Second Edition

NEUROLOGICAL SURGERY

Volume 2

A Comprehensive Reference Guide to the Diagnosis and Management of Neurosurgical Problems

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Pediatric Kidney Disease

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Volume II

Little, Brown and Company Boston

Published November 1978

First Edition

Library of Congress Catalog Card No. 78-61278

ISBN 0-316-21071-4

Printed in the United States of America

Notice

The indications and dosages of all drugs in this book have been recommended in the medical literature and conform to the practices of the general medical community. The medications described do not necessarily have specific approval by the Food and Drug Administration for use in the diseases and dosages for which they are recommended. The package insert for each drug should be consulted for use and dosage as approved by the FDA. Because standards for usage change, it is advisable to keep abreast of revised recommendations, particularly those concerning new drugs.

Contents

Volume II

II. Diseases of the Kidney

38. Diseases of the Kidney in the Newborn

Adrian Spitzer

It is characteristic of the seriously ill newborn to have nonspecific signs of illness such as fever, irritability, poor feeding, and failure to thrive. In these infants, disease of the kidneys and urinary tract must be considered in the differential diagnosis. Certain signs point directly toward urinary tract disease, and these are discussed in the following sections.

Disorders of Micturition

Within the first 24 hr after birth 92 percent of healthy infants pass urine, and 99 percent have done so by 48 hr [16, 20]. Often, however, the first micturition takes place in the delivery room and passes unnoticed. In the rare instance in which the newborn does not urinate within 72 hrs, serious consideration should be given to the possibility of bilateral renal agenesis, urinary tract obstruction, or a renovascular accident. Of these possibilities, the most important to diagnose is obstructive uropathy, since it is amenable to surgical correction.

Abnormalities in the volume of urine passed by the newborn during each 24-hr period are practically impossible to assess unless special attention is directed to the urinary system. The frequency of micturition varies from two to six times during the first and second days of life and from five to twenty-five times per 24 hr subsequently. The daily urinary volume is 30 to 60 ml during the first and second day, 100 to 300 ml during the following week, and between 200 and 400 for the rest of the first month.

Oliguria (urinary output below 15 to 20 ml/kg/24 hr) most often is a consequence of dehydration. Oliguria or anuria can also result from malformation, renovascular accident, or urinary tract obstruction. Oliguria of prerenal origin, as in association with diarrheal disease, maternal diabetes, or respiratory distress syndrome, usually can be identified by the high solute content of the urine, whereas in the oliguria of true renal insufficiency, urinary osmolality is low. Urinary retention can mimic anuria of renal origin. This retention can result from neurologic abnormalities, such as meningitis or disturbances in the innervation of the bladder (e.g., meningomyelocele), or from obstruction secondary to phimosis, posterior urethral valves, balanoposthitis, or vulvovaginitis. Palpation of the urinary bladder, which is easy to perform during the newborn period, and, if necessary, bladder catheterization establish the diagnosis.

Polyuria is most often the result of a defect in concentrating capacity, secondary to medullary abnormalities in renal dysplasia, to renal hypoplasia, or to nephronophthisis or medullary cystic disease. It is seen also in association with lack of antidiuretic hormone or with nephrogenic diabetes insipidus (Chap. 82).

Proteinuria

It is generally accepted that small amounts of protein ordinarily pass through the semipermeable glomerular basement membrane. De Luna and Hullet [4] reported a mean urinary excretion of 45 mg per day in newborns. However, we rarely find more than trace proteinuria in random urines from newborn infants. When protein is present in higher amounts, proteinuria suggests glomerular disease such as congenital nephrotic syndrome (Chap. 54) or glomerulonephritis (Chap. 43).

Hematuria

In the normal newborn, the excretion of erythrocytes in urine does not exceed 100 per minute or 75,000 per 12 hr. Reddish urine usually indicates hematuria [6], but it may also be caused by the presence of bile pigments, porphyrins, urate, or hemoglobin [1]. The differential diagnosis between hemoglobinuria and hematuria is easy to make if the urine is examined soon after collection. With standing, erythrocytes may hemolyze, especially in hypotonic urine, and no longer appear as formed elements. Hematuria in the newborn may result from a renovascular accident, cortical and medullary necrosis [2], neoplasia, obstructive uropathy, infection, nephritis, or coagulopathy.

