

## PDF hosted at the Radboud Repository of the Radboud University Nijmegen

The following full text is a publisher's version.

For additional information about this publication click this link.

<http://hdl.handle.net/2066/21030>

Please be advised that this information was generated on 2019-04-25 and may be subject to change.

Margot van de Bor

Division of Neonatology,  
Department of Pediatrics,  
University Hospital Leiden,  
The Netherlands

## Renal Blood Flow Velocity in Non-Distressed Preterm Infants during the First 72 Hours of Life

### Key Words

Renal blood flow velocity  
Preterm infant  
Doppler ultrasound

### Abstract

Renal blood flow velocity (RBFV) was studied with two-dimensional/pulsed Doppler ultrasound in 28 non-distressed very preterm infants (mean  $\pm$  SD gestational age was  $27.3 \pm 2.1$  weeks and birth weight  $907 \pm 214$  g) at 6, 12, 24, 36, 48, and 72 h of age. Mean arterial blood pressure (MABP), PaCO<sub>2</sub>, PaO<sub>2</sub>, and Hct were determined simultaneously. Mean RBFV increased significantly from  $14.5 \pm 1.9$  cm/s at 6 h to  $20.2 \pm 2.5$  cm/s at 72 h ( $p < 0.005$ ). MABP decreased slightly though significantly between 6 h ( $36.5 \pm 1.8$  mm Hg) and 12 h ( $34.3 \pm 1.5$  mm Hg), but rose thereafter to significantly higher values at 72 h ( $41.4 \pm 1.3$  mm Hg). Renal vascular resistance (RVR = MABP/RBFV) decreased rapidly during the first day of life ( $2.6 \pm 0.1$  mm Hg/cm $\cdot$ s<sup>-1</sup> at 6 h vs.  $2.0 \pm 0.05$  mm Hg/cm $\cdot$ s<sup>-1</sup> at 24 h). In conclusion, RBFV increases whereas RVR decreases during the first days of life.

### Introduction

Urine output depends on renal perfusion, glomerular filtration, renal tubular function, and urinary tract anatomy. Preterm as well as term infants produce less urine during the first days of life than during the remainder of the neonatal period. Animal studies suggest that renal hemodynamics follow a pattern of change that is determined by biological signals other than the functional demands imposed at

birth [1]. The development of renal blood flow during the first days of life in preterm human infants has not been studied. Pulsed Doppler ultrasonography has been applied to estimate renal blood flow by measuring mean blood flow velocity in the renal arteries (RBFV) in preterm and term neonates [2–4] as well as in older children [5]. The aim of this study was to measure RBFV with pulsed Doppler ultrasonography in non-distressed very preterm infants during the first 72 h of life.

## Methods

Thirty-one appropriate-for-date preterm infants of less than 32 weeks of gestation were initially enrolled in the study after informed parental consent had been obtained. The study was approved by the Bioethics Committee of the hospital. All infants were born in the Department of Obstetrics and admitted immediately after birth to the Neonatal Intensive Care Unit of the University Hospital Leiden. None of the infants suffered from birth asphyxia (defined as Apgar score at 5 min of  $<7$  and/or umbilical cord pH of  $<7.10$ ), respiratory distress syndrome, pneumonia, septicemia, a hemodynamically important patent ductus arteriosus (diagnosed by Doppler echocardiography before the RBFV measurements), congenital heart defect, and/or extreme weight loss ( $>15\%$  of birth weight) during the first week of life. As part of the routine clinical care of infants of less than 30 weeks gestational age, an endotracheal tube is placed at birth and mechanical ventilation continued as long as a tendency towards apnea is observed during the weaning process. Infants receiving vasoactive drugs (e.g. dopamine) or volume expanders were excluded from the study. Three infants were secondarily excluded from the study due to violation of the enrollment criteria. All 3 developed a hemodynamically important patent ductus arteriosus. The infants were nursed in Draeger type 8000 incubators (Draeger AG, Lübeck, Germany). The humidity in the incubators was kept at approximately 80%, and the temperature was maintained according to the guidelines described by Hey and Scopes [6]. The fluid intake of the infants was 60, 80, and 100 ml/kg on days 1, 2, and 3, respectively. All infants had an indwelling umbilical artery catheter in situ with its tip between L3 and L4.

