Urol Res (1985) 13:85–89

Urological Research

Construction and Experimental Application of a Catheter for Selective Arterial Kidney Perfusion in Situ

G. Kehrer[1], M. Kallerhoff[1], R. Probst[1], W. Siekmann[1], M. Blech[2], H. J. Bretschneider[1] and U. Helmchen[3]

1 Zentrum Physiologie und Pathophysiologie der Universität Göttingen
2 Zentrum Chirurgie I, Abt. Urologie, der Universität Göttingen
3 Zentrum Pathologie der Universität Göttingen, Göttingen, FRG

Accepted: September 25, 1984

Summary. In order to improve dog kidney perfusion in situ with a protective solution, a perfusion catheter was constructed which allowed continuous pressure measurement in the center of the catheter tip during perfusion. Using this catheter, the equilibration of the extracellular space with a protective solution (HTK solution) was found to be pressure dependent. Continuous pressure and resistance control is therefore a prerequisite for reliable organ protection.

Key words: Renal protection – Perfusion catheter – Perfusion pressure – Equilibration.

Introduction

The normothermic kidney tolerates ischemia for 20–30 min [4, 8]; lengthy renal operations are only possible, if the renal ischemia tolerance can be substantially improved. Only preischemic perfusion with a cold organ protective solution is likely to improve ischemia tolerance without external cooling.

An organ protective solution will exhibit its full effect only, if it can disperse rapidly throughout the whole extracellular space. This requires a low renal vascular resistance and a good diuresis during perfusion. Reliable measurement of perfusion pressure and perfusion rate are important. Using a newly constructed perfusion catheter, allowing pressure measurement at the tip of the catheter largely independent of the flow, this prerequisite can be fulfilled in dog kidney perfusion in situ.

Materials and Methods

Experimental Procedure. Mongrel dogs of either sex with a mean body weight of 30 kg were laparotomized and kidneys and renal vessels were exposed. 30 min after premedication with 90 mg piritramide[1] and 0.5 mg atropine[2] anaesthesia was induced by 5–7 mg/kg$_{bw}$ sodium thiopental[3] and maintained by nitrous oxide, isoflurane[4] and fentanyl[5]. During the preparation period lasting for some 2 h 500 ml/h Tutofusin®[6] were infused. The dogs received a total of 25–75 g glucose in a 5% solution[7] and 2,500 I.U. heparin[8] 20 min before perfusion. Prior to perfusion urine was sampled for 10 min by a ureteral catheter. Urine volume and osmolality were determined. The perfusion catheter was introduced into the aorta. After advancing the catheter into the renal artery with a slow perfusion rate and fixing it with a tape, the dog kidneys were perfused with 5–8 °C cold cardioplegic solution HTK[9]. Immediately after the beginning of perfusion, the renal vein was clamped near the vena cava and incised close to the kidney to let the perfusate flow out without restriction. In intervals of 1 or 2 min the urine arising during perfusion was collected using the ureteral catheter. In these samples urine volume and sodium concentration[10] were measured. During perfusion the pressure in the renal artery was recorded continuously. The number of revolutions of the roller pump[11] was recorded to determine the perfusion volumes.

Calculated Values. The corrected renal wet weight was ascertained by multiplication of the renal dry weight by a factor 5.9; this assumes the average water content of an untreated kidney to be 83%. The renal perfusion resistance was the perfusion pressure divided by the perfusion volume per 100 g renal wet weight per min. The calculated resistance values were not corrected for viscosity. As a parameter for renal equilibration with the "HTK" solution the dif-

1 Dipidolor®, Janssen GmbH, Neuß, FRG
2 Atropinsulfat Drobena, Drobena Arzneimittel GmbH, Berlin, FRG
3 Trapanal®, Byk Gulden Lomberg Chemische Fabrik GmbH, Konstanz, FRG
4 AErrane-Isofluran™ (Isofluran), Ohio Medical Pharma-Vertrieb GmbH, Puchheim, FRG
5 Fentanyl®-Janssen, Janssen GmbH, Neuß, FRG
6 Tutofusin®, Pfrimmer & Co, Pharmazeutische Werke Erlangen GmbH, Erlangen, FRG
7 Glucose 5% Braun, B. Braun Melsungen AG, Melsungen, FRG
8 Heparin-Natrium Braun 2500 IE/5 ml, B. Braun Melsungen AG, Melsungen, FRG
9 Kardioplegische Lösung HTK nach Bretschneider, Dr. Franz Köhler Chemie GmbH, Alsbach-Hähnlein, FRG
10 IL543 Flame Photometer, Instrumentation Laboratory GmbH, Hersel, FRG
11 American Optical Company, Bredford, USA

