# Paediatric Urology

## Second Edition

Edited by

**D. Innes Williams**

**J.H. Johnston**

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第二版

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# Preface to the Second Edition

This book was first published in 1968 under the editorship of D. Innes Williams and, although the rapidity of change in medical science is sometimes exaggerated, a new edition is clearly overdue. The scope of paediatric urology was defined in the 1960s and the groundwork of knowledge of the disorders to be treated was established, but the 1970s have seen a considerable increase in our understanding of the physiological aspects of urinary tract malformation and a much greater appreciation of the contributions that can be made to urology by other disciplines in medicine and science. The more diverse authorship of chapters in this new edition reflects our growing dependence upon the cooperative interests of our colleagues in nephrology, radiology, endocrinology, oncology and pathology, a reliance that has gone further in paediatric than in adult urology.

In clinical practice such collaborative work can only be fully achieved within a large hospital or a unit devoted to children. Both editors have been fortunate to work in such an environment and believe that the highest standards of paediatric urology can only be reached in such circumstances.

However, even in countries with advanced health care systems large numbers of children with urological disorders must be treated outside paediatric hospitals and this book is directed to all surgeons who undertake such work. Many will no doubt be urologists in training or in practice, whose chief concern is with adult disease; their continued interest in paediatrics is essential to the provision of appropriate care for the many children living long distances from specialized centres, but they also have a particular role to play in ensuring that the advances made in the more widely researched and better funded field of adult urology are applied to children's disorders. Equally, paediatric surgeons have a contribution to make to the treatment of urological disease and it is to be hoped that our book will be of value to them in training. For specialists outside surgery we aim at a reciprocal exchange of information. The urological surgeon needs to know something of oncology and similarly the oncologist must understand the problems and the possibilities of surgical treatment. This text is therefore intended for a wider audience than surgeons alone.

We are grateful to the various contributors to this volume for their cooperation in its production. Also we express our sincere thanks to the large number of junior staff and visitors in our respective departments who over many years have been involved in the management of patients, have helped in the assessment of results and, by their searching questions, have often stimulated reflection and research.