RBFV was determined as previously described [3]. The infants were lying in a supine position. All infants were awake though quiet during the examinations. The blood flow velocity in the right renal artery was measured with two-dimensional, pulsed Doppler ultrasonography (Ultramark 4, Advanced Technology Laboratories, Inc., Bothell, Wash., USA). The transducer, with a 7.5-MHz imaging system and a 5-MHz Doppler crystal, was positioned below the costal margin in the dorsolateral area of the right flank. The sample volume of the Doppler system was set at 1.5 mm, and a 100-Hz high-pass filter was used to reduce the noise of the arterial wall. The sample volume was placed in the relatively straight proximal course of the right renal artery, 3–5 mm from the right side of the wall of the aorta. The artery was thus insonated in an almost orthograde direction ( $0$ – $25^\circ$ ). Peak systolic, end diastolic, and temporal mean (RBFV) flow velocities were

calculated from five sequential cardiac cycles of optimal quality. RBFV measurements were performed at 6, 12, 24, 36, 48, and 72 h of age.

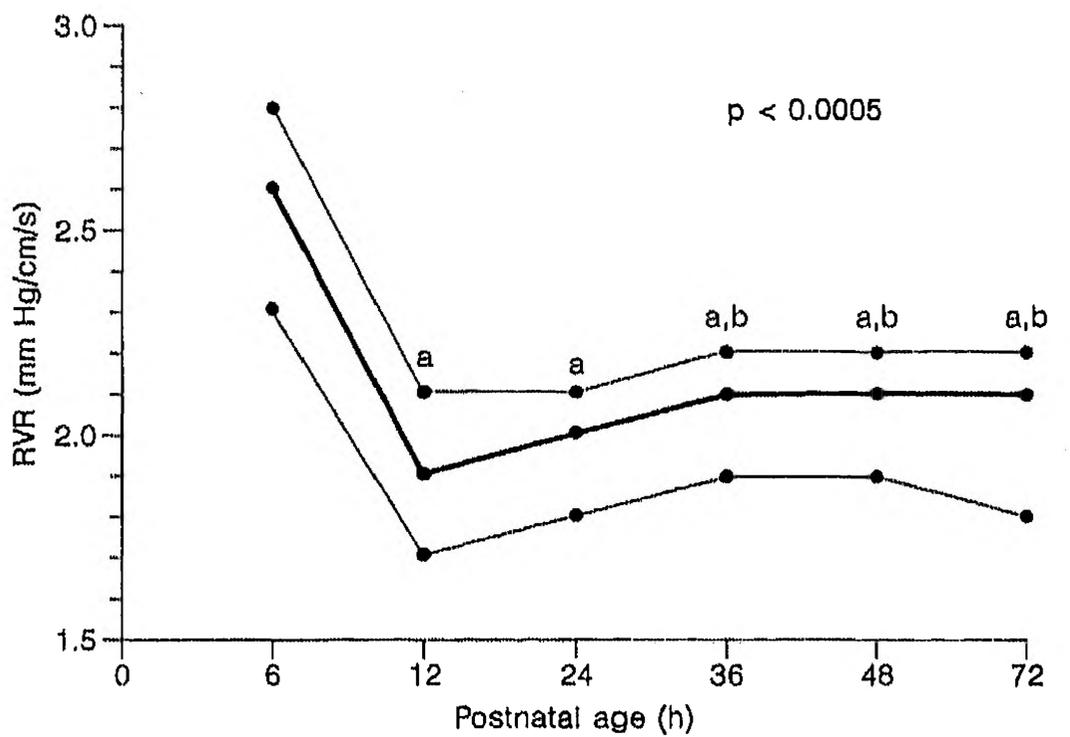
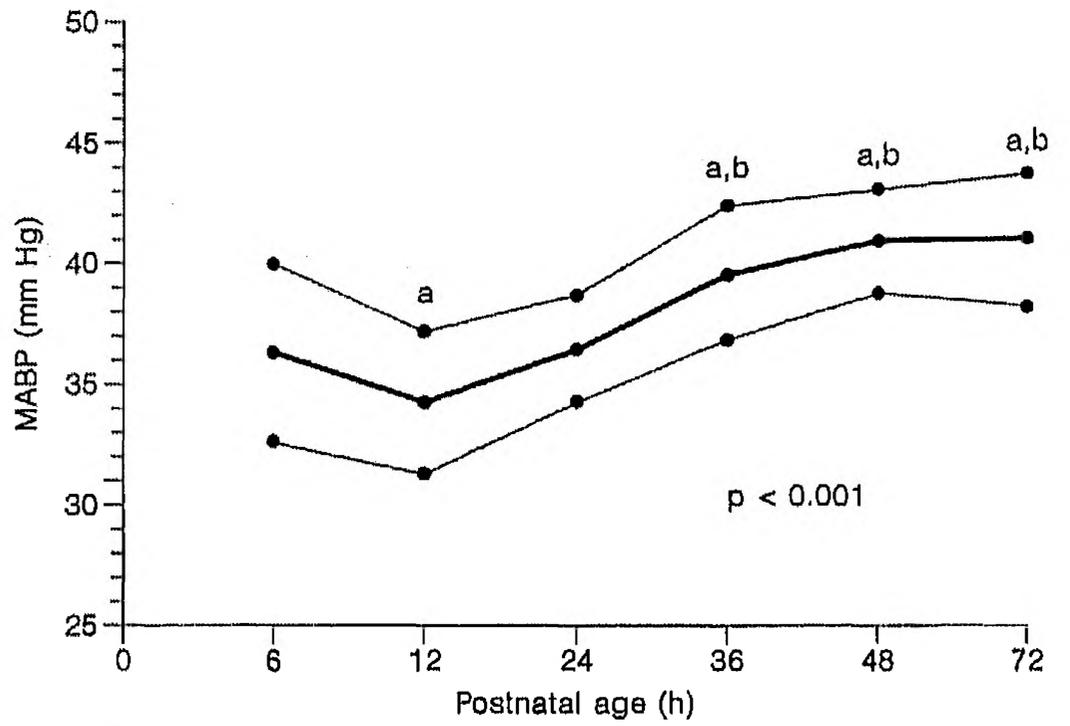
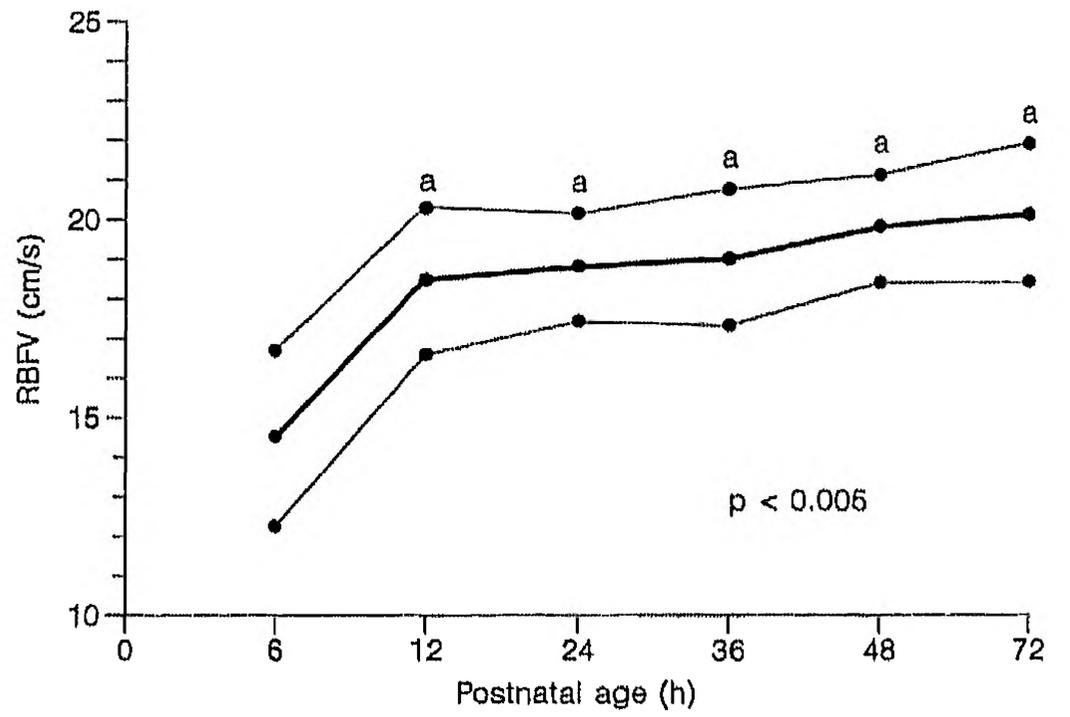
Just prior to the Doppler studies, blood samples were drawn from the umbilical artery for arterial oxygen pressure ( $\text{PaO}_2$ ), carbon dioxide pressure ( $\text{PaCO}_2$ ), and hematocrit (Hct) measurements. Simultaneous with the RBFV measurements mean arterial blood pressure (MABP) from an indwelling umbilical artery catheter was determined. Urine production was recorded continuously during the whole study period.

