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RENAL RESPONSE TO TOLAZOLINE IN NORMAL AND HYPOXEMIC NEWBORN PUPPIES. John, E.G., Bhat, R., and Vidyasagar, D.; University of Illinois Hospital, ALSM, Chicago, Illinois, U.S.A.

The present study was designed to investigate the effect of tolazoline (T), hypoxia (H), and tolazoline and hypoxia (TH) on renal functions. Each animal served as its own control. Hypoxia was induced by administering 5% O₂ and 95% N₂O for 45 minutes. Following a bolus injection of tolazoline (2mg/kg), a continuous infusion was given (2mg/kg/hr). Blood pressure (BP), renal blood flow (RBF), glomerular filtration rate (GFR), fractional excretion of sodium (FENA), and urine volume (UV) were measured by conventional methods. The change in PaO₂ were similar in H and TH groups. In T, there were no changes in BP, RBF, GFR, FENA, and UV during control and experimental periods. In H, at the onset of the experiment, BP increased from a mean value of 50±10mmHg to 65±20mmHg, then remained at 50±10mmHg. In TH, following the administration of tolazoline, BP decreased from 49±5mmHg to 29±2mmHg and remained low thereafter. A greater than 40% decrease in GFR was observed in H and 60% in TH group. RBF decreased 1.5 fold (P<.05) in H while 4 fold in TH (P<.05). FENA and UV however, increased 17 and 6 fold in H (P<.05) while the increase was 21 (P<.05) and 2.4 fold in TH. These results suggest: 1. Tolazoline does not have an adverse effect on BP and renal functions. 2. Hypoxia produces decrease in GFR and RBF. 3. Tolazoline in the presence of hypoxia produces more severe changes in renal functions.

PHYSIOLOGY

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RENAL HANDLING OF PHOSPHATE IN CHILDREN WITH VARIOUS STAGES OF RENAL INSUFFICIENCY.

Brodehl, J., Offner, G., Wegener, G. Abteilung Pädiatrische Nephrologie, Kinderklinik, Medizinische Hochschule, D-3000 Hannover-61, West-Germany. In order to determine the adaptive mechanism of impaired kidney in phosphate homeostasis, the renal transport of phosphate (plasma = Pp, urinary excretion = UpV, clearance = Cp, fractional tubular reabsorption = Tp/Cin, and fractional clearance = Cp/Cin) was measured in 42 children with chronic renal insufficiency. Three stages of impaired glomerular filtration rate (stage I = Cin 51-80 ml/min/1.73 m², II = 21-50, III = 3-20) are compared with normals of the same age group (see table). The results demonstrate that the kidney can sustain phosphate homeostasis down to GFR = 30 ml/min/1.73 m². Below this limit phosphate retention occurs despite secondary hyperparathyroidism.

	normal n = 142	Stage I n = 20	Stage II n = 12	Stage III n = 10
Cin	113 ± 18.4	67.6 ± 8.5	31.1 ± 8.2	12.9 ± 6.3
Pp	1.43 ± 0.19	1.35 ± 0.19	1.50 ± 0.14	2.12 ± 0.78
UpV	13.0 ± 6.4	15.7 ± 6.3	14.4 ± 5.3	10.6 ± 5.0
Cp	8.8 ± 4.1	11.6 ± 4.2	9.7 ± 3.9	5.3 ± 2.9
Tp/Cin	1.32 ± 0.18	1.12 ± 0.18	1.03 ± 0.23	1.01 ± 0.51
Cp/Cin	8.1 ± 4.1	17.6 ± 7.0	30.6 ± 11.4	49.2 ± 23.9

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PHOSPHATE TRANSPORT IN RENAL TUBULAR BRUSH BORDER VESICLES IN A PIG STRAIN OF VITAMIN D DEPENDENT RICKETS.