D. Innes Williams
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# Contents


1 Renal function 1
*T.M. Barratt*

2 Renal diagnostic imaging 11
*Isky Gordon*

3 Acute renal failure 27
*T.M. Barratt and Susan P.A. Rigden*

4 Chronic renal failure and regular dialysis 37
*T.M. Barratt and Rosemarie A. Raillod*

5 Renal transplantation in children 49
*Oswald N. Fernando*

6 Hypertension 57
*Michael J. Dillon*

7 Renal arterial disease 73
*J.H. Johnston*

8 Glomerular diseases and haematuria 79
*T.M. Barratt*

9 Urinary tract infection 89
*J.D. Williams*

10 Urinary tract infections: clinical aspects 95
*Jean M. Smellie and I.C.S. Normand*

11 Urinary tract infections: localized inflammatory lesions 113
*J.H. Johnston*

12 Urinary tract infections: tuberculosis and other specific infections 121
*J.H. Johnston*

13 Anomalies of the kidney 129
*D. Innes Williams*

14 Hypoplastic, dysplastic and cystic kidneys 137
*D. Innes Williams and J. Risdon*

15 Vesicoureteric reflux 151
*P.G. Ransley*

16 Ureteric duplications and ectopia 167
*D. Innes Williams*

17 Upper urinary tract obstruction 189
*J.H. Johnston*

18 Investigation of bladder function 215
*J.H. Johnston and Neville Harrison*

19 Bladder disorders 225
*J.H. Johnston*

20 Male urethral anomalies 239
*D. Innes Williams*

21 Male urethral obstructions 251
*D. Innes Williams*

22 Urinary tract complications of imperforate anus 271
*D. Innes Williams*

23 Female urethral anomalies and obstructions 279
*D. Innes Williams*

24 Prune belly syndrome 289
*D. Innes Williams*

25 The exstrophic anomalies 299
*J.H. Johnston*

26 Enuresis 317
*W. Keith Yeates*

27 Neuropathic bladder 325
*H.B. Eckstein and D. Innes Williams*

28 Urinary diversion 337
*J.H. Johnston*

29 Urolithiasis: medical aspects 351
*T.M. Barratt*

30 Urolithiasis: surgical aspects 361
*J.H. Johnston*

**31** Urinary tract injuries 369
*J.H. Johnston*
**32** Renal tumours 381
*D. Innes Williams and John Martin*
**33** Neuroblastoma, teratoma and other retroperitoneal tumours 401
*J.H. Johnston*
**34** Tumours of the lower genitourinary tract 411
*D. Innes Williams and John Martin*
**35** Normal and abnormal sexual development 423
*David B. Grant and D. Innes Williams*
**36** Abnormalities of the penis 435
*J.H. Johnston*
**37** Abnormalities of the scrotum and the testes 451
*J.H. Johnston*
**38** Acquired lesions of the penis, the scrotum and the testes 467
*J.H. Johnston*
**39** Male intersex disorders and male hypogonadism 477
*Frank Harris and J.H. Johnston*
**40** Female genital tract anomalies 495
*J.H. Johnston*
**41** Acquired female genital disorders 503
*J.H. Johnston*
**42** Turner's syndrome 509
*Frank Harris*
**43** Sexual precocity 515
*Frank Harris*
**44** Congenital adrenal hyperplasia and female pseudohermaphroditism 525
*David B. Grant and J.H. Johnston*
**45** True hermaphroditism and mixed gonadal dysgenesis 537
*David B. Grant and D. Innes Williams*
**46** Disorders of sexual development: investigation and general management 543
*David B. Grant*
**47** Gonadal tumours 549
*D. Innes Williams*
**48** Adrenocortical tumours and Cushing's syndrome 557
*David B. Grant and D. Innes Williams*

# 1 Renal Function

T.M. Barratt

## Introduction

The primary goal of the urologist is the preservation of renal function. With children there is an additional obligation to ensure optimum conditions for growth of the immature kidney. In this chapter basic aspects of renal physiology are not described because several accounts are readily available (Barratt, 1976). Instead the physiological development of the kidney, problems of assessment of renal function, metabolic aspects of young children and some fluid and electrolyte disturbances are reviewed.

## Development of the kidney

### Morphological aspects

#### Embryology

The pronephros develops in the human embryo during the third gestational week. Little is known of its function and it is rapidly superseded by the mesonephros which persists up to the 12th gestational week. The metanephros, which is the definitive kidney, is formed by the interaction of the ureteric bud arising from the lower end of the mesonephric duct with the nephrogenic blastema lying caudal to the mesonephros. The growing tip of the ureteric bud divides, undergoing 16 generations of branching, and secretes a substance that induces nephron formation in the blastema. Within the metanephros nephron development is centrifugal, the nephrogenic zone being in the outer cortex. The formation of new nephrons is essentially complete by the 36th week of gestation so that the full-term infant enters extrauterine life with his complete array of one million nephrons in each kidney (Potter and Thierstein, 1943; McCrory, 1972).

#### Postnatal growth

The combined weight of the kidneys at birth is approximately 25 g and this rises to 300 g in the adult. On the basis of DNA content Widdowson, Crobb and Milner (1972) concluded that the kidney of the full-term infant contains about 17 per cent of the adult number of cells. Net DNA synthesis ceases at 6 months of age and subsequent growth of the kidney is due to an increase in cell size rather than cell number. However, working on the rat kidney, Sands, Dobbing and Greatrix (1979) cast doubt on the neat division of phases of growth into hyperplasia characterized by an increase in cell number and hypertrophy in which there is an increase in cell size alone.

Microdissection studies show that the mean glomerular diameter in the middle cortical level of the neonatal kidney is 0.12 mm compared with an adult figure of 0.28 mm, whereas the proximal tubular length is only 1.73 mm in the neonate compared with 19.4 mm in the adult. The anatomical data suggest relative glomerular preponderance in the infant, and much of the increase in bulk of the kidney during early life is

due to growth of the proximal tubules, particularly in the most recently formed cortical nephrons (Fetterman *et al.*, 1965).

## Renal function *in utero*

From the ninth week of gestation the metanephros secretes urine consisting essentially of an ultrafiltrate of plasma. In mid term there is still little tubular reabsorption of glomerular filtrate and the urinary flow rate is high (Alexander and Nixon, 1961); towards term salt and water reabsorption increases so that the urinary flow rate falls. The only known function of the fetal kidney is the maintenance of amniotic fluid volume: bilateral renal agenesis results in oligohydramnios with consequent intrauterine compression deformities and pulmonary hypoplasia but otherwise little disturbance of homeostasis because the placenta functions as an efficient kidney *in utero*.

