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CONTRIBUTIONS OF PLASMA, SERUM AND RED BLOOD CELLS (RBC) TO VICOSITY REDUCTION OF BLOOD FROM TERM AND PRETERM INFANTS STUDIED IN NARROW TUBES

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In blood vessels and in artificial tubes with diameters of less than 500 µm blood viscosity decreases with decreasing tube diameter (Fahraeus - Lindqvist effect). For RBC-buffer suspensions this effect is stronger for neonatal than for adult RBC.(Pediatr.Res.25:595,1989) In the present investigation we studied the effect of autologous plasma, adult plasma and serum on the viscosity of RBC from 10 adults, 10 term and 10 preterm infants. The hematocrits of the samples were adjusted at 20, 40 and 60 %. Glass tubes with diameters of 270, 100 and 55 µm were perfused with these suspensions.The table shows the viscosity reductions for RBC suspensions with a hematocrit of 60 % when going from 270 to 55 µm tubes.

Suspending medium	Adult	Term	Preterm
Autologous plasma	-34.73	-37.55	-41.39
Adult plasma	-34.84	-38.50	-41.21
Serum	-33.22	-39.11	-41.21

At a given feed hematocrit there was no difference in viscosity reduction among the suspension media in the three age groups. We conclude that differences in Fahraeus-Linqvist effect among adults, term and preterm neonates are due to specific properties of RBC and independent of plasma properties.

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PLASMA VISCOSITY IN POLYCYTHAEMIC NEWBORN INFANTS.

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Polycythaemia in newborn infants may lead to a variety of clinical symptoms, probably as a result of impaired blood flow. Besides haematocrit (Hct), plasma viscosity (PV) is an important determinant for blood viscosity. We studied PV in 46 polycythaemic (mean Hct 72%, range 65-80) newborn infants. Fifteen were preterm, 12 small for gestational age (SGA), and 19 appropriate for gestational age (AGA). A control group (mean Hct 58%, range 52-64) consisted of 42 newborn infants. PV was measured using a capillary tube viscometer. Polycythaemic infants had a significantly ($p< 0.05$) lower PV level [1.060 (range 0.950-1.230)m Pa.s] than control infants [1.120 (range 0.960-1.540)m Pa.s]. Preterm polycythaemic and control infants had significantly lower PV levels than SGA and AGA polycythaemic and control infants. Thirty-three (71.7%) polycythaemic infants had clinical symptoms. The PV level in the group with clinical symptoms was significantly ($p< 0.05$) higher [1.067 (range 0.985-1.230)m Pa.s] than in the group without clinical symptoms [1.013 (range 0.950-1.183)m Pa.s]. We conclude that 1) PV in polycythaemic newborn infants is lower than in control infants, and 2) clinical symptoms seem to be associated with a combination of polycythaemia and higher PV.

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ATRIAL NATRIURETIC PEPTIDE (ANP), RENAL FUNCTION, AND PDA IN PRETERM INFANTS

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In the neonate, the role of ANP in the regulation of fluid balance is not clear. We assessed the relation of ANP in preterm infants to renal function and PDA on days 2 and 5. P-ANP was measured by RIA; G1 (<30 wk, n=11) and G2 (30-34 wk, n=12). PDA was assessed on day 2. P-ANP was higher in G1 than in G2 ($p<0.01$) and decreased by day 5 ($p<0.02$). A negative correlation between P-ANP and GA was found (day 2: $r=-0.54$, $p< 0.01$; day 5: $r=-0.45$, $p<0.05$). No correlation between P-ANP and C_{Cr} or $U_{Na}V$ was found. Infants with PDA had higher P-ANP than infants without PDA in G1 ($p<0.02$), but not in G2. Preterm infants are able to release huge amounts of ANP postnatally. The high P-ANP concentrations seen postnatally do not directly correlate to the renal regulation of sodium and water balance.