Pyuria

The dividing line between a normal and an abnormal number of white blood cells in the urine is uncertain. We do not expect to find more than two to three leukocytes per high-power field in a cen-

trifuged specimen of urine [9, 12]. Bag specimens of well-mixed, uncentrifuged urine obtained from 600 newborns on the sixth or seventh day of life contained five or fewer leukocytes per cubic millimeter in 98 percent of boys but in only 56 percent of girls. The percentage in girls increased to 94 when a clean-catch technique was used, suggesting perineal contamination of the bag specimens [13]. The most common cause of pyuria is urinary tract infection (Chap. 92). Increased rates of excretion of white blood cells also can accompany nephritis and nephrosis and can be indicative of any type of inflammatory process within the urinary tract, including those associated with drug reactions.

Edema

At an early stage, the retention of fluid can be detected only by repeated, accurate measurements of weight. Later, swelling becomes obvious. It is generally stated that the edema of renal disease involves primarily the face and is soft, whitish, and painless. None of these characteristics, however, is specific.

Edema is occasionally found in prematurely born infants during the first few days of life [7] and has been shown to be the result of shifts of fluid between body water compartments [14]. So-called late edema develops among some newborns with a birth weight below 1,300 gm and a short gestational age. The accumulation of fluid seems to correspond to the thirty-fifth to thirty-sixth week of gestational age. No other gross abnormalities are found in these babies, and the edema usually is transitory. Studies performed in infants with late edema and in healthy control subjects have not detected significant differences in external water and electrolyte balance. A difference was observed, however, in the distribution of fluids between various body compartments, with the extracellular compartment being larger than normal in the edematous babies [21]. The cause of this condition remains obscure, although some of these cases have been shown to be associated with vitamin E deficiency and anemia.

There are many extrarenal causes of edema in the newborn, such as primary lymphedema (Milroy's disease), congenital lymphedema with gonadal dysgenesis, the syndrome of inappropriate antidiuretic hormone secretion, hyperaldosteronism, congenital analbuminemia, severe protein deficiency, protein-losing gastroenteropathy, scleredema, syphilis, erythroblastosis fetalis, and hereditary angioneurotic edema. The differential diagnosis also should include maternal diabetes.

Ascites can occur in the congenital nephrotic syndrome, in which case the fluid has the character of an exudate with a protein content that usually does not exceed 500 mg per deciliter. A more common cause of ascites in the newborn is obstruction of the lower urinary tract, particularly in association with posterior urethral valves. At least 50 cases have been described in the literature, although this is an unusual complication of urinary tract obstruction. The ascitic fluid apparently represents urine that has leaked through a ruptured pelvis or calyx. The differential diagnosis includes chylous ascites, ascites caused by syphilis, hepatobiliary obstruction, ruptured intraabdominal cyst, meconium peritonitis, and bile ascites.

Abdominal Masses

Examination of the abdomen by palpation usually can be performed easily during the first 48 hr of extrauterine life because of the laxity of the abdominal muscles. The kidneys of the newborn are in a lower position than they are later in life, the right kidney usually being lower than the left. Using a very meticulous method of deep abdominal palpation in 10,000 infants, Mussels et al. [17] suspected renal anomalies in 77; 55 of these were confirmed by intravenous pyelography. The most common anomaly was a horseshoe-shaped, or fused, kidney, which occurred in 16 infants. Other conditions accounting for an apparently large kidney are hydronephrosis, tumor, thrombosis of the renal vein, and cystic disease. The possibility of an adrenal hemorrhage also should be kept in mind. A smooth mass is more likely to be the result of hydronephrosis or renal vein thrombosis, whereas an irregular surface suggests malformation or cystic disease.

Infection of the Urinary Tract

Asymptomatic bacteriuria has been found in less than 1 percent of apparently healthy full-term infants with equal frequency in males and females [5, 8, 11]. By contrast, studies in premature infants have demonstrated bacteriuria, confirmed by suprapubic puncture, in 2 to 5 percent [5] (see also Chap. 92).