## Physiology of the infant kidney

### Renal blood flow

Blood flow to the infant kidney is low compared to the adult organ, with a preferential distribution to the juxtamedullary area (Spitzer, 1978). During the first year of life there is a fourfold increase in the proportion of the cardiac output going to the kidneys, and the same phenomenon is evident whether renal blood flow is related to kidney weight or body surface area. Indirect estimation of renal plasma flow from the clearance of para-aminohippurate (PAH) is inaccurate, however, since the extraction of PAH is low, probably due to the higher fraction of renal blood flow perfusing medullary tissue. In the newborn puppy the ratio of blood flow in the superficial cortical nephrons to that in the juxtamedullary nephrons is 2:1, rising to 10:1 in the mature animal (Olbing *et al.*, 1973). Renal vascular resistance is high in the newborn and in the piglet it falls 10-fold during the first month of life (Gruskin, Edelmann and Yuan, 1970). Much of the rapid rise in renal blood flow in early life is due to the opening up of the vasculature in the superficial cortex.

### Glomerular filtration

Inulin clearance, which is a measure of glomerular filtration rate (GFR), is low in relation to body surface area or kidney weight during infancy (*Table 1.1*), principally due to the vascular factors described above. Permselectivity studies with polydisperse dextrans indicate restricted filtration of macromolecules by the neonatal glomerulus (Arturson, Groth and Grotte, 1971).

**Table 1.1** Glomerular filtration rate (ml/min per 1.73m$^2$ surface area) measured by inulin clearance in healthy individuals of different ages (data from Barratt and Chantler, 1975)

| *Age* | *GFR mean* | *GFR range ± 2 sd* |
|---|---|---|
| Premature | 47 | 29–65 |
| 2–8 days | 38 | 26–60 |
| 4–28 days | 48 | 28–68 |
| 35–95 days | 58 | 30–86 |
| 1–5.9 months | 77 | 41–103 |
| 6–11.9 months | 103 | 49–157 |
| 12–19 months | 127 | 63–191 |
| 2–12 years | 127 | 89–165 |
| Adult male | 131 | 88–174 |
| Adult female | 117 | 87–147 |

### Proximal tubular function

The anatomical evidence of proximal tubular immaturity is reflected in decreased tubular reabsorption of endogenous amino acids, a low bicarbonate threshold and a low tubular maximum secretory capacity for PAH which is related to GFR. Data on the tubular maximum reabsorptive capacity for glucose are inconclusive. The excretion of low molecular weight protein, which is characteristic of renal tubular disease, is not a feature of the infant kidney, presumably because of a low filtered load resulting from the reduced permeability of the neonatal glomerulus to macromolecules (Barratt and Crawford, 1970).

### Salt and water excretion

The infant kidney is less able than the adult organ to excrete a sodium load. For example, the fractional excretion of filtered sodium (sodium clearance/GFR) in an adult dog rises to 17 per cent following an infusion of isotonic saline 100 ml/kg body weight, but in a puppy only reaches 5 per cent (Goldsmith *et al.*, 1975). This phenomenon may be related to the diminished perfusion of the superficial nephrons which, with their short loops of Henle, are best adapted to the excretion of a sodium load.

During water diuresis the infant excretes a greater fraction of filtered water than the adult, suggesting that a larger proportion of the filtered sodium is reabsorbed by the distal nephron. The greater dependence on distal sodium reabsorption in the neonate is reflected in much higher plasma renin activity and aldosterone concentration (Dillon and Ryness, 1975) and in the more severe clinical expression of defects of mineralocorticoid biosynthesis such as congenital adrenal hyperplasia.

In response to water deprivation or exogenous ADH newborn infants concentrate their urine to only 600–700 mosmol/ℓ, whereas adults generally achieve 1200 mosmol/ℓ. This is largely due to low rates of urea excretion in neonates because the urinary concentrations of nonurea solutes are similar and the discrepancy is minimized by urea supplements or a high protein diet (Edelmann, Barnett and Tropkou, 1960).