Analysis of variance for repeated measurements was used to analyze differences in RBFV, MABP, renal vascular resistance ( $\text{RVR} = \text{MABP}/\text{RBFV}$ ; in  $\text{mm Hg}/\text{cm}\cdot\text{s}^{-1}$ ),  $\text{PaCO}_2$ ,  $\text{PaO}_2$ , Hct, and urine output during the study period, followed by the Student-Newman-Keuls test when a significant difference was found. Ninety-five percent confidence limits of RBFV, MABP, RVR,  $\text{PaCO}_2$ ,  $\text{PaO}_2$ , and Hct were calculated by the statistical package (StatView, Abacus Concepts Inc., Berkeley, Calif., USA). Regression analysis was performed to study the relationship between MABP,  $\text{PaCO}_2$ ,  $\text{PaO}_2$ , and Hct, respectively, and RBFV. Multiple regression analysis with MABP,  $\text{PaCO}_2$ ,  $\text{PaO}_2$ , and Hct as independent variables was carried out to detect the most predictive factor for RBFV. A  $p$  value of  $<0.05$  was considered to be statistically significant.

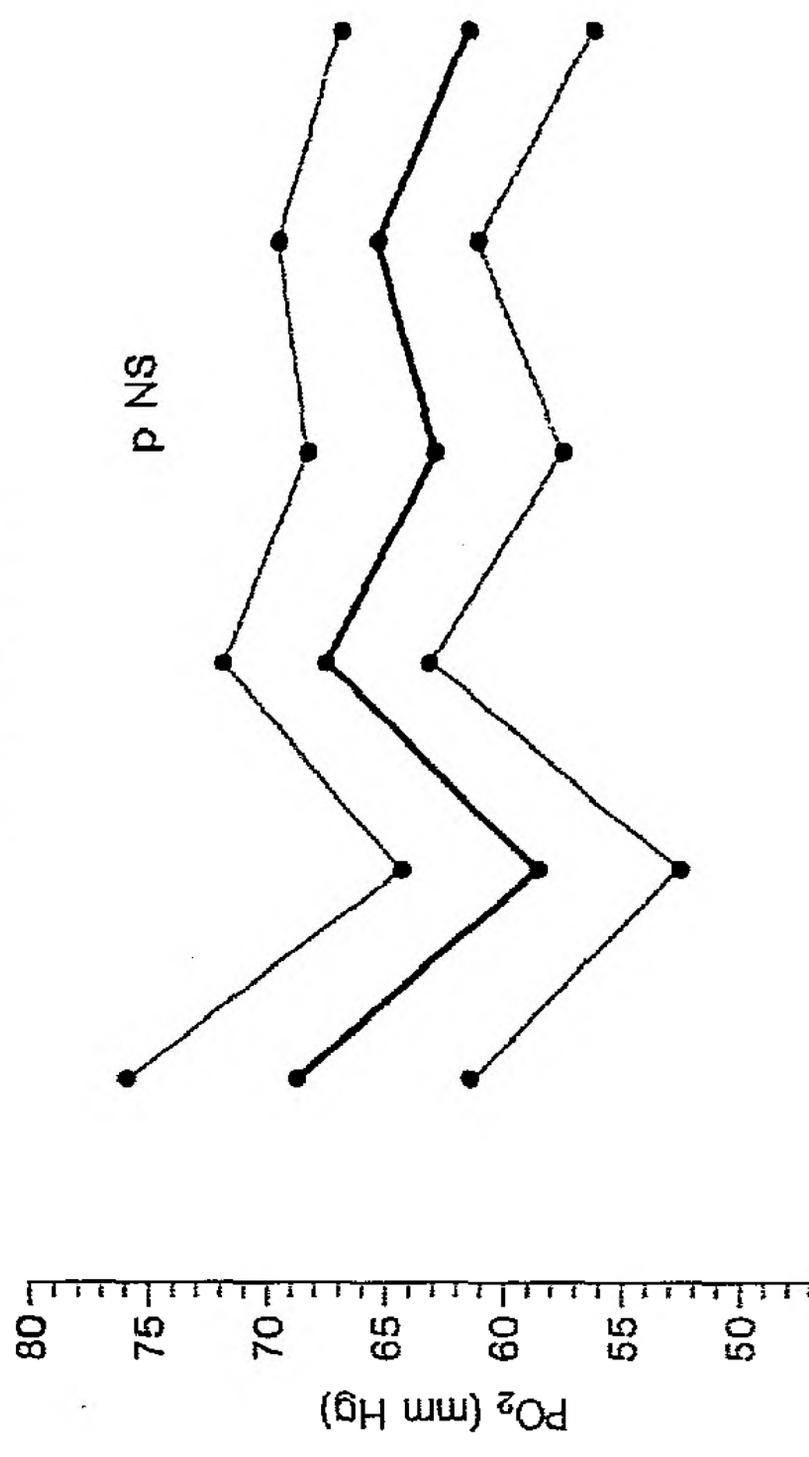
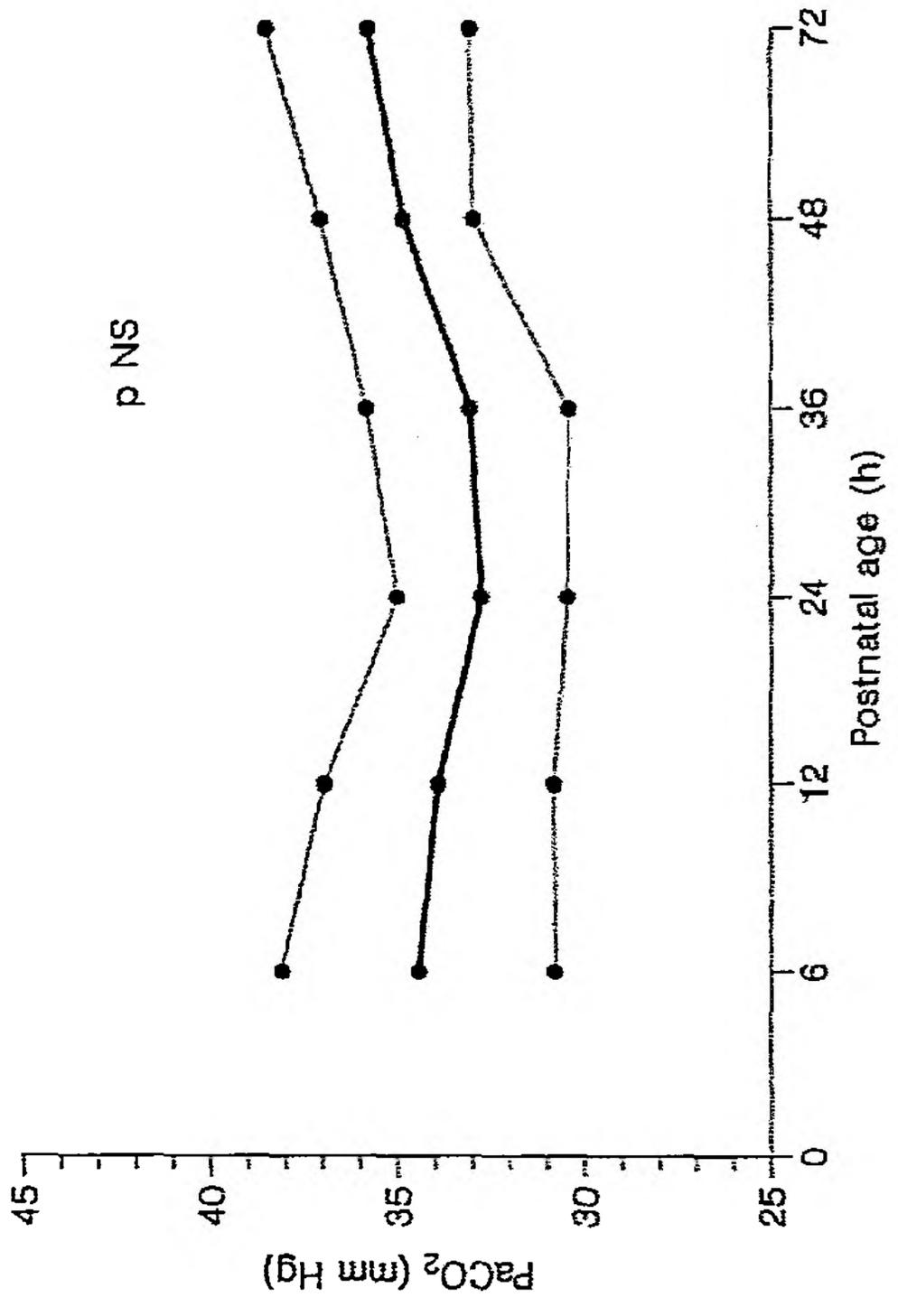
## Results

