اضطرابات الكلية والمسالك البولية

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كل الوسائط مسموحة:
تسجيل .. تصوير .. نسخ .. نقل الخ

19

Kidney and urinary tract disorders

Features of kidney and urinary tract disorders in children are:

• many structural abnormalities of the kidneys and urinary tract are identified on antenatal ultrasound Screening.

• urinary tract infection, vesicoureteric reflux, and urinary obstruction have the potential to damage the growing kidney.

• nephrotic syndrome is usually steroid sensitive and only rarely leads to chronic kidney disease.

• chronic renal disorders may affect growth and development.

Assessment of the kidneys and urinary tract

The glomerular filtration rate (GFR) is low in the newborn infant and is especially low in premature infants; the GFR at 28 weeks' gestation is only 10% of the term infant.

In term infants, the corrected GFR (15–20 ml/min per 1.73 m2) rapidly rises from 1-year to 2-years of age when the adult rate of 80 ml/min to 120 ml/min per 1.73 m2 is achieved (Fig. 19.1).

The assessment of renal function in children is listed in Table 19.1. The radiological investigations of the kidneys and urinary tract are presented in Table 19.2.

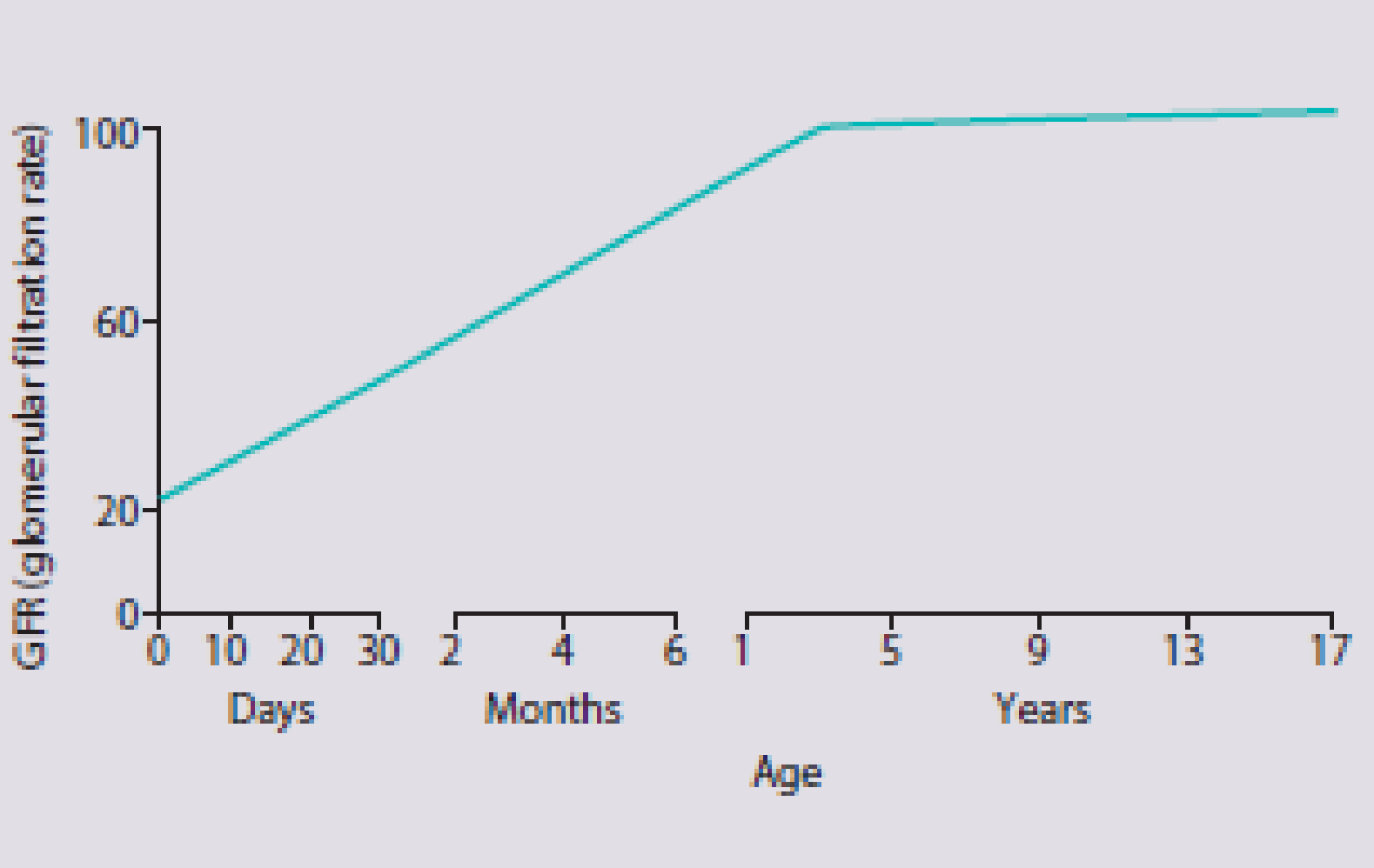


Figure 19.1 Increase in renal function (glomerular filtration rate, ml/min per 1.73 m^2) with age.

Table 19.1 Assessment of renal function in children

Plasma creatinine concentration	Main test of renal function. Rises progressively throughout childhood according to height and muscle bulk. May not be outside laboratory 'normal range' until renal function has fallen to less than half normal
Estimated glomerular filtration rate (eGFR)	The formula eGFR = k × height (cm) ÷ creatinine (μmol/L) provides estimate of GFR. Better measure of renal function than creatinine and useful to monitor renal function serially in children with renal impairment (k is 31 if measured enzymatically or 40 if creatinine measured using older Jaffe method)
Inulin or EDTA (ethylenediaminetetraacetic acid) glomerular filtration rate	More accurate as clearance from the plasma of substances freely filtered at the glomerulus, and is not secreted or reabsorbed by the tubules. Need for repeated blood sampling over several hours limits use in children
Creatinine clearance	Requires timed urine collection and blood tests. Rarely done in children as inconvenient and often becomes inaccurate
Plasma urea concentration	Increased in renal failure, often before creatinine starts rising, and raised levels may be symptomatic. Urea levels also increased by high protein diet, in catabolic states, or due to gastrointestinal bleeding

Table 19.2 Radiological investigation of the kidneys and urinary tract

Ultrasound	Standard imaging procedure of the kidneys and urinary tract provides anatomical assessment but not function. Excellent at visualizing urinary tract dilatation, stones, and nephrocalcinosis (small, multiple calcium deposits within renal parenchyma) Advantages: noninvasive, mobile Disadvantages: operator dependent, will not detect all renal scars
DMSA scan (^{99m}Tc dimercaptosuccinic acid)	*Static* scan of the renal cortex Detects functional defects, such as scars or areas of nonfunctioning renal tissue, but very sensitive, so need to wait at least 2 months after a urinary tract infection to avoid diagnosing false 'scars'
Micturating cystourethrogram (MCUG)	Contrast introduced into the bladder through urethral catheter Can visualize bladder and urethral anatomy. Detects vesicoureteric reflux (VUR) and urethral obstruction Disadvantages: invasive and unpleasant investigation especially beyond infancy, high radiation dose, and can introduce infection
MAG3 renogram (mercapto-acetyl-triglycine, labelled with ^{99m}Tc)	*Dynamic* scan, isotope-labelled substance MAG3 excreted from the blood into the urine. Measures drainage, best performed with a high urine flow so furosemide often given In children old enough to cooperate (usually >4 years of age), scan during micturition is used to identify VUR (indirect cystogram)
Plain abdominal X-ray	Identifies unsuspected spinal abnormalities May identify renal stones, but poor at showing nephrocalcinosis

Congenital abnormalities

Before antenatal ultrasound scanning became routine, few congenital abnormalities of the kidneys and urinary tract were diagnosed until they caused symptoms in infancy, childhood, or occasionally, adult life.

*Now the majority are identified in utero and can be managed prospectively.

*Abnormalities are identified in 1 in200 to 1 in 400 births. They are potentially important because they may:

- be associated with abnormal renal development or function (chronic kidney disease)
- predispose to postnatal infection
- involve urinary obstruction which requires surgical treatment

*The antenatal detection and early treatment of urinary tract anomalies provide an opportunity to minimize or prevent progressive renal damage.
*A disadvantage is that minor abnormalities are also detected, most commonly mild unilateral pelvic dilatation, which do not require intervention but may lead to over-investigation, unnecessary treatment, and unwarranted parental anxiety.

Anomalies detectable on antenatal ultrasound screening

Absence of both kidneys (*renal agenesis*) – As amniotic fluid is mainly derived from fetal urine, there is severe oligohydramnios resulting in Potter syndrome (Fig.19.2a,b), which is fatal.

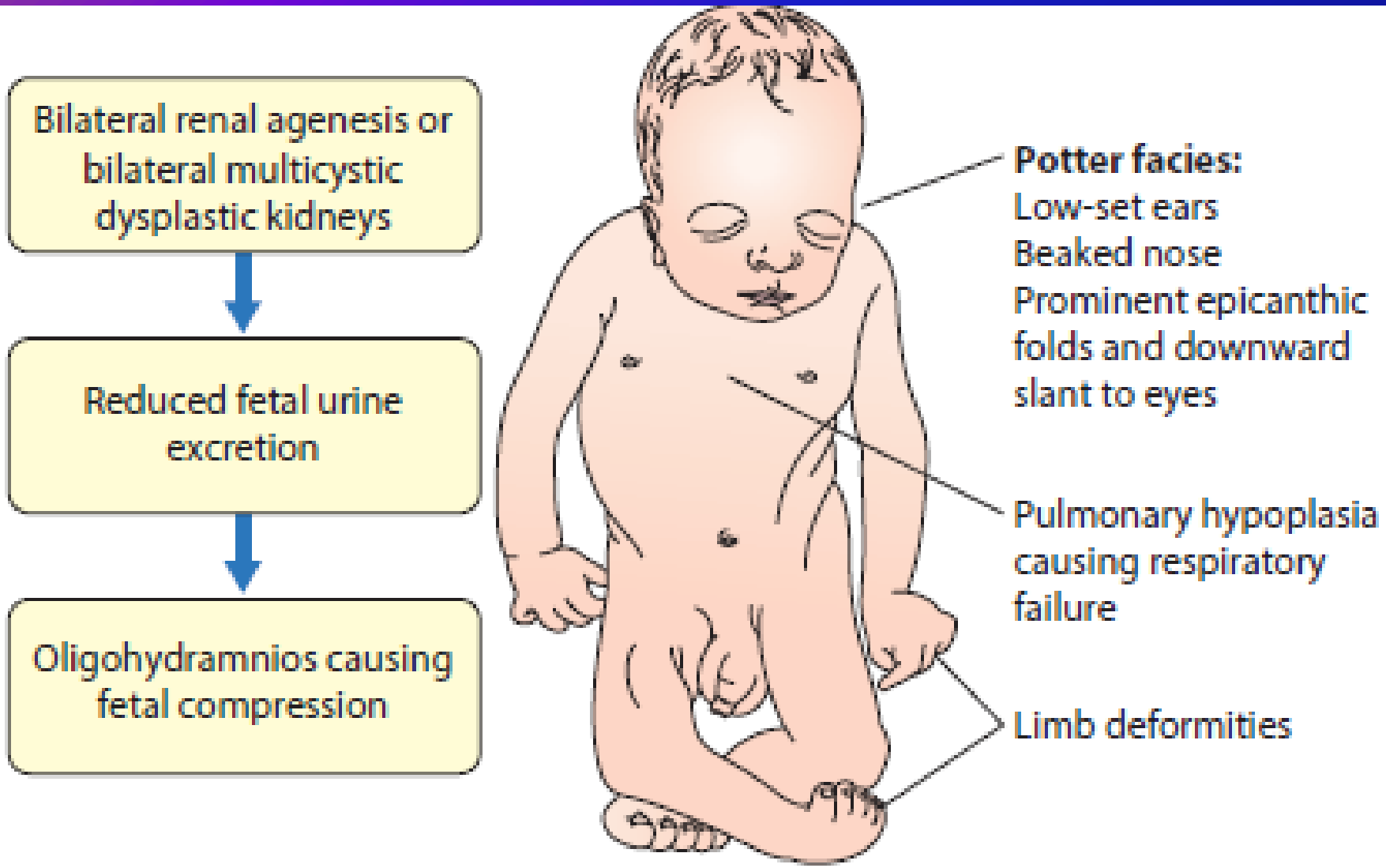


Figure 19.2a Potter syndrome. Intrauterine compression of the fetus from oligohydramnios caused by lack of fetal urine causes a characteristic facies, lung hypoplasia, and postural deformities including severe talipes. The infant may be stillborn or die soon after birth from respiratory failure.

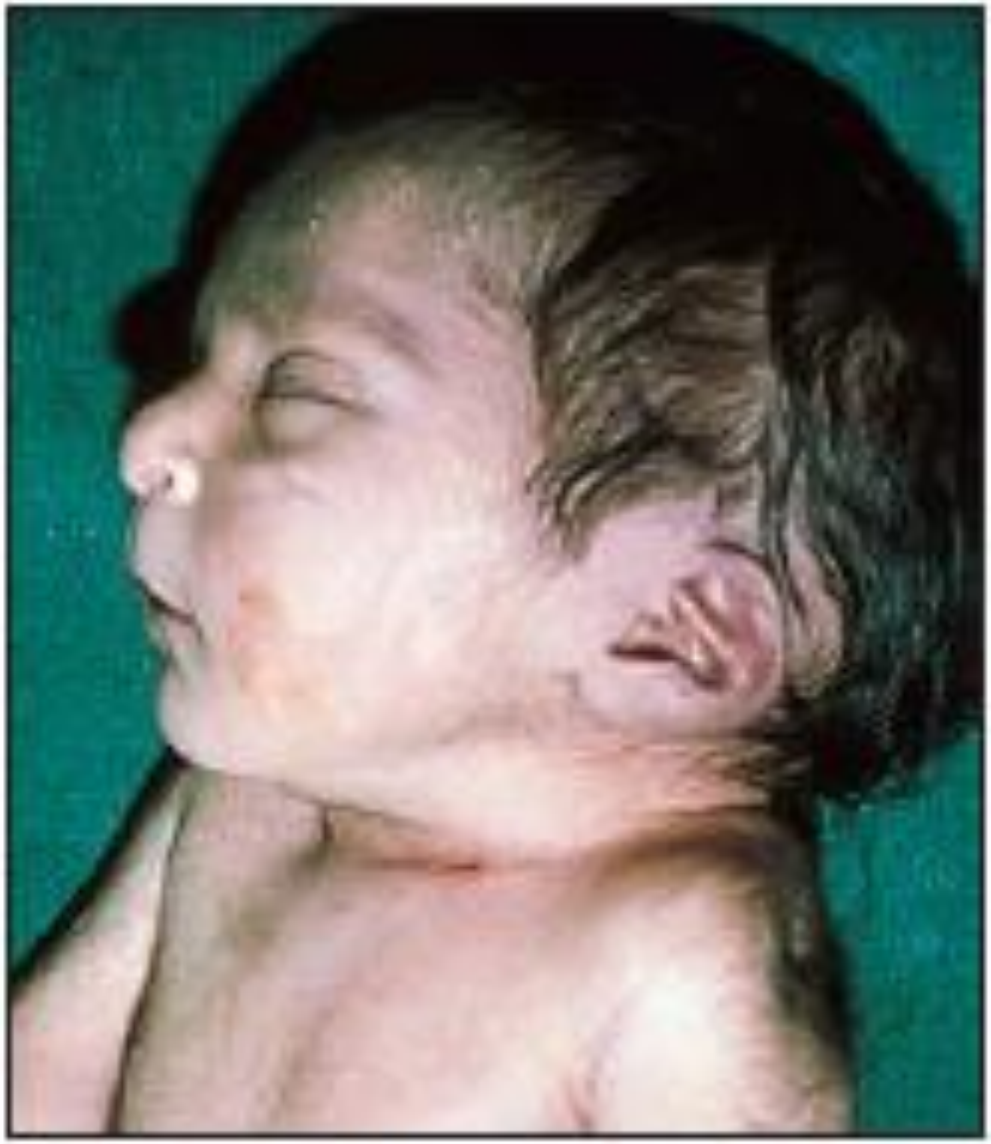
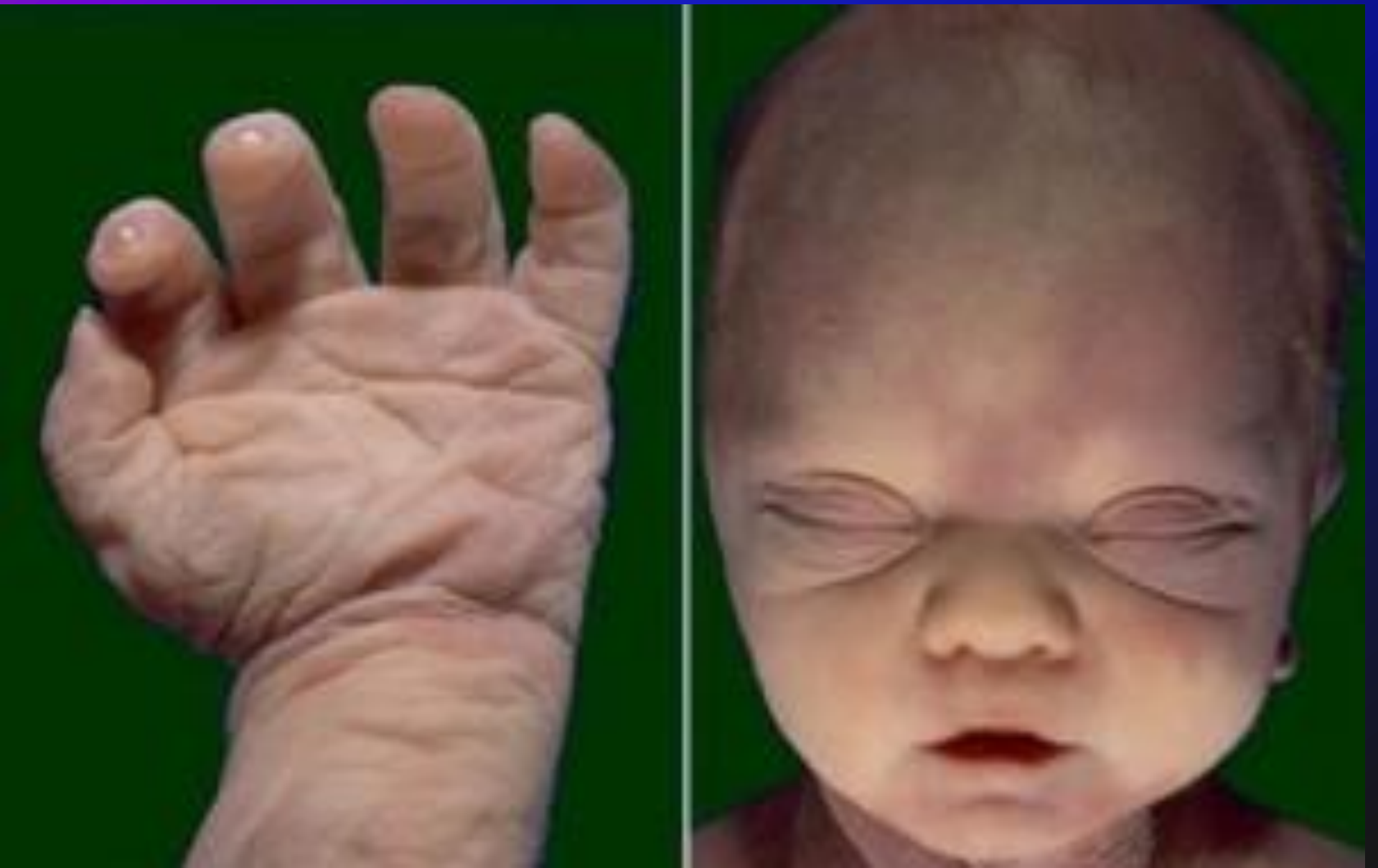


Figure 19.2b Facies in Potter syndrome.



Multicystic dysplastic kidney – Results from the failure of union of the ureteric bud (which forms the ureter, pelvis, calyces, and collecting ducts) with the nephrogenic mesenchyme. It is a non-functioning structure with large fluid-filled cysts with no renal tissue and no connection with the bladder (Fig. 19.3). Half will have involuted by 2 years of age, and nephrectomyis indicated only if it remains very large or hypertension develops, but this is rare. Because they produce no urine, Potter syndrome will result if the lesion is bilateral.

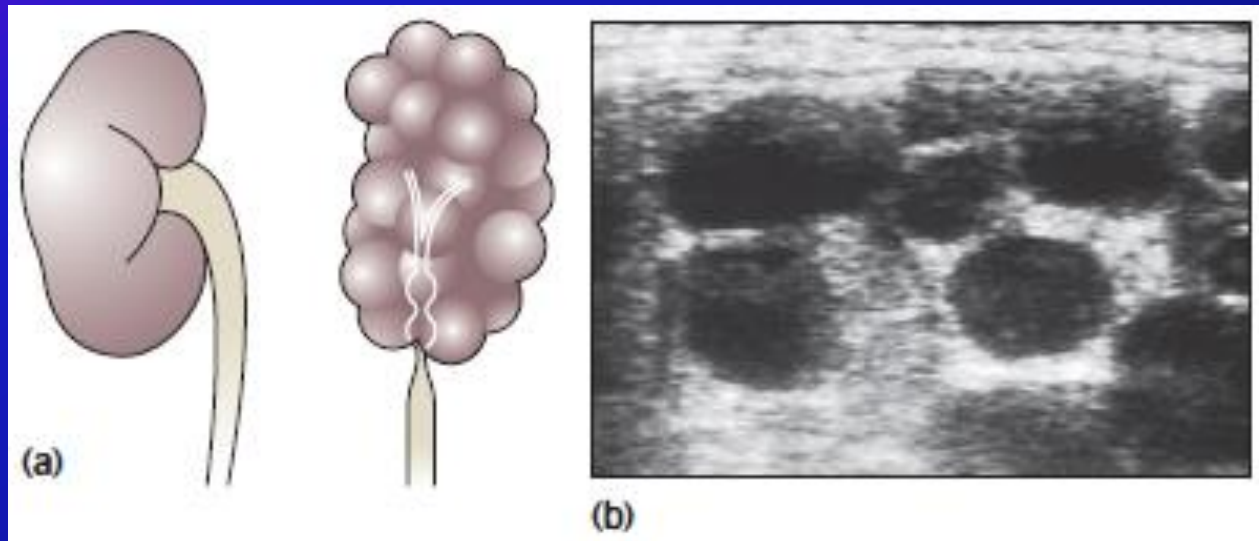


Figure 19.3 (a) Multicystic renal dysplasia. The kidney is replaced by cysts of variable size, with atresia of the ureter; and (b) renal ultrasound showing discrete cysts of variable size.

Other causes of large cystic kidneys are *autosomal recessive polycystic kidney disease* (ARPKD; Fig. 19.4), *autosomal dominant polycystic kidney disease* (*ADPKD*; Fig. 19.5), and tuberous sclerosis. In contrast to a multicystic dysplastic kidney, in these disorders some or normal renal function is maintained but both kidneys are always affected. ADPKD has an incidence of 1 in 1000; the main symptoms in childhood are hypertensionand it causes renal failure in late adulthood. It is associated with several extrarenal features including cysts in the liver and pancreas, cerebral aneurysms, and mitral valve prolapse.

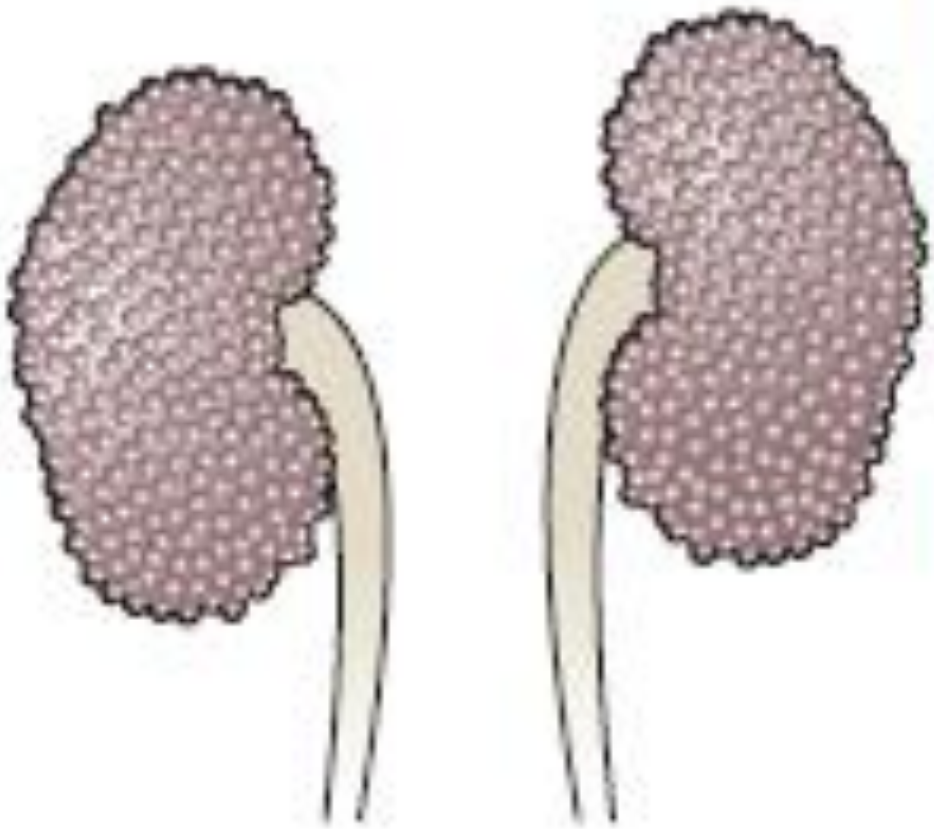


Figure 19.4 Autosomal recessive polycystic kidney disease (ARPKD). There is diffuse bilateral enlargement of both kidneys.

