Postnatal physiological renal function adaptation in newborn infants

Nils W. SVENNINGSEN
Yenidoğan Yoğunbakım Ünitesi, Lund Üniversitesi, İsveç

Introduction

In this presentation I will discuss certain data on the postnatal adaptation of renal functions of clinical importance during the first hours, days and weeks of life. A crucial question in this context is whether renal function after birth is sufficient in every aspect to meet the needs of extrauterine life? Will the transition of the kidney from its relatively dormant state in utero to its fully functional state after birth be influenced by excretory demands or is the postnatal development dependent only upon the degree of maturity at birth? And, finally, are some babies more vulnerable than others with regard to their various renal functions at birth? These questions are derived from practical clinical problems which can be met in the nursery in the clinical management of newborn infants and young infants, e.g. with dehydration, sudden edema, acidosis and problems related to fluid intake and drug administration[1].

The fetus is producing urine from about the 11th week of gestation. In the latter part of gestation a major contribution to the amount of amniotic fluid is the hypotonic urine excreted by the fetus[2].

In the following data on various renal functions will be presented with regard to glomerular filtration rate (GFR), water excretion (dilution) capacity, urine concentration capacity and the sodium excretion capacity in the postnatal period of life.

Some authors have compared different renal functions in infancy with the absolute values in percentage of adult function. By such comparison the picture looks rather gloomy for the newborn baby and young infant. It will take 6 weeks of more for tubular functions and about 6 months for the glomerular function to reach adult values[3, 4].

Early renal adaptation at birth and in the first hours of postnatal life

The renal excretion capacity following a water load within the first hours of life has been studied. After an initial period of 2-3 hours after birth, when spontaneous diuresis had occurred and urine output stabilized, these 7 infants received a water load by infusion of 1 to 2.5 ml/kg/minute of 5 % dextrose in water (DSW) over a period of 15 to 25 minutes. They were all fullterm infants (Fig. 1). This infusion caused a prompt increase in urine output (V), glomerular filtration (C_{In}), renal plasma flow (C_{PAH}) in all 7 infants. The urine/plasma ratio for osmolarity (U/P_{osm}) decreased in 5 of 7 newborns. These results show that the newborn infant is capable of increasing his glomerular filtration and renal plasma flow already at 2 to 3 hours of age[5].

The postnatal changes occurring spontaneously in these renal parameters are shown in 3 newborn infants from a large study. These infants were not receiving a water load (Fig.2).

Adres: Nils W. SEVENNINGSEN MD, Professor of Paediatrics and Neonatal Medicine.
Neonatal Intensive Care Unit, Department of Pediatrics, University Hospital. Lund, Sweden.

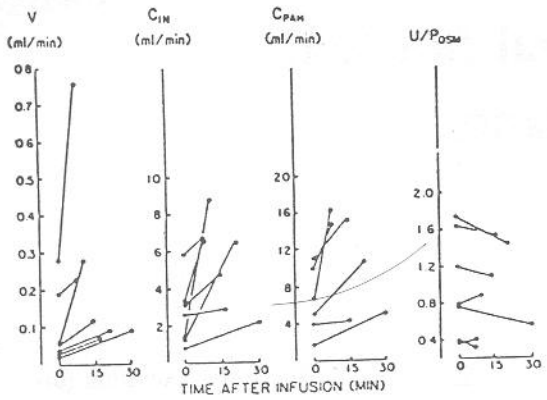

Fig. 1: Effect of rapid volume expansion in fullterm newborn infants at 2 to 3 hours of age (5). Urine output (V), inulin clearance (C_{IN}), p-aminohippuric acid clearance (C_{PAH}) and urine/plasma ratio before and after maximal diuresis.

The solid line[4] represents a baby after vaginal delivery **with** placental transfusion, the dotted line [14] a vaginally born baby **without** placental transfusion and the broken line [15] a baby born by Cesarean section. The highest rates of urine flow (V) were found after Cesarean section and the lowest in the vaginally born not transfused baby.

Despite variations in urine output all infants show increase in urine flow with maximum between 1 to 2 hours of age. The rates began to fall thereafter and by 3 to 4 hours of age values less than 0.02 ml/minute were recorded. Glomerular filtration (C_{In}) and renal plasma flow (C_{PAH}) follow a similar pattern. U/P_{osm} ratio changed in the opposite direction. The spontaneous transient postnatal diuresis could in part be due to expansion of extracellular volume by placenta blood transfusion[6].

