2
Osmolality	High	Low

2. Fractional excretion of sodium (FeNa)
   This is a good index of renal function as it is accurate even if the GFR is changing rapidly. This is obtained by urinary:plasma sodium divided by the urinary:plasma creatinine.

   <1% = prerenal failure
   >2.5% = intrinsic renal failure

   This may be difficult to interpret in a patient on diuretics as diuretic therapy results in high urinary sodium loss. However if FeNa is still low in the face of diuretics, the patient is clearly in pre-renal failure and is intravascularly volume depleted.

Summary of useful investigations

	Pre-renal	**Renal**
Urine osmolarity	High	Low
Urine sodium	Low	High
Urine creatinine	High	Low
FeNa	<1%	>2.5%

4. Imaging
   Ultrasound preferred as this avoids contrast which may be nephrotoxic. Renal perfusion scan using DTPA may help to distinguish between ATN (where perfusion is relatively preserved) from outflow obstruction.

5. Renal biopsy
   Indicated if the cause is unknown or the recovery is prolonged as this helps to differentiate the intra-renal cause of ARF and therefore affect longer term therapy.

Methods of preventing renal failure

Management
- Optimise cardiorespiratory function
- Ensure adequate circulating volume – use colloid if sepsis is likely cause

Knowledge of nephrotoxic drugs & monitoring; adjustment of doses.

Antibiotics
Antibiotics can cause renal failure through a variety of mechanisms including direct toxicity to the renal tubules, allergic interstitial nephritis, and crystallization of the antibiotic within the renal tubules. Allergic interstitial nephritis is an idiosyncratic reaction but reported as a possible side effect of a myriad of drugs. Antibiotics are by far the most common culprits. There is no way to prevent this side effect; one can only promptly recognize the syndrome and discontinue the offending agent. Although penicillins and cephalosporins are well-recognized culprits, almost any antibiotic can cause it occasionally. The fluoroquinolone ciprofloxacin is now a well-recognized cause of allergic interstitial nephritis. Crystallization of antibiotics in the renal tubules can lead to acute oliguric renal failure and has been reported with sulfa, acyclovir, and indinavir.
Aminoglycosides are well known for there nephrotoxic potential. Dose adjusting in renal impairment is well accepted. Regardless, proper dose adjustment is no guarantee of safety, and nephrotoxicity of aminoglycosides at therapeutic levels is well established. Aminoglycosides are excreted solely in the urine and are directly toxic to proximal tubular cells.

NSAIDS
There is no difference in the safety profile of these drug classes in renal insufficiency (Level 3 evidence). Both classes can lead to oedema, hypertension, CHF, and acute on chronic renal failure, sometimes leading to need for dialytic support. The effect is dose dependent and usually reversible, although permanent dialysis dependence can occur in patients with advanced renal failure. Acetaminophen is by far the safest analgesic in renal failure.

ACE inhibitors
In high risk patients, careful monitoring of BP, creatinine, and potassium should be undertaken when initiating or dose escalating these drugs. Some mild elevation in the serum creatinine is acceptable in order to get the benefits.

IV contrast dye
High molecular weight/ionic contrast dye can cause severe vasospasm in the afferent arteriole and acute renal failure in susceptible individuals. It is less common with newer lower molecular weight/non-ionic contrast dye. Hydration with I.V. saline is the simplest way to reduce contrast nephrotoxicity

ITU Management of clinical conditions:

Acute renal failure: diagnosis, investigation and management

- Diagnosis/ investigation as above
- Fluid restrict – insensible water loss of 400ml/m2/day plus ongoing losses. However this may not be practical or possible in the critically ill, and renal replacement therapy may be required to remove excess fluid.
- Watch out for polyuria during recovery phase and keep up with replacement
- Adequate nutrition to prevent catabolism but may need to reduce protein load
- Electrolyte control. Reduce sodium and potassium load
- Correct acidosis
- Modify drug doses and monitor levels if possible
- Renal replacement therapy indicated if
    - Uncontrolled hyperkalaemia
    - Uncontrolled symptomatic acidosis
    - Fluid overload

Electrolyte abnormalities : hyponatraemia, hypernatraemia, hyperkalaemia, hypo- & hyper phosphataemia, hypo- & hyper calcaemia.