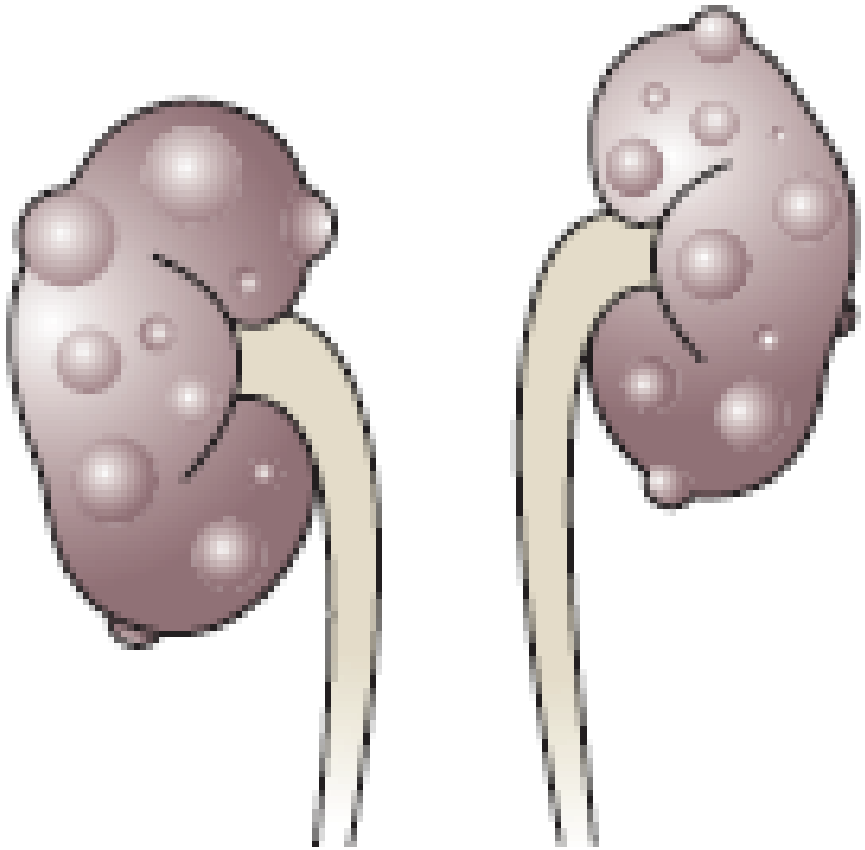


Figure 19.5 Autosomal dominant polycystic kidney disease (ADPKD). There are separate cysts of varying size between normal renal parenchyma. The kidneys are enlarged.

Abnormal caudal migration may result in a *pelvic kidney* or a *horseshoe kidney* (Fig. 19.6), when the lower poles are fused in the midline. The abnormal position may predispose to infection or obstruction of urinary drainage. Premature division of the ureteric bud gives rise to a *duplex system*, which can vary from simply a bifid renal pelvis to complete division with two ureters. These ureters frequently have an abnormal drainage so that the ureter from the lower pole moiety often refluxes, whereas the upper pole ureter may drain ectopically into the urethra or vagina or may prolapse into the bladder (ureterocele) and urine flow may be obstructed (Fig. 19.7).

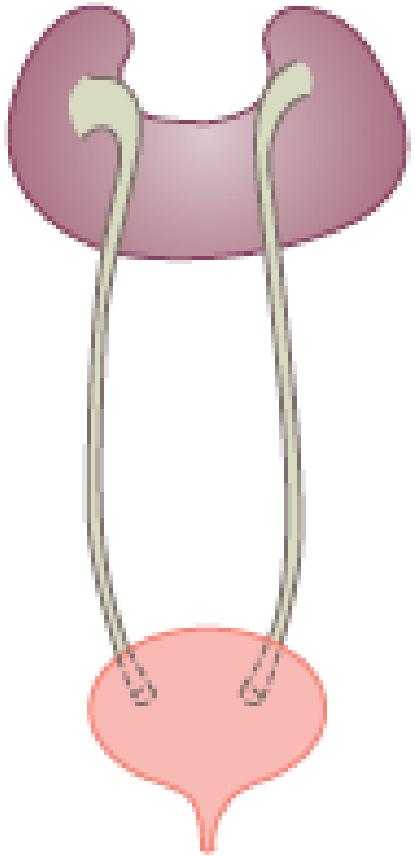


Figure 19.6
Horseshoe kidney.

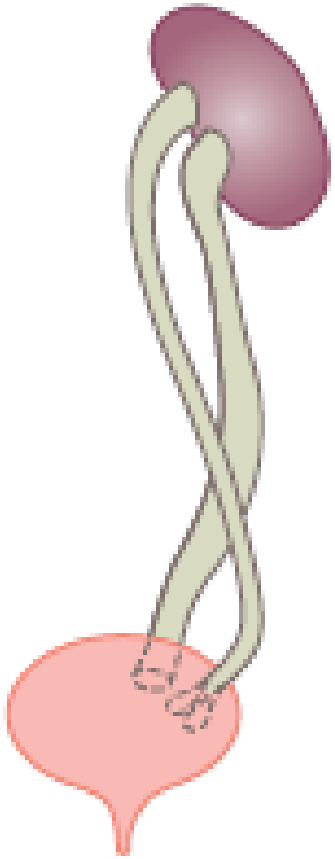
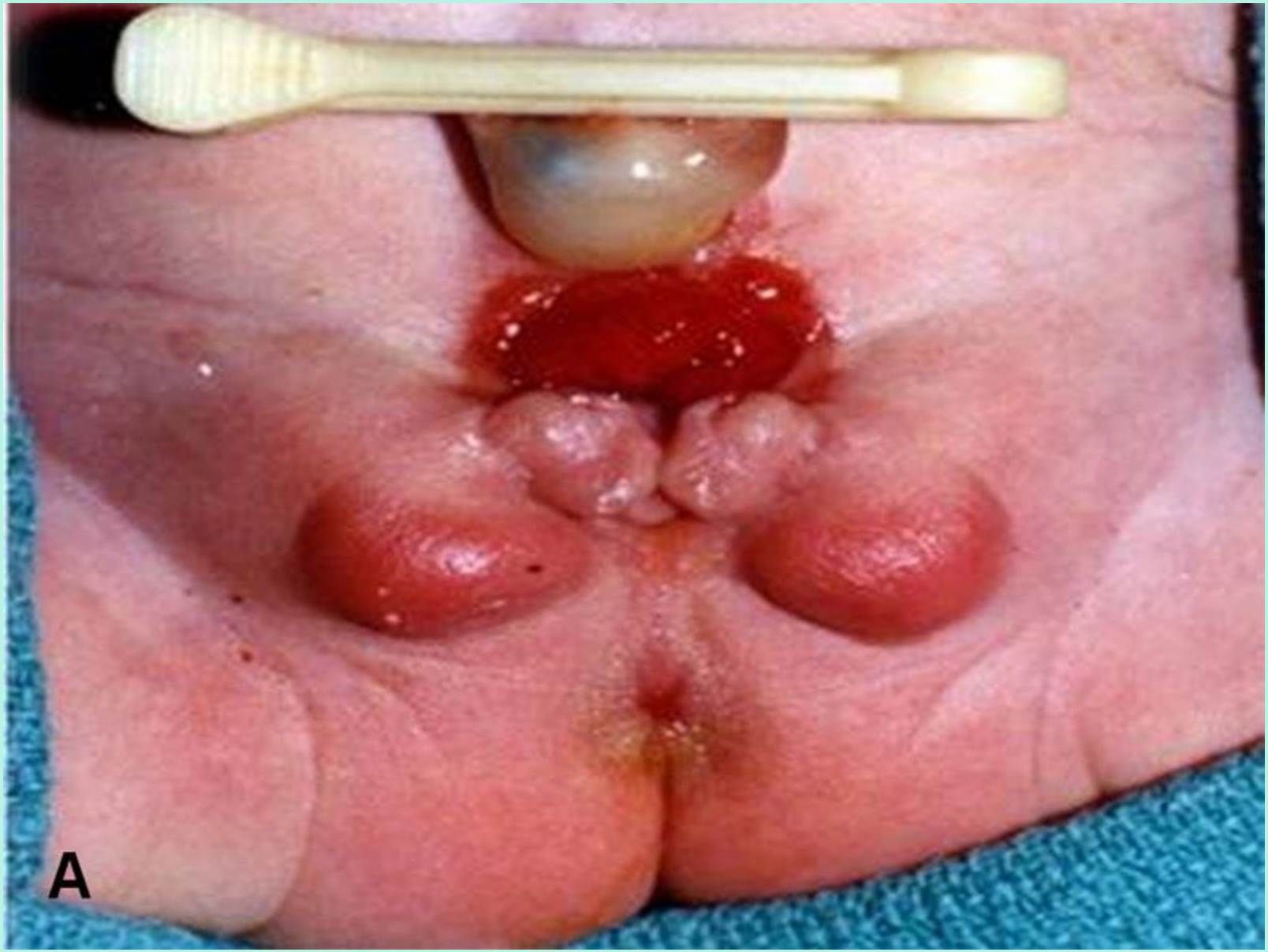


Figure 19.7
Duplex kidney showing ureterocele of upper moiety and reflux into lower pole moiety.

Failure of fusion of the infraumbilical midline structures results in exposed bladder mucosa (*bladder exstrophy*).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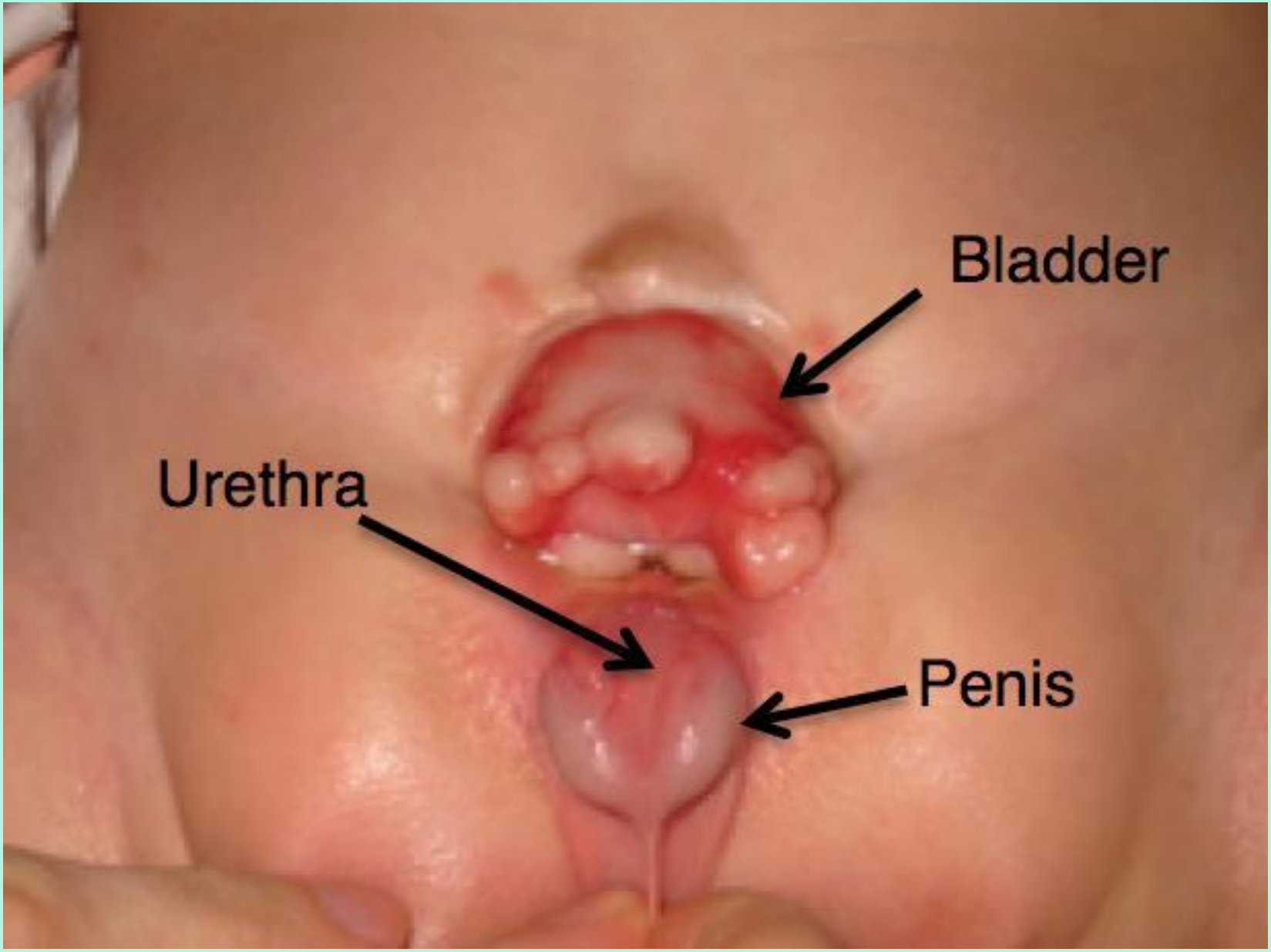

Bladder
Urethra
Penis

Absence or severe deficiency of the anterior abdominal wall muscles is frequently associated with a large bladder and dilated ureters (megacystismegaureter) and cryptorchidism, the *prune-belly syndrome* (*absent musculature syndrome*; Fig. 19.8).

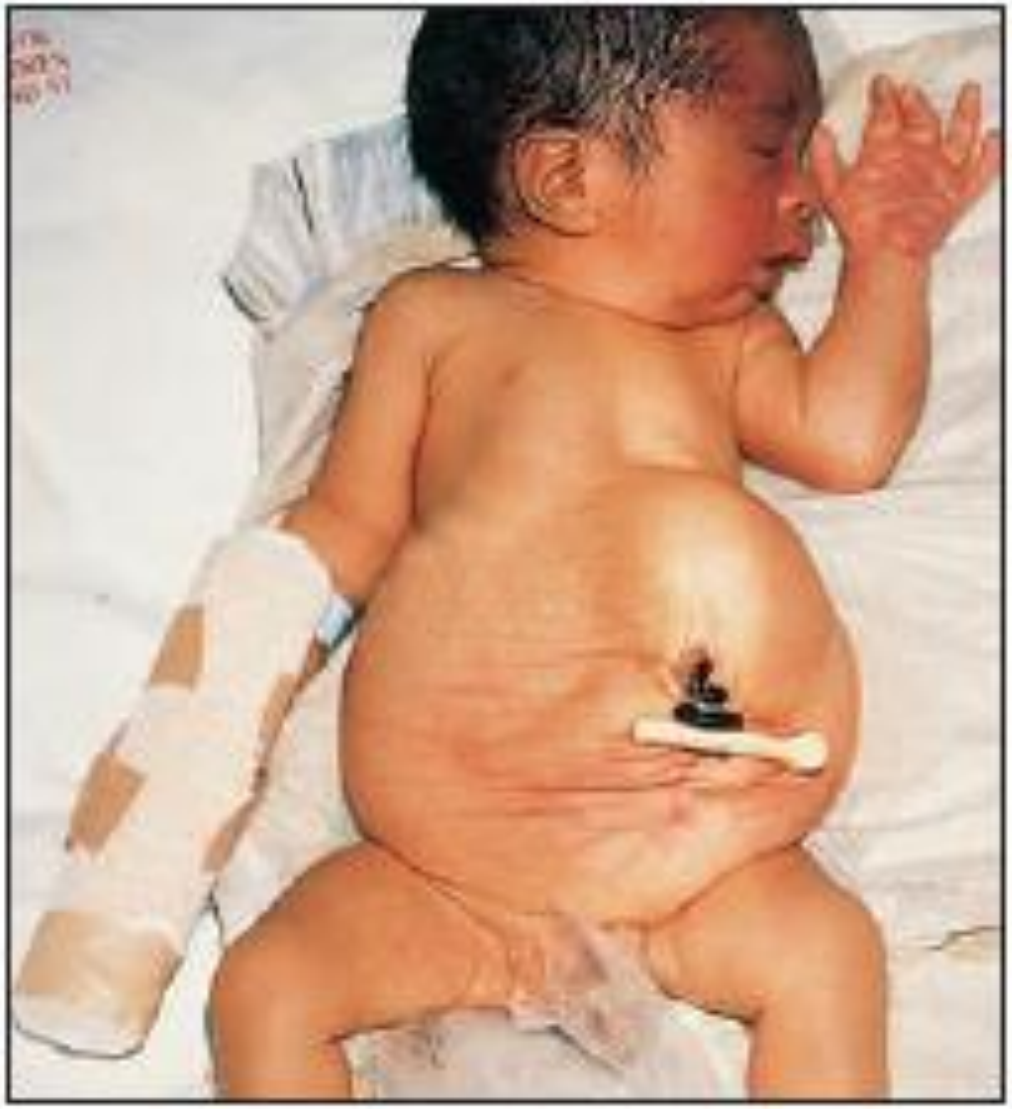
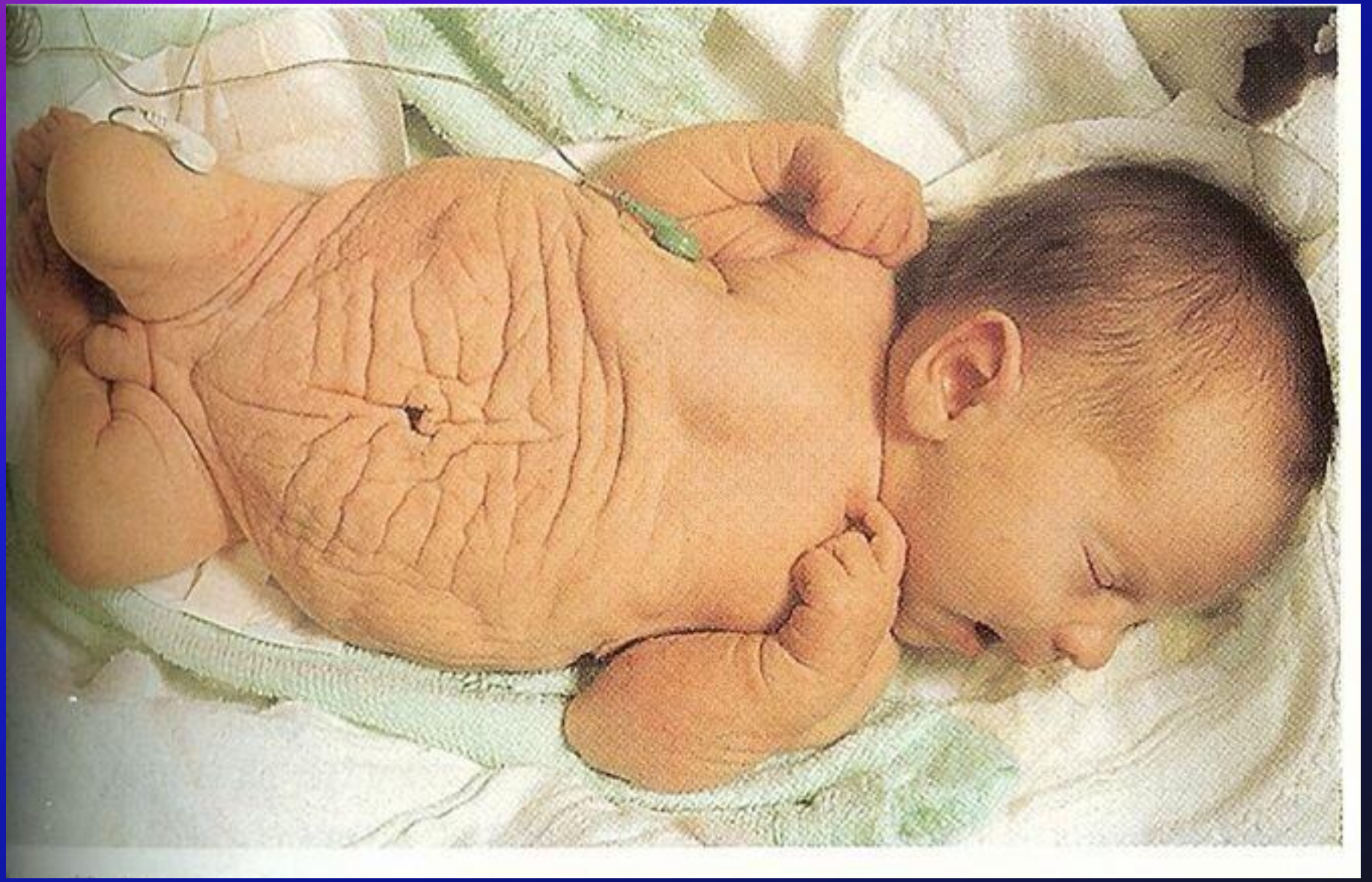
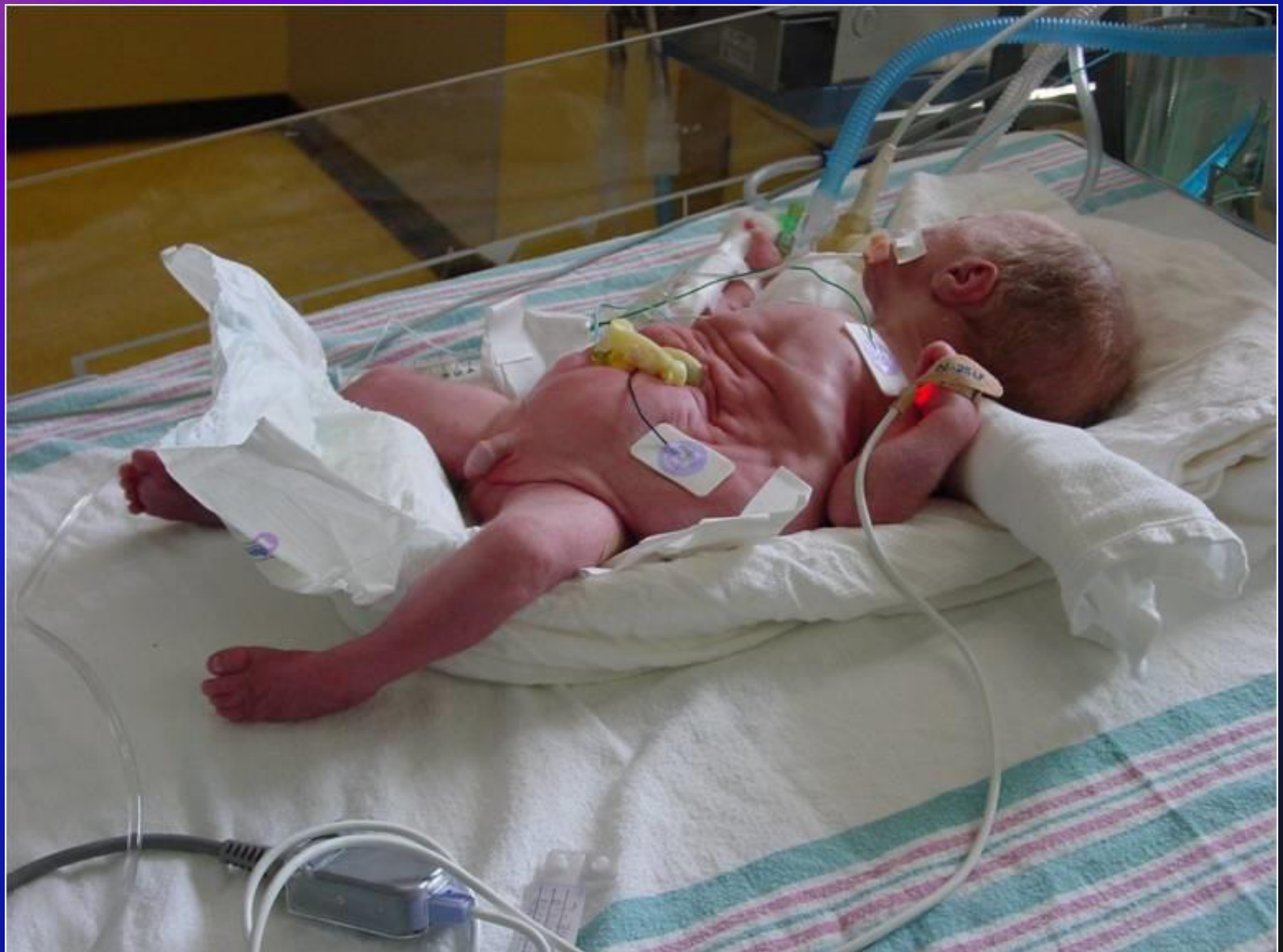


Figure 19.8 Prune-belly syndrome (absent musculature syndrome). The name arises from the wrinkled appearance of the abdomen. It is associated with a large bladder, dilated ureters, and cryptorchidism. (Courtesy of Jane Deal.)





Obstruction to urine flow may occur at the pelviureteric or vesicoureteric junction, at the *bladder neck* (e.g. due to disruption of the nerve supply, *neuropathic bladder*), or at the *posterior urethra* in a boy due to mucosal folds or a membrane, known as *posterior urethral valves*. The consequences of obstruction to urine flow are shown in Fig. 19.9a–d.

At worst, this
results in a *dysplastic kidney* which is small, poorly functioning, and may contain cysts. In the most severe and bilateral cases Potter syndrome is present. Renal dysplasia can also occur in association with severe intrauterine vesicoureteric reflux (VUR), in isolation, or in certain rare, inherited syndromes affecting multiple systems.