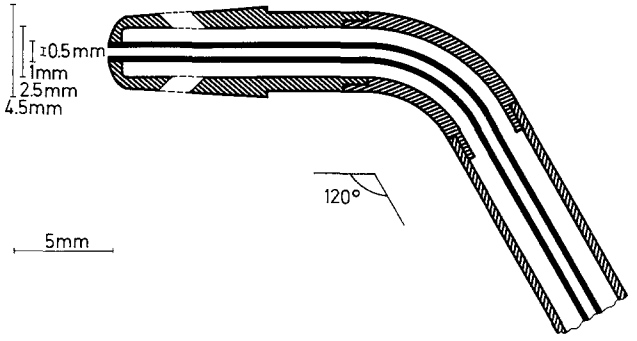

Fig. 1. Catheter (head) for dog kidney perfusion

Table 1. Catheter dimensions

	tip	connecting piece	shaft	pressure conduit
	mm	mm	mm	mm
inside diameter	2.5	2.5	3.0	0.5
outside diameter	max. 4.5	4.0	4.0	1.0
length	14.0	9.0–12.0	500	·/.
outlets	1.7	·/.	·/.	0.5

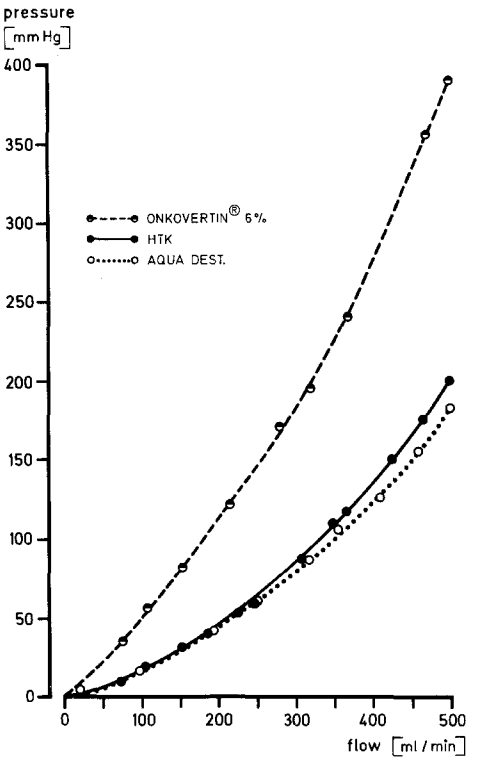

Fig. 2. Pressure-flow-relationship of the kidney perfusion catheter at 10 °C

ference between the sodium concentrations of the urine and of the "HTK" solution ($Na_{URINE-HTK}$) was calculated. Significance levels were determined using the Wilcoxon-Mann-Whitney test.

Perfusion System. The length of the tube system amounted to 3 meters without the catheter. It consisted of a PVC tube[12] (2.70 m), interrupted by a plastic three-way stopcock for "arterial" samples and a 30 cm long latex tube[13] proximal to the catheter. The latex tube damped roller pump pressure undulations.

Composition of the Perfusate. For kidney perfusion Bretschneider's "HTK" solution was used. Composition (mmol/l): NaCl 15, KCl 9, K-α-ketoglutarate 1, $MgCl_2$ 4, tryptophan 2, histidine 180, histidine-HCl 18, mannitol 30. The pH at 25 °C is 7.1, the total osmolarity is 310 mosmol/l.

To find out the pressure-flow-relationship of the catheter, "HTK" solution, 6% dextran[14] solution and aqua destillata were used.

Catheter Specification. The anterior part of the catheter consists of a tip piece which tapers conically, a curved connection piece and a shaft (Fig. 1). A grip-piece connects the shaft and the tube system. At this point also an interior pressure conduit branches out. The pressure conduit leads to the tip of the catheter and ends there with a central opening. At the other end it is connected to a pressure transducer[15]. The whole tip of the catheter and the grip are made of Plexiglass, the 50 cm long shaft (inside diameter 3 mm) and the pressure conduit (inside diameter 0.5 mm) are made of polyethylene. The junctions of the single parts of the catheter are glued with the Plexiglas adhesive Acrifix 92[16]. The outside diameter of the conical tip widens backwards from 3.2 mm to 4.5 mm. Then it falls to 4 mm in a 0.25 mm high step (Table 1). Here the catheter can be bound in the renal artery. The tip of the catheter has 2 x 2 obliquely (45°) bored lateral outlets for the perfusate, staggered to each other by 90° at a distance from the end of the catheter of 2.5 or 4 mm. The diameter of the outlets is 1.7 mm. The inside diameter of the tip is 2.5 mm.