Hyponatremia
Sodium is the main extracellular solute and the main determinant of the osmolality and tonicity of the ECF. Causes of hyponatremia is reviewed in a recent article in the Education and Practice edition of Archives [4] The symptoms depend on aetiology, severity and acuteness of the condition, with seizures and coma occurring at serum sodium levels <115 mmol/l. Hyponatremia can be caused by water retention or sodium loss hence assessment of ECF volume and urine sodium are important in determining the aetiology, and the plan of management. See appendix 1.

Shock should be corrected by 20 ml/kg boluses of 0.9% saline until arterial BP is restored. Acute severe symptomatic hyponatremia is a medical emergency and should be corrected as an emergency with hypertonic saline to bring the serum Na level to 125mmol/l. Subsequent correction can be at a slower rate. Correction of non-acute hyponatremia should occur at a rate of 0.5mmol/hr increase in serum sodium, as rapid correction of chronic hyponatremia could result in pontine myelinolysis.

Hypernatremia
Hypernatremia can be due to water loss or excess sodium ingestion, and assessment of the state of hydration will help in determination of the cause – see appendix 2.

Hypernatremic dehydration can be difficult to detect as the movement of water from cells initially maintains the plasma volume, until 10-15% loss of body weight occurs. The

movement of water from brain cells generally result in CNS symptoms of irritability, depressed sensorium or seizures. The severity of neurologic symptoms is related to the degree and rate of rise in plasma osmolality. Brain cell volume can be protected by their ability to generate new solutes intracellularly (ie. idiogenic osmoles). However when hypertonicity develops too quickly these may not form quickly enough to prevent brain damage from intracellular volume depletion. The speed at which these idiogenic osmoles are removed or inactivated is unknown; hence rapid correction of hypernatremia with hypotonic solutions may cause cerebral edema and seizures.

Hypernatremia from iatrogenic, accidental or non-accidental salt intoxication results in overhydration. Excess salt should be removed by inducing diuresis if renal function is normal, or by peritoneal dialysis if renal function is poor.

Hypokalemia
Potassium is entirely intracellular. Causes of hypokalemia include
- decreased intake
- increased movement into intracellular compartment (e.g. correction of acidosis, alkalosis, administration of insulin)
- increased urine losses (e.g. loop diuretics, renal tubular acidosis, hyperaldosteronism)
- increased gastrointestinal losses (vomiting, diarrhoea, continuous GI suction)

Rapid correction of potassium can be potentially dangerous as cells have a limited rate at which they can restore their K content. Replace potassium slowly at infusion rates of <0.3 mmol/kg/hr, and use intravenous correction only if severe or in cardiac patients at risk of arrhythmia **MUST consult with on call consultant**. Otherwise use the slower but safer oral route.

Hyperkalemia
Hyperkalemia causes muscle weakness and abnormal cardiac conduction, with ECG changes occurring at serum K of >6.5 mmol/l followed by ventricular fibrillation and cardiac standstill at increasing levels. Causes of hyperkalemia include
- increased intake
- increased movement into the extracellular space (acidosis, tissue catabolism, cell destruction, tumour lysis)
- impaired renal excretion (renal failure, adrenal insufficiency)

True hyperkalemia (with K>7mmol/l and/or ECG changes) is a medical emergency. Therapy includes
- diluting the ECF
- creating a chemical antagonism to the membrane effect by administering sodium bicarbonate and calcium gluconate
- increasing the cellular uptake of K by the use of glucose and insulin infusion
- removing K by the use of exchange resins, diuretics or dialysis.

Haemolytic uraemic syndrome (HUS)

This is the most common cause of intra-renal ARF in children in developed countries, and occurs most frequently in children under 3 years. The diagnosis is based on the triad of uraemia, thrombocytopenia, and microangiopathic haemolytic anaemia with microvascular thrombosis [5-7]. Extrarenal manifestations can occur in 20-30% of patients (e.g. seizures and hypertension) and may be life threatening. Peripheral blood film shows schistocytes and burr cells, and increased lactate dehydrogenase is a sensitive index of ongoing haemolysis. Serum levels of fibrin degradation product-E may be a useful marker of HUS as it is significantly raised.