Urinary tract obstruction

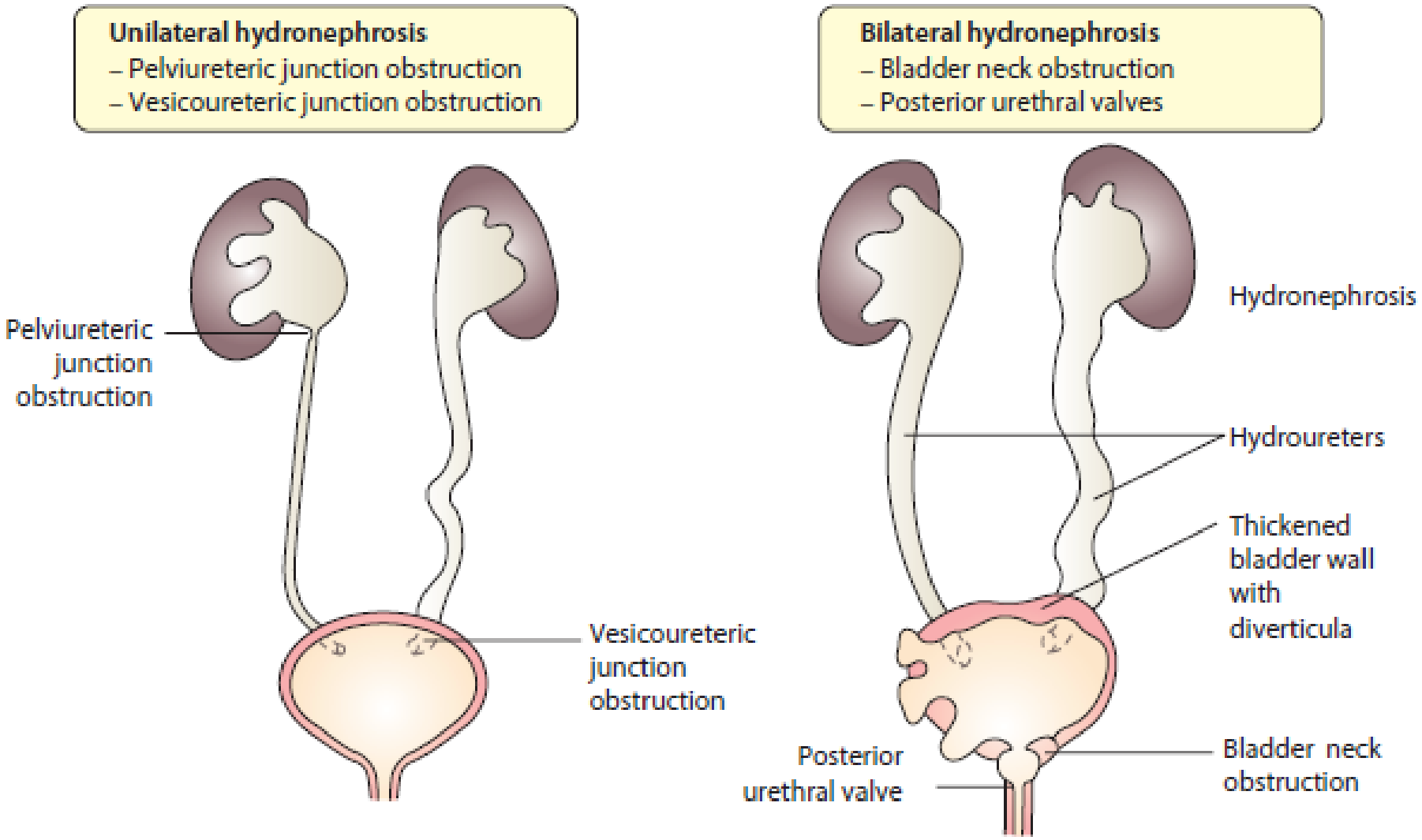


Figure 19.9a Obstruction to urine flow results in dilatation of the urinary tract proximal to the site of obstruction. Obstruction may be at the pelviureteric or vesicoureteric junction (left), the bladder neck, or urethra (right).

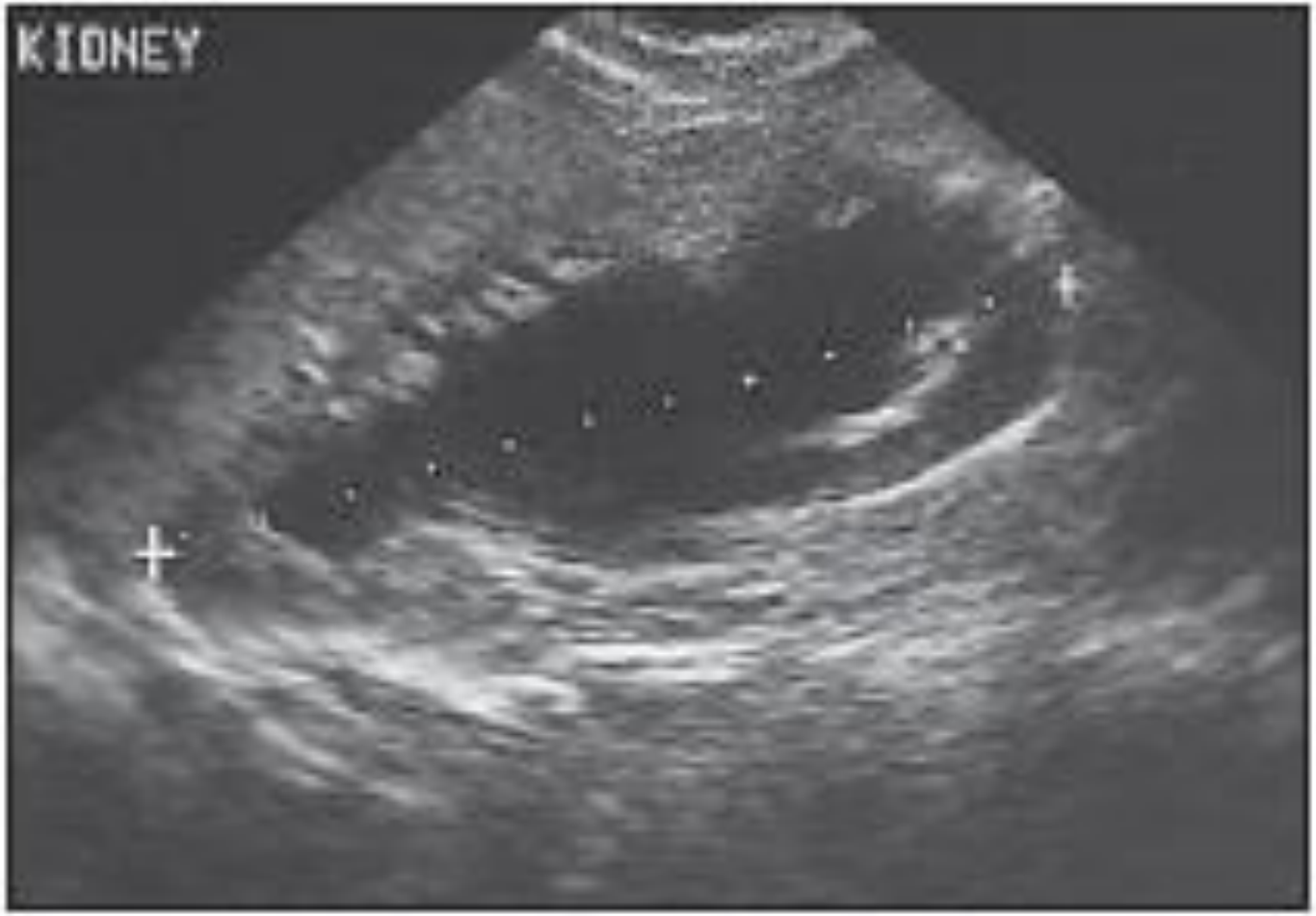


Figure 19.9b An ultrasound showing a dilated renal pelvis from pelviureteric junction obstruction.

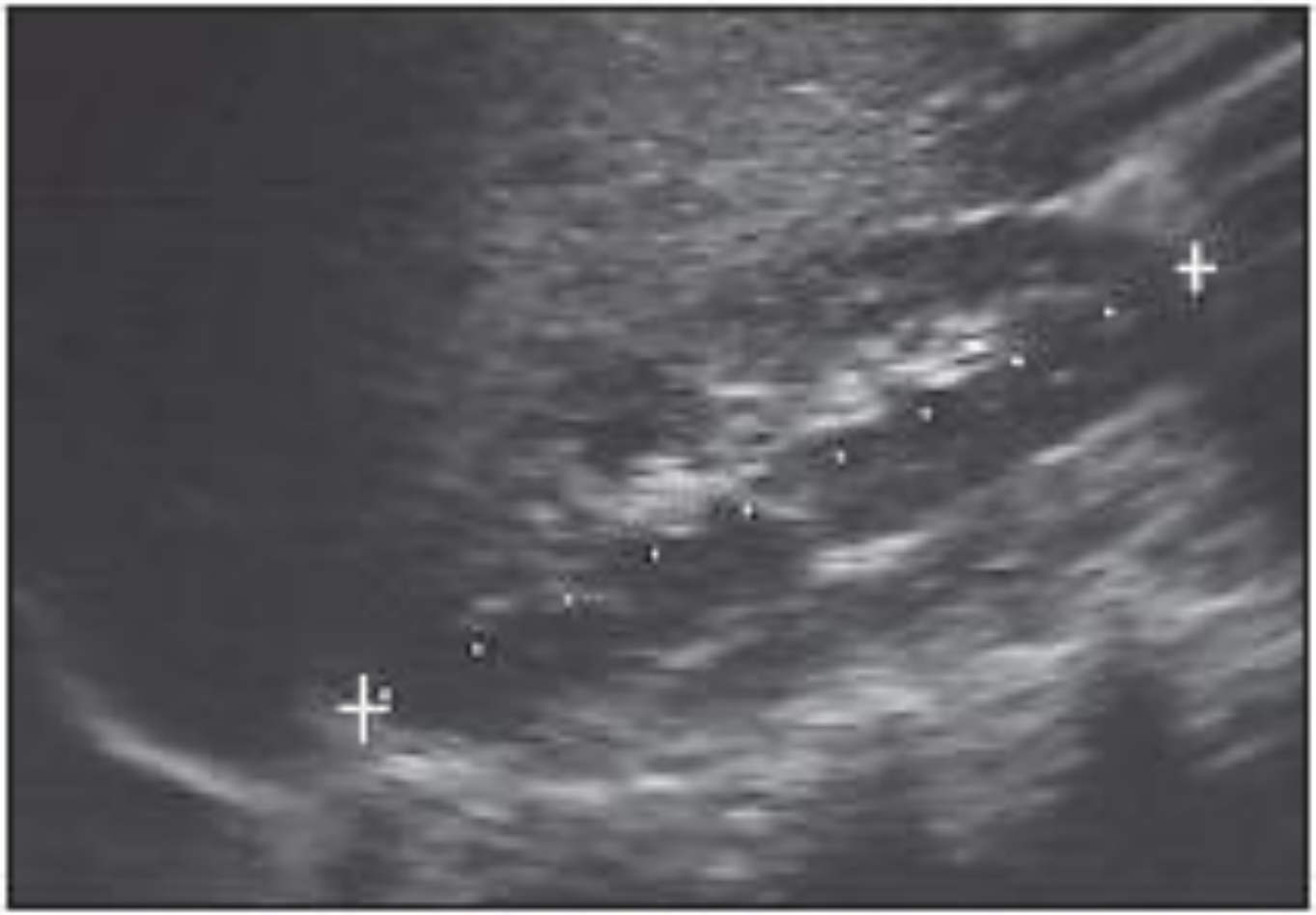


Figure 19.9c A normal ultrasound of the kidney is shown for comparison.

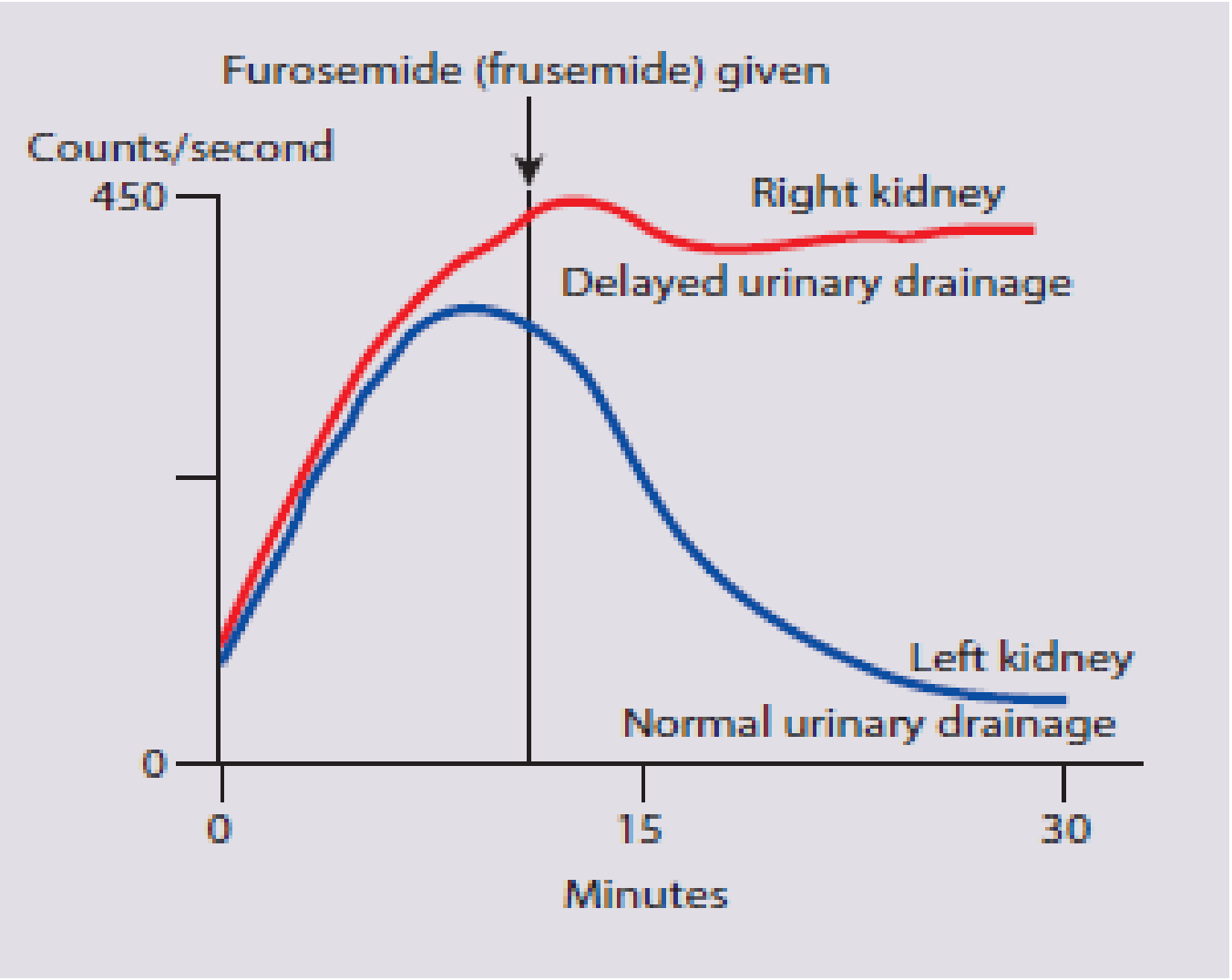


Figure 19.9d Graph from dynamic nuclear medicine scan MAG3 showing delayed excretion from a pelviureteric junction obstruction.

Antenatal treatment

The male fetus with posterior urethral valves may develop severe urinary outflow obstruction resulting in progressive bilateral hydronephrosis, poor renal growth, and declining liquor volume with the potential to lead to pulmonary hypoplasia. Intrauterine bladder drainage procedures to prevent severe renal damage have been attempted but results have been disappointing.

Early delivery is rarely indicated.

Postnatal management

An example of a protocol for infants with antenatally diagnosed anomalies is shown in Fig. 19.10.

Prophylactic antibiotics may be started at birth to try to prevent urinary tract infection (UTI), although practice varies between centres. As the newborn kidney has a low GFR, urine flow is low and mild outflow obstruction may not be evident in the first few days of life. The ultrasound scan should therefore be delayed for a few weeks. However, bilateral hydronephrosis in a male infant warrants investigations including an ultrasound and micturating cystourethrogram (MCUG) shortly after birth to exclude posterior urethral valves, which always requires urological intervention such as cystoscopic ablation (Case History 19.1).

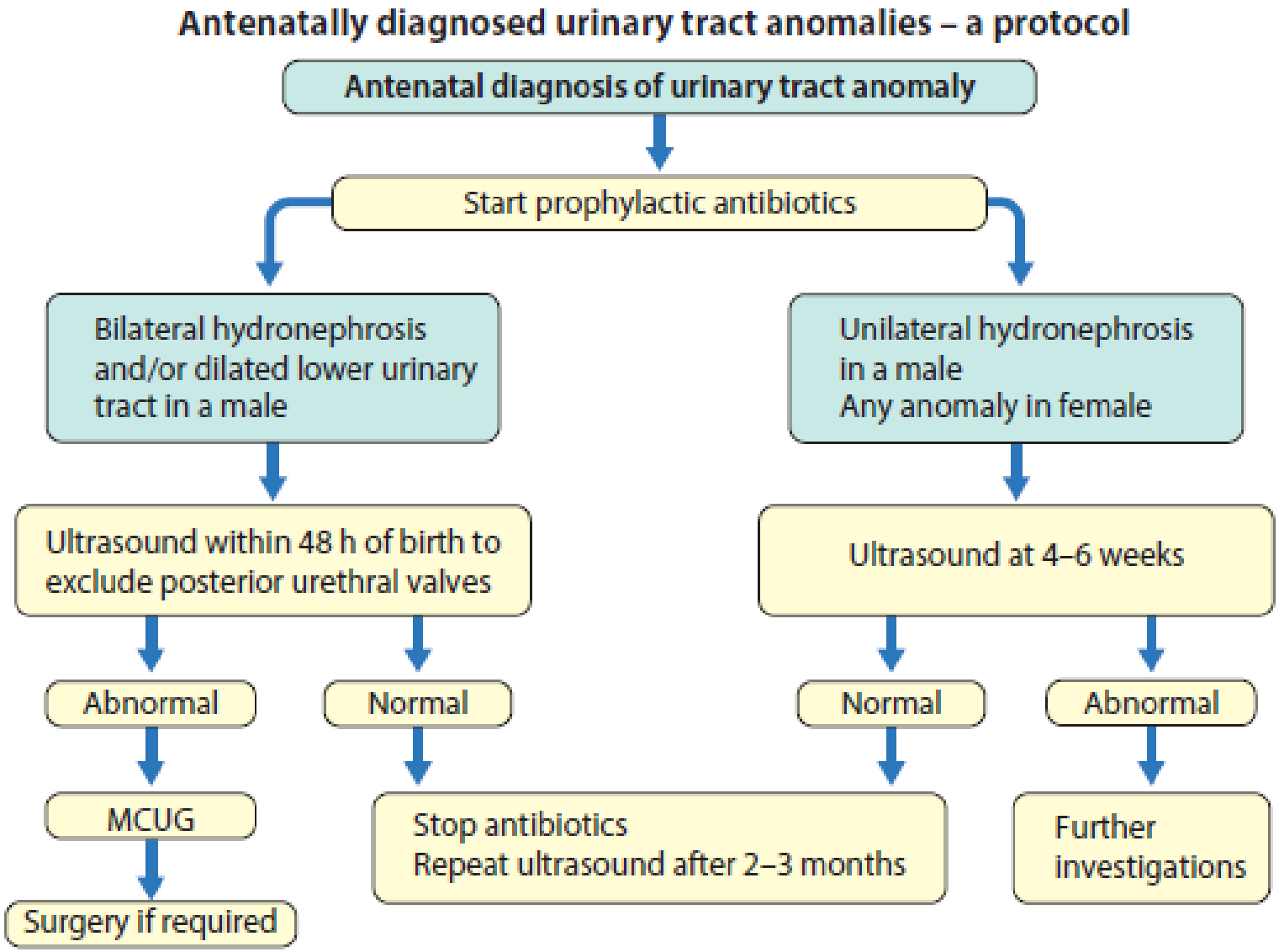


Figure 19.10 An example of a protocol for the management of infants with antenatally diagnosed urinary tract anomalies. MCUG, micturating cystourethrogram.

Case history 19.1

Posterior urethral valves

Bilateral hydronephrosis was noted on antenatal ultrasound at 20 weeks' gestation in a male fetus. There was progressive hydronephrosis, poor renal growth with reduced renal cortex, and decreasing volume of amniotic fluid on repeated scans (Fig. 19.11a). After birth, a urethral catheter was inserted and prophylactic antibiotics were started. An urgent ultrasound showed bilateral hydronephrosis with small dysplastic kidneys and cyst formation. A micturating cystourethrogram showed severe, bilateral vesicoureteric reflux, a small thickened bladder, and a dilated posterior urethra(Fig. 19.11b). Posterior urethral valves were confirmed on cystoscopy and ablated surgically. Caden's subsequent progress is described in Case history 19.4.

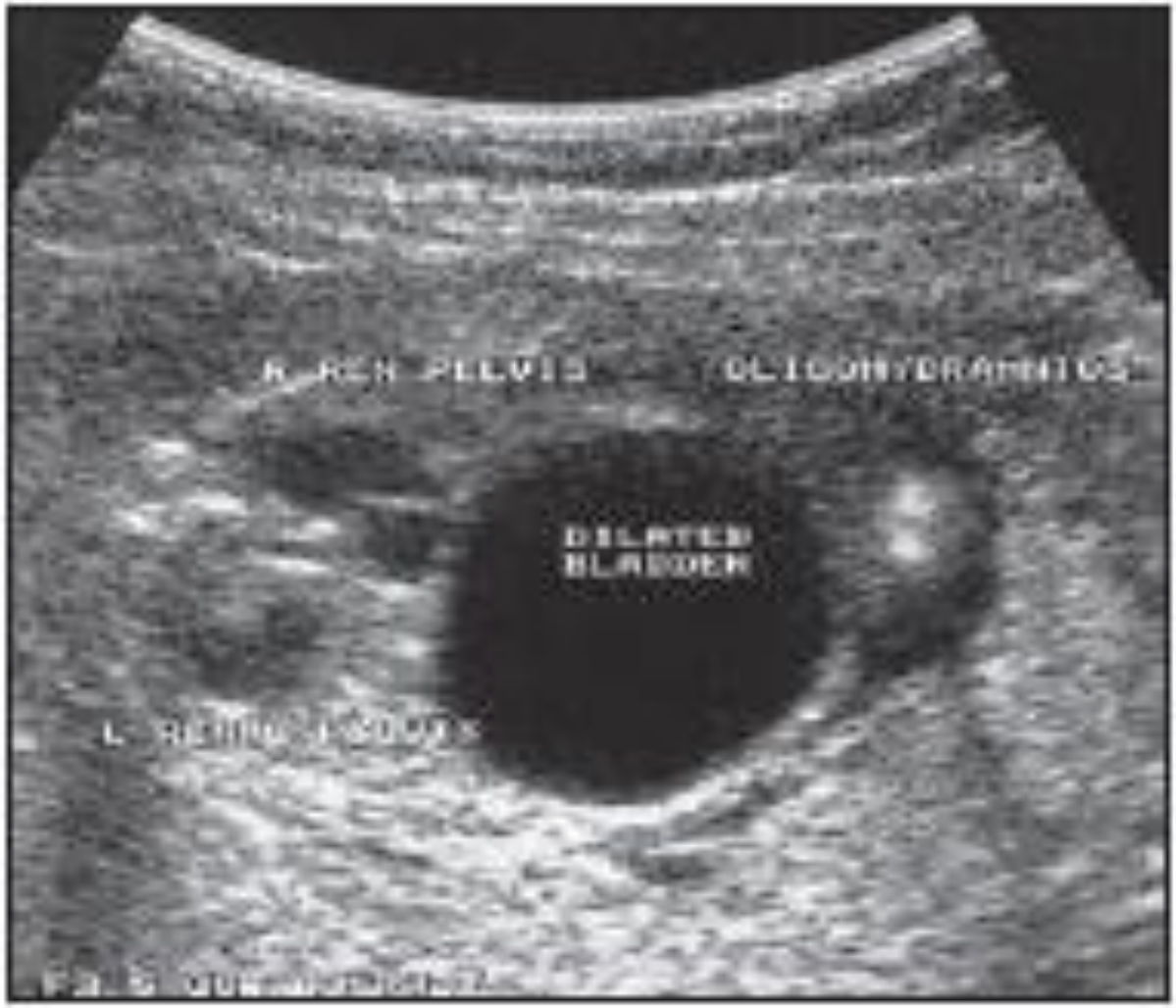


Figure 19.11a Antenatal ultrasound scan in an infant with urinary outflow obstruction from posterior urethral valve. (Courtesy of Karl Murphy.)

