21.1 Introduction

Many children who suffer from congenital, hereditary, or severe acquired renal disease, basically or caused by injury, have a substantially diminished number of functioning nephrons. Loss of nephrons cannot be replaced by new units, and recovery is impossible. Consequently, according to the patient’s age, different diseases enter a common pathway of progressive renal dysfunction called chronic renal failure (CRF). Further deterioration is associated with clinical symptoms and loss of metabolic control. End-stage renal disease (ESRD) is reached when survival is possible with only renal replacement therapy. Aside from all medical and psychosocial care during CRF and ESRD, renal transplantation is the ultimate goal to optimize rehabilitation and lifestyle. This chapter is devoted to these children who need lifelong multidisciplinary care and treatment, including pediatric radiology.

21.2 Definitions

Loss of one kidney during life or being born with a single kidney may cause slight renal dysfunction but, in general, does not lead to CRF even in late adulthood (Wikstad et al. 1988). CRF can be defined as a disease state with the loss of more than 50% of nephrons, persistently increased serum creatinine above +2 SD of the age-adjusted mean, and a decreased glomerular filtration rate (GFR). It is important to note that serum creatinine must be adjusted for age as, for example, a value of 1.0 mg/dl (88 μmol/l) is normal for an adolescent, but means CRF for an infant. CRF implicates a relentless pro-
gression to ESRD without the possibility of cure. In the early stages, it is a silent disease mostly defined by biochemical values. When GFR is reduced to 25% of normal and correspondingly the number of functioning nephrons to 12% of normal, clinical symptoms of uremia appear and dominate in ESRD. To improve the detection and the treatment of children with renal disorders the term chronic kidney disease (CKD) was established (Hogg et al. 2003). Patients suffer from CKD if kidney damage—with or without a reduced GFR—is present for at least 3 months, characterized by abnormalities in the composition of the blood or urine, abnormalities on imaging tests, or lesions on renal biopsy. CKD is classified into five stages with stage 1 having a normal GFR and stage 5 meaning the need for renal replacement therapy.

21.3 Incidence

The development of registries for dialysis and transplantation has made it possible to calculate the incidence of ESRD. These data may underestimate the true incidence as probably not all children with ESRD are offered therapy. There are few epidemiological data concerning CRF. In addition, studies are not always comparable as different populations and cut-off levels for age are used. Nevertheless, the incidence of ESRD is approximately one to three children aged 0–18 years per million total population and year (Wassner and Baum 1999). The incidence seems to be similar in Europe and Northern America.

The largest survey on chronic renal insufficiency (CRI) with 4,666 patients shows that 33% of patients were 6–12 years of age and 19% less than 2 years of age (Seikaly et al. 2003). Obstructive uropathy was the most common diagnosis (23%), and 18% suffered from renal aplasia, dysplasia, or hypoplasia. Reflux nephropathy (9%), focal segmental glomerulosclerosis (8%), and polycystic kidney disease (4%) were the next most frequent diagnoses. In general, nearly two-thirds of patients had a structural anomaly. A previous study had shown that 41% had already had urological surgery. Urinary tract malformations and hypoplasia dominated even more in patients aged less than 2 years, accounting for 67% of cases (Fivush et al. 1998). The largest study from Europe showed similar results with somewhat different groups of diagnoses (Ardisson et al. 2003). Renal hypoplasia with or without urological malformations accounted for 58% of cases. Hypoplasia with VUR was the most frequent single cause of childhood CRF responsible for 25.8% of cases. Almost 70% of patients with CRF reached ESRD by 20 years of age with an increasing number of patients with glomerular disorders and a decreasing number of children with hypoplasia as primary diagnosis. Age and GFR at presentation, the primary disease, and factors like anemia or hypoalbuminemia influence the progression to ESRD (Seikaly et al. 2003). Data for patients on dialysis or after renal transplantation are similar. Obstructive uropathy is less frequent and focal glomerulosclerosis more frequent (Warady et al. 1997; Neu et al. 2002).

21.4 Pathophysiology

Whatever the underlying disease (e.g., structural anomaly, glomerulopathy, hereditary nephropathy), there is a remarkably similar histological appearance of kidneys with progressive disease, suggesting a common final pathway. Glomerulosclerosis and tubulointerstitial fibrosis are the dominant features (El Nahas and Bello 2005). Various changes seem to perpetuate a vicious cycle with permanent loss of nephrons and ESRD as the endpoint. Extensive nephron loss leads to glomerular hypertrophy (increase in cell size and number). Hyperperfusion and hyperfiltration are the consequence, and glomerular hypertension correlates best with glomerulosclerosis (Fogo and Kon 1999). There is a central role of renal hemodynamics and the renin-angiotensin system. Yet other factors such as increased glomerular metabolism, mesangial macromolecular deposition, local hypercoagulopathy, and hyperlipidemia are of importance. They influence glomerular growth promoters. These promoters (e.g., growth hormone, transforming growth factor-β, insulin-like growth factor-I, angiotensin II, endothelin) can induce glomerular hypertrophy and mesangial matrix accumulation with glomerular sclerosis as a result. There is a remarkable diversity in morphologic appearance concerning sclerosis and disease progression. Young age at onset and