### Urinary excretion of acid

Infants tend to have a slightly lower plasma pH and bicarbonate concentration than adults. Although the bicarbonate threshold is also low in infants, data on the tubular maximum capacity to reabsorb bicarbonate are inconclusive because of the effects of concomitant volume expansion inherent in these studies. Immediately after birth there is a diminished urinary pH response to acidaemia, but by one week of age urinary pH values are as low as those of adults. Nevertheless net rates of acid excretion are low in babies because of low rates of excretion of phosphate and ammonia, which are the principal hydrogen ion acceptors. The infant excretes hydrogen ions in health at a rate close to maximum and has little reserve to cope with an acidotic stress.

# Assessment of renal function

## General considerations

Assessment of renal function in children with urological disorders necessitates care and familiarity with the methods, the precision and the sources of error of the techniques employed (Barratt, 1974a). Sick infants tolerate investigation poorly and methods that require repeated venepunctures, intravenous infusions or bladder catheterizations are rarely applicable in clinical practice. Problems arise with accurate timed urine collections because of losses and incomplete bladder emptying, and it is always prudent to check that creatinine excretion rates (urinary creatinine concentration times urinary flow rate) are of the expected order.

urinary creatinine concentration (mmol/kg body weight per day) = $0.132 + 0.004 \times$ age (years) $\pm$ 0.026 (sd)

## Allowance for body size

When evaluating renal function it is clear that some consideration must be given to the size of the individual as a whole. The problem of how to do so has not been satisfactorily resolved. It is customary to relate many physiological observations to body surface area, with a notional normal adult value of 1.73 $m^2$. On this basis most aspects of renal function appear immature, reaching 'adult' levels by the age of 2 years. However, the practice has insubstantial theoretical foundations. McCance and Widdowson (1952) proposed instead that it would be more logical to relate GFR to total body water, the domain over which the kidney exercises its excretory and regulatory function. A case can also be made for using extracellular fluid volume.

A similar problem arises in the estimation of surface area itself. The formula of Dubois and Dubois (1916) is commonly used, but it is based on meagre data in small infants.

surface area ($cm^2$) = weight $(kg)^{0.425} \times$ height $(cm)^{0.725} \times 71.84$

The logarithmic transformation, which is convenient for pocket calculators, is

surface area ($m^2$) = antilog (0.425 log weight + 0.725 log height − 2.144)

An analysis of the estimation of surface area in infants was given by Haycock, Schwartz and Wisotsky (1978).

## Glomerular function

There is no single test that gives an overall assessment of renal function, reflecting perhaps

the bulk of functioning renal parenchyma. The GFR approaches this, but filtration equilibrium is achieved within the glomerular capillaries with reserve filtration area and therefore substantial damage to the glomerular capillary bed must occur before the GFR falls.

From the physiological point of view the glomeruli are ultrafilters and thus there are two functional expressions of damage, namely blockage, which is reflected in a fall in GFR, and leakage, which is manifested by the appearance in the urine of blood and protein. Assessment of leakage is described in Chapter 8. There are five tests commonly employed to assess GFR and they are ranked here in order of simplicity and inverse order of precision.

## Plasma urea concentration

Urea production varies at least fourfold on conventional diets (see below). Urea clearance is less than GFR, due to back-diffusion, by an amount depending on the rate of urine flow. Thus metabolic factors are predominant in determining the plasma urea concentration. Although plasma urea concentration is deeply imbedded in the professional consciousness as a test of renal function, it is best discarded except as a measure of the degree of uraemia.

## Plasma creatinine concentration

The plasma creatinine concentration is determined by the balance between creatinine production and creatinine clearance (excretion/plasma concentration). Creatinine production is a function of body weight (see above) and thus of the cube of height while creatinine clearance is related to body surface area and thus to the square of height. Hence plasma creatinine concentration rises with age (*Table 1.2*) and GFR can be predicted from the child's height and plasma creatinine concentration (Counahan *et al.*, 1976).

GFR/surface area (ml/min per 1.73 $m^2$ surface area) = 38 height (cm)/plasma creatinine concentration (μmol/ℓ)

Measurement of plasma creatinine concentration in the laboratory has some technical problems, principally the detection of noncreatinine chromogens by the alkaline picrate reagent used. Biochemistry laboratories serving paediatric urology departments should be encouraged to devote sufficient resources to providing a rapid, specific and reproducible service for plasma creatinine determination.