Typical HUS occurs in epidemics commonly in the summer months, and is associated with diarrhoea (D+) from Shiga toxin producing enteropathogenic E coli (STEC) 0157:H7. This is the cause in 90% of cases of HUS in Europe and USA although Shigella dysenteriae is more

frequently associated with HUS in developing countries, and is associated with a higher mortality and morbidity. Other pathogens (S. pneumonia, Staphylococcus etc) are now recognized that are not associated with diarrhoea (D-) and present as atypical HUS. There is controversy about whether antibiotic therapy for E coli enteritis predisposes to development of HUS, but there is no evidence to support this [8]. Drugs and other conditions (e.g. SLE, BMT, cancers, malignant hypertension, etc) can also initiate the triad that defines HUS. Familial HUS can occur with factor H deficiency (gene locus identified at chromosome 1q32) or reduced expression of membrane co-factor CD46, although these are rare causes of atypical HUS. These factors are important regulators of the complement pathway and their deficiency leads to activation and complement deposition on glomerular endothelial cells.

Renal prognosis is better for patients with typical HUS, where 95% have total renal recovery compared to <50% in the D- HUS group. Adequate parenteral volume expansion with isotonic solutions in STEC infections before the development of HUS has been shown to be nephroprotective and may attenuate renal injury [5,9]. Treatment is mainly supportive with about 50% of D+ HUS patients requiring a short period of dialysis for renal failure. In the ITU setting haemofiltration may be more appropriate for the cardiovascularly unstable child. Plasmapheresis and immunosuppressive agents have a place in the D- group, especially in the familial group or HUS associated with auto-immune conditions. Permanent loss of renal function can occur in 5-25% of cases [10]. Renal transplant may not be a suitable option for atypical familial HUS where the recurrence rate of HUS in the transplanted kidney may be as high as 80%.

Other sources of information:

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- Goonasekaran C, Wilkins B and Dillon M. Renal disease and disturbances of water and electrolytes. In: Care of the Critically Ill Child. Eds Macnab, Macrae, Henning. Churchill Livingstone
- Halperin and Goldstein. Fluid, electrolyte and acid base physiology: a problem based approach. Saunders
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4. Haycock GB. Hyponatremia: Diagnosis and management. *Arch Dis Child* Educ Pract Ed 2006; 91:ep37-ep41
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7. Amirlak I, Amirlak B. Haemolytic uraemic syndrome: an overview. *Nephrology* 2006; 11:213-218
8. Safdar N, Said A, Gangnon RE, Maki DG. Risk of hemolytic uremic syndrome after antibiotic treatment of Escherichia coli 0157:H7 enteritis. A meta-analysis. *JAMA* 2002; 288: 996-1001
9. Ake JA, Jelacic S, Ciol MA et al. Relative hephroprotection during Escherichia coli O157:H7 infections: association with intravenous volume expansion. *Pediatrics* 2005; 115: 673-80
10. Garg AX, Suri RS, Barrowman N et al. Long term renal prognosis of diarrhoea associated hemolytic uremic syndrome. A systematic review, meta-analysis, and meta-regression. *JAMA* 2003; 290: 1360-70

Information for Year 2 ITU Training (advanced):

Year 2 ITU curriculum

ITU Management of clinical conditions:
- Renal manifestations of systemic disease including vasculitides
- Transplantation: immediate post op management, blood transfusion, immune suppression, perfusion issues.
- Post infectious Glomerulonephritis.
- Renal vein thrombosis.
- Pyelonephritis
- Nephrotic syndrome
- Hydronephrosis: posterior urethral valves, neuropathic bladder, role of nephrostomy, post obstructive diuresis.
- Hypertension: life threatening complications

Curriculum Notes for Year 2:

Renal manifestations of systemic disease including vasculitides

Renal involvement is common in any of the forms of systemic vasculitis. The clinical manifestations commonly include renal insufficiency that may be severe enough to initially require dialysis and hypertension.