However, other factors may be involved in the regulation of the diuresis shortly after delivery. Thus the amount of fluid given to the mother during the last 4 hours of labour has a large impact on the newborn baby's fluid balance. In recent studies it was shown that when the mother was given i.v. glucose solutions more than 1500 ml per 4 hours prior to birth the plasma sodium level of the baby was decreased considerably to around 128 mM/1 versus 133 mM/1 found after normal delivery[7].

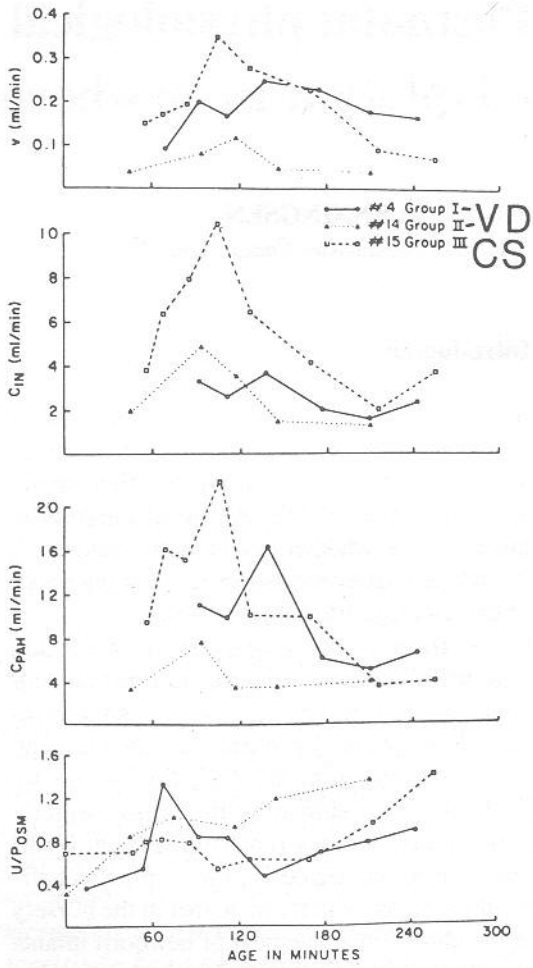

Fig. 2: Serial urine output, inulin-and PAH-clearance and urine/plasma osmolity ratio in three representative infants (6).

The response to a water load after birth appears to be mediated by an increase in GFR. It may thus be inferred that both renal plasma flow and GFR are normally maintained below maximal capacity in the newborn baby. Vasoactive factors (renin-angiotensin) may play a role since studies of the correlation between glomerular filtration rate measured by single injection polyfructosan clearance has shown an increase in GFR with increasing arterial oxygen tension (PAO_2) in the lower abdominal aorta. These ifants were studied at 6 to 12 hours of age (Fig. 3)[8].

In summary: It is evident that stabilization of

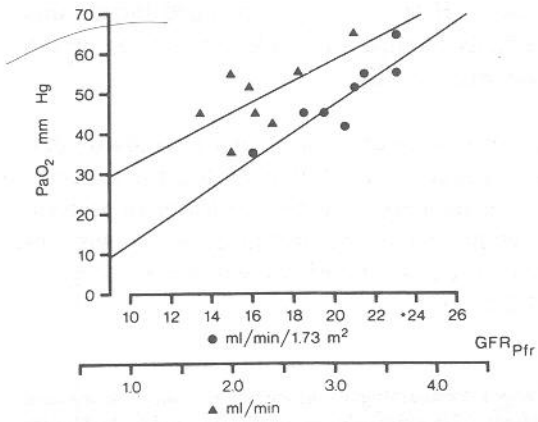

Fig. 3: GFR in relatin to PaO_2 in newborn infants at 6-12 hours of age (8).