**Table 1.2** True plasma creatinine concentration (μmol/ℓ) measured by autoanalyser (data from Schwartz, Haycock and Spitzer, 1976)

| *Age* | *Plasma creatinine concentration* | | | |
|---|---|---|---|---|
| | *Female* | | *Male* | |
| | *mean* | *sd* | *mean* | *sd* |
| 1 | 31 | 4.4 | 36 | 8.8 |
| 2 | 40 | 6.2 | 38 | 10.6 |
| 3 | 37 | 7.0 | 40 | 9.7 |
| 4 | 41 | 10.6 | 40 | 9.7 |
| 5 | 40 | 9.7 | 44 | 9.7 |
| 6 | 42 | 9.7 | 46 | 10.6 |
| 7 | 47 | 10.6 | 48 | 12.3 |
| 8 | 47 | 9.7 | 50 | 12.3 |
| 9 | 48 | 9.7 | 52 | 14.1 |
| 10 | 48 | 11.4 | 54 | 19.4 |
| 11 | 53 | 11.4 | 55 | 12.3 |
| 12 | 52 | 11.4 | 57 | 14.1 |
| 13 | 55 | 12.3 | 60 | 18.5 |
| 14 | 57 | 11.4 | 63 | 21.1 |
| 15 | 59 | 19.4 | 67 | 19.4 |
| 16 | 57 | 13.2 | 65 | 22.0 |
| 17 | 62 | 17.6 | 70 | 15.8 |
| 18–20 | 63 | 16.7 | 81 | 15.0 |

## Creatinine clearance

This overestimates GFR as there is some tubular secretion of creatinine. It may be counterbalanced fortuitously by the tendency to overestimate plasma creatinine concentration due to noncreatinine chromogens. In some units a 24-hour urine collection is taken to minimize bladder emptying errors and to smooth out diurnal variation, but obviously the risks of urine losses are great and there are some advantages in short-term urine collections under diuretic conditions instead. Counahan *et al.* (1976) found that GFR could be predicted as accurately from the plasma creatinine concentration as from the 24-hour creatinine clearance, and there is therefore little to be gained from the additional burden of urine collection. However, there are circumstances in which the creatinine clearance rate is valuable, such as in divided renal function studies when the kidneys are drained separately, as an internal reference clearance for the assessment of for example phosphate or albumin excretion, and as an estimate of GFR where there is either muscle wasting with decreased

creatinine production or oedema when single-shot techniques are inappropriate.

### GFR estimates without urine collection

The difficulty inherent in accurate timed urine collections, particularly in children, has prompted research for other methods. Two are in current use, that is single-shot slope clearances and constant infusion techniques.

If a substance is rapidly mixed within its volume of distribution ($V_D$) and only cleared from the body by glomerular filtration, the GFR can be estimated from the rate of fall of plasma concentration after a single intravenous injection. Accurate measurement of low concentrations of the substance in plasma is essential and methods using radio-labelled compounds are generally the most suitable; $^{51}$Cr-edetic acid ($^{51}$Cr-EDTA) and $^{99m}$Tc-diethylenetriaminepentacetic acid ($^{99m}$Tc-DTPA) have proved useful. Several mathematical analyses are possible and the simplest requires only two blood samples 2 and 4 hours after the intravenous injection (Chantler and Barratt, 1972). The half-time ($t_{1/2}$) of the exponential disappearance is determined by plotting the plasma concentrations on a semilogarithmic scale, and an estimate of the volume of distribution is obtained by dividing the administered dose by the extrapolated zero-time plasma concentration. The GFR can then be calculated.

$$GFR = V_D \frac{0.693}{t_{1/2}}$$

This method has the merit of being very reproducible in the same individual, with a coefficient of variation of replicate GFR estimates that is 5 per cent. It is thus well suited to the detection of minor degrees of deterioration of renal function in urological patients.

If a substance cleared only by glomerular filtration is administered by constant intravenous infusion then in the equilibrium state the rate of infusion equals the rate of excretion. It can then be substituted in the clearance formula so that GFR can be calculated from the rate of infusion and the plasma concentration. The problem is that equilibrium may take a long time to achieve.