The urinalysis typically reveals urine sediment similar to that found in acute glomerulonephritis: red cells, red cell and other cellular and granular casts, and proteinuria (that is usually not in the nephrotic range) all may be seen. These findings are primarily due to glomerular inflammation and necrosis that may be induced either by direct immune-mediated injury of the glomerular capillaries or by ischemia resulting from narrowing of the lumen of affected arteries and arterioles. One exception may occur in patients with classic polyarteritis nodosa in which the muscular arteries are involved. If this process leads only to incomplete narrowing, then there may only be glomerular ischemia (not necrosis) and the urinalysis may be relatively normal.

Renal Transplant

Most patients following renal transplant are managed on the renal ward in GOSH but younger patients are managed on ICU as they are likely to need ventilatory support. The renal team generally like the CVP maintained at 10 cmH2O, but this measurement needs to take into account the effect of PEEP, and a different value may need to be agreed. CVP cannot be measured via the Permacath and another central line will need to be inserted

Also one needs to be aware of the conflicting aims of the renal team of maintaining renal perfusion and urine flow of 2 ml/kg/hr, and the ICU team of preventing fluid overload to facilitate weaning from ventilatory support. It is important to prevent hypovolaemia and graft thrombosis. Therefore the fluid regimen needs to be discussed between the 2 teams. The transplant surgeon is also aware of the condition of the donor kidney at the time of transplant, and may have specific requests.

If there is primary non-function of the graft an ultrasound scan with Doppler must be organized as soon as possible, and the renal team and transplant surgeon informed.

To prevent graft thrombosis, aspirin is now the recommendation. Anticoagulation with heparin was apparently associated with increased incidence of graft thrombosis. If heparin is necessary unfractionated heparin infusion should be used rather than low molecular weight heparin, as this can be stopped or easily reversed with protamine in the event of bleeding or the need for further surgical procedures.

The renal team is still keen on "renal" dopamine at 2 mcg/kg/min although there is no evidence for this.

Hypertension may occur and likely to need treatment. Ensure this is not reflex vasoconstriction in response to hypovolaemia. Preferred therapies are with vasodilators in the first instance (hydralazine, nifedipine) and with beta-blockers if hypertension is persistent. Please be aware of the likely BP that the donar kidney used to.

Cadaveric graft recipients require antibiotics (ciprofloxacin) until culture results are available. No antibiotics are required for live related donors. Recipients will also require prophylaxis for pneumocystis because of immunosuppression. No routine CMV prophylaxis is given but all sero-negative patients will receive CMV negative blood products, and have a weekly CMV and EBV surveillance by PCR.

Immunosuppression as per recommendation of renal team, depending on
- whether it is first or second transplant
- the presence or absence of cytotoxic antibodies
- the underlying reason for transplant

Levels of some immunosuppressant drugs will need to be monitored regularly. There are on-going trials of different newer immunosuppressants

Post infectious Glomerulonephritis.
Post-infectious glomerulonephritis is inflammation of glomeruli in the kidneys after streptococcal infection of the throat or, the skin. It can also be associated with other bacterial, viral and parasitic infections. As a consequence of immune complexes (formed from streptococcal antigen, antibodies, and complement) becoming trapped in the glomeruli of the kidneys, the glomeruli become inflamed. AType III Hypersensitivity reaction. Immune complexes (antigen-antibody complexes formed during an infection) become lodged in the glomerular basement membrane. Compliment activation leads to destruction of the basement membrane. It has also been proposed that specific antigens from certain nephrotoxic streptococcal infections have a high affinity for basement membrane proteins, giving rise to particularly severe, long lasting antibody response.
Glomerulonephritis can occur at any age. But it's most common in children between the ages of 4 and 7. The exact cause isn't known. Signs and symptoms of glomerulonephritis usually appear 10 to 21 days after a strep infection and include:

Fluid accumulation
Elevated blood pressure
Increased number of red blood cells in the urine
High levels of protein in the urine

There is no specific treatment for post-streptococcal glomerulonephritis. Treatment is focused on relief of symptoms.Treatment with antibiotics may occur to get rid of any remaining streptococcal bacteria. In most cases, the kidneys heal with time although renal support may be necessary.