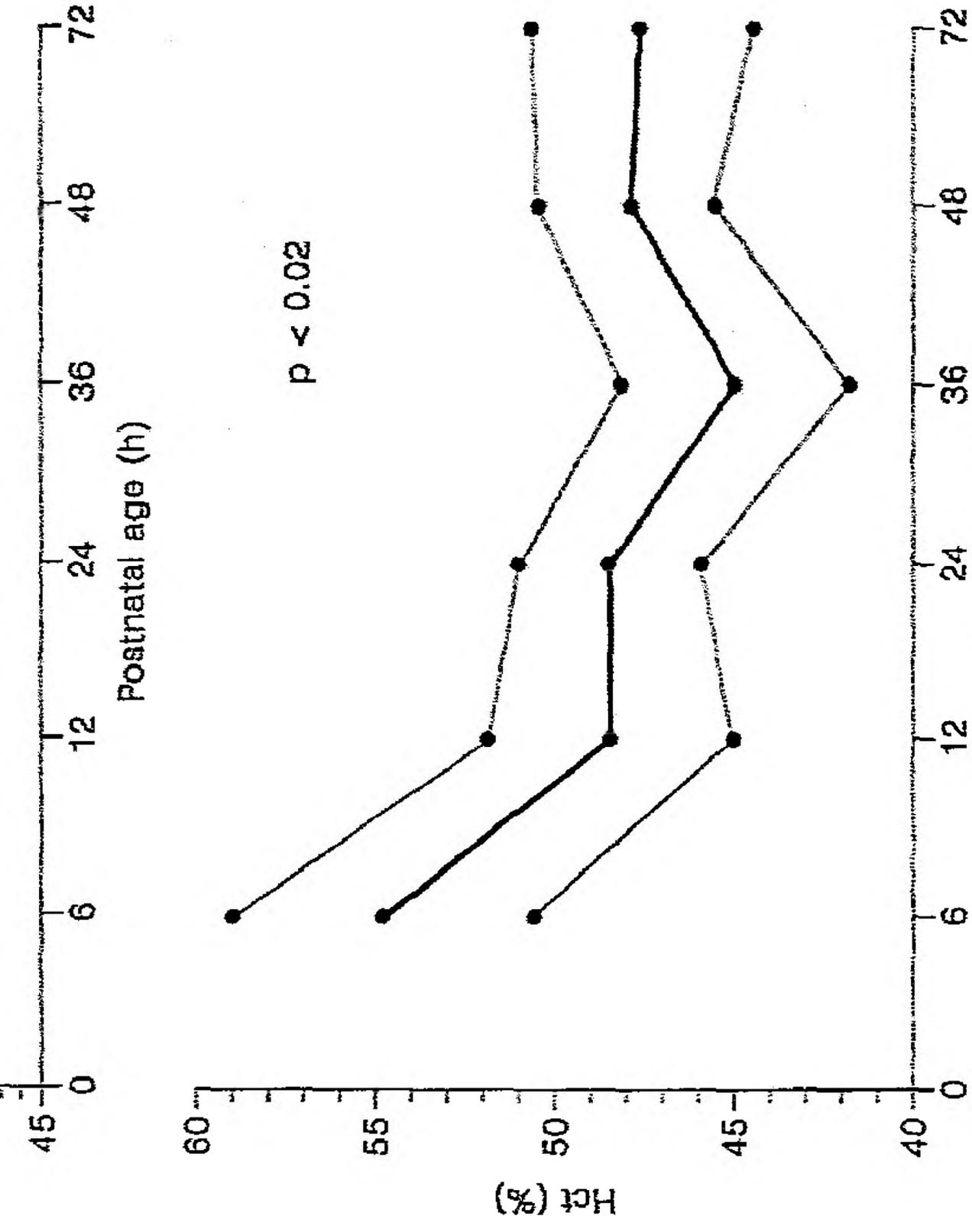
The final study population of 28 preterm infants had a mean gestational age of  $27.3 \pm 2.1$  ( $\pm$  SD) weeks (range 26–32) and a birth weight of  $907 \pm 214$  g (range 620–1,470). The mean umbilical cord pH was  $7.29 \pm 0.07$  (range 7.20–7.40) and the median Apgar score at 5 min was 9 (range 7–10). Six infants were born by cesarean section and 6 infants were born vaginally in breech position. All other infants were born vaginally in a cephalic position. Twenty-two infants had to be ventilated during the study period because of apnea. The ventilator settings could be kept very low in all cases (mean airway pressure  $<5.0$  cm  $\text{H}_2\text{O}$ ).

