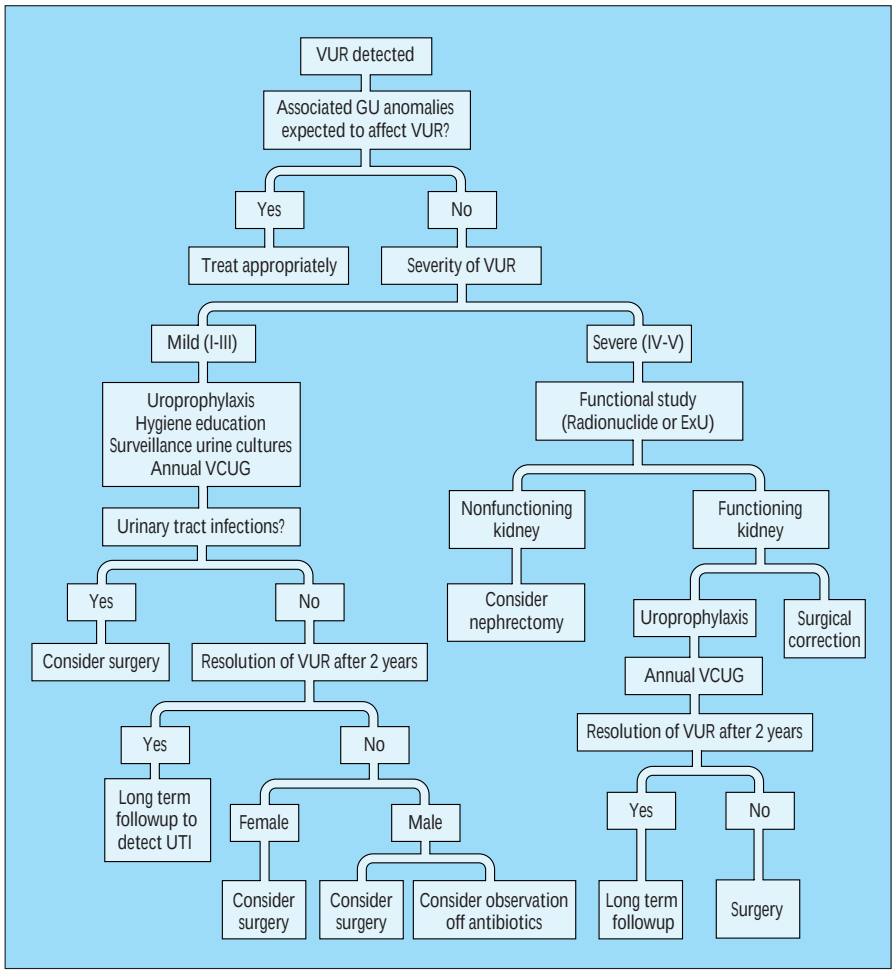

FIGURE 8-30

Proposed treatment of vesicoureteral reflux (VUR) in children. This algorithm provides an approach to evaluate and treat VUR in children. In VUR associated with other genitourinary anomalies, therapy for reflux should be part of a comprehensive treatment plan directed toward correcting the underlying urologic malformation. Children with mild VUR should be treated with prophylactic antibiotics, attention to perineal hygiene and regular bowel habits, surveillance urine cultures, and annual voiding cystourethrogram (VCUG). Children with recurrent urinary tract infection on this regimen should be considered for surgical correction. In children in whom VUR resolves spontaneously, a high index of suspicion for urinary tract infection should be maintained, and urine cultures should be obtained at times of febrile illness without ready clinical explanation.