Catheter Function. To perfuse a single kidney alone the catheter must be small enough to be inserted into the renal artery. On the other hand the flow resistance of the catheter must be low enough to allow the transport of the necessary perfusion volume without excessively high pressures with consequent overload on tubing and pump. For perfusion of dog kidneys weighing 80 g with a saline solution, perfusion rates of about 500 ml/min can become necessary, at least for a short time. At 10 °C this flow rate corresponds to a pressure decrease over the length of the catheter of about 200 mmHg (Fig. 2). A simple roller pump system is not overloaded by such a pressure. Using a colloidal solution such as Onkovertin® 6% (dextran) a pressure of about 400 mmHg is necessary at identical flow and temperature (Fig. 2). In experimental application one has to add the pressures of the catheter system to the pressures for the organ perfusion itself.

The flow resistance of a catheter not only depends on its dimensions but also on the flow conditions resulting from form and size. At a flow rate of 320 ml/min the mean flow velocity in the tip of the catheter amounts to 1.3 m/s. For this velocity the Reynold number (effective radius 1.15 mm in regard to the cross-section of the pressure conduit) is 940, being lower than the critical Reynold number. However, the influence of the annular cross-section on the flow characteristics has not been taken into consideration. But at a

12 Laboflex PVC-Schlauch 6 x 8, Labomatic GmbH, Sinsheim, FRG
13 Rüsch-Latexschlauch 6 x 9, Fa. Rüsch, Rommelshausen, FRG
14 Onkovertin® 6%, B. Braun Melsungen AG, Melsungen, FRG
15 P23D Pressure Transducer, Gould Medical GmbH, Düsseldorf, FRG
16 Acrifix 92, Röhm GmbH Chemische Fabrik, Darmstadt, FRG

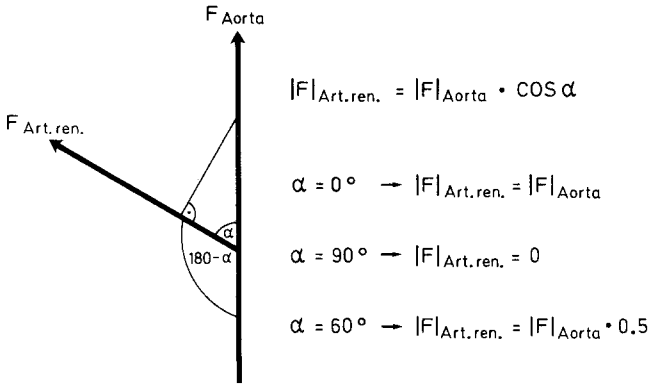

Fig. 3. Influence of bend angle of the kidney perfusion catheter on insertion into the renal artery

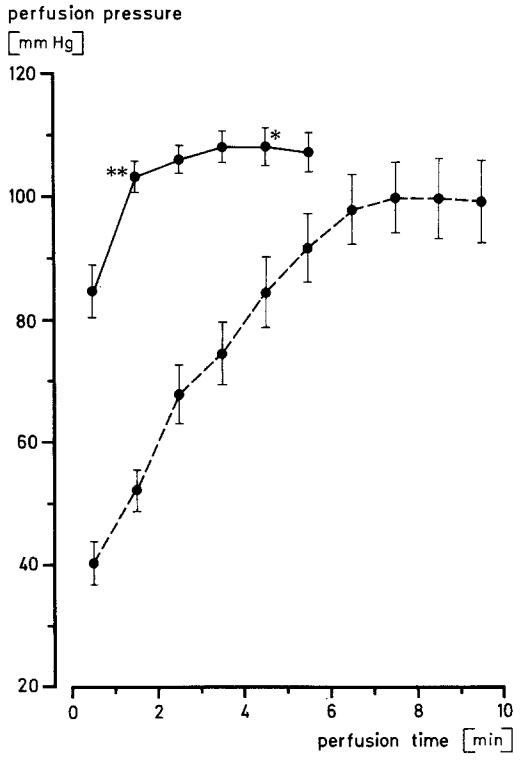

Fig. 4. Different perfusion pressures at dog kidney perfusion ($\bar{x} \pm s_{\bar{x}}$). ** $p < 0.001$, * $p < 0.025$. ●——● $n = 26$, baseline urine osmolality 529 ± 274 [mosmol/kg H_2O] ●– – –● $n = 18$, baseline urine osmolality 533 ± 191 [mosmol/kg H_2O]