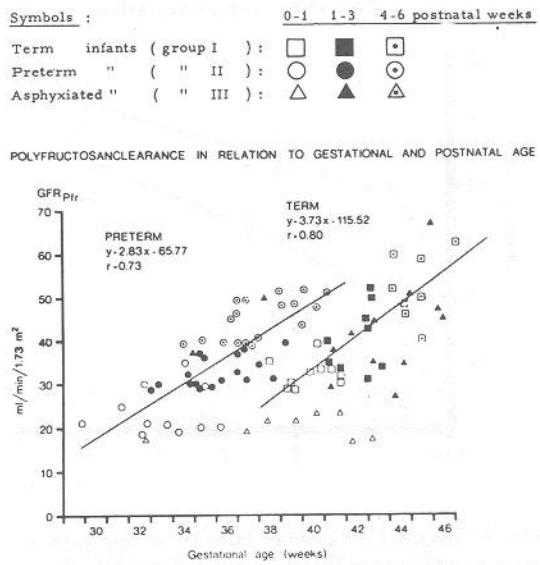

Fig. 4: GFR in relation to gestational age at birth and repeated in the same infants in the 1st, 2nd-3rd and 4th-6th postnatal week, respectively.

renal function in the first hours of life reflects the achievement of stability or renal circulation following adaptation to a variety of stresses during the birth process.

The main factors comprise: Placental blood transfusion and birth asphyxia. These will cause an increase of blood viscocity and vasoactive factors, e.g. catecholamines or vasopressin levels and furthermore an extracullular volume expansion. In contrary a high fluid load in the mother, e.g. during Cesarean section, will have an opposite effect with hyponatremia in the newborn. Thus various renal function changes after birth may be predictable from the mode of delivery. To a certain extent the stabilization of renal function after birth follows a general course of event pattern similar to that observed in acid-base indices after delivery.

Postnatal renal adaptation in the first days and weeks of life glomerular filtration rate (GFR)

The postnatal development after the first hours of life for glomerular filtration, concentration capacity and sodium excretion capacity is related to a certain extent to degree of maturity at birth. In a sutdy of repeated measurements in the 1st, 2nd, 3rd and 4th-6th weeks of life we have followed these changes in term infants (squares), preterm (circles) and babies with severe asphyxia with Apgar scores less than 6 stillat 10 minutes of age (triangles) (Fig.4).

For preterm infants the postnatal increase in GFR is slightly lower than in term infants. For asphyxiated infants born at term in the 38th week of gestation or later the initial GFR during the first days of life is comparable to preterm infants born before the 34the week of gestation. However, in the 2nd-3rd postnatal week of life there is a considerale increase in the asphyxiated infants, and even more at 4-6 weeks in both term and preterm infants[8].

Thus there is a progressive increase in GFR after birth to both term and preterm infants. The difference is largest in the first week of life. Generally the preterm infants have a delay in increase of GFR not starting until after the first postnatal week. As shown in Fig. 5 this delay is especially important for fluid electrolyte balance in very preterm infants born before 34 weeks of gestation[8,9].

In summary: The main factors influencing postnatal development of GFR are related to renal immaturity with anatomical heterogeneity

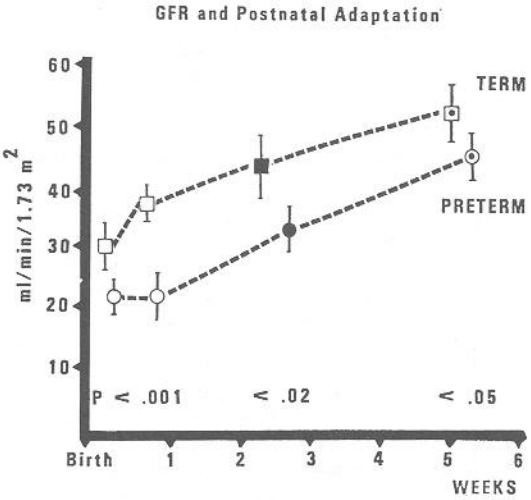

Fig. 5: Mean GFR values in fullterm as compared to preterm infants born before 34 weeks of gestation (8,9).

in the glomerulo-tubular morphology and the fact that after 34 weeks of gestation new glomeruli are added[3]. The high renal vascular resistance in the fetus and newborn at birth decreases rapidly after delivery during the first hours and days of life. This is partly related to renal blood flow bypassing secretory sites, partly to postnatal disappearence of turgid (obstructive) cells of the juxtaglomerular apparatus surrounding the afferent arterioli obstructing the blood flow into the glomeruli[2]. Thus hemodynamic adjustment of the renal blood flow will balance the GFR to the tubular reabsorption capacity. As judged from morphological findings the newborn has a large filtration potential which is not fully utilized[10]. However, for the clinician (neonatologist and pediatric surgeon) it is important to remember that the renal vascular resistance may rise considerably in hypoxic or acidotic infants. This will lower the fluid excretion (GFR) capacity in asphyxiated newborn babies and therefore a limited fluid input (60-80 ml/kg/24 hours) is preferable inthe first day of life in such infants[8, 10].