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PROSTACYCLINE - AN ALTERNATIVE TO ECMO IN THE TREATMENT OF PULMONARY HYPERTENSION

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Severe pulmonary hypertension (PH) of the newborn with mortality at or above 80% is an accepted indication for ECMO. We treated 30 term neonates with severe PH fulfilling ECMO criteria with prostacycline (PC). Mean gestational age was 39+4 wk (range 35-42+6), mean birth weight 3.42 kg and mean 1 min Apgar score 5.3. Before treatment paO_2/pAO_2 was 0.064 (0.03-0.14), and $A\text{-}aDO_2$ was 643 mmHg (596-658) and all received domapine. PC (10-200 ng/kg/min) was started at a mean age of 28.6 hr (range 2.8-87). Oxygenation improved usually within minutes. Mean duration of PC was 3.4 days, and extubation age 8 days (1.8-16). The main side effect was hypotension, easily controlled by pressors. Four children died at 1-3 days of age (2 asphyxia, 1 pneumothorax, 1 pneumonia). Only 3 of the 26 surviving infants had minor neurological or pulmonary sequelae. Prostacycline should be considered as an alternative to ECMO in severe PH.

DEVELOPMENTAL/NEUROLOGY/FOLLOW-UP

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CYTOSINE ARABINOSIDE INDUCES NEUROBLAST DIFFERENTIATION.

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In the last few years we have been able to produce a large body of evidences that ARA-C is capable of inducing neuronal differentiation of human neuroblasts in vitro. Three different human neuroblastoma (NB) cell lines have been tested with ARA-C, LAN-1, LAN-5 and GI-ME-N. ARA-C actually modifies both surface and cytoskeleton markers' expression while inducing substained morphologic differentiation of all three NB cell lines. Specifically, ARA-C induces concentration- dependent growth inhibition, neurite sprouting, and neurofilaments expression in GI-ME-N cells, while decreasing the level of membrane antigens specific for neuroblast cells. The maximum effect was obtained using a dose as low as 0.1 mg/ml. Similar modifications were recorded inducing both LAN-1 and LAN-5 human NB cells with ARA-C. The fact that ARA-C treatment of human NB cells started one day after plating with no subsequent decrease in cell viability in the cultures, strongly suggests that its effects were not the result of selection of more differentiated cells by differences in plating efficiency or ARA-C cytotoxicity. This conclusion was supported by time-lapse photomycroscopic observations, which clearly showed individual ARA-C treated NB cells undergoing morphologic differentiation.

The results rise the suspicious that the interpretation of ARA-C mechanisms of action on P19 carcinoembrional cells is oversemplicistic. We actually do not thing that "...one can selectively enrich for neurons by treating the induced culture with the anti/metabolyte ARA-C" as suggested by Chung JJM et al. (Cell 64, 189-200, 1991).

In fact, as previously demonstrated by our group, ARA-C is not only capable of arrest the overgrowing of non-neuronal cells, but is actively capable of pushing neuroblast cells along the neuronal differentiation pathway.

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INTRAUTERINE VERSUS EXTRAUTERINE MATURATION OF AUDITORY EVOKED RESPONSES (BMC ARs).

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Brainstem (ABR), Middle Latency (MLR) and Cortical (ACR) Auditory Responses were studied in 65 healthy preterm and 25 healthy term infants at 40 weeks conceptional age (CA) and at 52 weeks CA in order to establish the differences between intrauterine and extrauterine maturation of BMC ARs. The latencies of the ipsilateral ABR components I, II, V and the contralateral ABR components IIc and Vc at 40 and 52 weeks CA showed no significant differences between preterm infants and term infants, although in preterm infants a consistent tendency towards longer latencies was found. The latency of MLR component P0 was significantly longer in preterm infants compared to term infants, whereas MLR component Na showed no significant latency differences. The most interesting findings are related to the latency differences of the ACR components between term infants and preterm infants. At 40 weeks CA the latencies of components Na, N1 and P2 were significantly shorter in preterm infants, whereas at 52 weeks CA these latencies were significantly longer in preterm infants. Further, it was notable that at 40 and 52 weeks CA there was a striking difference in ACR wave form between preterm infants and term infants. At 40 and 52 weeks CA in preterm infants ACR wave form showed a less mature than in term infants, whereas term infants show a more mature wave form.