flow rate of 320 ml/min there is no longer a linear relationship between the pressure of the catheter and the flow rate, i.e. the flow resistance of the catheter rises with increasing flow. One reason for this is the fact that the parabolic profile of a fully developed laminar flow appears only after the passage of an entrance length (x) ($x = 0.13 \cdot \frac{r^2 \cdot v \cdot \rho}{\eta}$, r = radius, v = velocity, ρ = density, η = viscosity) [1, 2]. Turbulences at smaller steps, at the outlets and at the bend of the catheter may be involved as well. The pulsation amplitude of the roller pump, in connection with the latex tube, has no influence on flow as comparable experiments with a simple hydrostatic perfusion technique have proved.

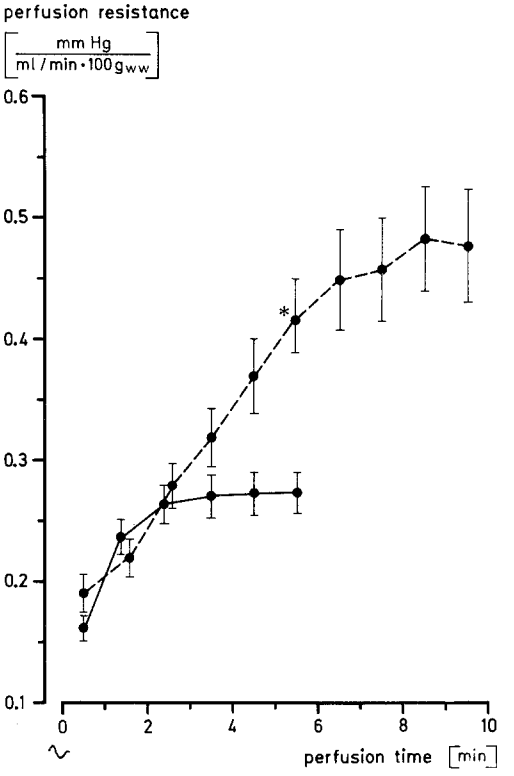

Fig. 5. Perfusion resistance ($\bar{x} \pm s_{\bar{x}}$) at different perfusion pressures ($\bar{x} \pm s_x$). * $p < 0.025$. ●——● pressure at 2nd min: 103 ± 13 [mmHg], $n = 26$ ●– – –● pressure at 2nd min: 52 ± 15 [mmHg], $n = 18$

Insertion of the Catheter. For the insertion of the catheter into a peripheral artery some flexibility of the shaft is necessary, but it must also have a sufficient torsion stiffness and pressure strength so that it can be brought into the renal artery. For this also the angle of the connecting piece of the catheter is of considerable importance (Fig. 3). An angle of 120° seems to be the best compromise to find the ostium of the renal artery on one hand to push forward the tip of the catheter in the renal artery on the other hand.

Results

Application of the Catheter in Animal Experiments. Kidney perfusions were assigned to two groups according to the level of the perfusion pressure. In the first group ($n = 18$) perfusion was initiated at a lower level and then gradually increased. A pressure of 60 mmHg was not exceeded in the 1st min. The mean perfusion pressure in the 2nd min of perfusion was 52 ± 15 mmHg ($\bar{x} \pm s_x$). The second group ($n = 26$) includes experiments with a minimum pressure of 80 mmHg at the end of the 1st min. The mean perfusion pressure in the 2nd min was 103 ± 13 mmHg ($\bar{x} \pm s_x$). Urine osmolality (mosmol/kg H_2O) before the perfusion and the mean renal weight (g_{ww}) were comparable in both groups ($\bar{x} \pm s_x$: 533 ± 191 or 80 ± 17 in group 1, 529 ± 274 or 76 ± 14 in group 2). The protective perfusion lasted 10 min in group 1 and 6 min in group 2. The "artificial urine" was collected in 2-min-periods in group 1, in 1-min-periods in the second group. Depending on the perfusion pressure