Bilateral hydronephrosis in a male infant requires urgent investigation to exclude posterior urethral valves

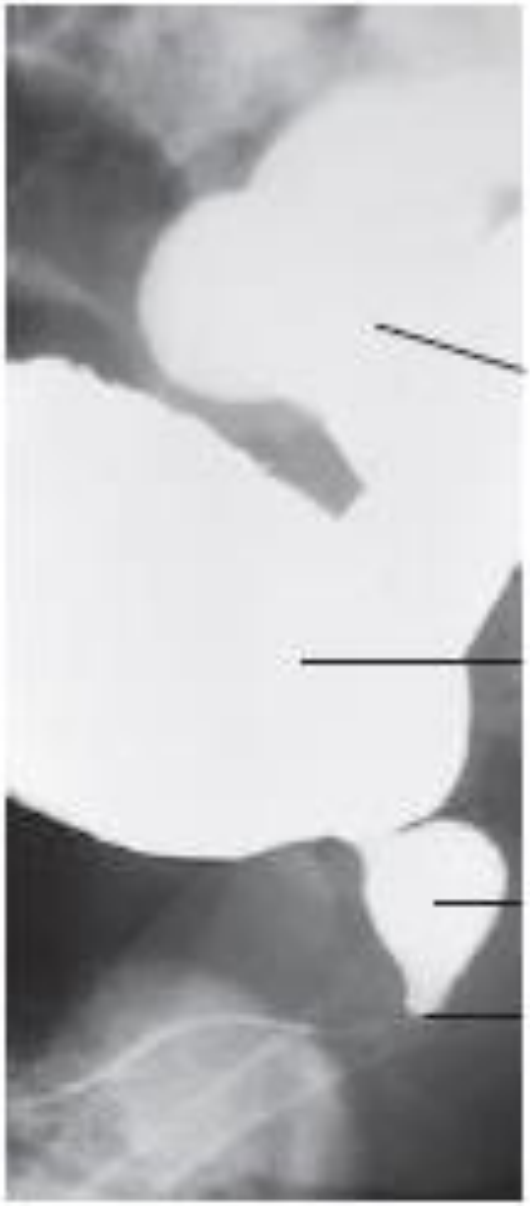


Figure 19.11b Micturating cystourethrogram (MCUG) in the same patient.

Urinary tract infection

About 3–7% of girls and 1–2% of boys have at least one symptomatic UTI before the age of 6 years, and 12–30% of them have a recurrence within a year. UTI may involve the kidneys (pyelonephritis), when it is usually associated with fever and systemic involvement, or may be due to cystitis, when there may be no fever.

UTI in childhood is important because:

- up to half of patients have a structural abnormality of their urinary tract
- pyelonephritis may damage the growing kidney by forming a scar, predisposing to hypertension and to progressive chronic kidney disease if the scarring is bilateral.

The NICE (National Institute for Health and Care Excellence) guidelines on UTI in children were published in 2007, although they have proved to be controversial as they recommend fewer children being investigated and the investigations are less extensive.

Clinical features

Presentation of UTI varies with age (Box 19.1). In infants, symptoms are nonspecific; fever is usually but not always present, and septicaemia may develop rapidly. The classical symptoms of dysuria, frequency, and loin pain become more common with increasingage. Serious illness from septicaemia is described in Chapter 6. Dysuria alone is usually due to cystitis, or vulvitis in girls or balanitis in uncircumcised boys. Symptoms suggestive of a UTI may also occur following sexual abuse.

Box 19.1 Presentation of urinary tract infection in infants and children

Infants

- Fever
- Vomiting
- Lethargy or irritability
- Poor feeding/ faltering growth
- Jaundice
- Septicaemia
- Offensive urine
- Febrile seizure (>6 months)

Children

- Dysuria, frequency and urgency
- Abdominal pain or loin tenderness
- Fever with or without rigors (exaggerated shivering)
- Lethargy and anorexia
- Vomiting, diarrhoea
- Haematuria
- Offensive/cloudy urine
- Febrile seizure
- Recurrence of enuresis

Methods of dipstick testing	
Nitrite stick testing	Positive result useful as very likely to indicate a true urinary tract infection (UTI) But some children with a UTI are nitrite negative
Leucocyte esterase stick testing (for white blood cells)	May be present in children with UTI but may also be negative Present in children with febrile illness without UTIs Positive in balanitis and vulvovaginitis
Interpretation of results	
Leucocyte esterase and nitrite positive	Regard as UTI
Leucocyte esterase negative and nitrite positive	Start antibiotic treatment if clinical evidence of UTI Diagnosis depends on urine culture
Leucocyte esterase positive and nitrite negative	Only start antibiotic treatment if clinical evidence of UTI Diagnosis depends on urine culture
Leucocyte esterase and nitrite negative	UTI unlikely. Repeat or send urine for culture if clinical history suggests UTI
Blood, protein, and glucose present on stick testing	Useful in any unwell child to identify other diseases, e.g. nephritis, diabetes mellitus, but will not discriminate between children with and without UTIs

Collection of samples

The most common error in the management of UTI in children, and especially in infants, is failure to establish the diagnosis properly in the first place. If the diagnosis of a UTI is not made, the opportunity to prevent renal damage may be missed, or, if incorrectly diagnosed, may lead to unnecessary invasive investigations.

For the child in nappies, urine can be collected by:

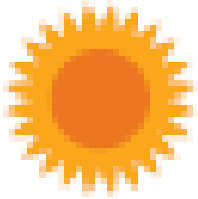
- a ‘clean-catch’ sample into a waiting clean pot when the nappy is removed. This is the recommended method
- an adhesive plastic bag applied to the perineum after careful washing, although there may be contamination from the skin
- a urethral catheter if there is urgency in obtaining a sample and no urine has been passed
- suprapubic aspiration, when a fine needle attached to a syringe is inserted directly into the bladder just above the symphysis pubis under ultrasound guidance; it may be used in severely ill infants requiring urgent diagnosis and treatment, but it is an invasive procedure, and is increasingly replaced by urethral catheter sampling.

In the older child, urine can be obtained by collecting a midstream sample. Careful cleaning and collection are necessary, as contamination with both white cells and bacteria can occur from under the foreskin in boys, and from reflux of urine into the vagina during voiding in girls.

Ideally, the urine sample should be observed under a microscope to identify organisms and cultured straight away. This is indicated in all infants and children under the age of 3 years with a suspected UTI. If this is not possible, the urine sample should be refrigerated to prevent the overgrowth of contaminating bacteria.

Urinary white cells are not a reliable feature of a UTI, as they may lyse during storage and may be present in febrile children without a UTI and in children with balanitis or vulvovaginitis. Dipsticks can be used as a screening test. Urine culture should still be performed unless both leucocyte esterase and nitrite are negative or if the clinical symptoms and dipstick tests do not correlate (Table 19.3).

A bacterial culture of more than 105 colony-forming units (CFU) of a single organism per millilitre in a properly collected specimen gives a 90% probability of infection. If the same result is found in a second sample, the probability rises to 95%. A growth of mixed organisms
usually represents contamination, but if there is doubt, another sample should be collected. Any bacterial growth of a single organism per millilitre in a catheter sample or suprapubic aspirate is considered diagnostic of infection.



A urine sample should be tested in all infants with an unexplained fever >38°C

Bacterial and host factors that predispose to infection

Infecting organism

UTI is usually the result of bowel flora entering the urinary tract via the urethra, although it can be haematogenous,
e.g. in the newborn. The most common organism is *Escherichia coli*, followed by *Klebsiella*, *Proteus, Pseudomonas,* and *Streptococcus faecalis*. *Proteus* infection is more commonly diagnosed in boys than in girls, possibly because of its presence under the prepuce. *Proteus* infection predisposes to the formation of phosphate stones by splitting urea to ammonia, and thus alkalinizing the urine. *Pseudomonas* infection may indicate the presence of some structural abnormality in the urinary tract affecting drainage and it is also more common in children with plastic catheters.

Antenatally diagnosed renal or urinary tract abnormality

Increases risk of infection and investigation of a UTI may
lead to urinary tract abnormality being detected if antenatal
diagnosis was not made or missed to follow-up.

Incomplete bladder emptying

Contributing factors in some children are:

- infrequent voiding, resulting in bladder enlargement
- vulvitis
- incomplete micturition with residual postmicturition bladder volumes
- obstruction by a loaded rectum from constipation
- neuropathic bladder
- vesicoureteric reflux.

Vesicoureteric reflux

VUR is a developmental anomaly of the vesicoureteric junctions. The ureters are displaced laterally and enter directly into the bladder rather than at an angle, with a shortened or absent intramural course. Severe cases may be associated with renal dysplasia. It is familial, with a 30% to 50% chance of occurring in first-degree relatives. It may also occur with bladder pathology, e.g. a neuropathic bladder or urethral obstruction, or temporarily after a UTI. Its severity varies from reflux into the lower end of an undilated ureter during micturition to the severest form with reflux during bladder filling and voiding, with a distended ureter, renal pelvis, and clubbed calyces (Fig. 19.12).

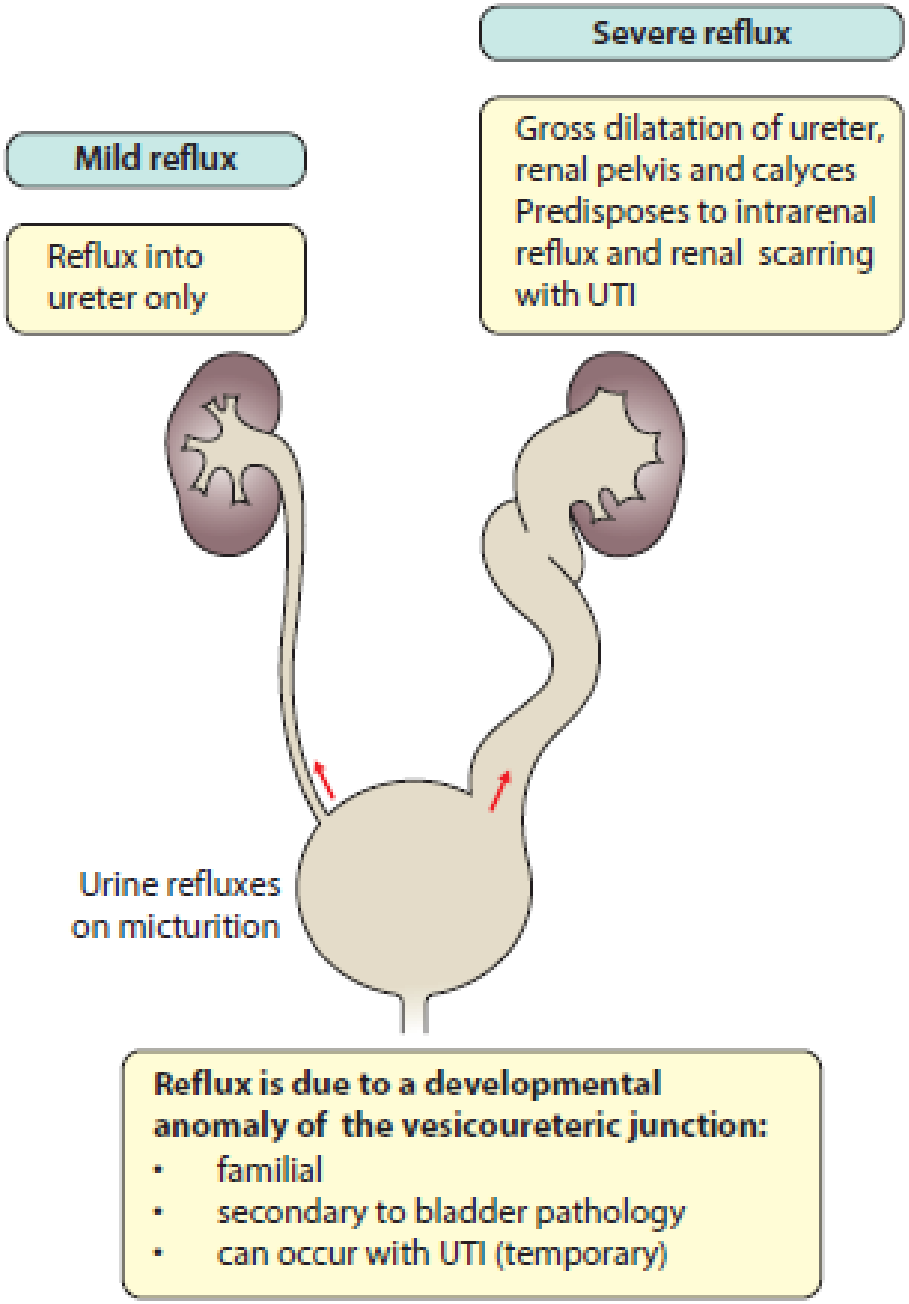


Figure 19.12 Vesicoureteric reflux.

Mild reflux is unlikely to be of significance, but the more severe degrees of VUR may be associated with *intrarenal reflux*, which is the backflow of urine from the renal pelvis into the papillary collecting ducts and is associated with a particularly high risk of renal scarring if UTIs occur. The incidence of renal defects increases with increasing severity of reflux. There is considerable controversy as to whether renal scarring is a congenital abnormality already present in children with reflux and which predisposes to infection or if children with reflux have normal kidneys at birth which are damaged by UTIs and that preventing UTIs in these children prevents scars. VUR tends to resolve with age, especially lower grades of VUR.

VUR-associated ureteric dilatation is important as:

- urine returning to the bladder from the ureters after voiding results in incomplete bladder emptying which encourages infection
- the kidneys may become infected (pyelonephritis) especially if there is intrarenal reflux
- bladder voiding pressure is transmitted to the renal papillae which may contribute to renal damage if voiding pressures are high.

Infection may destroy renal tissue, leaving a scar, resulting in a shrunken, poorly functioning segment of kidney (reflux nephropathy). If scarring is bilateral and severe, progressive chronic kidney disease maydevelop. The risk of hypertension in childhood or early
adult life is variously estimated to be up to 10%.

Investigation

The extent to which a child with a UTI should be investigated
is controversial. This is not only because of the invasive nature and radiation burden of the tests but also because of the lack of an evidence base to show that outcome is improved (unless urinary obstruction is demonstrated). Mild VUR usually resolves spontaneously
and operative intervention to stop mild VUR has not been shown to decrease renal damage.

Furthermore,
there is no evidence that antibiotic prophylaxis is any better than prompt treatment. There has, therefore, been a move away from extensive investigation of all children with UTIs to those who have had atypical or recurrent UTIs. Atypical UTI includes:

- seriously ill or septicaemia
- poor urine flow
- abdominal or bladder mass
- raised creatinine
- failure to respond to suitable antibiotics within 48 hours
- infection with atypical (non-*E. coli*) organisms.

An initial ultrasound will identify:

- serious structural abnormalities and urinary obstruction
- renal defects (although it is not the gold standard for detecting renal scars).

Subsequent investigations will depend on the results of the ultrasound. The need for any investigations in a child with only bladder symptoms (lower UTI/ cystitis) is also controversial. If urethral obstruction is suspected (abnormal bladder in a boy), MCUG should be performed promptly. Functional scans should be deferred for 3 months after a UTI, unless the ultrasound is suggestive of obstruction, to avoid missing a newly developed scar and because of false-positive results from transient inflammation. Medical measures for the prevention of UTI should be initiated.

A suggested schema for investigation of the first proven UTI is shown in Fig. 19.13, but there is significant variation of practice.

First urinary tract infection - a protocol for initial management and investigation

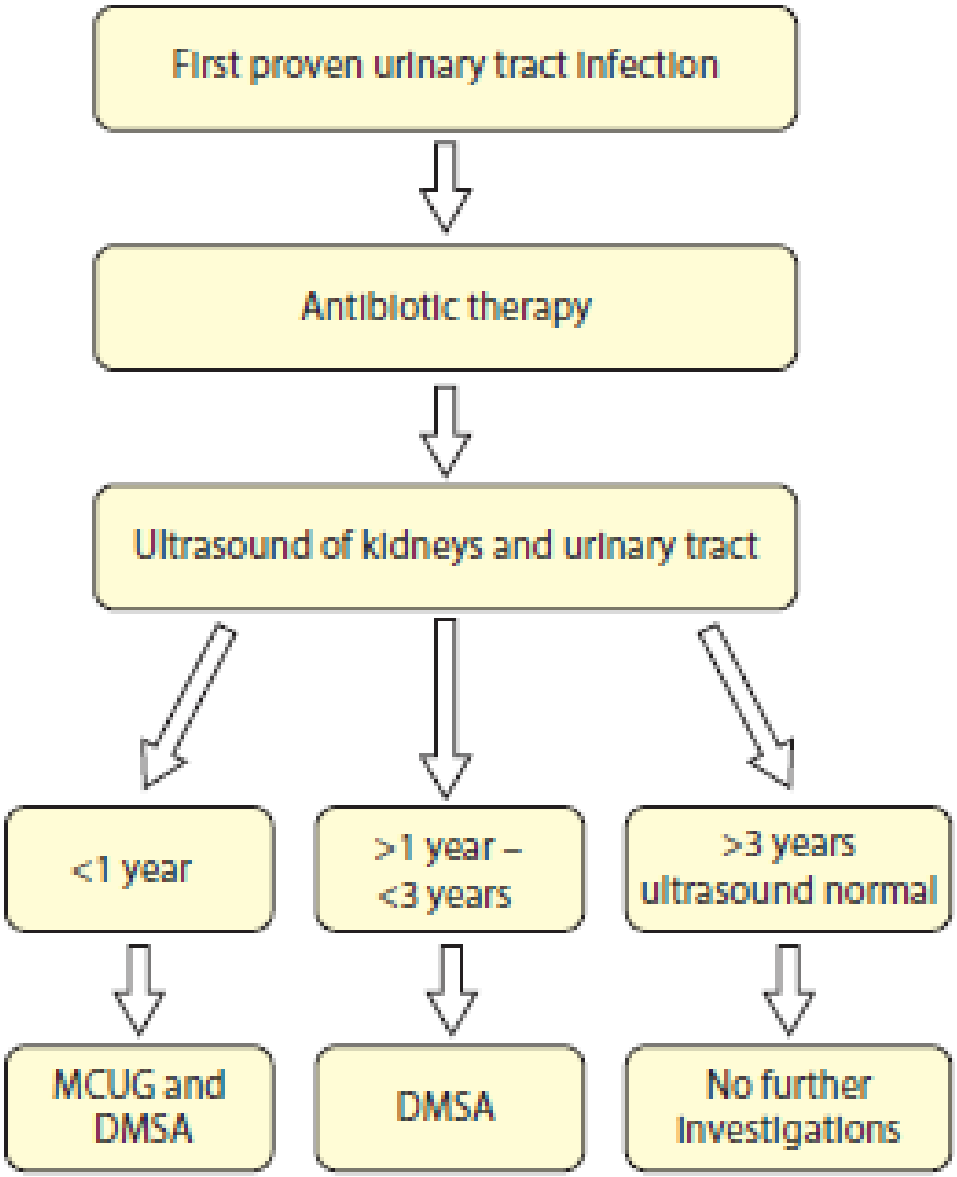


Figure 19.13 An example of a protocol for the initial management and investigation of a first urinary tract infection. This is controversial. The 2007 UK NICE (National Institute for Health and Care Excellence) guidelines do not recommend ultrasound examination for first urinary tract infection if there was response to antibiotic treatment within 48 hours, unless under 6 months of age or atypical or recurrent, but many paediatric nephrologists consider this approach too minimalistic and follow protocols like the one shown here.

Management

All infants under 3 months of age with suspicion of a UTI or if seriously ill should be referred immediately to hospital. They require intravenous antibiotic therapy (e.g. co-amoxiclav) for at least 5–7 days at which point oral prophylaxis can then be commenced (see Case History 19.2).

Management

Infants aged over 3 months and children with acute pyelonephritis/upper UTI (bacteriuria and fever ≥38° C or bacteriuria and loin pain/tenderness even if fever is <38° C) are usually treated with oral antibiotics (e.g. trimethoprim for 7 days); or else intravenous antibiotics, e.g. co-amoxiclav, are given for 2–4 days followed by oral antibiotics for a total of 7–10 days. The choice of antibiotic is adjusted according to sensitivity on urine culture.

Management

Children with cystitis/lower UTI (dysuria but no systemic symptoms or signs) can be treated with oral antibiotics such as trimethoprim or nitrofurantoin for 3 days.

Medical measures for the prevention of UTI

The aim is to ensure washout of organisms that ascend
into the bladder from the perineum; and to reduce the presence of aggressive organisms in the stool, perineum, and under the foreskin:

- high fluid intake to produce a high urine output
- regular voiding
- ensure complete bladder emptying by encouraging the child to try a second time to empty his bladder after a minute or two, commonly known as double voiding, which empties any urine residue or refluxed urine returning to the bladder
- treatment and/or prevention of constipation
- good perineal hygiene

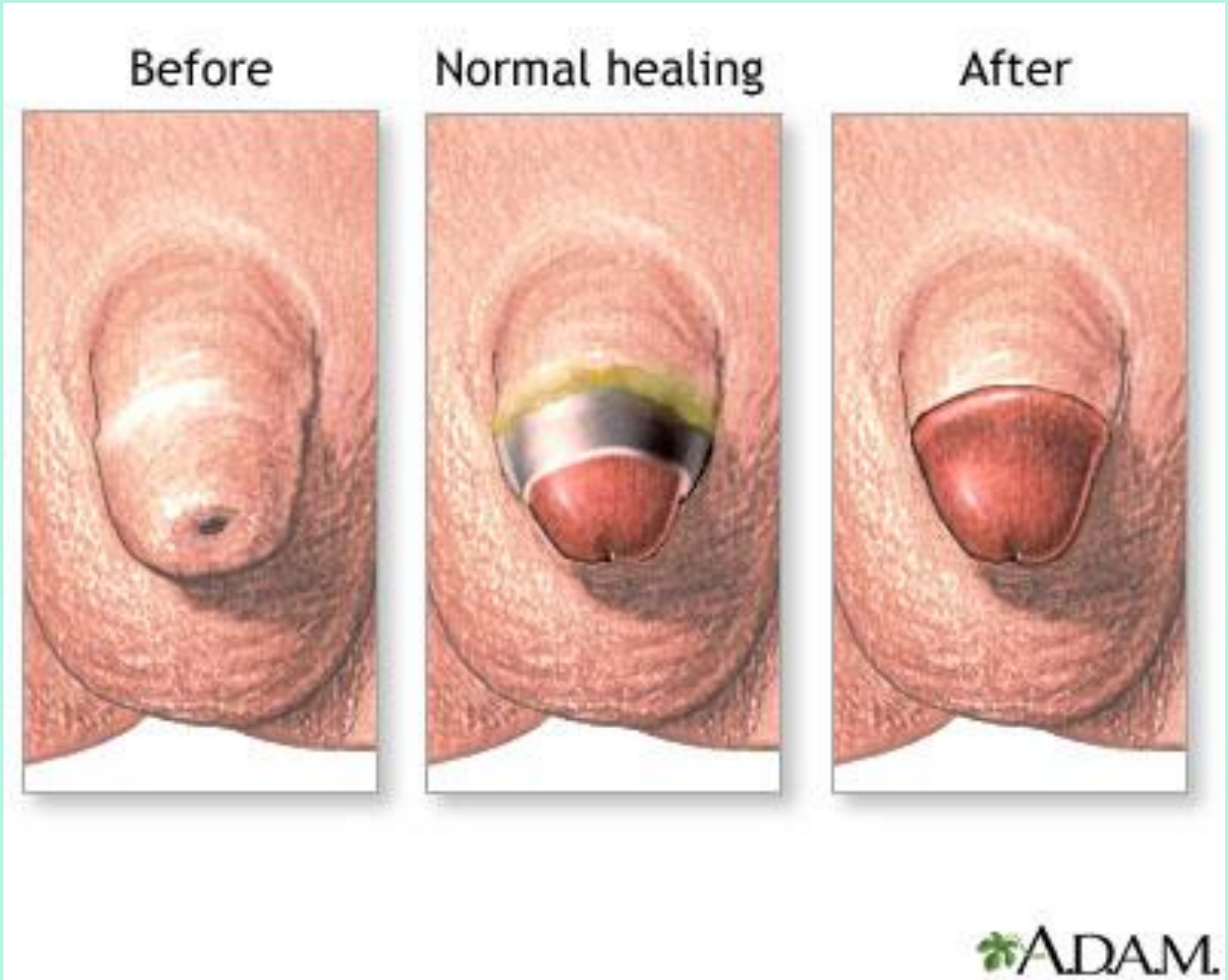
- *Lactobacillus acidophilus*, a probiotic to encourage colonization of the gut by this organism and reduce the number of pathogenic organisms that might potentially cause invasive disease
- antibiotic prophylaxis, although this is controversial. It is often used in those under 2 years to 3 years of age with a congenital abnormality of the kidneys or urinary tract or who have had an upper UTI and those with severe reflux until out of nappies. Trimethoprim (2 mg/kg at night) is used most often, but nitrofurantoin or cephalexin may be given. Broad-spectrum, poorly absorbed antibiotics such as amoxicillin should be avoided.

Follow-up of children with recurrent UTIs, renal scarring, or reflux

In these children:

- urine should be dipsticked with any nonspecific illness in case it is caused by a UTI and urine sent for microscopy and culture if suggestive of UTI

- long-term, low-dose antibiotic prophylaxis can be used. There is no evidence for when antibiotic prophylaxis should be stopped
- circumcision in boys may sometimes be considered as there is evidence that it reduces the incidence of UTI
- anti-VUR surgery may be indicated if there is progression of scarring with ongoing VUR but it has not been shown to improve outcome in mild VUR


Before
Normal healing
After
A.D.A.M.

- blood pressure should be checked annually if renal defects are present
- urinalysis to check for proteinuria which is indicative of progressive chronic kidney disease
- regular assessment of renal growth and function is necessary if there are bilateral defects because of the risk of progressive chronic kidney disease.

If there are further symptomatic UTIs in younger children, investigations may be required to determine whether there is new scar formation and if so whether there is ongoing VUR, which may require prophylactic antibiotic therapy or surgical anti-VUR treatment.