Renal vein thrombosis.
Renal vein thrombosis is a fairly uncommon that occur after trauma to the abdomen or back, or it may occur because of a tumour, stricture or other blockage of the vein. It may be associated with nephrotic syndrome. In some children it occurs after severe dehydration. Dehydration is the most common cause of RVT in infants.presentation is with pain, blood in urine, reduced urine output,Urinalysis may show large quantities ofprotein and blood in urine. Imaging will shoew an obstruction.The treatment is focused on preventing new clot formations and reducing the riskrisk of embolization. Anticoagulants may be given to prevent formation of new clots

Pyelonephritis

Acute pyelonephritis is an, *exudative purulent localized inflammation* of kidney and renal pelvis. Pyelonephritis most often occurs as a result of a uti particularly in the presence of occasional or persistent reflux of urine from the bladder into the ureters or kidney pelvis.

Tubules are damaged by exudate and may contain neutrophil casts. In the early stages, glomeruli and vessels are normal. Urine commonly reveals white or red blood cells in the urine. A urine and blood cultures may reveal an organism. Scans may show enlarged kidneys with poor flow of dye through the kidneys. IVP and CT scan of the abdomen can also indicate underlying disorders. Gross pathology often reveals pathognomonic radiations of haemorrhage and pus through therenal pelvis and cortex. Chronic infections can result in fibrosis and scarring.

Nephrotic syndrome
Nephrotic syndrome is where the kidneys have been damaged, causing them to leak protein. It is characterised by proteinuria (>3.5g/ day) hypoalbuminemia, and edema. The following are baseline, essential investigations
Urine sample looking for protein, albumin levels in blood < 30g/L
High levels of cholesterol, specifically elevated LDL usually with concomitantly elevated VLDL. Abnormal electrolytes, urea and creatinine. Furher investigations are indicated if the cause is not clear. Auto-immune markers (ANA, ASOT, C3, cryoglobulins, serum electrophoresis. Causes include

- Primary renal diseases
- Any of the glomerulonephritides
- Secondary renal diseases
    Diabetes
    SLE
    Amyloidosis

Treatment includes general supportive measures and specific treatment of underlying cause Immunosupression for the glomerulonephritides. Complications include venous thrombosis: due to leak of anti-thrombin 3, which helps prevent thrombosis. This often occurs in the renal veins. Acute renal failure due to hypovolemia. Pulmonary edema. The prognosis depends on the cause of nephrotic syndrome. It is usually good in children, because Minimal change disease responds very well to steriods. However other causes such as focal segmental glomerulersclerosis frequently leads to renal failure.

Hydronephrosis: posterior urethral valves, neuropathic bladder, role of nephrostomy, post obstructive diuresis.
Hydronephrosis is dilation of the area of kidneys where urine collects that can occur when there is an obstruction of urine flow somewhere along the urinary tract, most often in the upper section. Another cause of hydronephrosis is reflux. Most children with hydronephrosis are born with the condition although it can develop during childhood. It is the most common urinary tract anomaly (abnormality) and ranges in severity. In mild hydronephrosis, the pelvic dilation is barely noticeable, whereas in severe hydronephrosis the swelling occupies much of the abdomen. In mild cases and even some moderate cases of hydronephrosis, children will have no symptoms and the condition may disappear on its own within the first year of life. In more severe cases, when kidney function is affected, the infant or child can experience pain, bleeding and infections. These symptoms may not develop until months or years after hydronephrosis is first detected. In most cases, hydronephrosis is detected on a prenatal ultrasound. Treatment depends on the underlying cause and the severity of the symptoms.

Hypertension (HTN)
HTN is defined as BP elevation above the 95th centile for a population matched for age, sex, size, genetics and environmental factors. Guidelines of BP centiles for age, sex and height are available from the National Blood Pressure Education Program Working group published in Pediatrics and on the internet [1]. An acute hypertensive emergency arises when the BP increases rapidly or exceeds the upper limits of diastolic BP for age by 55%. Most children with hypertensive crisis have an underlying secondary cause for the HTN, usually renal or renovascular in origin, although one also needs to exclude CNS causes, tumours (e.g. phaeochromocytoma) and drugs.