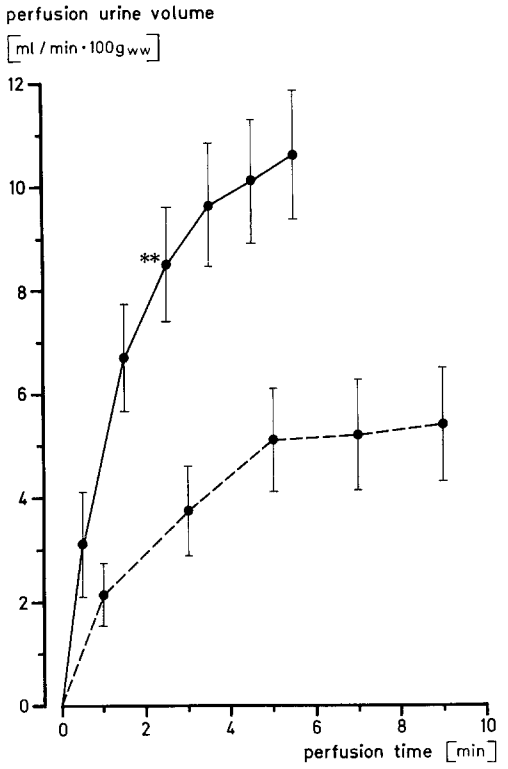

Fig. 6. Urine volume ($\bar{x} \pm s_{\bar{x}}$) during perfusion at different perfusion pressures ($\bar{x} \pm s_{\bar{x}}$). ** $p < 0.001$. •——• pressure at 2nd min: 103 ± 13 [mmHg], $n = 26$ •– – –• pressure at 2nd min: 52 ± 15 [mmHg], $n = 18$

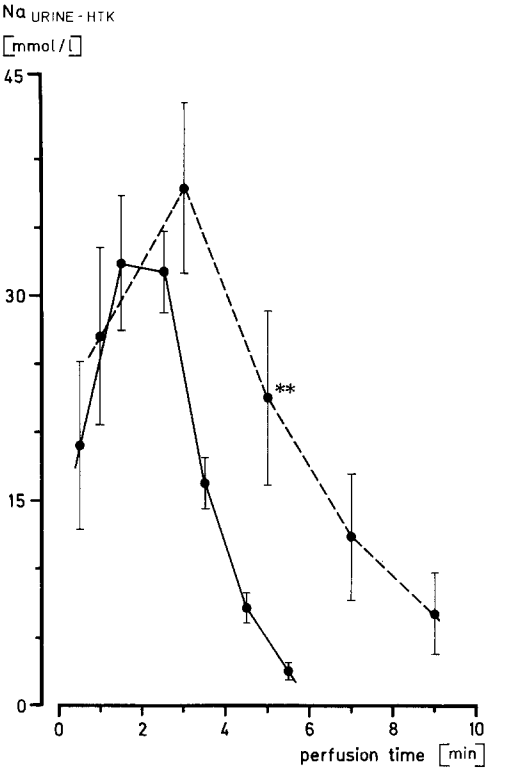

Fig. 7. Renal equilibration ($Na_{URINE\text{-}HTK}$, $\bar{x} \pm s_{\bar{x}}$) at different perfusion pressures ($\bar{x} \pm s_{\bar{x}}$). ** $p < 0.001$ •——• pressure at 2nd min: 103 ± 13 [mmHg], $n = 26$ •– – –• pressure at 2nd min: 52 ± 15 [mmHg], $n = 18$

at the beginning of the perfusion, also the further course of the pressures during perfusion was different in both groups (Fig. 4). In group two the mean pressure, reaching 85 mmHg in the 1st min, continued to increase during the 2nd min. Later on there was only a small increase. In group 1 the pressure rose continuously from 40 mmHg in the 1st min up to about 100 mmHg in the 8.–10. min of perfusion, although perfusion volume had hardly changed. Parallel to the increase of the perfusion pressure there was an increase of the perfusion resistance (Fig. 5). Its value of 0.42 mmHg · ml^{-1} · min · 100 g_{ww} was significantly higher ($p < 0.025$) in this group than in group 2. Similar to the perfusion pressure the perfusion resistance in group 2 reached a plateau in the 2.–3. min at 0.27 mmHg · ml^{-1} · min · 100 g_{ww}.