Case history 19.2

Urinary tract infection

Jack, a 2-month-old infant, stopped feeding and had a high, intermittent fever. He was referred to hospital, where he had an infection screen. Urine microscopy showed more than 100 white blood cells and cultured more than 105 *E. coli* CFU/ml. He was treated with intravenous antibiotics. An ultrasound showed that the left kidney was smaller than the right kidney with dilated ureters. He was started on prophylactic antibiotics. A DMSA (dimercaptosuccinic acid) scan (Fig. 19.14) performed 3 months later confirmed bilateral renal scarring, with the left kidney contributing 33% of renal function. The MCUG (Fig. 19.15) showed bilateral vesicoureteric reflux. At 4 years of age, the reflux had resolved and antibiotic prophylaxis was stopped. His blood pressure, urine protein-to-creatinine ratio, and renal growth and function continue to be monitored in clinic.

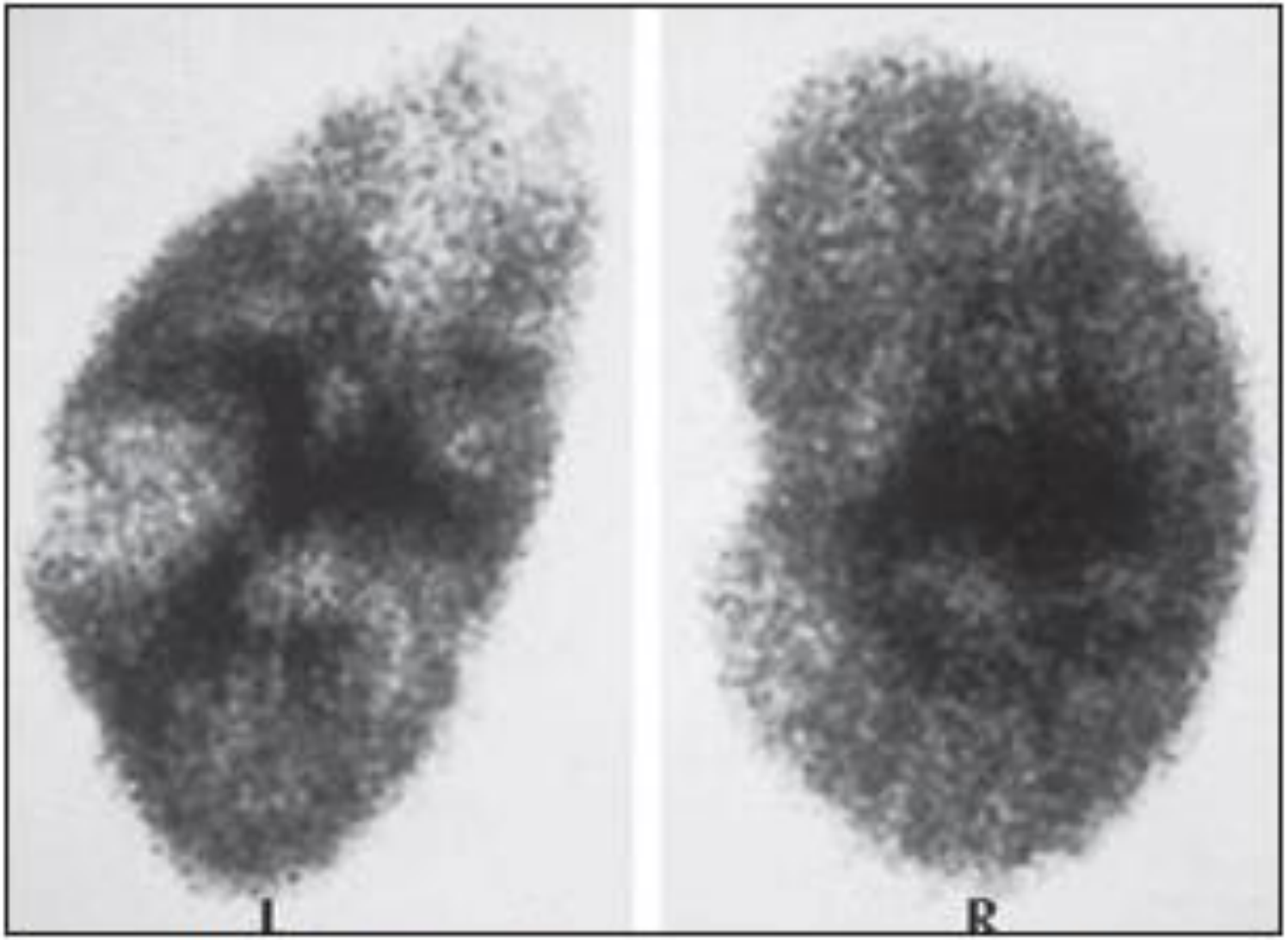


Figure 19.14 DMSA (Dimercaptosuccinic acid) scan showing bilateral renal scarring, more severe on left upper pole.

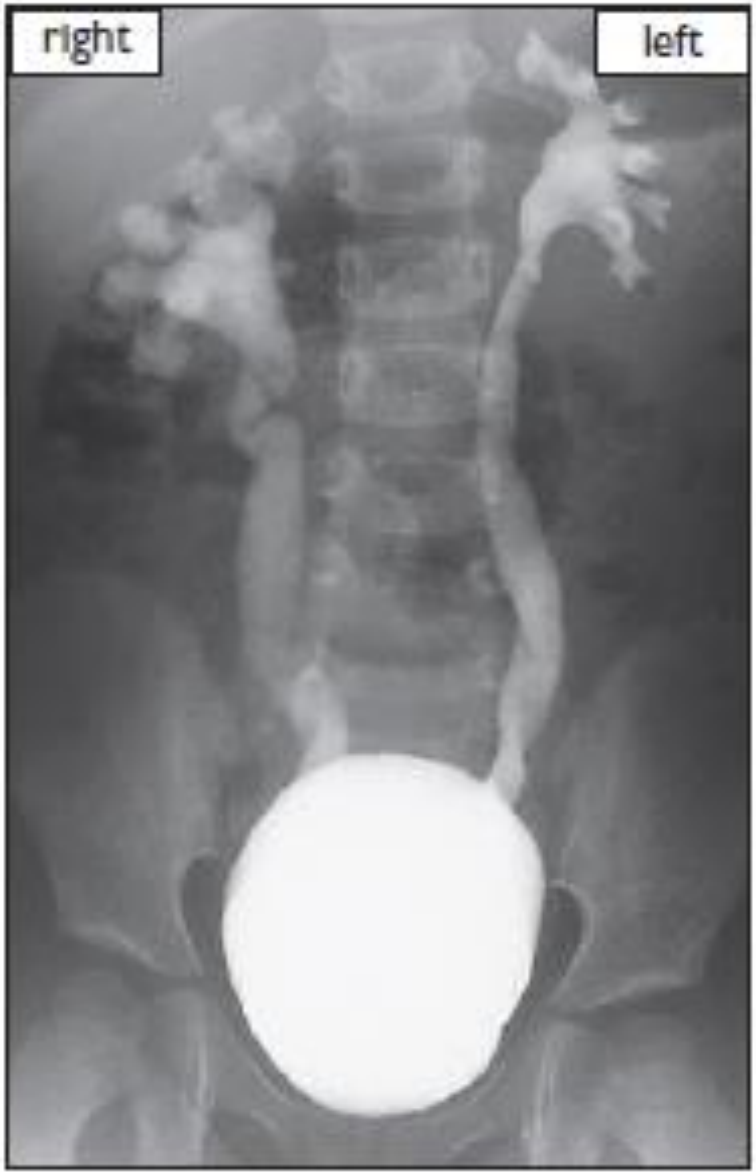


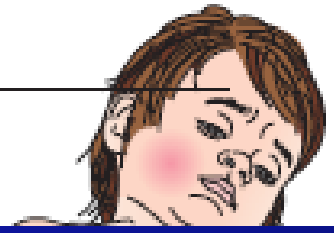
Figure 19.15 Micturating cystourethrogram (MCUG) showing bilateral vesicoureteric reflux with ureteric dilatation and dilated clubbed calyces on the right.

A child with a first urinary tract infection

Why important?
Up to half have a structural abnormality of their urinary tract
Pyelonephritis may damage the growing kidney by forming a renal scar, which may result in hypertension and chronic renal failure

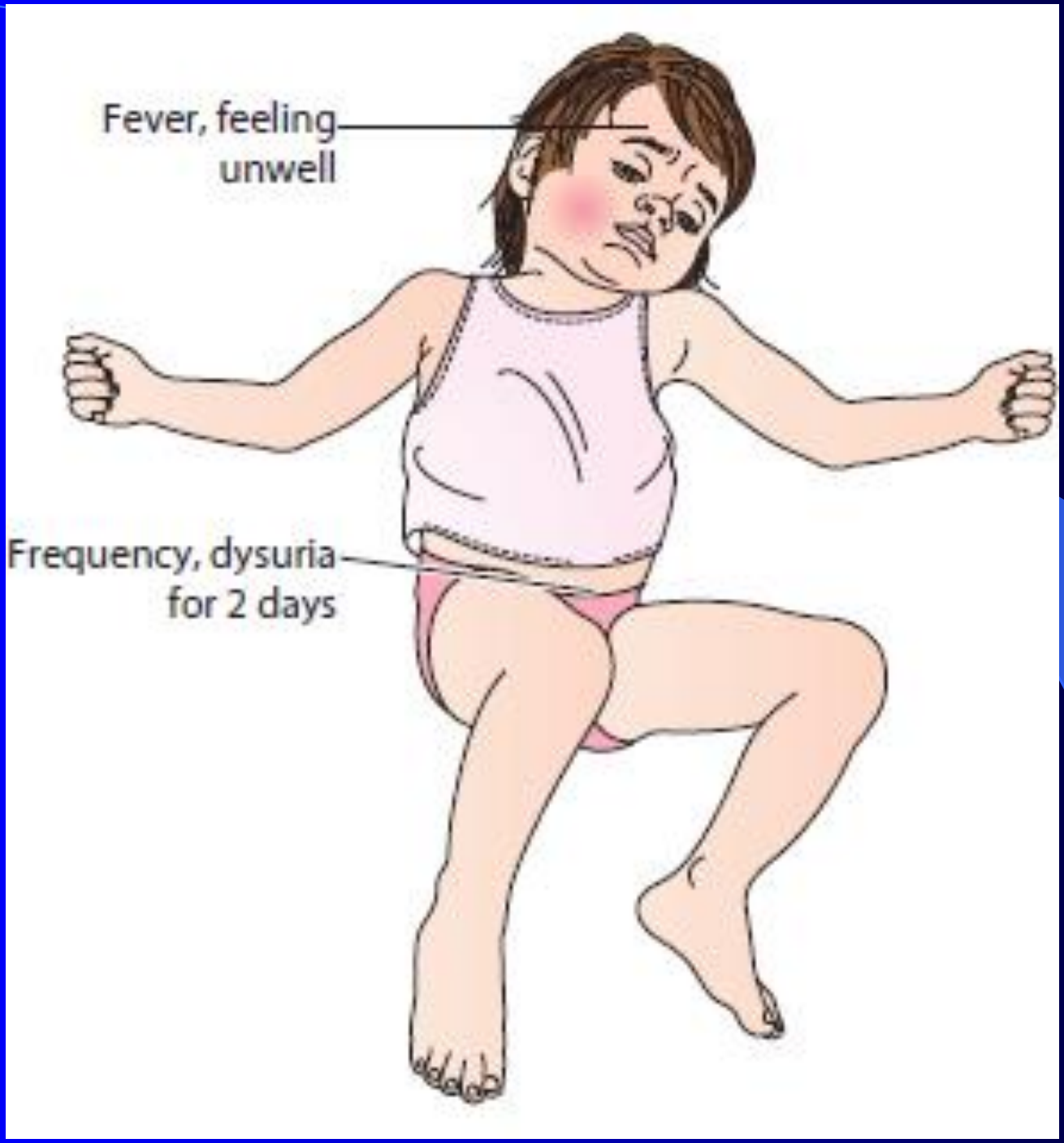
Diagnosis secure?
- Suggestive clinical features?
- Upper or lower urinary tract infection?
- Urine sample properly collected and processed?
- Culture of single organism >10^5/ml if clean catch or mid-stream urine or else any organisms on suprapubic aspirate or catheter sample?

Predisposing factors?
Incomplete bladder emptying
Constipation
Vesicoureteric reflux



Why investigate?
To identify serious structural abnormalities, urinary obstruction, renal scars, vesicoureteric reflux.

What investigation?
Consider:
- Ultrasound of kidneys and urinary tract
- DMSA to check for renal scars 3 months after UTI
- MAG3 or MCUG to detect obstruction and vesicouretic reflux.


Fever, feeling unwell
Frequency, dysuria for 2 days

Management

Treat infection with antibiotics

Advice about medical preventative measures to consider:

- High fluid intake
- Regular voiding, double micturition
- Prevent or treat constipation
- Good perineal hygiene
- *Lactobacillus acidophilus*

Advise to check urine culture if develops clinical features suggestive of non-specific illness

If renal scarring or reflux on investigation, or develops recurrent UTIs:

- Consider low-dose antibiotic prophylaxis
- Monitor blood pressure, renal growth and function

Enuresis

Primary nocturnal enuresis

This is considered in Chapter 24. Child and Adolescent Mental Health.

Daytime enuresis

This is a lack of bladder control during the day in a child old enough to be continent (over the age of 3–5 years). Nocturnal enuresis is also usually present. It may be caused by:

- lack of attention to bladder sensation: a manifestation of a developmental or psychogenic problem, although it may occur in otherwise normal children who are too preoccupied with what they are doing to respond to the sensation of a full bladder
- detrusor instability (sudden, urgent urge to void induced by sudden bladder contractions)

Daytime enuresis

- bladder neck weakness
- a neuropathic bladder (bladder is enlarged and fails to empty properly, irregular thick wall, and is associated with spina bifida and other neurological conditions)
- a UTI (rarely in the absence of other symptoms)
- constipation
- an ectopic ureter, causes constant dribbling and child is always damp.

Examination may reveal evidence of a neuropathic bladder, i.e. the bladder may be distended, there may be abnormal perineal sensation and anal tone, or abnormal leg reflexes and gait. Sensory loss in the distribution of the S2, S3, and S4 dermatomes should be sought. A spinal lesion may be present. Girls who are dry at night but wet on getting up are likely to have pooling of urine from an ectopic ureter opening into the vagina. A urine sample should be examined for microscopy, culture, and sensitivity. Other investigations are performed if indicated. An ultrasound may show bladder pathology, with incomplete bladder emptying or thickening of the bladder wall. Urodynamic studies may be required. An X-ray of the spine may reveal a vertebral anomaly. A MRI scan may be required to confirm or exclude a spinal defect such as tethering

Affected children in whom a neurological cause has been excluded may benefit from star charts, bladder training, and pelvic floor exercises. Constipation should be treated. A small portable alarm with a pad in the pants, which is activated by urine, can be used when there is lack of attention to bladder sensation. Anticholinergic drugs, such as oxybutynin, to dampen down bladder contractions, may be helpful if other measures fail.

Secondary (onset) enuresis

The loss of previously achieved urinary continence may be due to:

- emotional upset, which is the most common cause
- UTI
- polyuria from an osmotic diuresis in diabetes mellitus or a renal concentrating disorder, e.g. sickle cell disease or chronic kidney disease or very rarely diabetes insipidus, which can be central or nephrogenic.

Investigation should include:

- testing a urine sample for infection, glycosuria, and proteinuria using a dipstick

• assessment of urinary concentrating ability by measuring the osmolality of an early morning urine sample. Rarely, a formal water deprivation test may be needed to exclude a urinary concentrating defect
• ultrasound of the renal tract.

Summary

Enuresis

Daytime enuresis

- Consider possible causes: developmental or psychogenic, bladder instability or neuropathy, UTI, constipation, ectopic ureter.

Secondary (onset) enuresis

- Consider – emotional upset, UTI, polyuria from an osmotic diuresis in diabetes mellitus or a renal concentrating disorder.

Proteinuria

Transient proteinuria may occur during febrile illnesses or after exercise and does not require investigation. Persistent proteinuria is significant and should be quantified by measuring the urine protein-to-creatinine ratio in an early morning sample (normal protein-to creatinine ratio <20 mg/mmol).

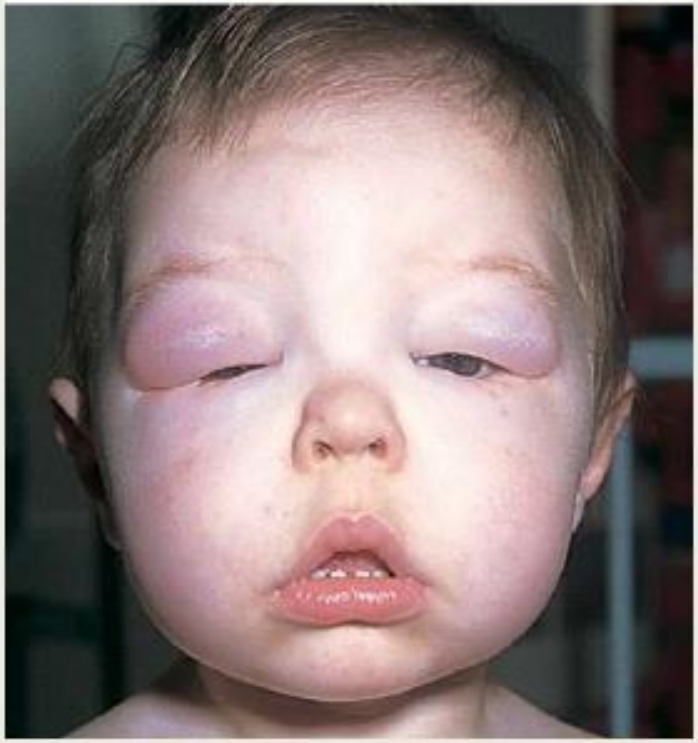
A common cause is orthostatic (postural) proteinuria when proteinuria is only found when the child is upright during the day. It can be diagnosed by measuring the urine protein-to-creatinine ratio in a series of early morning urine specimens. The prognosis is excellent and further investigations are not necessary.

Other causes of proteinuria, which need further evaluation,are listed in Box 19.2.

Box 19.2 Causes of proteinuria

- Orthostatic proteinuria
- Glomerular abnormalities
  - Minimal change disease
  - Glomerulonephritis
  - Abnormal glomerular basement membrane (familial nephritides)
- Increased glomerular filtration pressure
- Reduced renal mass in chronic kidney disease
- Hypertension
- Tubular proteinuria

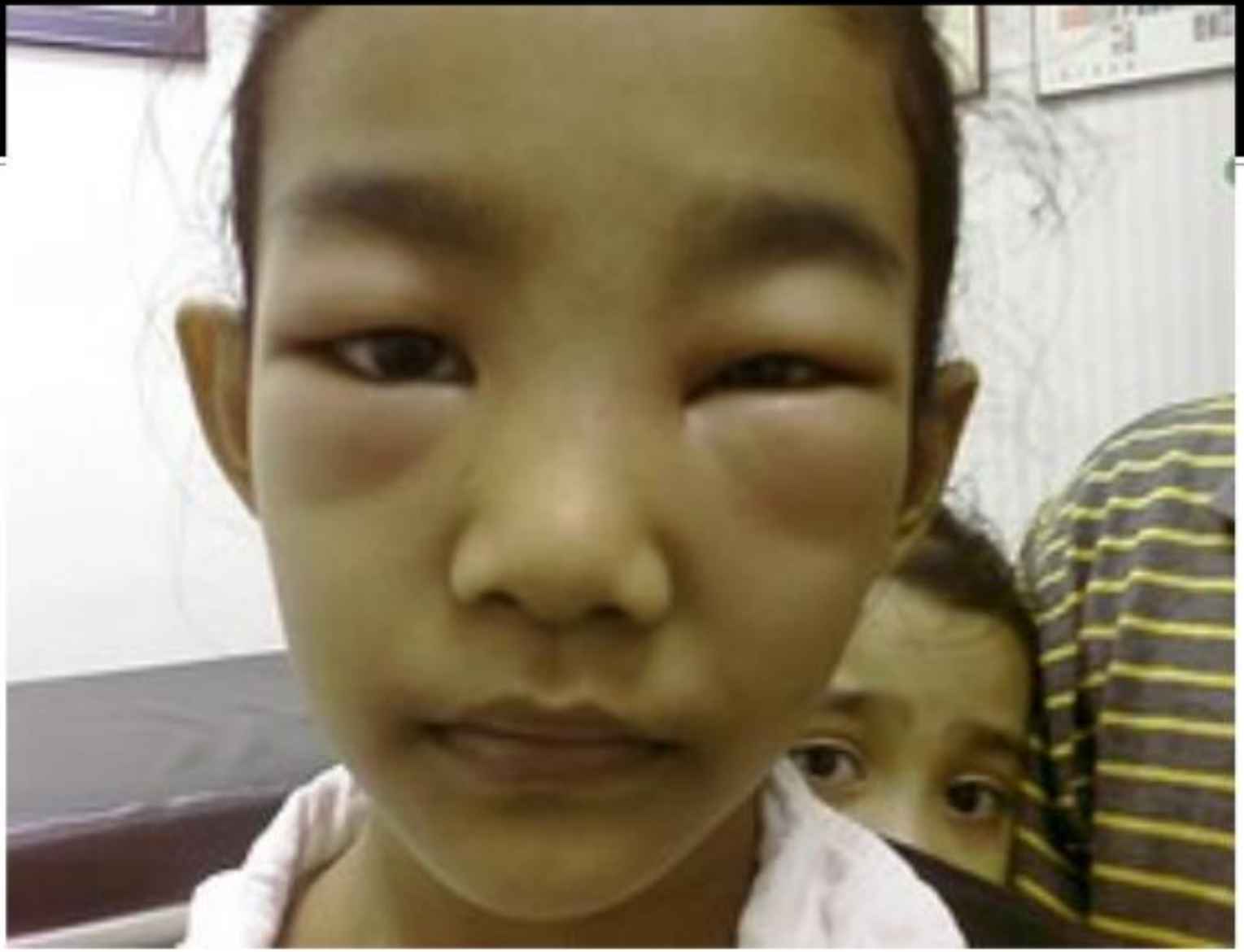
NEPHROTIC SYNDROME



THE SWOLLEN CHILD

Nephrotic syndrome

In nephrotic syndrome, heavy proteinuria results in a low plasma albumin and oedema. The cause of the condition is unknown, but a few cases are secondary to systemic diseases such as Henoch–Schönlein purpura and other vasculitides, e.g. SLE (systemic lupus erythematosus),
infections (e.g. malaria) or allergens (e.g.
bee sting).



Clinical signs of the nephrotic syndrome are:

- periorbital oedema (particularly on waking) which is often the earliest sign
- scrotal or vulval, leg, and ankle oedema (Fig. 19.16)
- ascites
- breathlessness due to pleural effusions and abdominal distension
- infection such as peritonitis, septic arthritis, or sepsis due to loss of protective immunoglobulins in the urine.

Case history 19.3 shows typical presentation, and initial investigations are listed in Box 19.3.

Steroid-sensitive nephrotic syndrome

In 85–90% of children with nephrotic syndrome, the proteinuria resolves with corticosteroid therapy(steroid-sensitive nephrotic syndrome). These children
do not progress to chronic kidney disease. It is more common in boys than in girls, in Asian children than in Caucasians, and there is an association with atopy. It is often precipitated by respiratory infections.

Steroid-sensitive nephrotic syndrome

In 85–90% of children with nephrotic syndrome,

Features suggesting steroid-sensitive nephrotic syndrome are:

- age between 1–10 years
- no macroscopic haematuria
- normal blood pressure
- normal complement levels
- normal renal function.

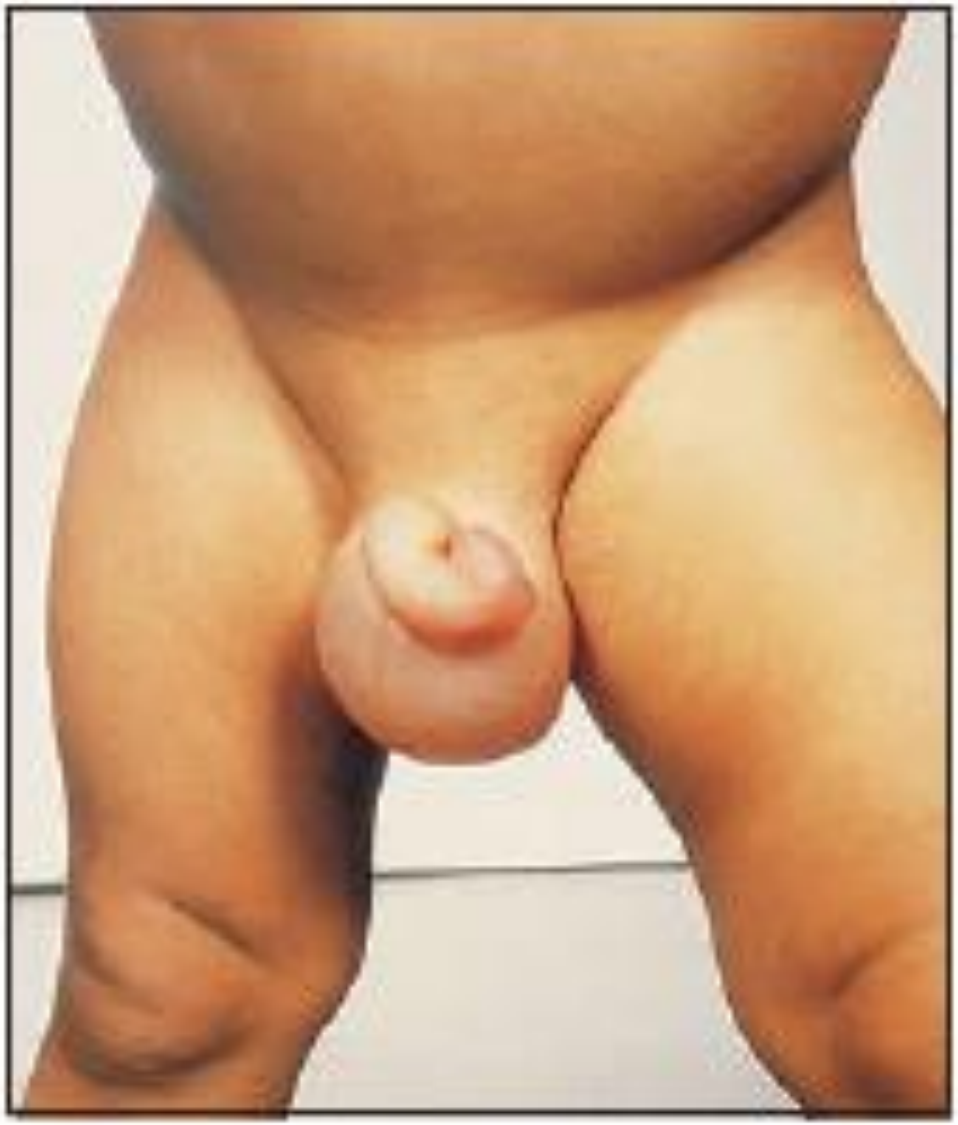


Figure 19.16 Gross oedema of the scrotum and legs as well as abdominal distension from ascites.