### Inulin clearance

This remains the definitive method for determination of GFR against which all other techniques should be assessed. It requires constant intravenous infusion and accurately timed short periods of urine collection often necessitating catheterization, and the analytical methods are not easy.

### Individual kidney GFR

In urological practice the need for an assessment of individual kidney function often arises. In these circumstances the relative function of the two kidneys is sufficient information, overall GFR being assessed in one of the ways described above. Clearly if urine from the two kidneys is draining separately then the divided creatinine clearance is a suitable measurement and opportunities to obtain such information should not be missed. Apart from this, methods of obtaining separate collections by ureteric catheterization or external occlusion are not convenient and radioisotopic means using 'area of interest' gamma camera analysis are most appropriate (*see* Chapter 2). In general such techniques depend on measurement of the rate of arrival of the radioisotope in the renal area and so depend on renal plasma flow rather than GFR.

## Proximal tubular function

Renal glycosuria indicates a defect of proximal tubular function. Hypophosphataemia is suggestive as well, although it can also result from hyperparathyroidism or dietary phosphate depletion. A generalized aminoaciduria is characteristic, but perhaps the simplest screening test is detection in the urine of low molecular weight proteins such as beta$_2$-microglobulin or lysozyme (Barratt and Crawford, 1970) which are normally filtered by the glomerulus and reabsorbed by a pinocytic mechanism in the proximal tubule.

## Urinary concentrating capacity

The capacity to concentrate the urine is an aspect of renal function very sensitive to urological disorders since it depends upon the integrity of the countercurrent system in the medulla. Obstructive uropathy in particular causes a major defect of urinary concentration. In most children over the age of 2 years deprived of fluid

overnight the osmolality of the first urine specimen passed in the morning is over 900 mosmol/ℓ and a single such observation excludes a defect of urinary concentration. Formal and more prolonged water deprivation tests should be monitored closely so that the child does not lose more than 2–3 per cent of body weight. Under such circumstances normal children achieve a urinary osmolality of 1127 ± 128 (sd) mosmol/ℓ (Edelmann *et al.*, 1967a).

Failure to respond adequately to water deprivation can be due to pituitary or renal causes and the problem can be dissected further by observing the response to antidiuretic hormone (ADH). A synthetic analogue of ADH, D-deamino (8-D-arginine) vasopressin (DDAVP) is now generally used. It can be given by intranasal instillation of 10 μg in infants and 20 μg in older children (Aronson and Svenningsen, 1974), but if the response is inadequate there may be doubt as to whether the dose was properly administered. Thus intramuscular injection of 0.04 μg/kg body weight is preferable in critical cases. Urinary osmolality should rise above 750 mosmol/ℓ. In infants fluid intake should be restricted to match urine output and insensible losses in order to avoid the possibility of water intoxication.

## Urinary acidification

The healthy kidney responds to metabolic acidosis by producing urine of pH less than 5.3 at any age with the exception of premature infants. A urinary pH less than 5.3 with a normal or only slightly reduced plasma bicarbonate concentration indicates an essentially normal acidification mechanism and certainly excludes distal renal tubular acidosis (*see* Chapter 29). Such an acidity is often found in the overnight urine specimen and obviates the need for further testing. Otherwise, ammonium chloride 75 mEq(4 g)/$m^2$ body surface area can be used as a moderate acid load, and the urinary pH should then fall below 5.3 (Edelmann *et al.*, 1967b). Urinary infection, particularly with Proteus, may interfere with urinary pH observations due to urea splitting and ammonia production.

# Metabolic aspects of young children

## Growth

The growing infant gains some 30 g in weight daily and of this approximately 25 g is water. About 1 g protein/kg body weight per day is incorporated into growing tissues and bone, along with sodium, potassium, calcium, phosphorus and other elements. In this respect growth relieves the kidney of an excretory load. McCance (1959) described growth as 'the third kidney' and reported protection from the effects of uraemia, hyperkalaemia and hyperphosphataemia by anabolism in the nephrectomized puppy (providing calorie intake was sufficient). The interaction of growth, calorie intake amd uraemia is further considered in Chapter 4.