In persons in whom mild VUR fails to resolve after 2 to 3 years of observation, consideration should be given to voiding pattern. A careful voiding history and an evaluation of urinary flow rate may reveal abnormalities in bladder function that impede resolution of reflux. Correction of dysfunctional voiding patterns may result in resolution of VUR. In the absence of dysfunctional voiding, it is controversial whether older women with persistent VUR are best served by surgical correction or close observation with uroprophylactic antibiotic therapy and surveillance urine cultures, especially during pregnancy. Males with persistent low-grade VUR may be candidates for close observation with surveillance urine cultures while not receiving antibiotic therapy, especially if they are over 4 years of age and circumcised. Circumcision lowers the incidence of urinary tract infection. In severe VUR the function of the affected kidney should be evaluated with a functional study (radionuclide renal scan). High-grade VUR in nonfunctioning kidneys is unlikely to resolve spontaneously, and nephrectomy may be indicated to decrease the risk of urinary tract infection and avoid the need for uroprophylactic antibiotic therapy. In patients with functioning kidneys who have high-grade VUR, the likelihood for resolution should be considered. Severe VUR, especially if bilateral, is unlikely to resolve spontaneously. Proceeding directly to repeat implantation may be indicated in some cases. Medical therapy with uroprophylactic antibiotics and serial VCUG may also be used, reserving surgical therapy for those in whom resolution fails to occur.

Complications of Reflux Nephropathy

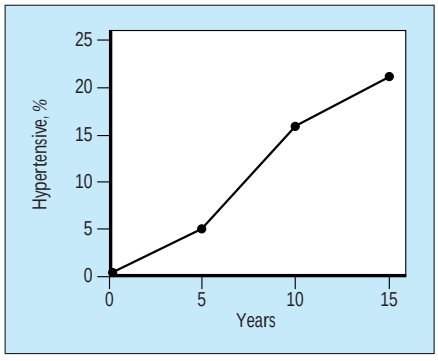

FIGURE 8-31

Development of hypertension in 55 normotensive subjects with reflux nephropathy at follow-up examinations over 15 years. The incidence of hypertension in persons with reflux nephropathy increases with age and appears to develop most commonly in young adults within 10 to 15 years of diagnosis. In a cohort of 55 normotensive persons with reflux nephropathy observed for 15 years, 5% became hypertensive after 5 years. This percentage increased to 16% at 10 years, and 21% at 15 years. The grading system for severity of scarring was different from the system adopted by the International Reflux Study Committee. Nevertheless, using this system, 78% of persons in the group could be classified as having reflux nephropathy severity scores between 1 and 4 [42].

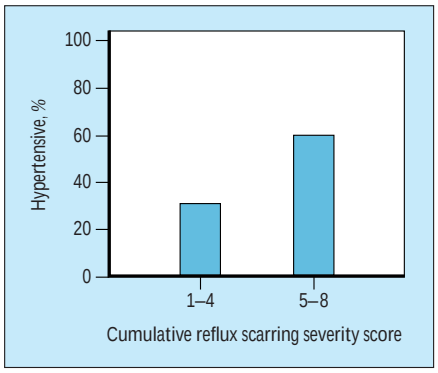

FIGURE 8-32

Frequency of hypertension versus severity of parenchymal scarring. The frequency of hypertension in persons with vesicoureteral reflux–related renal scars is higher than in the normal population. In adults with reflux nephropathy the incidence of hypertension can be correlated with the severity of renal scarring. Adding the individual grade of reflux (0–4) for the two kidneys results in a scale ranging from 0 (no scars) to 8 (severe bilateral scarring). Persons with cumulative scores of parenchymal scarring from 1 to 4 have a 30% incidence of hypertension, whereas 60% of those with scarring scores ranging from 5 to 8 have hypertension [42,43].