Box 19.3 Investigations performed at presentation of nephrotic syndrome

- Urine protein – on test strips (dipstick)
- Full blood count and erythrocyte sedimentation rate
- Urea, electrolytes, creatinine, albumin
- Complement levels – C3, C4
- Antistreptolysin O or anti-DNAse B titres and throat swab
- Urine microscopy and culture
- Urinary sodium concentration
- Hepatitis B and hepatitis C screen
- Malaria screen if travel abroad

Management

The most widely used protocol is to initially give oral corticosteroids (60 mg/m2 per day of prednisolone), unless there are atypical features. After 4 weeks, the dose is reduced to 40 mg/m2 on alternate days for 4 weeks and then weaned or stopped. The median time for the urine to become free of protein is 11 days. However, there is now good evidence that extending the initial course of steroids by gradually tapering the alternate day part of the course leads to a marked reduction in the proportion of children who develop a frequently relapsing or steroid-dependent course, although there are increased side-effects from steroid treatment.

Management

Children who do not respond to 4–6 weeks of corticosteroid therapy or have atypical features may have a more complex diagnosis and require a renal biopsy. Renal histology in steroid-sensitive nephrotic syndrome is usually normal on light microscopy but fusion of the specialized epithelial cells that invest the glomerular capillaries (podocytes) is seen on electron microscopy. For this reason, it is called minimal change disease.

The child with nephrotic syndrome is susceptible to several serious complications at presentation or relapse

- *Hypovolaemia* – during the initial phase of oedema formation, the intravascular compartment may become volume depleted. The child who becomes hypovolaemic characteristically complains of abdominal pain and may feel faint. There is peripheral vasoconstriction and urinary sodium retention. A low urinary sodium (<10 mmol/L) and a high packed cell volume of red blood cells are indications of hypovolaemia, which requires urgent treatment with intravenous fluid (0.9% saline or 4.5% albumin solution) as the child is at risk of vascular thrombosis and shock.

Increasing peripheral oedema, assessed clinically and by daily weight, may cause discomfort and respiratory compromise. If severe, this may need treatment with intravenous 20% albumin infusion with furosemide. Care must be taken with the use of 20% albumin as it may precipitate pulmonary oedema and hypertension from fluid overload, and also with diuretics, which may cause or worsen hypovolaemia.

- *Thrombosis* – a hypercoagulable state, due to urinary losses of antithrombin III, thrombocytosis which may be exacerbated by steroid therapy, increased synthesis of clotting factors, and increased blood viscosity from the raised haematocrit, all predispose to thrombosis. This may affect the lungs, brain, limbs, and splanchnic circulation with potentially catastrophic results.

- *Infection* – children in relapse are at risk of infection with capsulated bacteria, especially *Pneumococcus*. Spontaneous peritonitis may occur. Pneumococcal and seasonal influenza vaccination is widely recommended. Chickenpox and shingles should be treated with aciclovir.
- *Hypercholesterolaemia* – this correlates inversely with the serum albumin, but the cause of the hyperlipidaemia is not fully understood.

Prognosis

This is summarized in Fig. 19.18. Relapses are identified by parents on urine testing. The side-effects of corticosteroid therapy may be reduced by an alternate-day regimen. If relapses are frequent, or if a high maintenance dose is required, involvement of a paediatric nephrologist is advisable as steroid-sparing agents may be considered to enable reduction in steroid use. Possible steroid-sparing agents include the immunomodulator levamisole, alkylating agents (e.g. cyclophosphamide), calcineurin inhibitors such as tacrolimus and cyclosporin A, the immunosuppressant mycophenolate mofetil, and for difficult cases the anti-B-cell monoclonal antibody rituximab.

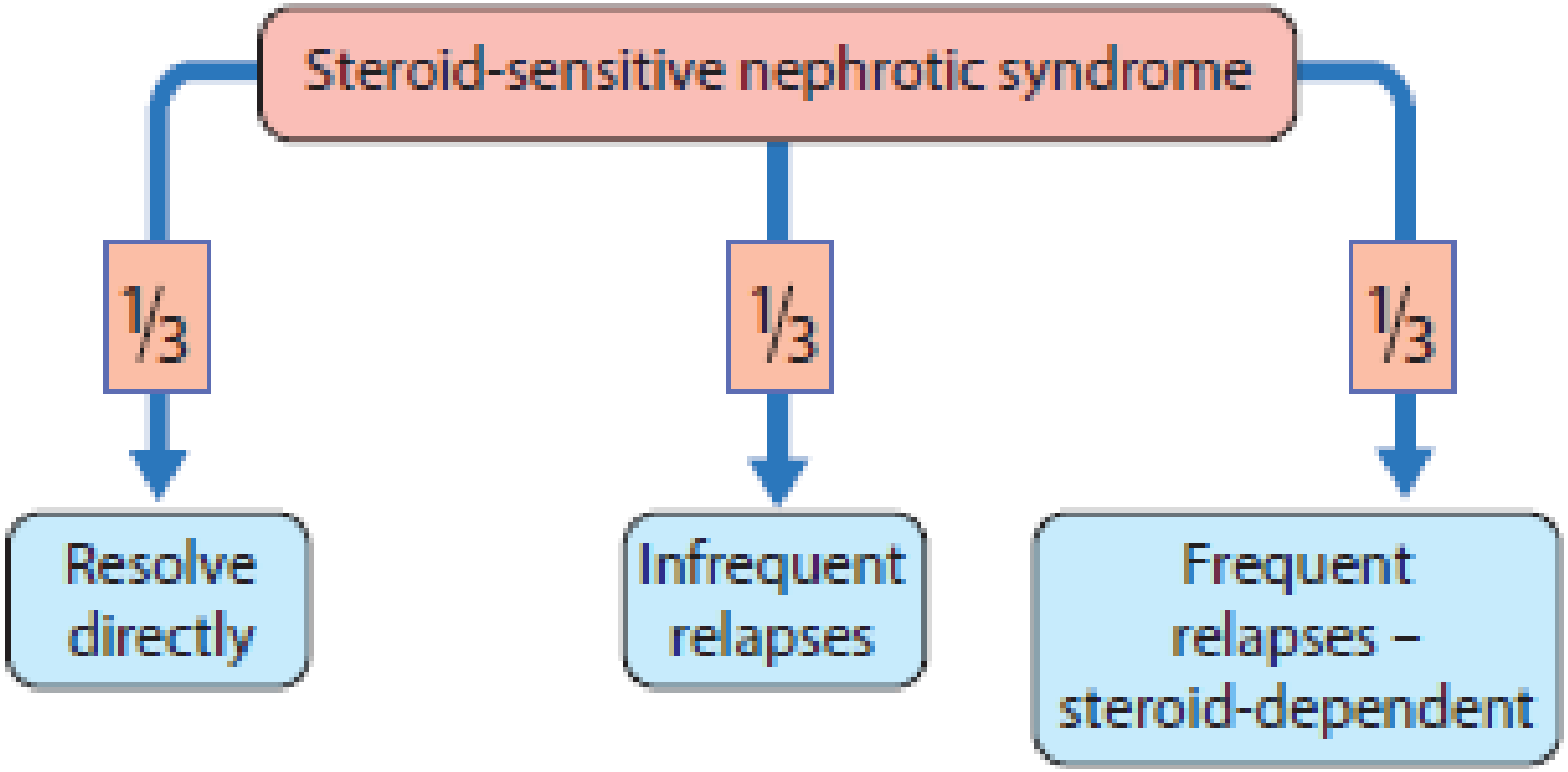


Figure 19.18 Clinical course in steroid-responsive nephrotic syndrome.

Steroid-resistant nephrotic syndrome

These children should be referred to a paediatric nephrologist (Table 19.4). Management of the oedema is by diuretic therapy, salt restriction, angiotensin-converting enzyme inhibitors, and sometimes nonsteroidal antiinflammatory drugs, which may reduce proteinuria.

Genetic testing for steroid-resistant nephrotic syndrome is available and helps in the management of children, e.g. withdrawal of immunosuppression or supplementation of CoQ10 if there is a CoQ10 pathway defect.

Congenital nephrotic syndrome

Congenital nephrotic syndrome presents in the first 3 months of life. It is rare. The most common kind is recessively inherited and the gene frequency is particularly high in Finns. In the UK, it is more common in consanguineous families. It is associated with a high mortality, usually due to complications of hypoalbuminaemia rather than progressive chronic kidney disease. The albuminuria is so severe that unilateral nephrectomy may be necessary for its control, followed by dialysis for stage 5 (most severe) chronic kidney disease, which is continued until the child is no longer nephrotic and old enough for renal transplantation.

Table 19.4 Steroid-resistant nephrotic syndrome

Cause	Specific features	Prognosis
Focal segmental glomerulosclerosis	Most common Familial or idiopathic	30% progress to end-stage renal failure in 5 years; 20% respond to cyclophosphamide, cyclosporin, tacrolimus, or rituximab Recurrence post-transplant is common
Mesangiocapillary glomerulonephritis (membranoproliferative glomerulonephritis)	More common in older children Haematuria and low complement level present	Decline in renal function over many years
Membranous nephropathy	Associated with hepatitis B May precede SLE (systemic lupus erythematosus)	Most remit spontaneously within 5 years

Summary

Nephrotic syndrome

- Clinical signs: oedema (periorbital, scrotal or vulval, leg, and ankle oedema; ascites; pleural effusions).
- Diagnosis: heavy proteinuria and low plasma albumin.

Steroid-sensitive nephrotic syndrome

- Characteristic features: 1–10-years-old; no macroscopic haematuria; and normal blood pressure, complement levels, and renal function.
- Management: oral corticosteroids, renal biopsy if unresponsive or atypical features.
- Complications: hypovolaemia, thrombosis, infection (pneumococcal), hypercholesterolaemia.
- Prognosis: may resolve or else there may be infrequent or frequent relapses.

- An oedematous child – test for proteinuria to diagnose nephrotic syndrome

Case history 19.3

Nephrotic syndrome

Zakariya developed periorbital oedema (Fig. 19.17) which improved during day. He was seen by several doctors who diagnosed allergy, conjunctivitis, and hay fever. When he developed ascites and bilateral leg oedema his urine was dipsticked and showed 4+ protein and nephrotic syndrome was diagnosed. Periorbital oedema is often the initial sign of nephrotic syndrome but diagnosis is often delayed until other complications develop. Investigations performed are listed in Box 19.3. He is most likely to have steroid responsive nephrotic syndrome, and the clinical course is outlined in Fig. 19.18.

Figure 19.17 Facial oedema in nephrotic syndrome which improves during the day and is often misdiagnosed as an allergy.

Haematuria

Urine that is red in colour or tests positive for haemoglobin
on urine sticks should be examined under the microscope to confirm haematuria (>10 red blood cells per high-power field). Glomerular haematuria is suggested
by brown urine, the presence of deformed red cells (which occurs as they pass through the basement membrane), and casts, and is often accompanied by proteinuria. Lower urinary tract haematuria is usually red, occurs at the beginning or end of the urinary stream, is not accompanied by proteinuria, and is unusual in children.

UTI is the most common cause of haematuria (Box 19.4), although seldom as the only symptom. The history and examination may suggest the diagnosis, e.g. a family history of stone formation or nephritis or a history of trauma. A plan of investigation is outlined in Box 19.5.

Box 19.4 Causes of haematuria

Nonglomerular

- Infection (bacterial, viral, tuberculosis, schistosomiasis)
- Trauma to genitalia, urinary tract, or kidneys
- Stones
- Tumours
- Sickle cell disease
- Bleeding disorders
- Renal vein thrombosis
- Hypercalciuria

Glomerular

- Acute glomerulonephritis (usually with proteinuria)
- Chronic glomerulonephritis (usually with proteinuria)
- IgA nephropathy
- Familial nephritis, e.g. Alport syndrome
- Thin basement membrane disease

Box 19.5 Investigation of haematuria

All patients

- Urine microscopy (with phase contrast) and culture
- Protein and calcium excretion
- Kidney and urinary tract ultrasound
- Plasma urea, electrolytes, creatinine, calcium, phosphate, albumin
- Full blood count, platelets, coagulation screen, sickle cell screen

If suggestive of glomerular haematuria

- ESR, complement levels, and anti-DNA antibodies
- Throat swab and antistreptolysin O/anti-DNAse B titres
- Hepatitis B and C screen
- Renal biopsy if indicated
- Test mother's urine for blood (if Alport syndrome suspected)
- Hearing test (if Alport syndrome suspected)

A renal biopsy may be indicated if:

- there is significant persistent proteinuria
- there is recurrent macroscopic haematuria
- renal function is abnormal
- the complement levels are persistently abnormal.

Acute nephritis

The causes of acute nephritis in childhood are listed in Box 19.6. Increased glomerular cellularity restricts glomerular blood flow, and therefore glomerular filtration is decreased. This leads to:

- decreased urine output and volume overload
- hypertension, which may cause seizures
- oedema, characteristically initially periorbital
- haematuria and proteinuria.

Management is by attention to both water and electrolyte balance and the use of diuretics when necessary.
Rarely, there may be a rapid deterioration in renal function (rapidly progressive glomerulonephritis).
This may occur with any cause of acute nephritis, but is uncommon when the cause is poststreptococcal.
If left untreated, irreversible chronic kidney disease may occur over weeks or months, so renal biopsy and subsequent treatment with immunosuppression and plasma exchange may be necessary.

Box 19.6 Causes of acute nephritis

- Post-infectious (including streptococcus)
- Vasculitis (Henoch–Schönlein purpura or, rarely, SLE (systemic lupus erythematosus), Wegener granulomatosis, microscopic polyarteritis, polyarteritis nodosa)
- IgA nephropathy and mesangiocapillary glomerulonephritis
- Antiglomerular basement membrane disease (Goodpasture syndrome) – very rare

Post-streptococcal and post-infectious nephritis

Usually follows a streptococcal sore throat or skin infection and is diagnosed by evidence of a recent streptococcal infection (culture of the organism, raised ASO/anti-DNAse B titres), and low complement C3 levels that return to normal after 3 weeks to 4 weeks. Streptococcal nephritis is a common condition in developing countries, but has become uncommon in developed countries. Long-term prognosis is good.

Summary

Acute nephritis

- Cause: usually post-infectious or follows a streptococcal infection, but also vasculitis (including Henoch–Schönlein purpura), IgA nephropathy, and familial nephritis.
- Clinical features: oedema (around the eyes), hypertension, decreased urine output, haematuria and proteinuria.
- Management: fluid and electrolyte balance, diuretics, monitor for rapid deterioration in renal function.

Henoch–Schönlein purpura

Henoch–Schönlein purpura is the combination of some of the following features:

- characteristic skin rash on extensor surfaces
- arthralgia
- periarticular oedema
- abdominal pain
- glomerulonephritis.

Henoch–Schönlein purpura

It usually occurs between the ages of 3–10 years, is twice as common in boys, peaks during the winter months, and is often preceded by an upper respiratory infection. Despite much research, the cause is unknown. It is postulated that genetic predisposition and antigen exposure increase circulating IgA levels and disrupt IgG synthesis. The IgA and IgG interact to produce complexes that activate complement and are deposited in affected organs, precipitating an inflammatory
response with vasculitis.

Clinical findings

At presentation, affected children often have a fever. The *rash* is the most obvious feature (Fig. 19.19). It is symmetrically distributed over the buttocks, the extensor surfaces of the arms and legs, and the ankles. The trunk is usually spared. The rash may initially be urticarial, rapidly becoming maculopapular and purpuric, is characteristically palpable, and may recur over several weeks. The rash is the first clinical feature in about 50% and is the cornerstone of the diagnosis, which is clinical.

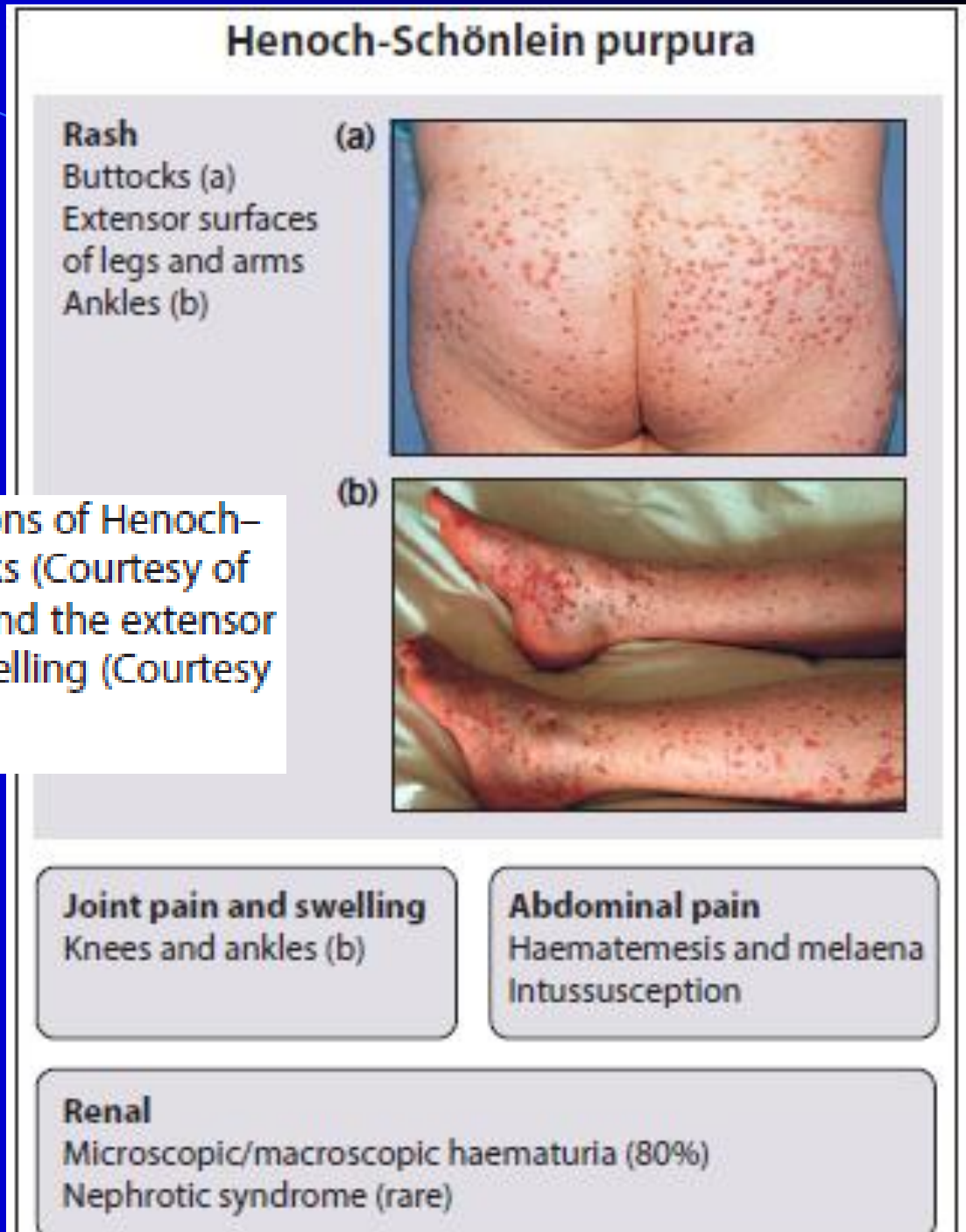
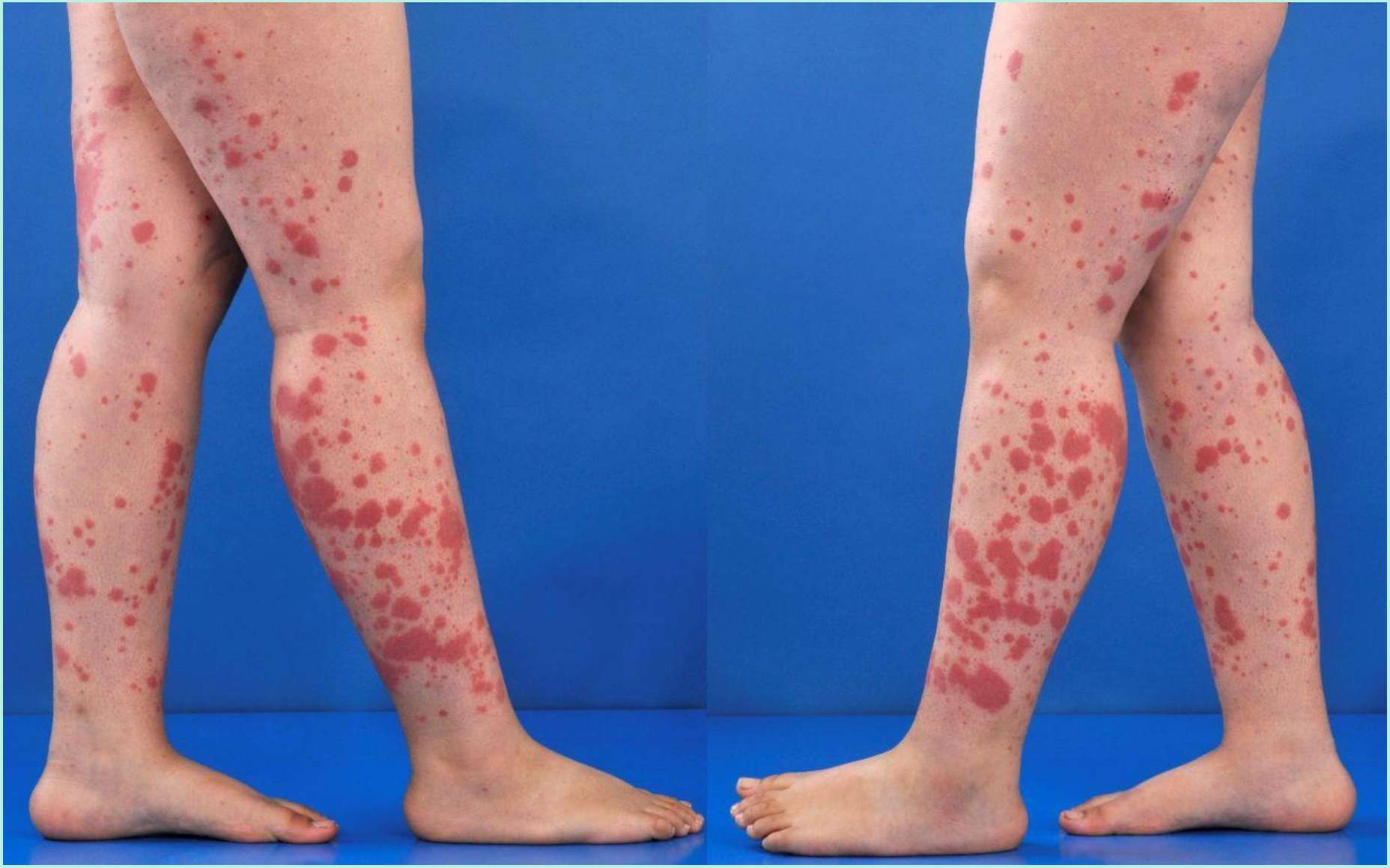


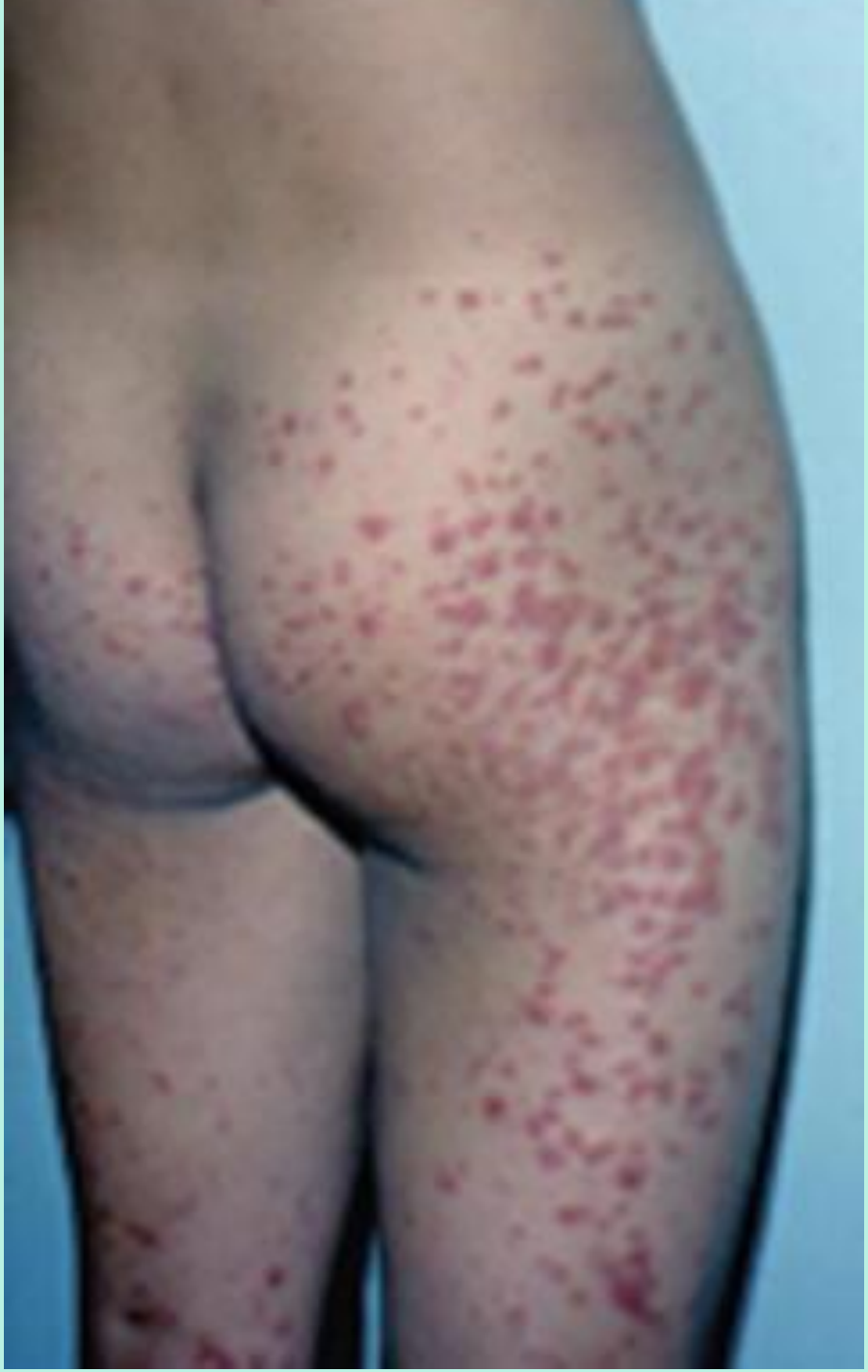
Figure 19.19 Main clinical manifestations of Henoch–Schönlein purpura. (a) Rash on buttocks (Courtesy of Michael Markiewicz); and (b) rash around the extensor surfaces of the legs and slight joint swelling (Courtesy of Tauny Southwood).