The usual presentation in children is with hypertensive encephalopathy because of the intense arteriolar vasospasm due to "over-autoregulation" of cerebral flow. This leads to ischaemia and microinfarcts in the brain, causing severe headache and vomiting, blurred

vision, altered sensorium, focal neurological signs and convulsions. Other target organ damage can also occur on the eyes (exudates and haemorrhages), heart (left ventricular failure) and kidneys (proteinuria or haematuria) [2]. The effect of fibrinoid necrosis on the vascular system causes thrombosis and haemolytic anaemia.

In chronic HTN functional and structural adaptations may have occurred, shifting autoregulation to a higher BP range. Attempts to lower BP too rapidly to avoid target-organ damage may lead to organ hypoperfusion. Therefore it is important to find out if HTN is acute or chronic.

Safest way to treat hypertensive crisis is to lower BP using continuous IV infusion of short-acting antihypertensive medication, with continuous monitoring of BP. Lower BP by 25% in first 8 hours, followed by gradual reduction in BP over the next 26-48 hours [1].

Sodium nitroprusside is a powerful arteriolar and venous vasodilator. Ideal because fast acting (within seconds) and very short half-life, thus easy to titrate dose. Start at dose of 0.5mcg/kg/min, up to 8mcg/kg/min. Potential for cyanide toxicity, especially if used longer term. Potential to increase cerebral blood flow and intracranial pressure.

Nicardipine is a calcium channel blocker and mainly an arteriolar vasodilator. Slightly longer onset of action and half-life compared to nitroprusside. Dose 1-3 mcg/kg/min. Potential to increase cerebral blood flow and intracranial pressure.

Hydralazine causes reflex tachycardia as well as salt and water retention

Labetolol is a combined α/β-blocker and can be given as an IV infusion (0.5-3 mg/kg/h) or IV bolus, but has a longer duration of action and should be used with caution.
 Esmolol is a pure β-blocker and decreases BP by reducing cardiac output. Dose 50-300 mcg/kg/min. It has a very short onset of action and short half-life. Avoid in patients with obstructive airway disease e.g.asthma and use with caution in patients with congestive heart failure.

Fenoldopam is the newest class of antihypertensive agents and the first available peripheral dopamine receptor DA1 agonist. Works as vasodilator by increasing cAMP, leading to smooth muscle relaxation, with greatest effects on renal and splanchnic arterial beds, and less effects on cerebral and coronary circulation. Dose 0.5-2 mcg/kg/min. Tolerance develops after 48 hours of use. Potential to increase intraocular pressure. Limited experience with children.

Other sources of information:

- Seikaly MG. Hypertensive crisis. In Essentials of Pediatric Intensive Care. Ed Levin and Morriss. Quality Medical Publishing Incorporated.
- GOSH renal transplant protocol (attached – please do not circulate widely as this is from renal team and only available to nephro-urology trainees). Relevant sections are the anaesthetic/operation check list, the immediate post-operative management and immunosuppression.
- GOSH hypertension protocol (renal unit)