Discussion

Recently it was shown [6] that the renal perfusion resistance during perfusion with the "HTK" solution is lower at higher diuresis or with lower urine osmolality. The artificial diuresis during perfusion depends on the baseline diuresis. A high perfusion diuresis and a low perfusion resistance lead to a better washout of blood and urine from the kidney. These equilibration processes in the kidney can be shown among other things by the course of the sodium concentration in the urine [5]. Since a change in urine osmolality is associated with a parallel change of osmolality of the renal medulla [3], the more advantageous perfusion at a high baseline diuresis could occur as a consequence of a reduction of the medullar osmolality. The osmotic concentration in the medulla is influenced by the blood flow through the medulla which depends on the pressure in the renal artery [9]. Thus it is possible that an increase in the initial perfusion pressure can accelerate the medullar washout by an increased medullar perfusion and thus improve the renal equilibration. The results show that at a comparable urine baseline osmolality the perfusion resistance is considerably lower, when a high initial perfusion pressure of 80–100 mmHg causes a higher perfusion rate. The amelioration of the perfusion resistance via the perfusion pressure is accompanied by a corresponding higher perfusion diuresis and an accelerated adaptation of the urinary sodium concentration to the sodium concentration of the "HTK" solution (Figs. 6, 7). Thus it is possible to weaken negative effects of a high baseline urine osmolality on renal perfusion by a sufficiently high perfusion pressure. At least in the first minutes of perfusion, as long as the kidney is capable of autoregulation, perfusion pressures up to 120 mmHg are tolerated without risk according to the present results. If perfusion diuresis begins too slowly these high pressures can be used with an appropriate flow control,

provided that exceeding these pressure values can be avoided by a continuous pressure control. Also because of the variable outlet resistance of a catheter for single kidney perfusion depending on the width of the artery it is advisable, at least for experiments on animals, to perfuse, by volume control so that the flow rate conforms to the pressure in the renal artery.

The catheter described can only be used with a normal the catheter, and in some renal arteries intimal lesions may occur where the catheter is fixed so that a certain amount of care must be exercised when fastening the tape.

Acknowledgements. The authors wish to thank R. Dohrmann, E. Neumeyer, A. Orend and other co-workers of the Institute of Physiology for their skilful technical support.

References

1. Bretschneider HJ (1961) Methoden zur Messung der Durchblutung mit einem hohen zeitlichen Auflösungsvermögen. In: Kraus H, Klepzig H (eds) Kreislaufmessungen. Werk-Verlag Dr. E. Banaschewski, München-Gräfelfing, pp 157–174
2. Eck B (1961) Technische Strömungslehre. Sechste Auflage. Springer, Berlin Göttingen Heidelberg
3. Hirokawa W (1908) Über den osmotischen Druck des Nierenparenchyms. Hofmeisters Beitr Physiol Pathol 11:458–478
4. Hölscher M (1982) Verbesserung der Nierenprotektion zur Verlängerung der Ischämietoleranz bei in situ Operationen und bei Transplantationen. Habilitationsschrift, München
5. Kallerhoff M, Hölscher M, Kläß G, Bretschneider HJ (1980) The equilibration proceedings at a 12' long perfusion of kidneys with HTP-solution of Bretschneider. Pflügers Arch 389 (Suppl):R43
6. Kehrer G, Gebhard MM, Kallerhoff M, Siekmann W, Blech M, Helmchen U, Bretschneider HJ (1984) The influence of glucose premedication on perfusion resistance, perfusional diuresis and equilibration of the dog kidney during perfusion with Bretschneider's cardioplegic solution "HTK" in standardized anaesthesia. Pflügers Arch 400 (Suppl):R22
7. Marberger M (1983) In situ cooling of the kidney. In: Marberger M, Dreikorn K (eds) Renal preservation. Williams and Wilkins, Baltimore Londn, pp 38–63
8. Rosetti SR (1983) Impact of acute ischemia on human kidney. In: Marberger M, Dreikorn K (eds) Renal preservation. Williams and Wilkins, Baltimore London, pp 21–37
9. Thurau K, Deetjen P (1962) Die Diurese bei arteriellen Drucksteigerungen. Die Bedeutung der Hämodynamik des Nierenmarks für die Harnkonzentrierung. Pflügers Arch 274:567–580

Dr. G. Kehrer
Zentrum Physiologie und Pathophysiologie
Humboldtallee 23
D-3400 Göttingen