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IMPAIRED CHEMOTAXIS ASSOCIATED WITH DECREASED SERUM FACTOR B & INFECTION IN IDIOPATHIC NEPHROTIC SYNDROME OF CHILDHOOD (INSC). D. Anderson, C. Smith, D. Kaufman and T. York, Depts. of Anatomy & Human Development, Mich. State University (Spons. by M. Bailie), East Lansing, Michigan.

The increased incidence of severe systemic infections in INSC secondary to bacteria with polysaccharide capsules suggests a defect in serum complement activity relating to chemotactic activity. Chemotactic function was assessed in INSC during 1)"severe" relapse, 2) "mild" relapse, & 3)"remission" with respect to A) chemotactic activity generated by INSC sera (±zymosan activation) B)chemotactic responses of INSC PMNs to control sera, & C)inhibitory effects of INSC sera and/or plasma on control PMNs (modified Boyden method). Serum chemotactic activity in 14 "severe" relapsing INSC patients was diminished compared to controls ($p < 0.01$) and 21 "mild" and "remission" patients ($p<0.001$). Chemotactic activity of zymosan activated sera was diminished compared to controls and to "mild" or "remission" states ($p<0.025$). Decreased serum chemotactic activity was related to occurrence of systemic bacterial infection, and decreased serum Factor B and albumin values. Serial determinations in "severe" cases demonstrated increasing chemotactic activity, serum Factor B & albumin associated with a positive response to treatment and return to clinical remission. Normal chemotactic responses of patient PMNs to control sera (±zymosan) were shown in all patient groups, and patient sera did not inhibit chemotactic function of control PMNs. These findings suggest that bacterial infection in INSC may be causally related to impaired serum chemotactic activity related to an abnormality of properdin pathway complement activation.

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PROTEIN BINDING AND PHARMACOKINETIC DISPOSITION OF FUROSEMIDE (F) IN NEWBORN INFANTS. Jacob V. Aranda, Jorge Perez, Daniel Sitar, Judi Collinge, Ana Portuguez-Malavasi, Claire Dupont. McGill University-Montreal Children's Hosp. Depts of Ped, Pharmacol and Therap, Montreal, CANADA.

The pharmacokinetic disposition of F was studied in 8 premature and full-term neonates with fluid overload using a one compartment model. Mean (±S.E.) birth weight was 2391.3 ± 289.9 g; gestational age was 35.0 ± 1.8 wks and postnatal age was 11.5 ± 5.9 days. BUN was 10.4 ± 1.5 mg/dl and serum creatinine was 0.9 mg/dl. Following a single IV dose of F, (1-1.5 mg/kg) blood samples (0.2 ml/sample) were obtained from a heelstick or an arterial catheter at times 0, 0.5, 1,2,4,6,9,12 and 24 hrs and analyzed for F, measured by gas liquid chromatography. The mean (±S.E.) volume of distribution was 829.2 ±118.9 $ml.kg^{-1}$; $T_{\frac{1}{2}}$ was 7.7 ± 1.0 h; elimination rate constant (Kel) was 0.102 ± $0.013h^{-1}$ and plasma clearance was 81.61 ± 14.98 $ml.kg^{-1}.h^{-1}$. Compared to the disposition of F in normal adults, aV_d is almost 4-fold greater in the neonate with an 8-fold prolongation in plasma $T_{\frac{1}{2}}$, an 8-fold decrease in Kel and a 2-fold decrease in plasma clearance. Neither gestational and postnatal age nor birth weight correlated with the pharmacokinetic variables. F had no effect on the reserve bilirubin binding capacity (RBBC) measured by sephadex-gel filtration in 6 neonates (age 2.1 ± 0.3 d; weight 2329.9 ± 339.1 g). Mean RBBC 5 min before and 30-60 min after F were 6.2± 0.2 and 6.8 ± 0.5 mg/dl respectively. Slow F elimination may partly explain the prolonged diuretic and saluretic effect of F in the neonate. This must be taken into account whenever repetitive or chronic administration of F is used in the newborn infant.

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EFFECTS OF CHANGING PLASMA VOLUME (PV) AND OSMOLARITY (Posm) ON SODIUM EXCRETION BY THE NEONATAL KIDNEY. Billy S. Arant, Jr., (Spon. by James N. Etteldorf), Univ. of Tenn. Ctr. for Health Sciences, Dept. Peds., Memphis.

The developing kidney has been reported to have a limited capacity compared to the adult to excrete an acutely administered sodium load. Studies to date have presumed that the sodium administered is filtered and reabsorbed by the nephron. Preliminary studies of human infants in our laboratory indicated that fractional sodium excretion(FE_{Na}) varied with Posm and with fractional urine flow (V/GFR). The present study was designed to compare renal sodium excretion in puppies during the first month of life for 2 hours following IV saline loading(10ml/kg) given as (A) 0.9% saline(NS), (B) 10% albumin/NS or (C) 10% glucose/NS. Results are presented from studies completed to date as mean per cent changes from control values.

	n	ΔPV	ΔECFV[1]	ΔGFR	ΔV/GFR	ΔFE_{Na}	Load/excretedx100 Volume	Sodium
A	8	-11	+4	+55	+302	+242	40.4	29
B	10	+35	+7	+3	+342	+846	230	225
C	11	+15	+10	+15	+940	+1136	318	120

[1]extracellular fluid volume

It is concluded that following saline loading in the neonate, Na is distributed mainly in the expanded ECFV and less Na is presented to the kidney for excretion in the decreased PV. However, the neonatal kidney is capable of excreting a Na load when PV is preserved or increased with albumin or glucose.