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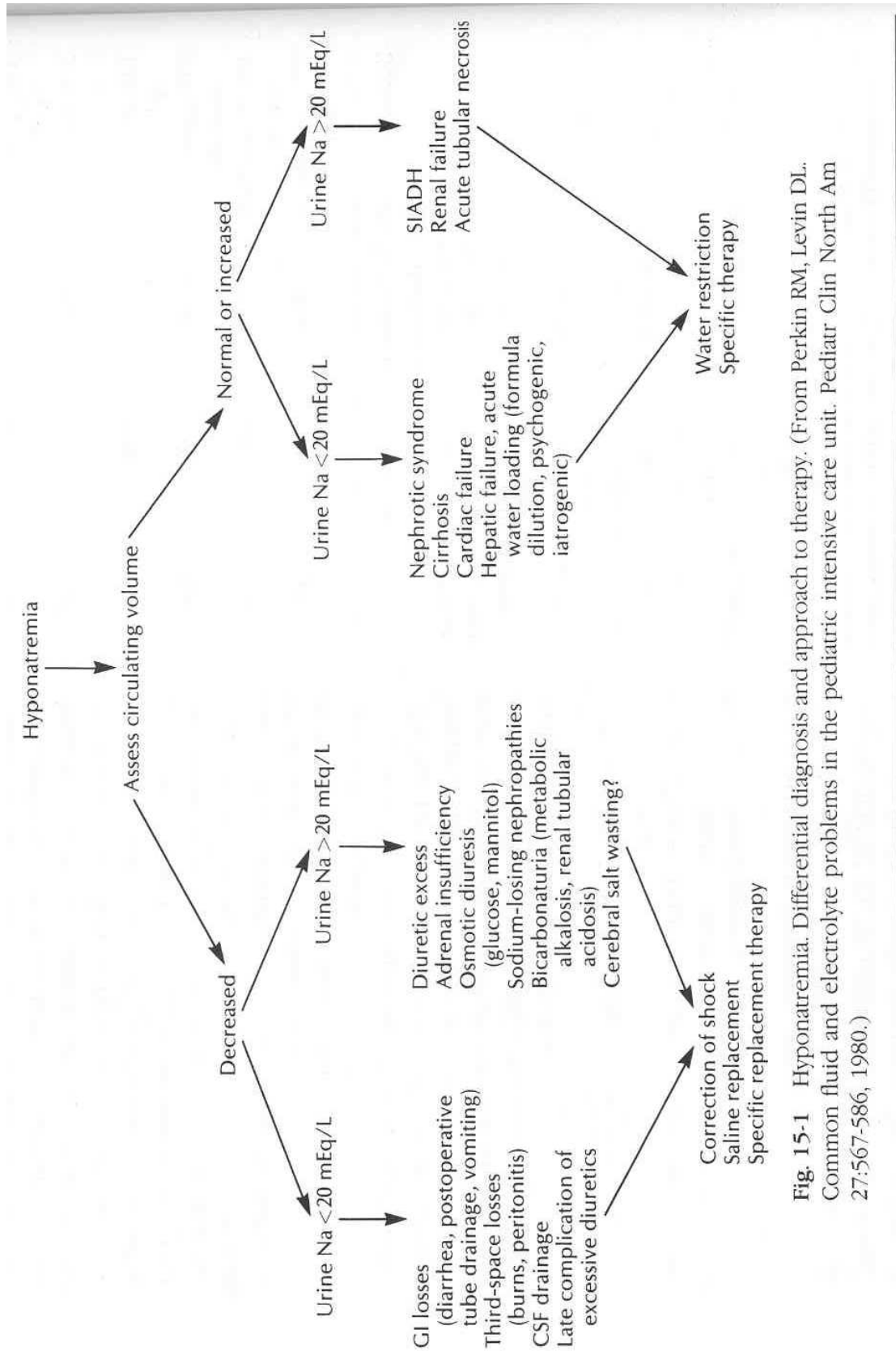
Hyponatremia

Assess circulating volume

Decreased

Urine Na <20 mEq/L

GI losses
(diarrhea, postoperative
tube drainage, vomiting)
Third-space losses
(burns, peritonitis)
CSF drainage
Late complication of
excessive diuretics

Urine Na >20 mEq/L

Diuretic excess
Adrenal insufficiency
Osmotic diuresis
(glucose, mannitol)
Sodium-losing nephropathies
Bicarbonaturia (metabolic
alkalosis, renal tubular
acidosis)
Cerebral salt wasting?

Correction of shock
Saline replacement
Specific replacement therapy

Normal or increased

Urine Na <20 mEq/L

Nephrotic syndrome
Cirrhosis
Cardiac failure
Hepatic failure, acute
water loading (formula
dilution, psychogenic,
iatrogenic)