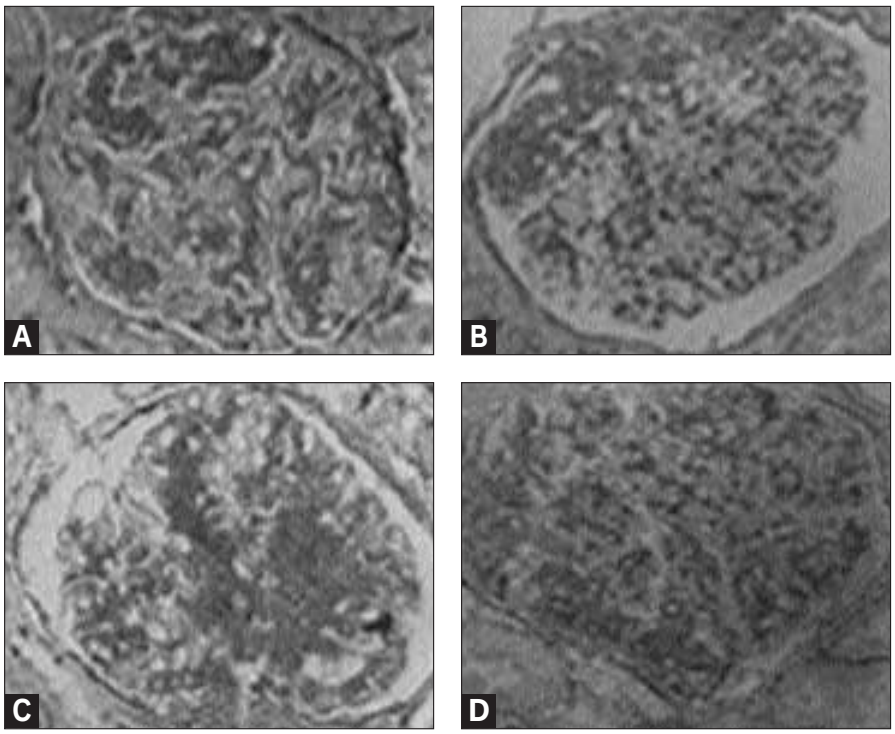

FIGURE 8-33

Glomerular hypertrophy and focal segmental glomerulosclerosis (FSGS) in severe reflux nephropathy. Reflux nephropathy resulting in reduced renal functional mass induces compensatory changes in glomerular and vascular hemodynamics. These changes initially maintain the glomerular filtration rate but are maladaptive over time. **A–D**, Compensatory hyperfiltration results in renal injury manifested histologically by glomerular hypertrophy and FSGS and clinically as persistent proteinuria [44]. In reflux nephropathy, proteinuria is a poor prognostic sign, indicating that renal injury has occurred. The severity of proteinuria is inversely proportional to functioning renal mass and the glomerular filtration rate and directly proportional to the degree of global glomerulosclerosis. Surgical correction of vesicoureteral reflux has not been found to prevent further deterioration of renal function after proteinuria has developed. Hyperfiltration resulting from decreased renal mass continues and produces progressive glomerulosclerosis and loss of renal function. Evidence exists that inhibition of the renin-angiotensin system through the use of angiotensin-converting enzyme inhibitors decreases the compensatory hemodynamic changes that produce hyperfiltration injury. Thus, these inhibitors may be effective in slowing the progress of renal failure in reflux nephropathy.

Pathogenesis of Obstructive Nephropathy

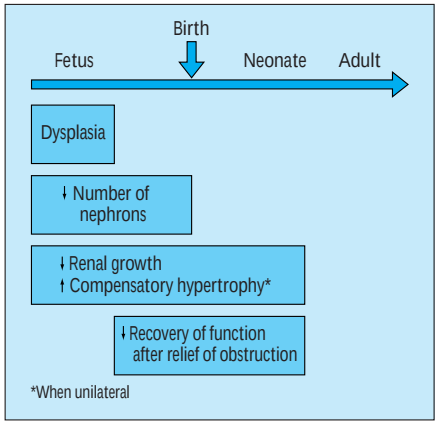

FIGURE 8-34

Consequences of urinary tract obstruction for the developing kidney in animals. The effects of urinary tract obstruction on the developing kidney depend on the time of onset, location, and degree of obstruction. Ureteral obstruction during early pregnancy results in disorganization of the renal parenchyma (dysplasia) and a reduction in the number of nephrons. Partial or complete ureteral obstruction in neonates causes vasoconstriction, glomerular hypoperfusion, impaired ipsilateral renal growth, and interstitial fibrosis. The degree of impairment of the ipsilateral kidney, in the case of partial unilateral ureteral obstruction, and of compensatory hypertrophy of the contralateral kidney, in the case of partial or complete unilateral ureteral obstruction, is inversely related to the age of the animal at the time of obstruction. The older the animal, the less the impairment of the ipsilateral kidney and the less the compensatory growth of the contralateral kidney. In addition, the recovery of renal function after relief of urinary tract obstruction also decreases with the age of the animal [45].