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SECRETION OF ACTIVE AND INACTIVE RENIN BY THE DEVELOPING KIDNEY. Michael D. Bailie, Franz Derkx, and Martin A.D.H. Schalekamp. Erasmus Univ., Rotterdam, Netherlands and Michigan State Univ., East Lansing, Michigan.

We have determined the concentration and secretion of active renin (ARC and ARS) and the acid-activated form of inactive renin (IRC and IRS) in anesthetized pigs between the ages of 3 and 57 days. IR was activated by dialysis of plasma at pH 3.3, and angiotensin I was estimated by radioimmunoassay. Both AR and IR were found in plasma of newborn and adult animals. ARC decreased from 4 ± 1 (sem) to 0.6 ± 0.1 ng/ml between 3 and 57 days while IRC declined from 11 ± 3 to 3 ± 1 ng/ml. However, ARS and IRS were unchanged during this time (ARS = 12 ± 5 and 8 ± 4 ng/min and IRS = 31 ± 16 and 55 ± 23 ng/min at 3 and 57 days, respectively). Isoproterenol significantly increased ARS and IRS at all ages. Intravenous furosemide also stimulated secretion of both forms of renin, while propranolol and indomethacin suppressed secretion. ARC as a percentage of the total renin concentration was the same in simultaneously drawn arterial and renal venous plasma. However, AR represented 31 ± 2% of total renin at 3 days and decreased to 20 ± 4% at 57 days. We conclude 1) IR is present in the newborn pig; 2) IRC and ARC decrease with age; 3) changes in IRC and ARC with age may be related to metabolic clearance of renin; 4) control of ARS and IRS are qualitatively similar at different ages. No evidence for systemic activation of IR was found. The change in proportions of AR and IR in plasma may be related to changes in intrarenal storage of renin.

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IMMUNE RESPONSE IN UREMIC AND POST-TRANSPLANT CHILDREN. Beale, Mary G., Hoffsten, Philip E., and Robson Alan M. Washington Univ. School of Medicine, Dept. of Pediatrics, St. Louis Children's Hospital, St. Louis.

Patients with chronic renal failure and renal allograft recipients have an increased incidence of infection. To define further the defect(s) in immune surveillance, children with chronic uremia, those on maintenance hemodialysis and those with well-functioning renal transplants were studied. Serum IgA, IgG and IgM levels, measured as an indicator of B-cell function, were reduced in all three groups. Intrinsic lymphocyte function was assayed by culturing patient cells in normal pooled plasma and stimulating them with phytohemagglutinin (PHA) or pokeweed mitogen (PWM). Mitogenic activity varied widely within each group but mean values were normal. The presence of an extrinsic inhibitor of lymphocyte activity was examined by culturing normal cells in patient plasma, again stimulating with PHA or PWM. Uremic plasma did not inhibit normal cell response to either PHA or PWM, but both pre- and post-dialysis plasma was markedly inhibitory. Plasma from transplant patients inhibited PHA response but not PWM response. Thus, uremic and transplant patients demonstrate a functional defect in B-cell activity. Although lymphocytes from these patients respond normally to mitogenic stimuli, plasma from dialysis (but not uremic patients) inhibits the mitogenic response of normal lymphocytes. Our data indicate that chronic hemodialysis affects humoral factors which influence lymphocyte activity. Immunosuppressive agents may contribute to the inhibition observed in transplant patient plasma.

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ANGIOTENSIN-I-CONVERTING ENZYME(ACE)ACTIVITY IN TERM AND PRETERM INFANTS. John W. Bender, Mary Kate Davitt and Pedro A. Jose. Georgetown Univ. Sch. of Med., Georgetown Univ. Hospital, Dept. of Pediatrics, Washington, D.C.

ACE is a carboxypeptidase whose activity includes conversion of angiotensin I to II and inactivation of bradykinin. The elevated ACE reported in infants with idiopathic respiratory distress (IRD) may reflect pulmonary immaturity. To evaluate the role of ACE on pulmonary vascular maturity, serum ACE levels were measured in cord and peripheral blood samples in 21 term and 21 preterm infants. ACE was measured spectrophotometrically using hippuryl-histidyl-leucine as substrate. Cord ACE activity(units/ml)was significantly higher($p<0.005$)in preterm(26.82±1.35 SE) than term infants(18.98 ± 1.43). There was a significant correlation between gestational age and cord ACE, best described as a parabola. From 27-34 wks, ACE activity decreased slowly; after 35 wks, a rapid decline in ACE was noted. ACE activity in peripheral blood during the first 24 hrs was also higher in preterm than term infants but values were similar among preterm infants, maternal and adult controls. Cord ACE in preterm infants who developed IRD(27.71 ± 1.89) was similar to preterms who remained healthy(26.27 ± 1.90). Cord ACE levels may not be used to predict the infant who will develop IRD. However, cord ACE may serve as an additional marker for pulmonary ontogenesis.