Concentration capacity

Postnatal renal concentration capacity also increases after birth faster in term than in preterm infants. However, in asphyxiated infants this capacity is impaired in the 1st and part in the 2nd week of life[11].

In absolute figures (mean and 1 standard deviation) according to DDAVP-test the concentration capacity is somewhat lower in preterm as compared to term breastfed infants, but considerably lower in infants with severe asphyxia (Table 1).

Table 1: Postnatalrenal concentration capacity in newborn infants: Maximum urine osmolality (mOSM/kg H_2O) with DDAVP-test i.e. 10 µg intranasally administered DDAVP=1-deamino-8-D-arginine-vasopressin.

Postnatal age	1-2 weeks	4-6 weeks
Term infants	385±9.0	565±17.9
Preterm infants	359±19.4	524±20.6
Term infants with asphyxia	300±5.7	525±18

The renal concentration capacity can be expressed not only as a function of maximal concentration but also of duration of increased osmolarity. In the first weeks of life the duration of concentration of preterm infants is significantly shorter than in fullterm infants but increasing with postnatal age reaching the capacity of the fullterm at 4-6 weeks of postnatal age (Fig. 6).

The implication of these findings is that for each mOsm urine solute to be excreted the minimum urine water needed is higher in the preterm than in the term infant or adult individual[2].

Sodium excretion capacity

The renal sodium excretion is comparatively low in fullterm infants in relation to the sodium intake. In preterm infants, however, the excretion of sodium is much higher indicating that the preterm infant is in a negative sodium balance in the first 10 days or more after birth. This underlines the importance of electrolyte balance in the preterm infants in the first weeks of life[1,12].

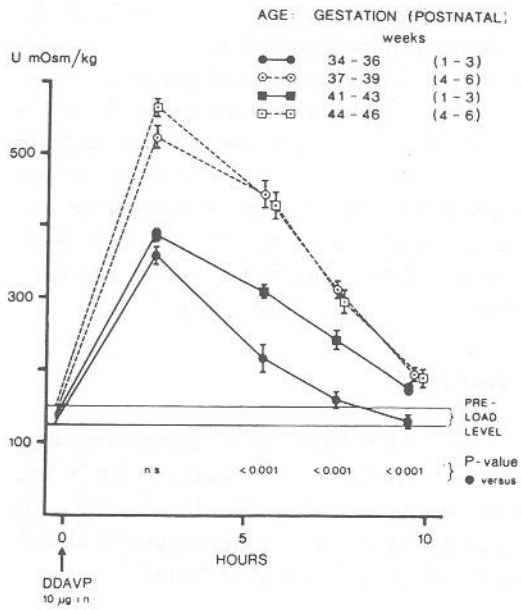

Fig. 6: Postnatal development of renal concentration capacity measured by DDAVP-test in preterm infants (11).

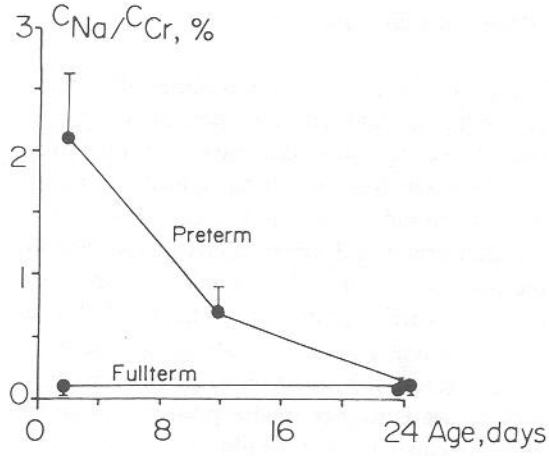

Fig. 7: Fractional sodium excretion in proximal renal tubules in preterm (34 weeks gestation) and fullterm infants during the first 3 weeks of life.

As shown in Fig. 7 the fractional sodium excretion (in relation to glomerular filtration rate) is much higher in preterm infants than in fullterm infants during the first weeks of life. This means that sodium reabsorption capacity in the tubuli is low in the preterm infants[12].