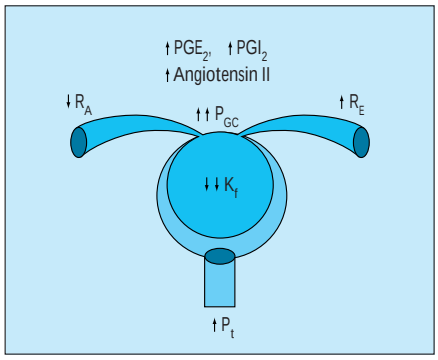

FIGURE 8-35

Renal hemodynamic response to mild partial ureteral obstruction. Renal blood flow and the glomerular filtration rate may not change in mild partial ureteral obstruction, despite a significant reduction in glomerular capillary ultrafiltration coefficient (Kf). This is due to the increase in glomerular capillary hydraulic pressure (P_{GC}) caused by a prostaglandin E2–induced reduction of afferent arteriolar resistance (R_A) and an angiotensin II–induced elevation of efferent arteriolar resistance (R_E). It is likely that other vasoactive factors, such as thromboxane A2, also play a role, particularly in more severe ureteral obstruction accompanied by reductions in renal blood flow and glomerular filtration rate [46]. PGE2—prostaglandin E2; PGI2—prostaglandin I2; Pt—tubule hydrostatic pressure.

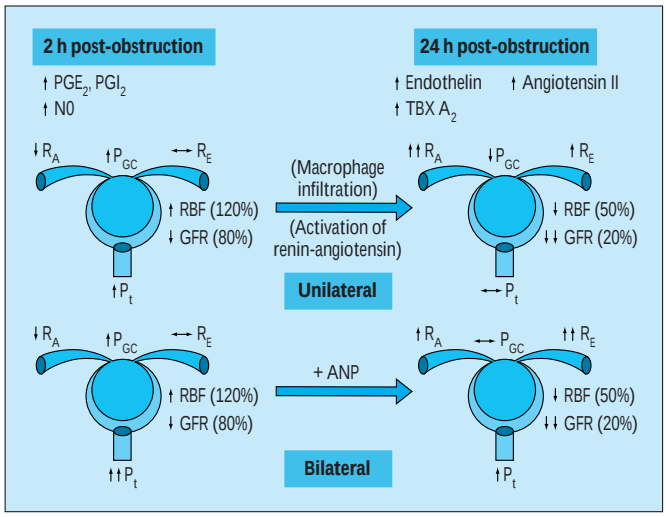

FIGURE 8-36

Acute renal hemodynamic response to unilateral or bilateral complete ureteral obstruction. In the first 2 hours after unilateral complete ureteral obstruction, there is a reduction in preglomerular vascular resistance and an increase in renal blood flow mediated by increased production of prostaglandin E2 (PGE2), prostacyclin, and nitric oxide (NO). The increase in renal blood flow (RBF) and glomerular capillary pressure maintain the glomerular filtration rate (GFR) at approximately 80% of normal, despite an increase in intratubular pressure. As the ureteral obstruction persists, activation of the renin-angiotensin system and increased production of thromboxane A2 (TBXA2) and endothelin result in progressive vasoconstriction, with reductions in renal blood flow and glomerular capillary pressure. The glomerular filtration rate decreases to approximately 20% of baseline, despite normalization of the intratubular pressures. The hemodynamic changes in the early phase (0–2 h) of bilateral ureteral obstruction are similar to those observed after unilateral obstruction. As bilateral obstruction persists, however, there is an accumulation of atrial natriuretic peptide (ANP) that does not occur after unilateral obstruction. The increased ANP levels attenuate the afferent and enhance the efferent vasoconstrictions, with maintenance of normal glomerular capillary and elevated tubular pressures. Despite these differences in hemodynamic changes between unilateral and bilateral ureteral obstruction, the reductions in renal blood flow and glomerular filtration rate 24 hours after obstruction are similar [47–49]. P_{GC}—glomerular capillary hydraulic pressure; PGI2—prostaglandin I2; Pt—tubule hydrostatic pressure; R_A—afferent arteriolar resistance; R_E—efferent arteriolar resistance.