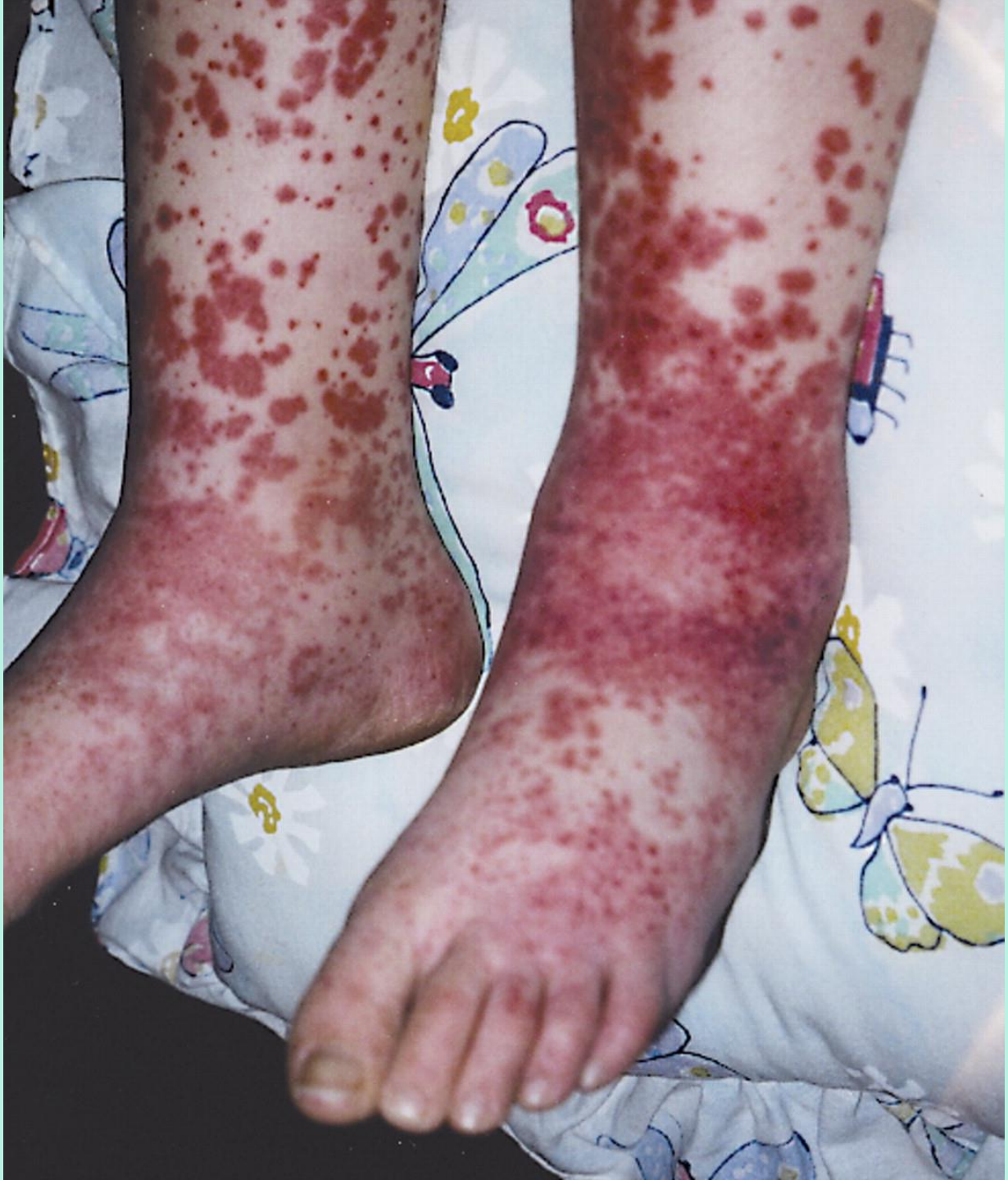
Joint pain occurs in two-thirds of patients, particularly of the knees and ankles. There is *periarticular oedema*. Long-term damage to the joints does not occur, and symptoms usually resolve before the rash goes.

Colicky abdominal pain occurs in many children and, if severe, can be treated with corticosteroids. Gastrointestinal involvement can cause haematemesis and melaena. Intussusception can occur and can be particularly difficult to diagnose under these circumstances. Ileus, protein-losing enteropathy, orchitis, and occasionally central nervous system involvement are other rare complications. *Renal involvement* is common, but is rarely the first symptom. Over 80% have microscopic or macroscopic haematuria or mild proteinuria. These children usually make a complete recovery. If proteinuria is more severe, nephrotic syndromemay result.

Risk factors for progressive chronic kidney disease are heavy proteinuria, oedema, hypertension, and deteriorating renal function, when a renal biopsy will determine if treatment is necessary. All children with Henoch–Schönlein purpura should be followed for a year to detect those with persisting haematuria or proteinuria (5–10%). Children who have persistent renal involvement or required treatment for Henoch–Schönlein purpura nephritis require long-term follow-up. This is necessary as hypertension and progressive chronic kidney disease may develop after an interval of several years.







IgA nephropathy

This may present with episodes of macroscopic haematuria, commonly in association with upper respiratory tract infections. Histological findings and management are as for Henoch–Schönlein purpura, which may be a variant of the same pathological process but not restricted to the kidney. The prognosis in children is better than that in adults.

Familial nephritis

The most common familial nephritis is Alport syndrome. This is usually an X-linked recessive disorder that progresses to progressive end-stage chronic kidney disease by early adult life in males and is associated with nerve deafness and ocular defects. The mother may have haematuria. The differential diagnosis is thin basement membrane disease, which also required long-term follow-up to detect proteinuria and chronic kidney disease, which rarely develops in later life.

Vasculitis

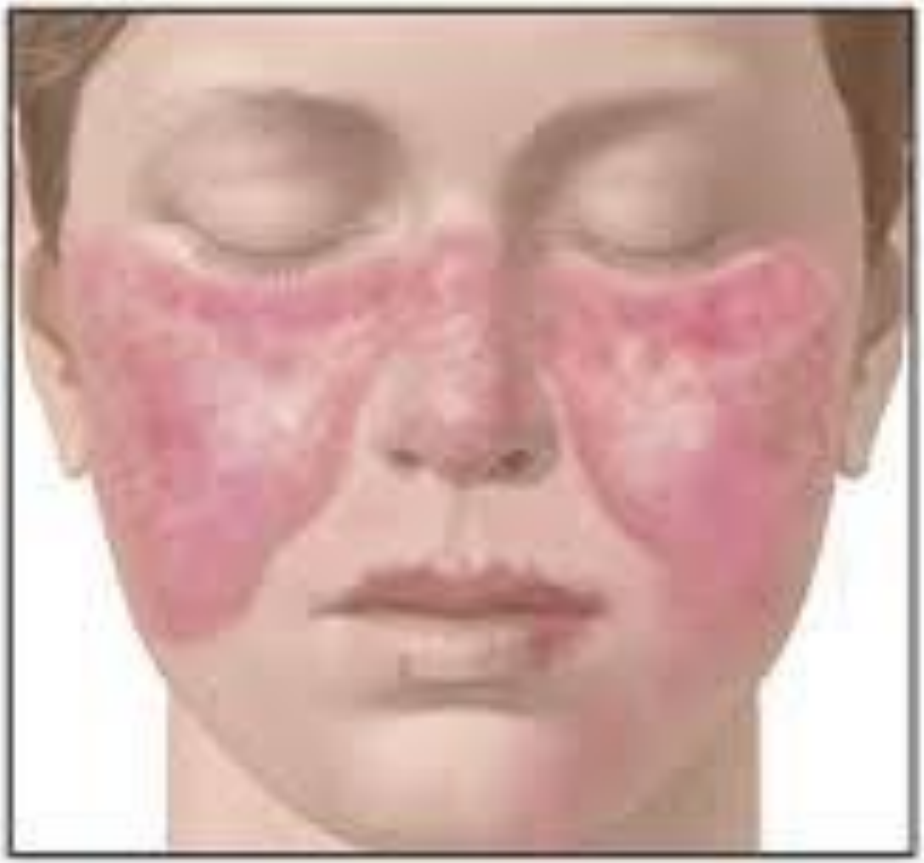
The most common vasculitis to involve the kidney is Henoch–Schonlein purpura (see the 'Henoch–Schonlein Purpura' section). However, renal involvement may occur in rarer vasculitides such as polyarteritis nodosa, microscopic polyarteritis, and granulomatosis with polyangiitis (formerly known as Wegener granulomatosis). Characteristic symptoms are fever, malaise, weight loss, skin rash, and arthropathy with prominent involvement of the respiratory tract in granulomatosis with polyangiitis. ANCA (antineutrophil cytoplasm antibodies) are present and diagnostic in these diseases.

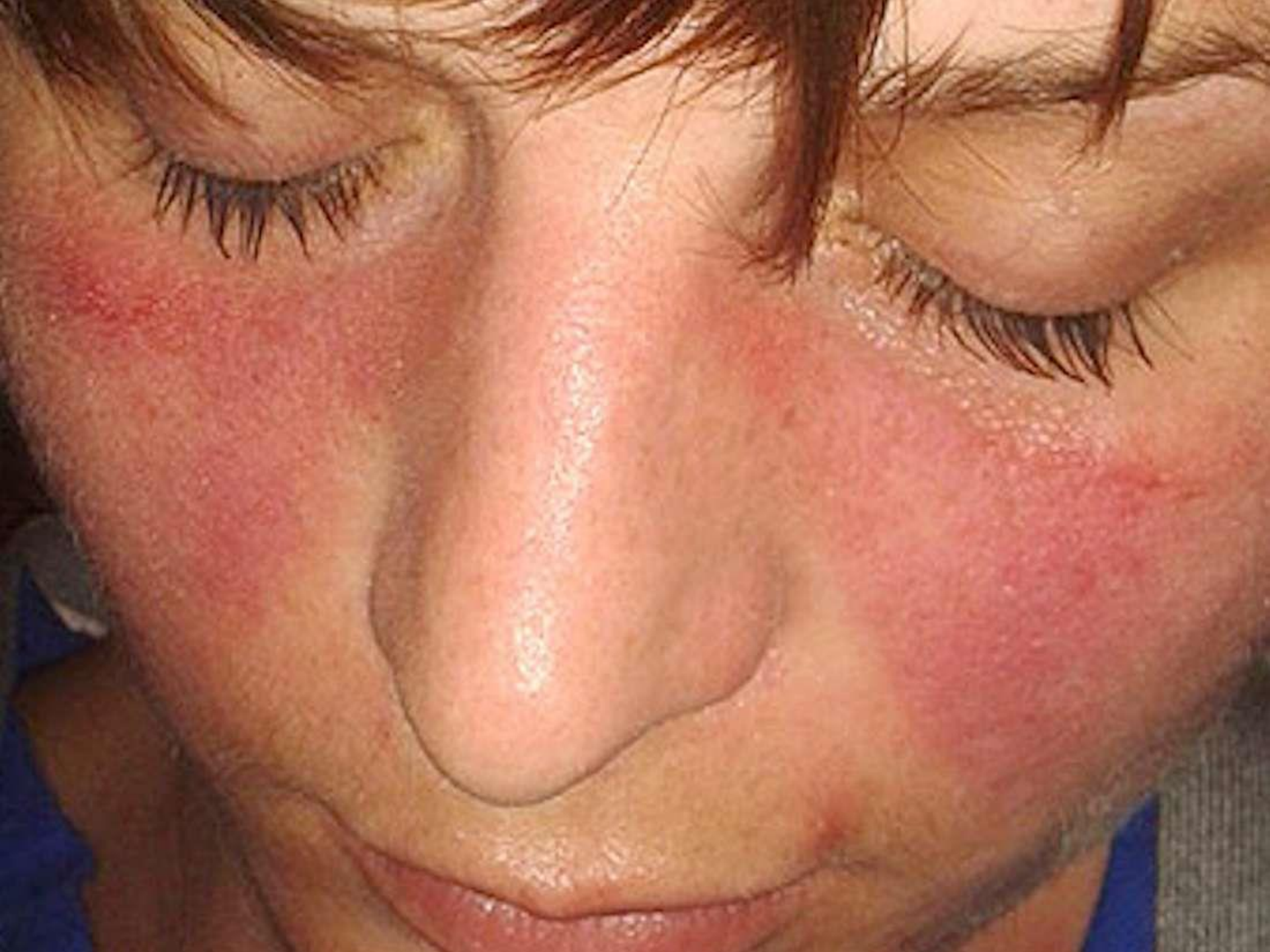
Renal arteriography, to demonstrate the presence of aneurysms, will diagnose polyarteritis nodosa. Renal involvement may be severe and rapidly progressive.

Treatment is with corticosteroids, plasma exchange, and intravenous cyclophosphamide, which may need to be continued for many months.

Systemic lupus erythematosus (SLE)

SLE is a disease that presents mainly in adolescent girls and young women. It is much more common in Asian and Black than White ethnic groups. It is characterized by the presence of multiple autoantibodies, including antibodies to double-stranded DNA. The C3 and C4 components of complement may be low, particularly during active phases of the disease. Haematuria and proteinuria are indications for renal biopsy, as immunosuppression
is always necessary and its intensity will
depend on the severity of renal involvement.





Hypertension

Blood pressure in children needs to be measured with a cuff over two-thirds the length of the upper arm (see Fig. 2.14). Blood pressure increases with age and height and readings should be plotted on a centile chart (see Appendix A4). Hypertension is blood pressure above 95th percentile for height, age, and sex. Children who are overweight or obese are at increased risk. Symptomatic hypertension in children is usually secondary to renal, cardiac, or endocrine causes (Box 19.7).

Box 19.7 Causes of hypertension

- **Renal**
  - Renal parenchymal disease
  - Renovascular, e.g. renal artery stenosis
  - Polycystic kidney disease (autosomal recessive polycystic kidney disease and autosomal dominant polycystic kidney disease)
  - Renal tumours
- **Coarctation of the aorta**
- **Catecholamine excess**
  - Pheochromocytoma
  - Neuroblastoma
- **Endocrine**
  - Congenital adrenal hyperplasia
  - Cushing syndrome or corticosteroid therapy
  - Hyperthyroidism
- **Essential hypertension**
  - A diagnosis of exclusion.

Presentation includes vomiting, headaches, facial palsy, hypertensive retinopathy, convulsions, or proteinuria. Faltering growth and cardiac failure are the most common features in infants. Pheochromocytoma may also cause paroxysmal palpitations and sweating.
Some causes are correctable, e.g. nephrectomy for unilateral scarring, angioplasty for renal artery stenosis, surgical repair of coarctation of the aorta, resection of a pheochromocytoma, but in most cases medical treatment is necessary with antihypertensive medications.
Early detection of hypertension is important. All children with a renal tract abnormality should have their blood pressure checked annually throughout life.
Children with a family history of essential hypertension should be encouraged to restrict their salt intake, avoid obesity, and have their blood pressure checked regularly.

Renal masses

An abdominal mass identified on palpating the abdomen should be investigated promptly by ultrasound scan. The causes of palpable kidneys are shown in Box 19.8. Bilaterally enlarged kidneys in early life are most frequently due to autosomal recessive polycystic kidney disease (ARPKD), which is associated with hypertension, hepatic fibrosis, and progression to chronic kidney disease. This form of polycystic kidney disease must be distinguished from ADPKD (autosomal dominant adult-type polycystic kidney disease), which has a more benign prognosis in childhood with onset of progressive chronic kidney disease in adulthood, although hypertension is found in at least 10% of affected children.

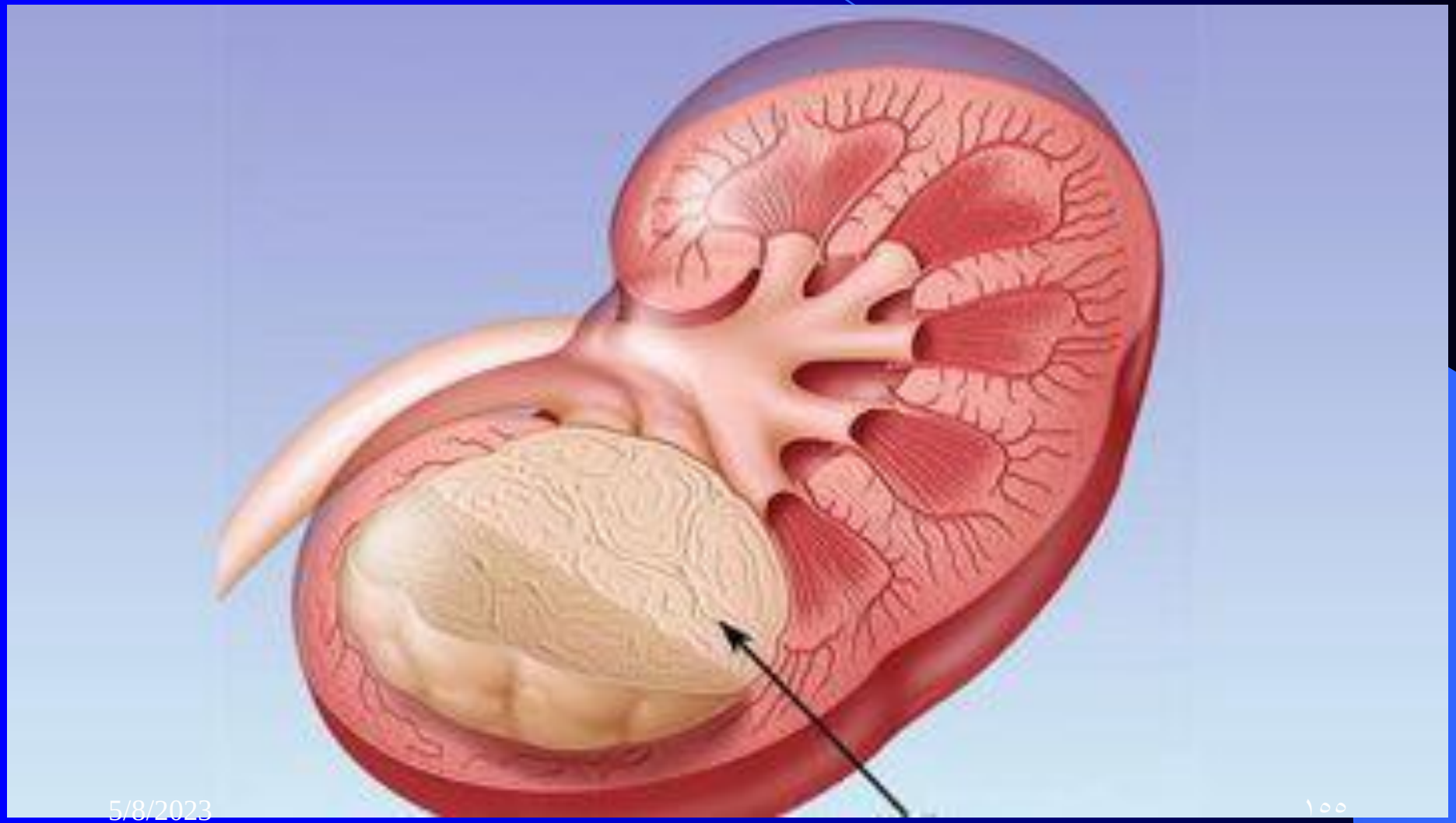
Box 19.8 Causes of palpable kidneys

Unilateral

- Multicystic kidney
- Compensatory hypertrophy
- Obstructed hydronephrosis
- Renal tumour (Wilms tumour)
- Renal vein thrombosis

Bilateral

- Autosomal recessive polycystic kidneys
- Autosomal dominant polycystic kidneys
- Tuberous sclerosis
- Renal vein thrombosis



Renal calculi

Renal stones are uncommon in childhood (Fig. 19.20). When they occur, predisposing causes must be sought:

- UTI
- structural anomalies of the urinary tract
- metabolic abnormalities.


1
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The most common are phosphate stones associated with infection, especially with *Proteus*. Calcium containing stones occur in idiopathic hypercalciuria, the most common metabolic abnormality, and with increased urinary urate and oxalate excretion. Deposition of calcium in the parenchyma (nephrocalcinosis) may occur with hypercalciuria, hyperoxaluria, and distal renal tubular acidosis. Nephrocalcinosis may be a complication of furosemide therapy in the neonate. Cystine and xanthine stones are rare.

Presentation may be with haematuria, loin or abdominal pain, UTI, or passage of a stone. Stones that are not passed spontaneously should be removed, by either lithotripsy or surgery, and any predisposing structural anomaly repaired if possible. A high fluid intake is recommended in all affected children. If the cause is a metabolic abnormality, specific therapy may be possible.

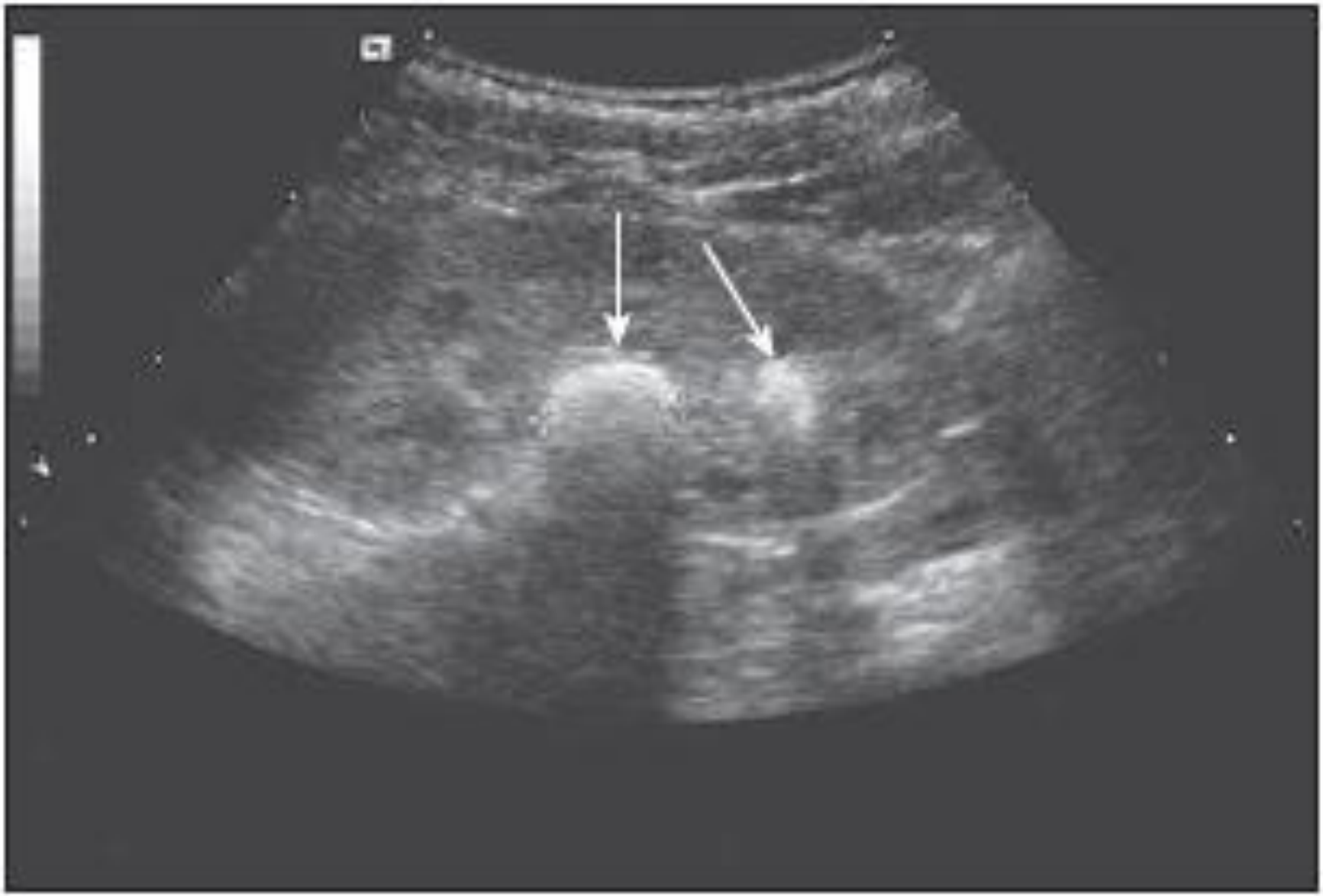


Figure 19.20 Renal ultrasound showing a staghorn calculus.

