Progressive nephron loss that occurs during the course of chronic renal failure (CRF) induces significant changes in the function of surviving nephrons, which appears to be geared to preserving fluid and electrolyte homeostasis. The adaptive functional changes in surviving nephrons show predictable patterns, regardless of the underlying renal disease. Exceptions to these patterns may occur when any component of the system responsible for the adaptation has been specifically damaged. In this chapter we will briefly describe how the chronically failing kidney copes with the demand for sodium (Na\(^+\)), potassium (K\(^+\)) and hydrogen ion (H\(^+\)) homeostasis.

**SODIUM**

During the course of chronic renal failure, patients generally retain their ability to maintain Na balance until GFR falls to a few percent of normal. In contrast to healthy persons, who excrete only 0.5–1\% of their filtered Na on a normal intake, patients with CFR excrete from 1\% to over 30\% of their filtered Na. Within these limits, Na fractional excretion (NaFe) will change in such a way as to match its intake.

Even though Na homeostasis appears qualitatively normal within the limits of renal adaptation, the rate at which Na excretion matches intake is much slower than normal. Only when weaning from salt is accomplished over a period of weeks or months can the appropriate renal response to the low intake be shown to occur. If, instead, Na intake is abruptly curtailed, patients con-
tinue to excrete salt at an inappropriate rate, leading to a further decline on GFR, a drop in arterial blood pressure, and the full-blown clinical picture of extracellular dehydration [1, 2].

Conversely, when salt intake is abruptly increased, the response in Na excretion is sluggish, leading to expansion of extracellular volume,—inappropriately partitioned towards the intravascular compartment [3],—increase in blood pressure, and a full-blown picture of sodium-water retention. Not all patients with severe CRF failure show adaptation to nephron loss. In some of them, the underlying renal disease may cause a tendency to either Na retention through persisting loss of large amounts of albumin into the urine (nephrotic syndrome) or to obligatory Na loss by a prominent effect on tubular transport of sodium (salt-wasting nephropathy).

**Regulation of Na excretion in CRF**

Changes in Na intake are reflected in variations of extracellular fluid volume that however small and even unmeasurable by currently available methods, appear to be the primary signal for eliciting the appropriate response in Na excretion. Not only changes in volume, but even the redistribution of a normal extracellular volume, as it occurs with upright posture or water neck immersion, lead to changes in Na excretion. How these changes are sensed and converted into the appropriate regulation of Na excretion is still incompletely understood. Theoretically, the marked increase in fractional Na excretion observed in patients with CRF could result either from an exaggerated volume signal or an abnormal response of the diseased kidney. Evidence for an exaggerated volume signal has been sought either directly, by measuring fluid spaces, or indirectly, by determining the levels of the putative humoral correlates of volume changes.

**Exaggerated volume signal**

Direct determinations of both extracellular and blood volumes indicate that these volumes are increased in uremia, but results have varied greatly from one study to another, probably due to shortcomings inherent in the methods of measurement, changes in nutritional status of patient populations, and so forth [4]; hence the conclusions should be regarded with great caution.

It appears plausible that in the face of a sluggish renal response, any salt load should cause an expansion of extracellular fluid (or of any of its compartments) of greater degree or longer duration than in healthy persons. This amplified signal should be reflected in the levels of the putative mediators of renal response.

Mediators responding to changes in extracellular volume are aldosterone, renin, ADH, catecholamines, still poorly defined natriuretic factors, and the atrial natriuretic factor (ANF).

Levels of aldosterone, renin, and ADH are tendentially increased in uremics, even in the presence of an expanded extracellular space; these hormones, how-