Figure 1 displays the mean values of RBFV, MABP, and RVR during the first 72 h of life. RBFV and MABP increased significantly (F ratio 3.9,  $p < 0.005$ , and F ratio 4.7,



**Fig. 1.** Mean  $\pm$  95% confidence limits of mean renal blood flow velocity (RBFV), mean arterial blood pressure (MABP), and renal vascular resistance (RVR) during the study period. <sup>a</sup>  $p < 0.05$  vs. 6 h of age; <sup>b</sup>  $p < 0.05$  vs. 12 h of age.





**Fig. 2.** Mean  $\pm$  95% confidence limits of PaCO<sub>2</sub>, PaO<sub>2</sub>, and Hct during the study period.

**Table 1.** Multiple regression analysis with mean renal blood flow velocity (RBFV) as dependent variable

	F ratio	p
MABP	33.90	0.0000
PaCO <sub>2</sub>	5.19	0.025
PaO <sub>2</sub>	0.00	0.99
Hct	0.18	0.67

$p < 0.001$  respectively), while RVR decreased significantly (F ratio 4.9,  $p < 0.0005$ ). The increase in RBFV occurred primarily during the first 12 h of life. From 12 h of age onwards RBFV was significantly higher than at 6 h. RBFV values did not differ significantly between 12 and 72 h. MABP decreased slightly though significantly between 6 and 12 h of age, but increased gradually thereafter until the age of 72 h. MABP values at 36, 48, and 72 h were significantly higher than at 6 and 12 h of age. No differences between the 36- and 72-hour values were observed. RVR was high at 6 h of age and decreased rapidly. From 12 h of age onwards RVR values were significantly lower than at 6 h. The RVR values at 36, 48, and 72 h were, however, significantly higher than at 12 h.

Figure 2 shows the mean values of PaCO<sub>2</sub>, PaO<sub>2</sub>, and Hct during the study period. PaCO<sub>2</sub> and PaO<sub>2</sub> remained within normal limits, whereas Hct values decreased significantly during the first 3 days of life (F ratio 3.0,  $p < 0.002$ ).

Mean urine output was significantly higher ( $p < 0.001$  on days 2 and 3 ( $3.7 \pm 0.2$  and  $3.4 \pm 0.3$  ml/kg/h, respectively) than on day 1 ( $2.0 \pm 0.2$  ml/kg/h). The mean percentage weight loss (daily weight compared to birth weight) was greater ( $p < 0.02$ ) on days 2 and 3 ( $7.6 \pm 0.8$  and  $7.2 \pm 1.0\%$ , respectively) than on day 1 ( $4.1 \pm 0.8\%$ ).

Multiple regression analysis, with RBFV as the dependent variable and MABP, PaCO<sub>2</sub>, PaO<sub>2</sub>, and Hct as independent variables, revealed that MABP was the most predictive variable for RBFV (table 1).

## Discussion

Two-dimensional pulsed Doppler provides a tool to measure blood flow velocity in the renal arteries under a sharp angle [2]. Reliable identification of the renal arteries is possible because they are the only two arteries to branch off pairwise in the upper abdominal aorta and to have a characteristic flow velocity pattern throughout the diastolic phase. Actual renal blood flow, however, cannot be measured with this technique because it is not sensitive enough to measure the diameter of the renal artery accurately. But in vitro and animal studies have shown that, under various conditions, RBFV correlates well with renal blood flow [7, 8].