Renal tubular disorders

Abnormalities of renal tubular function may occur at any point along the length of the nephron and affect any of the substances handled by it.

Generalized proximal tubular dysfunction (Fanconi syndrome)

Proximal tubule cells are among the most metabolically active in the body, so are especially vulnerable to cellular damage. The cardinal features are excessive urinary loss of amino acids, glucose, phosphate, bicarbonate, sodium, calcium, potassium, and magnesium.
The causes are listed in Box 19.9. Fanconi syndrome should be considered in a child presenting with:

- polydipsia and polyuria
- salt depletion and dehydration
- hyperchloraemic metabolic acidosis
- rickets
- faltering or poor growth.

Box 19.9 Causes of Fanconi syndrome

Idiopathic

Secondary to inborn errors of metabolism

- Cystinosis (an autosomal recessive disorder causing intracellular accumulation of cystine)
- Glycogen storage disorders
- Lowe syndrome (oculocerebrorenal dystrophy)
- Galactosaemia
- Fructose intolerance
- Tyrosinaemia
- Wilson disease

Acquired

- Heavy metals
- Drugs and toxins
- Vitamin D deficiency

Specific transport defects

See Fig. 19.21.

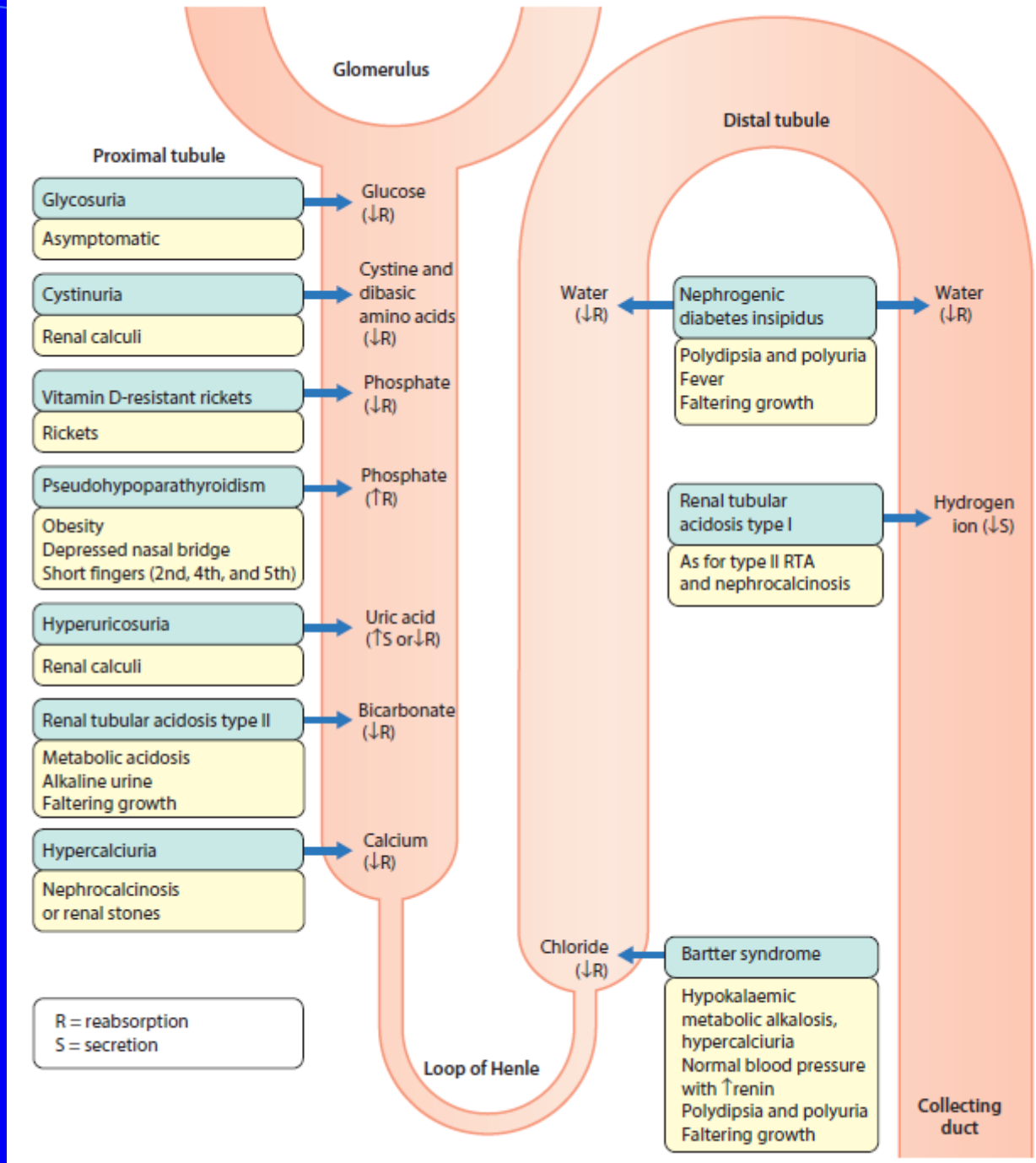
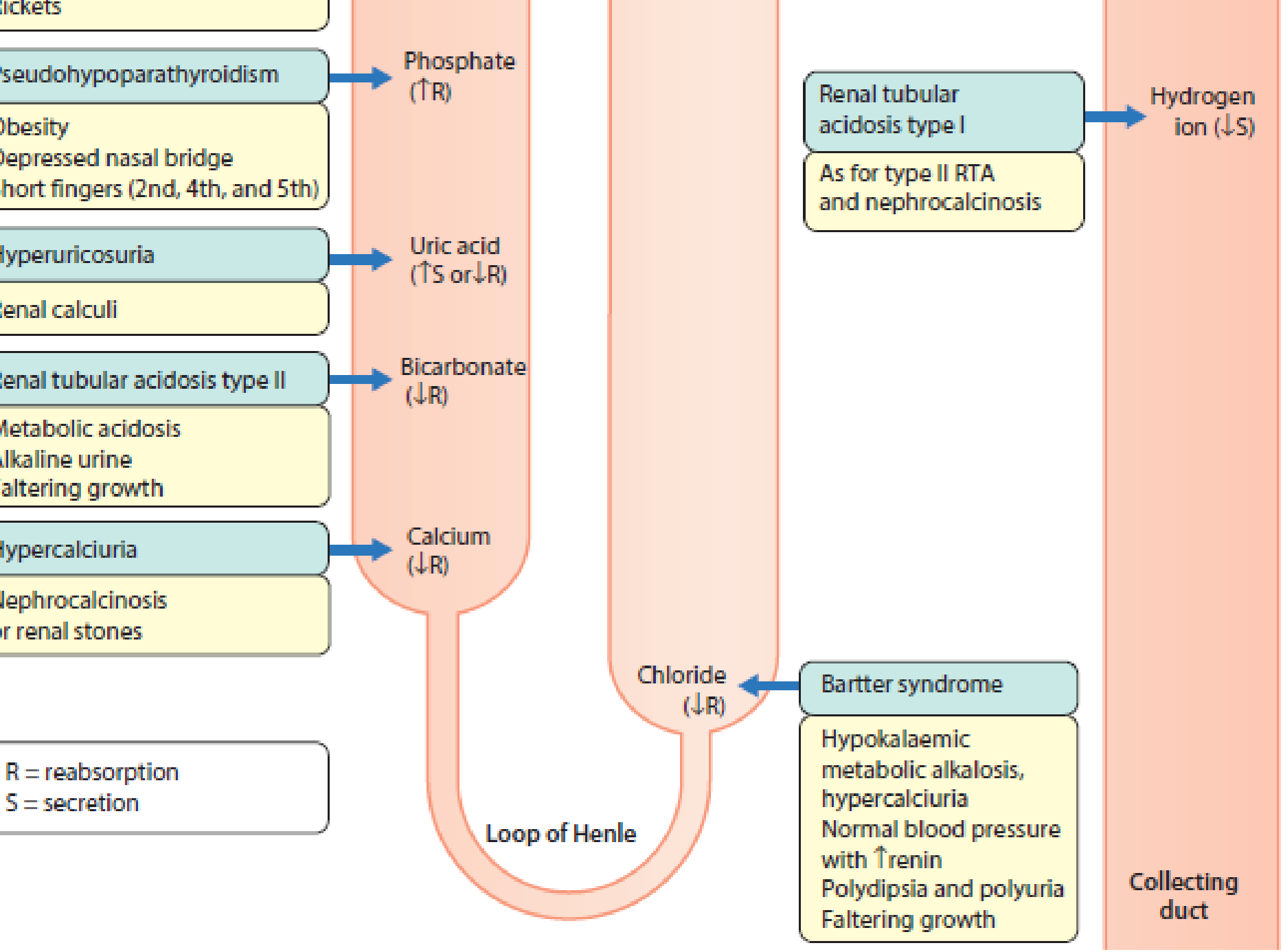


Figure 19.21 Schematic diagram of specific transport defects in some renal tubular disorders.



gure 19.21 Schematic diagram of specific transport defects in some renal tubular disorders.

Acute kidney injury

Acute kidney injury has acute renal failure at the most severe end of the spectrum where there is a sudden, potentially reversible, reduction in renal function. Oliguria (<0.5 ml/kg per hour) is usually present. It can be classified as (see Box 19.10):

- prerenal: the most common cause in children
- renal: there is salt and water retention; blood, protein, and casts are often present in the urine; and there may be symptoms specific to an accompanying disease [e.g. haemolytic uraemic syndrome (HUS)]
- postrenal: from urinary obstruction.

Acute-on-chronic renal failure is suggested by the child having growth failure, anaemia, and disordered bone mineralization (renal osteodystrophy).

Box 19.10 Causes of acute kidney injury

Prerenal

- Hypovolaemia:
  - gastroenteritis
  - burns
  - sepsis
  - haemorrhage
  - nephrotic syndrome
- Circulatory failure

Renal

- Vascular:
  - haemolytic uraemic syndrome
  - vasculitis
  - embolus
  - renal vein thrombosis
- Tubular:
  - acute tubular necrosis
  - ischaemic
  - toxic
  - obstructive
- Glomerular:
  - glomerulonephritis
- Interstitial:
  - interstitial nephritis
  - pyelonephritis

Postrenal

- Obstruction:
  - congenital, e.g. posterior urethral valves
  - acquired, e.g. blocked urinary catheter

Management

Children with acute renal failure should have their circulation and fluid balance meticulously monitored. Investigation by ultrasound scan will identify obstruction of the urinary tract, the small kidneys of chronic kidney disease, or large, bright kidneys with loss of cortical medullary differentiation typical of an acute process.

Prerenal failure

This is suggested by hypovolaemia. The fractional excretion
of sodium is very low as the body tries to retain volume. The hypovolaemia needs to be urgently corrected
with fluid replacement and circulatory support
if acute tubular injury and necrosis are to be avoided.

Renal failure

If there is circulatory overload, restriction of fluid intake and challenge with a diuretic may increase urine output sufficiently to allow gradual correction of sodium and water balance. A high-calorie, normal protein feed will decrease catabolism, uraemia, and hyperkalaemia. Emergency management of metabolic acidosis, hyperkalaemia, and hyperphosphataemia is shown in Table 19.5. If the cause of renal failure is not obvious, a renal biopsy should be performed to identify rapidly progressive glomerulonephritis, as this may need immediate treatment with immunosuppression. The two most common renal causes of acute renal failure in children in the UK are haemolytic uraemic syndrome and acute tubular necrosis, the latter usually in the setting of multisystem failure in the intensive care unit or following cardiac surgery.

Postrenal failure

This requires assessment of the site of obstruction and relief by nephrostomy or bladder catheterization.

Surgery can be performed once fluid volume and electrolyte abnormalities have been corrected.

Dialysis

Dialysis in acute kidney injury is indicated when there is:

- failure of conservative management
- hyperkalaemia
- severe hyponatraemia or hypernatraemia
- pulmonary oedema or severe hypertension due to volume overload
- severe metabolic acidosis
- multisystem failure.

Peritoneal dialysis or haemodialysis can be undertaken for acute kidney injury. If plasma exchange is part of the treatment (e.g. in vasculitis), haemodialysis is used. If there is cardiac decompensation or hypercatabolism, continuous arteriovenous or venovenous haemofiltration provides gentle, continuous dialysis and fluid removal. Acute kidney injury in childhood generally carries a good prognosis for renal recovery unless complicating a life-threatening condition, e.g. severe

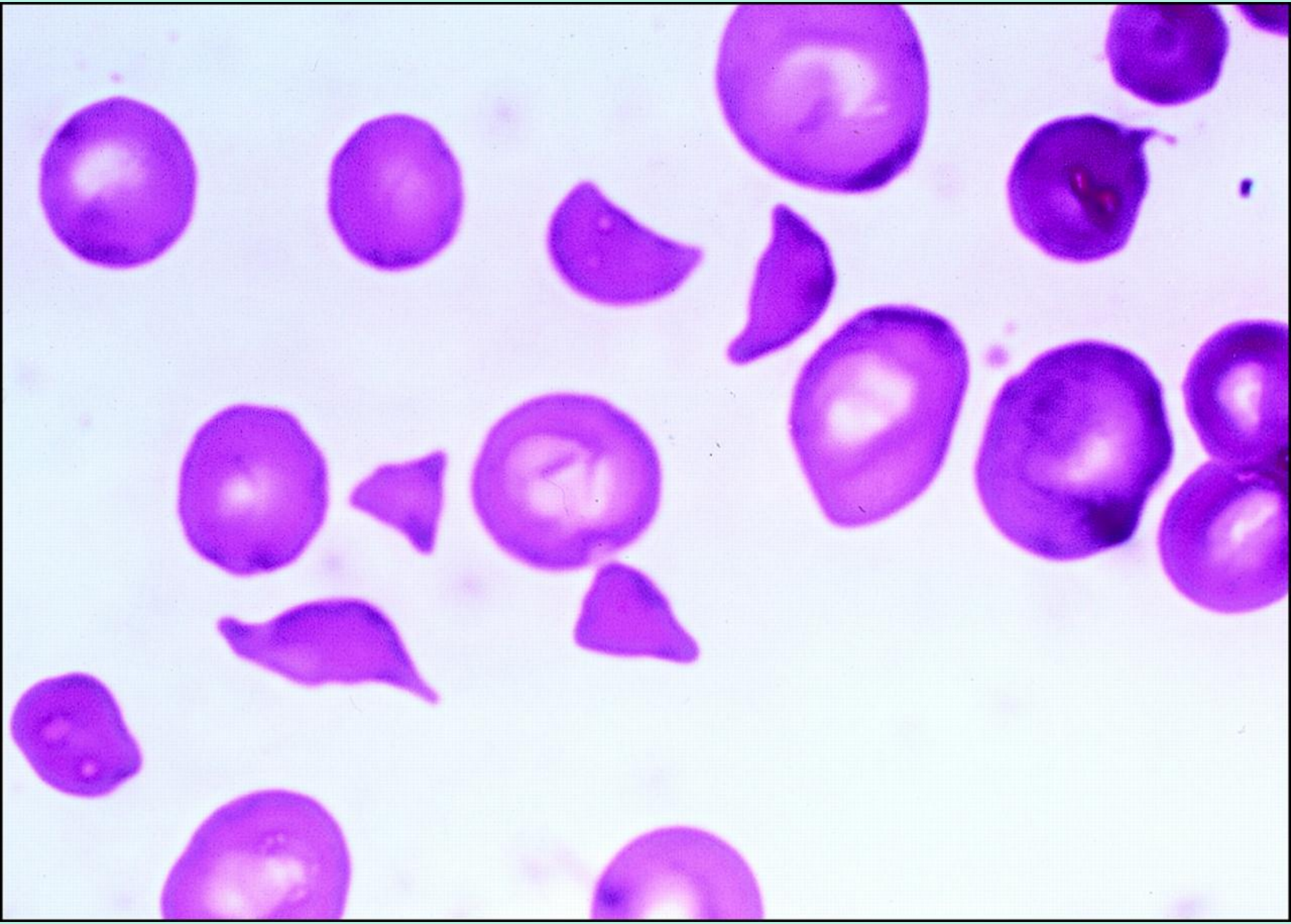
Summary

Acute kidney injury

- Prerenal: most common cause in children, from hypovolaemia and circulatory failure.
- Renal: most often haemolytic uraemic syndrome or multisystem failure.
- Postrenal: from urinary obstruction.
- Management: treat underlying cause, metabolic abnormalities, dialysis if necessary.

Haemolytic uraemic syndrome

HUS is a triad of acute renal failure, microangiopathic haemolytic anaemia, and thrombocytopenia. Typical HUS is secondary to gastrointestinal infection with verocytotoxin-producing *E. coli* O157:H7, acquired through contact with farm animals or eating uncooked beef, or, less often, *Shigella*. It follows a prodrome of bloody diarrhoea. The toxin from these organisms enters the gastrointestinal mucosa and preferentially localizes to the endothelial cells of the kidney where it causes intravascular thrombogenesis. Coagulation cascade is activated and clotting is normal (unlike in disseminated intravascular coagulation). Platelets are consumed in this process and microangiopathic haemolytic anaemia results from damage to red blood cells as they circulate through the microcirculation



With early supportive therapy, including dialysis, the typical diarrhoea-associated HUS usually has a good prognosis, although long-term follow-up is necessary as there may be persistent proteinuria and the development
of hypertension and progressive chronic kidney disease in subsequent years.

By contrast, atypical HUS
has no diarrhoeal prodrome, may be familial, and frequently relapses. It has a high risk of hypertension and progressive chronic kidney disease with a high mortality. A new treatment, the monoclonal anti-terminal complement antibody eculizumab, has greatly improved the prognosis of this condition although it is very expensive, and therefore plasma exchange is still used in many cases, especially in cerebral atypical HUS.

Table 19.5 Some metabolic abnormalities in acute renal failure and their therapy

Metabolic abnormality	Treatment
Metabolic acidosis	Sodium bicarbonate
Hyperphosphataemia	Calcium carbonate
	Dietary restriction
Hyperkalaemia	Calcium gluconate if ECG changes
	Salbutamol (nebulized or intravenous)
	Calcium exchange resin
	Glucose and insulin
	Dietary restriction
	Dialysis

- Haemolytic uraemic syndrome – the triad of:
  - acute kidney injury
  - haemolytic anaemia
  - thrombocytopenia

Chronic kidney disease

Chronic kidney disease is progressive loss of renal function due to numerous conditions and has five stages as shown in Table 19.6. Stage 5 chronic kidney disease, with GFR less than 15 ml/min per 1.73 m2, is much less common in children than in adults, with an incidence of only 10 per million of the child population each year. Congenital and familial causes are more common in childhood than are acquired diseases (Table 19.7).

Clinical features

Stage 4 and stage 5 chronic kidney disease presents with:

- anorexia and lethargy
- polydipsia and polyuria
- faltering growth/growth failure
- bony deformities from renal osteodystrophy (renal rickets)
- hypertension
- acute-on-chronic renal failure (precipitated by infection or dehydration)
- incidental finding of proteinuria
- unexplained normochromic, normocytic anaemia.

Many children with chronic kidney disease have had their renal disease detected before birth by antenatal ultrasound or have previously identified renal disease. Symptoms rarely develop before renal function falls to less than one-third of normal or chronic kidney disease stage 4.

Management

The aims of management are to prevent the symptoms and metabolic abnormalities of chronic kidney disease, to allow normal growth and development, and to preserve residual renal function. The management of these children should be conducted in a specialist paediatric nephrology centre.

Diet

Anorexia and vomiting are common. Improving nutrition using calorie supplements and nasogastric or gastrostomy feeding is often necessary to optimize growth. Protein intake should be sufficient to maintain growth and a normal albumin, whilst preventing the accumulation of toxic metabolic by-products.

Prevention of renal osteodystrophy

Phosphate retention and hypocalcaemia due to decreased activation of vitamin D lead to secondary hyperparathyroidism, which results in osteitis fibrosa and osteomalacia of the bones. Phosphate restriction by decreasing the dietary intake of milk products, calcium carbonate as a phosphate binder, and activated vitamin D supplements help to prevent renal osteodystrophy.

Control of salt and water balance and acidosis

Many children with chronic kidney disease caused by congenital structural malformations and renal dysplasia have an obligatory loss of salt and water. They need salt supplements and free access to water. Treatment with bicarbonate supplements is necessary to prevent acidosis.

Anaemia

Reduced production of erythropoietin and circulation of metabolites that are toxic to the bone marrow result in anaemia. This responds well to the administration of recombinant human erythropoietin which is administered subcutaneously.

Hormonal abnormalities

Many hormonal abnormalities occur in progressive chronic kidney disease. Most importantly, there is growth hormone resistance with high growth hormone levels but poor growth. Recombinant human growth hormone has been shown to be effective in improving growth for up to 5 years of treatment, but whether it improves final height remains unknown. Many children with stage 4 and stage 5 chronic kidney disease have delayed puberty and a subnormal pubertal growth spurt.

Dialysis and transplantation

It is now possible for all children to enter renal replacement therapy programmes when stage 5 chronic kidney disease is reached. The optimum management is by renal transplantation (Case History 19.4).

Table 19.6 Grading of severity of chronic kidney disease

Stage	Estimated glomerular filtration rate	Description
1	>90 ml/min per 1.73 m^2	Normal renal function but structural abnormality or persistent haematuria or proteinuria
2	60–89 ml/min per 1.73 m^2	Mildly reduced function, asymptomatic
3	30–59 ml/min per 1.73 m^2	Moderately reduced renal function, renal osteodystrophy
4	15–29 ml/min per 1.73 m^2	Severely reduced renal function with metabolic derangements and anaemia. Need to make plans for renal replacement therapy
5	<15 ml/min per 1.73 m^2	End stage renal failure, renal replacement therapy required

Table 19.7 Causes of chronic kidney disease

Cause	%
Renal dysplasia ± reflux	34
Obstructive uropathy	18
Glomerular disease	10
Congenital nephrotic syndrome	10
Tubulointerstitial diseases	7
Renovascular disease	5
Polycystic kidney disease	4
Metabolic	4

Data from UK Renal Registry 2014.

Technically, this is difficult in very small children and a minimum weight, e.g. 10 kg, needs to be reached before transplantation to avoid renal vein thrombosis. Kidneys obtained from living related donors have a higher success rate than deceased donor kidneys, which are matched as far as possible to the recipient's HLA (human leukocyte antigen) type. Patient survival is high and first-year graft survival is around 95% for living related and 96% for deceased kidneys in the UK. Graft losses from both acute and chronic rejection or recurrent disease mean that the 5-year graft survival is reduced to 94% for living related kidneys and 84% for deceased donor kidney transplants and some children need retransplantation. Current

Ideally, a child is transplanted before dialysis is required, but if this is not possible, a period of dialysis may be necessary. Peritoneal dialysis, either by cycling overnight using a machine (continuous cycling peritoneal dialysis) or by manual exchanges over 24 hours (continuous ambulatory peritoneal dialysis), can be done by the parents at home and is therefore less disruptive to family life and the child’s schooling. Haemodialysis is an alternative and is usually done in hospital three to four times a week.

Case history 19.4

Renal transplantation

Caden was born with a severe form of posterior urethral valves and had chronic kidney disease from birth (see Fig. 19.11a, b). He was managed for the first 3 years with intensive nutritional input. He underwent treatment for UTIs and received medications including salt supplements and erythropoietin. He needed to have his bladder augmented and went on to dialysis briefly (Fig. 19.22) before he had a live related transplant from his father at the age of 4 years. He is now growing and developing well although he continues to need immunosuppressants
and occasionally suffers from UTIs.

Figure 19.22 Caden enjoying treats whilst on dialysis. Children with chronic kidney disease have a diet restricted in potassium and phosphate, which means no chocolate, crisps, or pizza – unless on the dialysis machine!

Summary

Chronic kidney disease

- Causes: congenital (structural malformations and hereditary nephropathies) most common.
- Presentation: abnormal antenatal ultrasound, anorexia and lethargy, polydipsia and polyuria, faltering growth/growth failure, renal rickets (osteodystrophy), hypertension, proteinuria, anaemia.
- Management: diet and nasogastric or gastrostomy feeding, phosphate restriction and activated vitamin D to prevent renal osteodystrophy, salt supplements and free access to water to control salt and water balance, bicarbonate supplements to prevent acidosis, erythropoietin to prevent anaemia, growth hormone, and dialysis and transplantation.


Thank you!