## Nutrition

A consideration of paramount importance in the metabolism of young children with renal disease is the difference in composition of human breast milk and cows' milk formulas (*Table 1.3*), even though nowadays most of the artificial milks have protein and solute concentrations closer to those of human breast milk. The protein intake is more than twice as great from a cows' milk formula. Surplus protein not incorporated into growing tissues is broken down into urea, each gram of protein producing 0.3 g (5 mmol) of urea. With 1 g protein/kg per day being assimilated by growth then urea production on a protein intake of 2 g/kg per day is approximately 5 mmol/kg per day, whereas from a protein intake of 5 g/kg per day urea production is 20 mmol/kg per day. The implications for infants with chronic renal insufficiency are obvious.

**Table 1.3** Representative dietary intakes and excretory loads expressed per kilogram body weight per day of infants on cows' milk and breast milk diets (data from Barratt, 1974b)

| | *Cows' milk* | *Breast milk* |
|---|---|---|
| Water (ml) | 150 | 100 |
| Calories | 100 | 100 |
| Protein (g) | 5 | 2 |
| Sodium (mEq) | 4 | 1 |
| Potassium (mEq) | 5 | 2 |
| Phosphorus (mg) | 150 | 23 |
| Renal solute load (mosmol) | 33 | 13 |
| Hydrogen ion load (mEq) | 6 | 1 |

The principal urinary solutes are urea, sodium, potassium and chloride and the solute load presented for excretion is determined by dietary intake and not by renal function. It can be estimated roughly in milliosmoles as four

times the dietary protein intake in grams plus the dietary intake of sodium, potassium and chloride each expressed as milliequivalents (Ziegler and Fomon, 1971), and is thus 33 mosmol/kg per day in a baby fed cows' milk compared with 13 mosmol/kg per day in a breast-fed baby. With a conventional fluid intake urine volume is of the order of 100 ml/kg per day. Urinary osmolality in a breast-fed baby is thus about 130 mosmol/$\ell$ and in a baby fed cows' milk about 330 mosmol/$\ell$. An infant who has lost the ability to concentrate the urine above 300 mosmol/$\ell$, which is a defect commonly observed with urological disorders, is therefore in negative water balance on an intake of cows' milk of 150 ml/kg per day. He does not have effective thirst control and with impaired capacity to control urinary osmolality he has lost both limbs of the osmolar homeostatic mechanism. For such an infant cows' milk is like sea water for a shipwrecked sailor.

# Body fluids and electrolytes

## Water

Total body water (TBW) is 780 ml/kg in the full-term infant, falling to 600 ml/kg in the adult (Friis-Hansen, 1961). Extracellular fluid (ECF) is difficult to measure accurately or even to define with precision; it is generally taken to be the volume of distribution of a small solute whose intracellular concentration is negligible. The bromide space is easy to measure and amounts to 46 per cent of TBW in infants and 40 per cent in adults, but probably overestimates ECF by about 20 per cent (Barratt and Walser, 1969). Intracellular water (ICW) is taken as the difference between TBW and ECF.

The water intake of a baby is usually about 150 ml/kg per day. Of this about 25 ml/kg per day is incorporated into growing tissues and another 25 ml/kg per day is accounted for by insensible losses. Thus urine volume is about 100 ml/kg per day. Water balance is maintained by a homeostatic mechanism of which the afferent limb is ECF osmolality and the efferent limb is ADH which permits reabsorption of water from the collecting duct along the osmotic gradient established by the countercurrent system, thus reducing urine flow.

## Sodium

The distribution of water between the intracellular and extracellular phases is determined by osmotic forces. Sodium and its attendant anion are the principal determinants of ECF osmolality. Therefore in states of salt and water depletion it is mainly ECF that is diminished, resulting in circulatory collapse, whereas with pure water depletion it is ICW that is decreased and the organ principally affected is the brain because of the volume constraints imposed by the skull. Conversely with pure water excess ICW is expanded, causing the syndrome of water intoxication, whereas salt and water excess increases ECF and leads to hypertension and oedema.

The concentration of sodium in ECF is determined by the relative amounts of sodium and water: a normal plasma sodium concentration is quite compatible with severe saline depletion or overload if there are equivalent changes in TBW. On the other hand hyponatraemia can imply water excess with normal body sodium levels (dilutional), sodium depletion with normal body water levels (depletional) or usually a mixture of the two. The distinction usually hinges upon a clinical assessment of ECF volume, particularly blood pressure. In equivocal cases a raised plasma renin activity is a helpful pointer to a state of sodium depletion.