Urine Na >20 mEq/L

SIADH
Renal failure
Acute tubular necrosis

Water restriction
Specific therapy

Fig. 15-1 Hyponatremia. Differential diagnosis and approach to therapy. (From Perkin RM, Levin DL. Common fluid and electrolyte problems in the pediatric intensive care unit. Pediatr Clin North Am 27:567-586, 1980.)
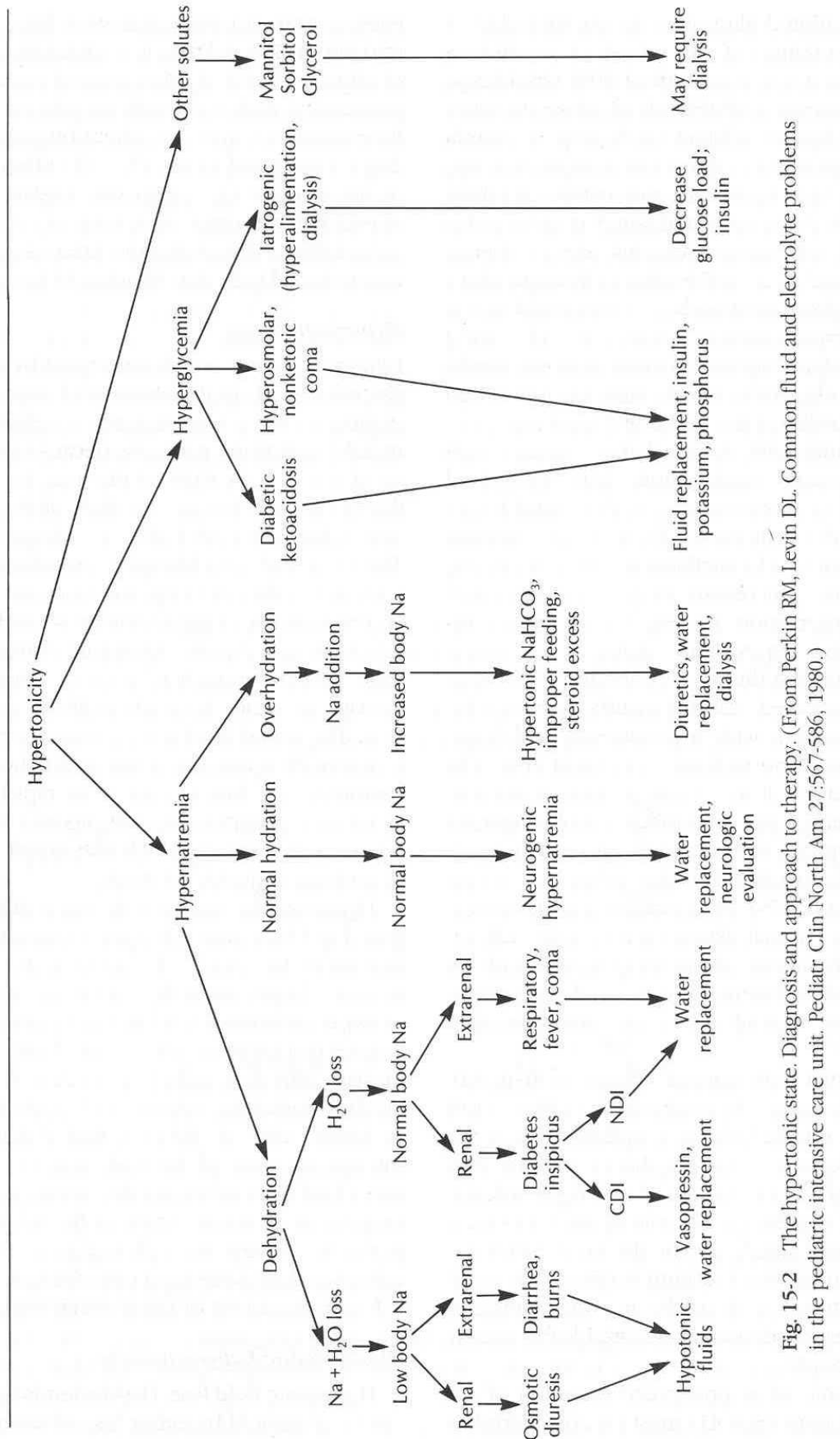
Appendix

2

Fig. 15-2 The hypertonic state. Diagnosis and approach to therapy. (From Perkin RM, Levin DL. Common fluid and electrolyte problems in the pediatric intensive care unit. Pediatr Clin North Am 27:567-586, 1980.)