This is related to the low aldosterone tubular response of preterm infants. As shown in Fig. 8a increased urine-potassium over urine-sodium excretion is seen with increasing aldosterone levels in fullterm babies. In preterm infants (filled circles represent 1-10 days old preterm infants and open circles 12-20 days old preterm infants in fig. 8b) there is no correlation with increasing aldosterone during the first 10 days but at 12 to 20 days there is a positive correlation as in fullterm infants.

In summary: The comparatively high sodium-excretion in preterm infants during the first weeks of life is due to a low tubular response to aldosterone and consequently a low tubular sodium reabsorption capacity in the preterm infants.

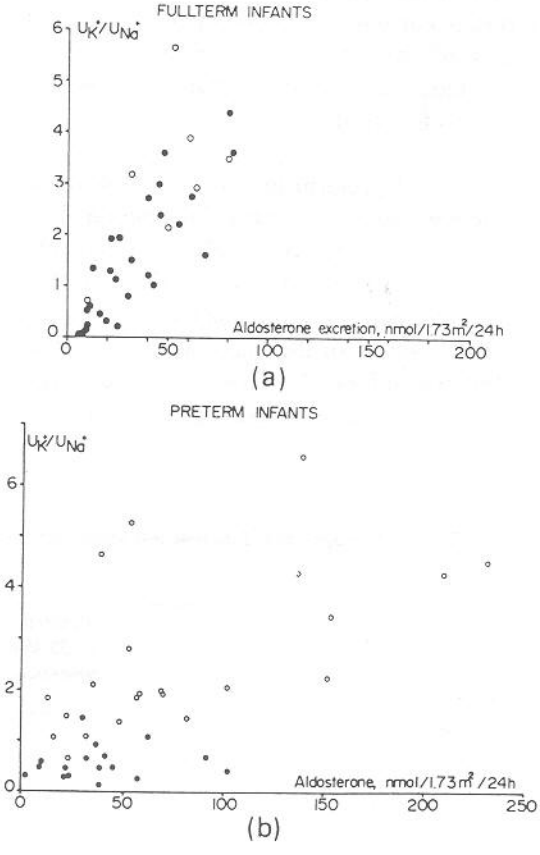

Fig. 8: Urine potassium/urine sodium excretion rate in relation to aldosterone urine levels in term and preterm infants. Filled circles 1-10 days, unfilled circles 12-21 days of age (12).

Other tubular functions

Filtration of small protein molecules also changes with gestational and postnatal age[13]. Beta-2-microglobulin is a marker of renal proximal tubular function. It has a molecular weight of around 12.000 and is easily filtered in the glomerulus and subsequently reabsorbed in the proximal tubule. The fractional reabsorption is less efficient in preterm than in fullterm infants. Still at 4 weeks of postnatal age the fractional excretion in relation to glomerular filtration rate is higher in the preterm infant[14]. This demonstrates that the glomerulotubular imbalance at the level of the proximal tubulus will persist in preterm infants all through the first month of postnatal life [1,11,14,15]. The postnatal development of various renal tubular functions has also been shown to be proportionate to gestational age at birth, e.g. glucose reabsorption capacity [16] and the hydrogen ion excretion capacity which is an important buffering mechanism for maintenance of acid-base balance after birth[17].

In studies of preterm infants at 2 to 4 weeks of age we found that their urine contains both titrable acid and ammonia and that both increase with net acid loading with NH_4Cl. However, titrable acid and ammonia increased to only 57 % and 43 % of the maximum values seen in fullterm infants[18]. This diminished capacity to increase tubular hydrogen ion secretion is a major determinant of late metabolic acidosis in preterm infants at 2 to 4 weeks of age. Because phosphate is the principal buffer in urine it is also essential that there is sufficient in urine to allow hydrogen ion secretion to proceed to within the limits set by the minimum urine pH 5.0-5.6 besides the capacity of the kidney to generate ammonia [19]. Average values of some of the major renal functions in early infancy are presented in Table 2.

Conclusion

Our present knowledge of the extrauterine adaptation of renal functions indicates that in fullterm infants the kidney is fully developed for the excretory demands of postnatal life already within the first hours after birth[15].