In the majority of neonates with urinary tract infection, urologic-radiologic examination reveals structurally normal kidneys and collecting systems. This finding is in striking contrast to that in infants diagnosed as having urinary tract infection during the remainder of the first year of life and in whom the incidence of urologic malformation has been reported to be as high as 50 to 80 percent. The low incidence of asymptomatic bacteriuria in healthy full-term infants suggests that routine screening in this age group is not a profit-

able undertaking. In contrast, the infant with any evidence of illness is likely to have an otherwise silent urinary tract infection; accordingly, he should be examined appropriately.

Neonates with pyelonephritis may show relatively little evidence of serious infection, or they may appear as toxic, septic, desperately ill infants. A peculiar syndrome consisting of pyelonephritis, hepatomegaly, hemolytic anemia, and jaundice (direct- and indirect-reacting bilirubin) has been described [19]. Other features include poor feeding, lethargy, irritability, occasional vomiting and diarrhea, and azotemia. Hemolysis may be severe enough to require transfusion. The pathogenesis of this syndrome is unknown. The organisms most commonly cultured are the low-numbered serotypes of *Escherichia coli* (especially 04:115). As in presumptive septicemia, treatment is urgent and cannot await the results of cultures. The response to antibiotic therapy usually is prompt, with a return of the blood urea to normal, resolution of hepatomegaly, clearing of jaundice, and cessation of hemolysis.

Renal Insufficiency and Renal Failure

Inadequacy of renal function may be a consequence of any of the developmental anomalies, may arise from prerenal factors such as dehydration and shock, or may be the result of acquired disease of the kidneys. The recognition and treatment of renal insufficiency is discussed here without consideration of the nature of the specific underlying cause.

DIAGNOSIS

In the majority of cases the history reveals nonspecific signs such as lethargy, poor appetite, vomiting, and convulsions. Oliguria, although often present, is easily missed until other findings direct the attention toward the urinary system. Urinary output less than 15 to 20 ml/kg/24 hr in the newborn (beyond the first few days of life) is indicative of oliguria. It is vital to determine whether the cause of oliguria or anuria is prerenal (i.e., caused by inadequacy of the blood supply to the kidney), postrenal (i.e., urine being formed but not voided, because of obstructive uropathy or a neurogenic bladder), or true renal failure (i.e., malfunction of the kidneys caused by intrinsic disease, whether congenital or acquired) (Table 38-1). This differentiation usually is simple. In some instances, extensive radiologic or urologic investigation may be required to demonstrate the cause of postrenal failure.

The adequacy of the circulation must be assessed to rule out prerenal failure. If insufficiency of the vascular volume is suspected, the response to administration of fluid may be helpful. For this purpose, isotonic saline in a dose of 15 to 20 ml per kilogram of body weight, or mannitol (0.5 to 1.0 gm per kilogram in a 20% solution) can be given IV. A prompt increase in urinary output suggests that additional fluids may be needed. If there is no response, care must be taken to avoid administration of excessive amounts of fluids in order to "force" a diuresis.

Table 38-1. Differentiation of Prerenal from True Renal Failure in Infancy

Measurement	Prerenal	True Renal
U_{Na}	<20 mEq/L	>70 mEq/L
U/P osmolality	>2	<1.1
U/P urea	>15	<5
U/P creatinine	>15	<5
Fractional excretion of sodium	<1.8%	>10%

CAUSES OF RENAL INSUFFICIENCY

Among 35 newborns with persistent renal insufficiency in one study, only 7 had normal kidneys [18]. The most common organic cause of renal failure in the newborn period is renal dysplasia, followed in frequency by urinary tract obstruction and cystic disease of the kidneys. Extrarenal causes are, in order of frequency, shock and dehydration, sepsis, and renal venous thrombosis. Perinatal anoxia [3] and respiratory distress syndrome [10] are additional causes of renal insufficiency.

TREATMENT

Treatment of renal insufficiency in the neonate is similar to treatment in the older child (see Chaps. 33, 34). Consideration must be given to maintenance of the balance of water, electrolytes, and hydrogen ions, and at the same time to provision of nutrition as near optimal as possible. Acute renal insufficiency is treated by providing a fluid intake equal to insensible water loss (25 to 40 ml/kg/24 hr) plus urinary output. In the anuric or severely oliguric patient, solute requiring urinary excretion is not given. In addition to withholding potassium, it may be necessary to reduce dangerously high plasma levels. When the concentration in plasma exceeds 6 mEq per liter, sodium or polystyrene sulfonate (Kayexalate) can be given (by enema or by mouth) in a starting dose of 0.5 to 1.5 gm per kilogram of body weight and is repeated as needed. Moderate or severe degrees of acidemia are treated by administration of sodium bicarbonate. Peritoneal dialysis may be indicated in the infant with total renal failure lasting more than 7 to 10 days or when severe

metabolic disturbances cannot be managed with medical treatment alone.