MABP Decreased slightly between 6 and 12 h of age. This decline might be caused by a rapid fall in the systemic vascular resistance, which is not yet fully compensated by an increase in left ventricular output [9]. Shunting of blood through a hemodynamically important patent ductus arteriosus, which may lead to a lower MABP, was excluded in all cases. The subsequent gradual increase in MABP is similar to observations by others [10]. The increase in RBFV during the first day of life is in accordance with blood flow velocity patterns found in other organs, such as the brain [11, 12]. This phenomenon is probably caused by the decline in RVR as well as by the redistribution of cardiac output to the kidneys [13]. In the first 12 h of life only 4–6% of the cardiac output is distributed to the kidneys, while this percentage increases to 8–10% during the first week of life. Animal

studies have demonstrated that the site of high RVR is localized mainly at the afferent arterioles [14]. The decline in RVR after 6 h of age is likely to be related to the generalized fall in systemic vascular resistance during the first day of life [8]. If the decrease in RVR is considered to be the cause of the increase in RBFV, this might indicate an intact renal autoregulatory system on the first day of life.

Changes in fluid intake have not affected the changes in RBFV during the first day of life, because all infants received a constant intravenous fluid infusion of 2.5 ml/kg/h (60 ml/kg/day) from birth until 24 h of age.

Control of basal renal blood flow may be affected by other factors as well. The renin-angiotensin system and prostaglandins do not seem to play a significant role in preterm infants [13]. The effect of factors, such as the kallikrein-kinin system, arginine vasopressin, and adenosine receptors, has yet to be determined [13]. Atrial natriuretic factor appeared to exert a direct vasodilatory effect on the neonatal renal vasculature [15].

In conclusion, RBFV increases whereas RVR decreases during the first day of life in non-distressed very preterm infants.

## References

- 1 Seikaly MG, Arant BS: Development of renal hemodynamics: glomerular filtration and renal blood flow. *Clin Perinatol* 1992;19:1-13.
- 2 Boemelburg T, Jorch G: Investigations of renal artery blood flow velocity in preterm and term neonates by pulsed Doppler ultrasonography. *Eur J Pediatr* 1988;147:283-287.
- 3 Van de Bor M, Van Bel F, Guit GL, Schipper J: Renal blood flow velocity in preterm infants with severe respiratory distress syndrome. *J Pediatr* 1990;117:785-788.
- 4 Visser MOJM, Leighton JO, Van de Bor M, Walther FJ: Renal blood flow in neonates: Quantification with color flow and pulsed Doppler US. *Radiology* 1992;183:441-444.
- 5 Grunert D, Schoening M, Rosendahl W: Renal blood flow and flow velocity in children and adolescents: Duplex Doppler evaluation. *Eur J Pediatr* 1990;149:287-292.
- 6 Hey E, Scopes JW: Thermoregulation in the newborn; in Avery GB (ed): *Neonatology; Pathophysiology and Management of the Newborn*. Philadelphia, Lippincott, 1987, pp 201-211.
- 7 Greene ER, Venters MD, Avasthi PS, Conn RL, Jahnke RW: Noninvasive characterization of renal artery blood flow. *Kidney Int* 1981;20:523-529.
- 8 Sampson D, Abramezyk J, Murphy GP: Ultrasonic measurement of blood flow velocity changes in canine renal allografts. *J Surg Res* 1972;12:388-393.
- 9 Nelson NM: The onset of respiration; in Avery GB (ed): *Neonatology; Pathophysiology and Management of the Newborn*. Philadelphia, Lippincott, 1987, pp 176-200.
- 10 Ingelfinger JR, Powers L, Epstein MF: Blood pressure norms in low-birth-weight infants: Birth through 4 weeks (abstract). *Pediatr Res* 1983;17:319.
- 11 Calvert SA, Ohlsson A, Hosking MC, Erskine L, Fong K, Shennan AT: Serial measurements of cerebral blood flow velocity in preterm infants during the first 72 hours of life. *Acta Paediatr Scand* 1988;77:625-631.
- 12 Van Bel F, Den Ouden L, Van de Bor M, Stijnen T, Baan J, Ruys JH: Cerebral blood flow velocity during the first week of life of preterm infants and neurodevelopment at two years. *Dev Med Child Neurol* 1989;31:320-328.
- 13 Jose PA, Harmati A, Fildes RD: Postnatal maturation of renal flow; in Polin RA, Fox WW (eds): *Fetal and Neonatal Physiology*. Philadelphia, Saunders, 1992, pp 1196-1200.
- 14 Spitzer A, Edelman CM Jr: Maturation changes in pressure gradients for glomerular filtration. *Am J Physiol* 1971;221:1431-1435.
- 15 Varille VA, Nakamura KT, Meweeny OJ, Matherne GP, Smith FG, Robillard JE: Renal hemodynamic response to atrial natriuretic factor in fetal and newborn sheep. *Pediatr Res* 1989;25:291-294.