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An autosomal recessive strain of pigs with Vit.D-dependent rickets has been thoroughly investigated in functional studies. Within 4-6 weeks after birth these animals develop severe rickets with hypophosphatemia, hyperaminoaciduria and osteomalacia. A defect of 1,25 hydroxylase is the postulated mechanism of this disease. Early treatment of high doses Vit D3 or 1,25 D prevents the rickets. The brush border membrane isolation (vesicle method, KINNE et al., 1975) was used to study the Na-coupled 32P-transport in hetero- and homozygote animals of the same litter. Serial renal biopsies (6 g per sample) were performed before and after high dose Vit. D3 treatment. The 32P- influx showed the typical overshoot phenomenon. The highest values showed 322 % accumulation in healthy animals. The lowest values only 127 % in Vit- D deficient animals. The results are interpreted as an indication for a disturbed phosphate transport at the luminal site of the proximal tubular membrane in Vit D- deficiency.

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THE RENIN-ANGIOTENSIN-ALDOSTERONE SYSTEM IN HEALTHY INFANTS AND CHILDREN.

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Previous investigations have shown that, in healthy children, active renin values, measured as plasma renin activity (PRA_{act}), and plasma aldosterone (PA) values are increased when compared to adult values. No correlation between PRA and PA was observed. Inactive renin values (PRA_{inact}) obtained after cryoactivation did not decrease with age. Moreover, in some children, mainly infants, PRA decreased after cold treatment.

In the present investigation it was shown that, in healthy children, active renin values, measured as plasma renin concentration (PRC), are also increased. There was a significant correlation with angiotensin II (AII) values. No correlation, however was found between AII and PA values, confirming the earlier suggestion that other factors than the RAA-system are involved in the high aldosterone secretion. Although the mean activation rate of inactive renin was higher with cold than with acid treatment, the difference between both methods was not obvious in individual cases. After addition of o-phenanthroline to the blood samples, no negative values for PRA_{inact} were observed. It is suggested that the previous negative values were due to insufficient inactivation of the Ca- and Zn-dependent enzymes involved in the system.

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URINARY PROSTAGLANDINS AND KALLIKREIN IN HEALTHY CHILDREN FROM BIRTH TO ADOLESCENCE. Godard C.M., Dale B.D., Favre H., Lucot G. and Vallotton M.B. Dept. of Pediatrics

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The aim of this study was to establish normal values for urinary excretion of prostaglandins (PG) E2 and P2α and of kallikrein (KALL) at different ages of development, and to correlate them with several parameters of renal function. In 55 healthy infants and children of both sexes, aged 2 days to 14 years, daily urinary PGE2 and PGP2α were determined by specific radioimmunoassays; KALL was measured by an enzymatic method. Results (mean ± SEM):

Age	1-3days	5-8days	2-3weeks	4-12months	4-9years	10-14years
n	10	10	4	7	14	10
PGE2	36.3	20.3	28.9	37.5	135.4	238.2
ng/24hr	± 10.2	± 6.8	± 11.9	± 6.4	± 15.8	± 44.3
PGP2α	134.4	104.4	161.0	231.7	625.8	710.6
ng/24hr	± 28.8	± 25.3	± 57.6	± 77.6	± 57.1	± 103.1
KALL	8.2	10.7	12.0	44.8	326.3	567.2
mU/24hr	± 1.0	± 2.0	± 6.1	± 6.1	± 70.1	± 97.1

In contrast to the activity of the renin-angiotensin-aldosterone system, which is known to decrease from birth on, urinary PGE2, PGP2α and KALL significantly increased with age. These changes were not correlated to blood pressure, UV, UNa+, Uosm or GFR, and were obliterated when results were corrected for surface area.

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Prostaglandins (PG) are involved in the hemodynamic adaptation at birth. Their effects during the further postnatal period is, however, more obscure. PG exert potent actions on general as well as renal circulation. There is also evidence for a direct effect of PG on the renal transtubular transport of water and sodium. A high production of PG in the perinatal period might therefore contribute to the renal functional adaptation to extra-uterine life.

This study was designed to examine the influence of indomethacin, an inhibitor of PG synthesis, on renal hemodynamics, i.e GFR and RBF, and on sodium excretory capacity during an isotonic volume expansion (VE). Anesthetized lambs aged 5-14 days and 27-44 days were examined. The results show a blunted natriuretic response to VE in the indomethacin-treated lambs as compared to controls (Fig). This effect was more prominent in the higher age-group and it was not related to the changes in renal hemodynamics. This implies the importance of PG for the control of sodium excretion during development. It is suggested that the age differences in PG effects on sodium homeostasis can partly be explained by a less responsiveness to PG in the younger as compared to the older lambs.