In infants with chronic renal insufficiency, special attention must be paid to provision of adequate nutrition. Mild to moderate degrees of renal insufficiency usually can be managed by utilizing humanized milk such as Similac PM 60-40 or SMA as the sole source of nutrition. The usual dose of supplemental vitamins should be given.

With lesser degrees of function, other specific therapy may be required. Normal levels of pH and bicarbonate in the blood should be maintained by administration of sodium bicarbonate. The dose is adjusted to the patient, starting with 1 to 2 mEq/kg/day and increased as needed. Concentrations of calcium and inorganic phosphate in the blood should be measured frequently. Hyperphosphatemia usually does not develop in young infants fed low-phosphate diets until they reach advanced stages of renal failure. In such cases, phosphate-binding gels (such as aluminum hydroxide gel [Amphojel]) can be administered, although they are usually poorly tolerated. A dose of 50 to 150 mg/kg/day given PO is customary. If the plasma calcium level falls significantly below normal, supplemental calcium (such as calcium gluconate [Neo-Calglucon]) is given in a daily dose of 10 to 20 mg (of elemental calcium) per kilogram of body weight.

If these measures are not successful in maintaining normal blood levels of calcium, pharmacologic doses of vitamin D should be prescribed, starting with a dosage of 10,000 units per day. Recently, dihydrotachysterol has gained wide acceptance. This is an analogue of vitamin D that is activated in the absence of the kidneys. The drug is given PO. Care must be taken to avoid too-vigorous therapy and induction of hypercalcemia. The serum calcium × phosphate product should not be allowed to exceed 70.

In infants with severe uremia, vomiting may be a most troublesome symptom. Treatment with one of the phenothiazine drugs may be helpful.

Hypertension in infants is treated as in older children (Chap. 32). Every effort should be made to maintain normal levels of blood pressure. Treatment is usually initiated with reserpine (0.01 to 0.02 mg/kg/day) or hydralazine hydrochloride (1 to 2 mg/kg/day in four divided doses), or both. If these drugs are not successful, guanethidine sulfate can be added (0.2 to 0.3 mg/kg/day as a single dose). Diazoxide (Hyperstat), 5 mg per kilogram IV, is used whenever a prompt decrease in diastolic pressure is required.

Infants who cannot be maintained in a satisfactory metabolic state by dietary and medical therapy alone are candidates for dialysis (Chap. 35). Peritoneal dialysis can be used for short periods but probably is inadvisable if prolonged treatment is anticipated [15]. Special peritoneal catheters with perforations that are not more than 3 to 4 cm from the tip are required. Prior to the insertion of the catheter, the bladder, which is an intraabdominal organ in the newborn, should be emptied, and the abdominal cavity should be distended by injection of 30 to 40 ml of dialysis fluid per kilogram of body weight. A similar amount is usually well tolerated for each cycle. Care should be taken to avoid interference with the respiratory mechanism, which, in the newborn, is more dependent on diaphragmatic movements than in older children. Special attention should be given to the prevention of dehydration or overloading, which requires continuous monitoring of the baby's weight or the use of an automatic cycling dialysis machine. To avoid the development of hypothermia, the solution should be heated to 37°C.

Hemodialysis is technically difficult in infants and should be reserved for patients in whom peritoneal dialysis cannot be performed.

PROGNOSIS

The mortality among newborns with renal failure is high, being around 50 percent in several relatively large series [3, 15, 18]. Most of these infants have severe congenital renal and extrarenal anomalies, although the immediate cause of death often is sepsis or shock. Death usually occurs within a few days after birth.

Renal transplantation has not improved the outcome of patients of this age with end-stage renal disease (Chap. 36). To our knowledge, none of the newborns so far given transplants has survived.

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