In infants with perinatal asphyxia and preterm infants the not fully developed GFR and renal functional concentration and hydrogen ion excretion capacities at birth certainly have clinical importance for neonatal and surgical care [1, 10]. Major problems in these infants are thus related to the increased susceptibility for fluid- and electrolyte imbalances with oedema, hyponatremia and hypoalbuminemia, to the lowered drug excretion capacity of the kidney and the risk of tubular leakage of low molecular peptides and glucose. In the light of recent investigations of renal function in the fetus and newborn baby moderate impairments of renal func-

TABLE II: Average renal function test values after birth.

	Preterm (33 W) gestation	Preterm (33 W)	Fullterm		
Postnatal age, weeks		0-1		2-6	7-8
Glomerular filtration rate (cc/min/1.73 m²)	7 (6-8.5)	18 (10-25)	23 (8-42)	50 (30-90)	69 (42-90)
Renal plasma flow (cc/min/1.73 m²)	—	53 (53-99)	82 (33-162)	135 (48-188)	244 (203-321)
Tubular reabsorption Tm glucose (mg/min/1.73 m²)	—	—	60	60	170
Tubular excretion Tm PAH (mg/min/1.73 m²)	—	—	16 (6-26)	14 (4-22)	50 (13-93)
Max. concentration capacity (mOsm/kg)	200-500	300-600	350-650	400-800	500-900
Urine volume (cc/day)	15-40		15-60	100-300	250-450

tion very likely remain unrecognized in many clinical situations, which indicates the continuous need for further studies within this field of neonatal medicine and pediatric surgery.

References

1. Oh W: Renal functions and clinical disorders in the neonate. Clin Perinatol 8; 215. 1981
2. Royer P, Habib R, Mathieu H et al: The kidney in the newborn. In: Pediatric Nephrology, Vol. XI, Major Problems in Clinical Pediatrics pp. 116-27, 1978
3. Edelmann CMJr, Spitzer A: The maturing kidney. J Pediatr 75: 509, 1969
4. Fetterman GH, Shuplock NA, Philippe FJ et al: The growth and maturation of human glomeruli and proximal convolutions from term to adulthood. Pediatrics 33: 601, 1965
5. Daniel S, James LS, Strauss J: Response to rapid volume expansion during the postnatal period. Pediatrics 68: 809, 1981
6. Strauss J, Daniel SS, James LS: Postnatal adjustment in renal function. Pediatrics 68: 802, 1981
7. Singhi SC, Chookang E: Maternal fluid overload during labour; transplacental hyponatremia and risk of transient neonatal tachypnoea in term infants. Arch Dis Child 59: 155, 1984
8. Svenningsen NW: Single injection polyfructosan clearance in normal and asphyxiated neonates. Acta Paediatr Scand 64:87, 1975
9. Aperia A, Broberger O, Elinder G et al: Postnatal development of renal function in preterm and full-term infants. Acta Paediatr Scand 70: 183, 1981
10. Daniel SS, James LS: Abnormal renal function in the newborn infant. J Pediatr 88: 856, 1976
11. Svenningsen NW, Aronson AS: Postnatal development of renal concentration capacity as estimated by DDAVP test in normal and asphyxiated neonates. Biol Neonate 25: 230, 1974
12. Aperia A, Broberger O, Herin P et al: Sodium excretion in relation to sodium intake and aldosterone excretion in newborn preterm and fullterm infants. Acta Paediatr Scans 68: 813, 1979
13. Miltényi M: Urinary protein excretion in healthy children. Clin Nephrol 12: 216, 1979
14. Aperia A, Broberger O: Beta-2-microglobulin - an indicator of renal tubular maturation and dysfunction in the newborn. Acta Paediatr Scand 68:669, 1979
15. Nash MA, Edelmann CM Jr: The developing kidney. Inappropriate function or inappropriate standard? Nephron 11:71, 1973
16. Brodehl J, Franken A, Gellisson K: Proximal tubular reabsorption of glucose in infants and children. Acta Paediatr Scand 61:413, 1972
17. Svenningsen NW, Lindquist B: Postnatal development of renal hydrogen ion excretion capacity in relation to age and protein intake. Acta Paediatr Scand 63: 721, 1974
18. Svenningsen NW: Renal acid-base titration studies in infants with and without metabolic acidosis in the postneonatal period. Pediatr Res 8: 659, 1974
19. Sutyok E, Heim T: Assessment of maximal urinary acidification in premature infants. Biol Neonate 19: 200, 1971