Sodium excretion is determined ultimately by sodium intake and the need to maintain sodium balance. In states of sodium depletion urinary sodium can be reduced below 0.1 mEq/kg per day, except perhaps in premature infants. The afferent limb of the sodium homeostatic mechanism is responsive to ECF volume. The efferent limbs are the renin-angiotensin-aldosterone system, which controls distal tubular sodium absorption in exchange for potassium, and an as yet unidentified hormonal system (natriuretic hormone), which controls proximal tubular sodium reabsorption.

## Potassium

Potassium is the principal intracellular cation. External potassium balance is under the control of the kidney and is regulated by aldosterone. If potassium excretion is impaired, as in renal failure, extracellular potassium concentration

rises leading to dysfunction of cardiac muscle. With renal or gastrointestinal potassium losses ECF potassium concentration is initially maintained at the expense of intracellular potassium, which leaves the cell in exchange for hydrogen ions resulting in intracellular acidosis and extracellular alkalosis.

## Hydrogen ions

Metabolism of a normal diet generates hydrogen ions in excess of bicarbonate, principally from breakdown of organic phosphates and sulphates. These hydrogen ions are excreted in the urine as titratable acidity and ammonium and amount to 1 mEq/kg per day in the breast-fed baby and as much as 6 mEq/kg per day in the infant fed cows' milk. Failure to excrete hydrogen ions results in a metabolic acidosis with a fall in plasma bicarbonate concentration. The change in ECF pH is minimized by compensatory hyperventilation (Kussmaul respiration) with hypocapnia.

## Principles of parenteral fluid therapy

Parenteral fluid therapy is only indicated if the oral route is inadequate.

### Correction of hypovolaemia

In states of circulatory collapse due to volume depletion 20 ml/kg body weight of blood, plasma or isotonic saline should be given rapidly.

### Deficit replacement

If dehydration is perceptible then the water deficit is probably about 50 ml/kg, if moderate around 100 ml/kg, and if severe approximately 150 ml/kg. Probable deficits in infants with moderately severe dehydration are shown in *Table 1.4*. Deficits should be replaced over 4–6 hours, and more slowly in hypertonic states. Acidosis can be corrected simultaneously; a useful solution for isotonic dehydration with acidosis is sodium bicarbonate 4 mmol added to each 100 ml burette of 1/5N dextrose saline to give a final sodium concentration of 70 mEq/ℓ.

**Table 1.4** Probable deficits of water and electrolytes in moderately severe dehydration in infants (data from Dell, 1973)

| *Type of dehydration* | *Plasma sodium (mEq/ℓ)* | *Probable deficit (ml/kg)* | *(mEq/kg)* |
|---|---|---|---|
| Hypertonic | >150 | 120–170 | 2–5 |
| Isotonic | 130–150 | 100–150 | 7–11 |
| Hypotonic | <130 | 40–80 | 10–14 |

### Maintenance requirements

The intravenous requirements for maintenance of fluid balance in infants are 120 ml/kg per day and approximately 2 mEq/kg per day of both sodium and potassium. About half this amount is required in the first few days of life and immediately after surgical operations. However, children with urological disorders frequently have defects of urinary concentration and sodium conservation so that they may not have the usual antidiuretic and antinatriuretic response to surgery. The practice of maintaining infants 'dry' in the postoperative period may not be appropriate for them.

### Replacement of abnormal losses

Children with major defects of urinary concentration require a fluid intake up to 200 ml/kg per day. They may not tolerate preoperative restriction of oral fluids and may therefore need intravenous fluids during this period.

Excessive urinary sodium losses can, if not replaced, lead to salt and water depletion with secondary deterioration of renal function. This may occur dramatically after relief of urinary tract obstruction. In these circumstances the urinary sodium excretion usually rises in the postoperative period to about 2.5 mEq/kg per day (Ghazali and Barratt, 1974). Occasionally there is massive salt loss.

### Nutrition

If it seems likely that there will be any delay in restitution of oral intake, early consideration should be given to the provision of amino acids, calories and vitamins parenterally (Harries, 1971).

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