CHAPTER 8

Summary, conclusions and a look toward the future

8.1 Summary

The subject of this thesis is the relation between hypertension and the excessively mobile kidney (nephroptosis). In the past a variety of complaints and symptoms, apart from hypertension, have been attributed to nephroptosis. However, the varying effect of numerous surgical fixations of the mobile kidney to relieve these conditions has led to some scepticism toward the pathogenetic role of nephroptosis. Apparently the degree of renal mobility is a poor indicator of the alleged effects of nephroptosis and therefore it was supposed to occur with or without symptoms or complaints.

As a result of this 'history of nephroptosis', described in chapter 1, further research on this phenomenon and its significance for the development of hypertension had become neglected. This is remarkable realizing that the condition is found rather frequently (20%) in the general female population. The high prevalence of both nephroptosis and 'essential' hypertension should be a compelling reason to investigate the causal relation between the two phenomena.

The results of our study on the frequency of nephroptosis in a normotensive and essential hypertensive population have indeed confirmed the existence of such a relation (chapter 2). Nephroptosis appeared to be present in 75 per cent of hypertensive females and in 20 per cent of a normotensive female control group.

Two possible mechanisms are thought to underlie the causal relation between nephroptosis and high blood pressure. The first is a direct relation, i.e. a narrowing of the artery of a mobile kidney through traction on its vascular pedicle in the upright position. This might cause a rise in blood pressure analogous to a 'Goldblatt hypertension'. The second mechanism may be an indirect relation, viz. nephroptosis causing a specific renal artery
stenosis (fibromuscular dysplasia) in the long run through an intermittent stretching of its artery. The high renal mobility observed in patients with FMD-affected kidneys supports the hypothesis of such an indirect relation (chapter 2).

Further investigations on a direct relation are described in chapters 3 and 4. The renal plasma flow (ERPF) in upright position appeared to be more reduced in nephroptotic patients than in subjects with a less mobile kidney. Moreover, a positive correlation was found between the degree of renal mobility and the degree of orthostatic ERPF-decrease. Computerized quantification of the artery diameter of kidneys with different degrees of renal mobility confirmed the earlier observation: the mobile kidney indeed caused an orthostatic diameter decrease of its artery. A positive correlation was found between the degree of artery narrowing and the degree of renal mobility. The 'length' of the renal artery however, had to be taken into account: a curved longer artery allows the kidney more movement without a reduction in the diameter than a shorter one. The effect of this artery narrowing was further confirmed by the observation that upright renin release (PRA) increased significantly more in nephroptotic patients.

The feasibility of relatively simple diagnostic tests to screen for 'nephroptotic hypertension' is discussed in chapter 5. Serial IVU and radionuclide renography, generally used for the detection of a renal artery stenosis, appeared to be adequate in patients having excessively mobile kidneys. The use of these methods however, is probably limited to cases with severe artery narrowing since the adaptive mechanisms of the kidney, maintaining a constant filtration pressure, seem to obscure the effects of a milder stenosis. Consequently, a study was performed to improve the benefits of these diagnostic procedures by interfering with the adaptive mechanisms of the post-stenotic kidney. Oral administration of a prostaglandin-synthesis inhibitor (indomethacin) prior to renography improved the detection sensitivity for a renal artery stenosis. However, a continuous monitoring of the blood flow in a ptotic kidney during posture changes would be preferable to the conventional methods. With such a method it would be also possible to monitor the adaptive mechanism of a kidney in response to a narrowing of its artery.

In theory, the $^{81}$Rb/$^{81m}$Kr ratio method would meet these exacting demands. The development of this novel technique through animal experiments and the final evaluation in a number of human studies is described in chapters 6 and 7. The method answered the theoretical expectations since it is feasible during at least tracer. The results of unilateral renal artery stenosis may render such a screening method preferable to use other methods already have an advantage.

8.2 Conclusions

The results of the existence and elucidation of nephroptotic hypertension. Apparent or nephroptotic hypertension is not only caused by the arterial stenosis but also by the artery mobility. A mobile kidney on its blood flow during upright posture appears drastically reduced contralateral, non-potent kidney to the fall in renal plasma flow. Continuous monitoring of the blood flow in a ptotic kidney during posture changes would be preferable to the conventional methods. With such a method it would be also possible to monitor the adaptive mechanism of a kidney in response to a narrowing of its artery.

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expected since the monitoring of renal blood flow changes appeared feasible during at least half an hour after an intravenous injection of the $^{81}$Rb tracer. The results of the $^{81}$Rb/$^{81m}$Kr ratio method in a patient with a unilateral renal artery stenosis and nephroptosis demonstrated the distinct advantages of this method over conventional methods of renal blood flow measurement. In addition, we could visualize the possible effects of a mobile kidney on its blood supply: the blood flow of the stenotic and ptotic kidney appeared drastically reduced in upright position, in contrast to the contralateral, non-ptotic kidney. Moreover, an adaptation of the involved kidney to the fall in filtration pressure could be observed in this unique experiment.

8.2 Conclusions

The results of the studies presented in this thesis have demonstrated the existence and elucidated the possible mechanisms of nephroptotic hypertension. Apparently the causal relation between nephroptosis and hypertension is not exclusively determined by the degree of renal mobility, but also by the artery 'length' of the mobile kidney. The latter can only be assessed with renal angiography, which should then be complemented with an upright angiogram in order to determine the orthostatic effect of the mobile kidney on its artery diameter. This procedure however, is invasive and hence some pre-screening examination will be mandatory. Serial IVU and radionuclide renography performed both in supine and upright position are the preferable methods, particularly after administration of a prostaglandin-synthesis inhibitor like indomethacin. The rather high prevalence of nephroptosis in female patients with essential hypertension may render such a screening worthwhile. On the other hand it might be preferable to use other techniques for this screening, since both mentioned methods already have shown to be of limited use for the detection of a renal artery stenosis. Probably the $^{81}$Rb/$^{81m}$Kr ratio method with its continuous and non-invasive character, will be the method of choice to detect a nephroptotic hypertension in the future.