

**ENDOTHELIN-1 (ET-1) IS A CIRCULATING HORMONE IN NEWBORN PRETERM AND TERM INFANTS.** Henrik Ekblad, Olli Arjamaa, Olli Vuolteenaho, Pekka Käähä and Pentti Kero. Department of Pediatrics, University of Turku, Turku and Department of Physiology, University of Oulu, Oulu, Finland.

Endothelin-1 (ET-1) is an endothelium-derived vasoconstrictor peptide. Animal studies have suggested a possible role of ET-1 in alveolar hypoxia. ET-1 may be of pathophysiological significance in the fetal as well as in the maternal circulation in pregnancies complicated with hypertension. ET-1 has been shown to induce a dose-related constriction in vitro of strips of ductus arteriosus from mature fetal lambs. It has also been shown to contract human umbilical vessels at extremely low concentrations. Its role in the newborn infant is not known.

In the present study we measured plasma ET-1 levels in preterm and term infants soon after birth as well as in healthy infants and children of different ages. ET-1 was determined by a commercial radioimmunoassay kit (RIK 6071, Peninsula Laboratories Europe Ltd).

The plasma levels of ET-1 were as follows (mean, range, pg/ml): preterm (<24 h) 26.8, 11.6-49.2 (n=9); term (<24 h) 19.9, 10.0-39.9 (n=10); 3 mo to 1 y 14.8, 10.2-26.6 (n=13); 2 y to 15 y 8.2, 2.9-16.7 (n=29). Preterm and term infants have relatively high plasma ET-1 levels. In the newborn infant ET-1 is a circulating hormone with possible physiological and pathophysiological roles.

**FETAL HAEMOPOIETIC RESPONSES TO INTRAVASCULAR TRANSFUSION** Graham Stewart, John Kingdom, Martin Whittle, Barbara Holland. Departments of Child Health and Midwifery, University of Glasgow, Scotland.

Intravascular transfusion therapy (IVT) is the accepted treatment for severe rhesus iso-immunisation. The timing and frequency of IVT is controversial, and is currently based on change in fetal haematocrit (Hct). The aims of this study were to measure fetal erythropoietin concentration (EPO), haematocrit and red cell volume following serial (IVT) and to study their inter-relationship as anaemia is corrected.

**Methods & Results:** Twelve pregnancies were studied with serial data in 4 cases. Pre-transfusion fetal EPO correlated inversely with Hct (R2 31%; p = .004) and fell significantly between IVT 1 and IVT 2 (314 to 31 mU/ml: mean values). Hct fell between IVT1 and IVT 2 (35 to 25% : mean values n=4). Neither fetal, or donor red cell volumes fell during this time, though circulating fetoplacental blood volume increased (179 to 357 mls: mean values n=4).

**Conclusions:** Fetal EPO is inversely related to Hct, and is suppressed by IVT through increases in total red cell volume. The fall in Hct between IVT 1 and IVT 2 is due to the physiological increase in fetoplacental blood volume rather than destruction of transfused red cells.

**CORRELATION OF PACKED CELL VOLUME (PCV) WITH RED CELL MASS (RCM): VARIATION WITH POST-NATAL AGE AND BLOOD VOLUME IN PRETERM NEONATES.** Alison Bedford Russell and Rodney PA Rivers Dept. Paediatrics, St. Mary's Hospital Medical School, London W2.

Reliance is widely placed on PCV to indicate blood transfusion requirements of neonates, although poor overall correlation between PCV and RCM has been demonstrated (Lancet. 1:882-4, 1986). The aim of this study was to investigate the relationship between PCV and RCM with increasing post-natal age (PNA) and with estimated baby total blood volume (TBV).

Pre-transfusion RCM and PCV were measured in 16 babies of 24 to 35 weeks gestation, receiving a total of 36 blood transfusions. Circulatory RCM was estimated using dilution of haemoglobin F by transfused red cells. TBV was calculated from the RCM divided by the measured PCV.

PCV correlated poorly with RCM in 9 babies studied on 17 occasions in the first 5 days PNA (r=0.152). In 7 babies studied on 13 occasions after 10 days PNA, correlation was good (r=0.820). Correlation was intermediate (r=0.629), in 5 babies studied on 6 occasions on days 6-10. At all ages, correlation of PCV with RCM was greatest in babies with a TBV in the range 70-90 ml/kg (r=0.827; n=14), compared to those with a TBV above or below these values (r=0.580; N=22).

In conclusion PCV is a particularly poor gauge of RCM in preterm infants in the first 5 days of life and when total blood volume is not in the range 70-90 ml/kg.

**AN INNOVATIVE METHOD FOR NEONATAL AUTOLOGOUS TRANSFUSION.** Robert A. Dracker, Kevin Lorah, Anuradha Palit, and Ellen M. Bifano. SUNY-Health Science Center, Departments of Pathology and Pediatrics, Syracuse, New York

During the first month of life, the majority of very low birthweight infants require multiple transfusions, thereby repeatedly exposing them to the risks of the administration of homologous blood. Autologous transfusions minimize the risks of transfusion related infections and alloimmunization. We have developed a novel system for the "closed" aseptic collection and storage of autologous placental blood in sterile bags containing the anticoagulant, citrate phosphate dextrose-adenine.

**Results:** Of 29 collections from placentas of vaginal and C-section deliveries, the average volume of blood collected was 76 cc (range 55-110 cc) over 1.5 min (range 1-2 min). Adequate anti-coagulation was achieved in all samples as defined by an APTT >90 sec. Over a four week storage period at 4°C, there was no significant intrasample decline in hemoglobin concentration (0.4±0.4 g/dl; mean change ± sd), red blood cell ATP content (0.1±0.6 µm/g), change in P<sub>i</sub> (0.1 mmHg±0.1), increase in hemolysis 0.1±0.1%, or change in red cell morphology (3±1% echinocytes). Surface cultures were positive in 2 of 29 swabs prior to preparation of the cord. All placental surface cultures taken after cord preparation as well as anaerobic and aerobic blood cultures remained negative over the four week storage interval.

**Conclusion:** This study demonstrates the feasibility of collecting and storing placental autologous blood for transfusions in neonates.

**MULTIPLE BLOOD TRANSFUSIONS INDUCE ANTI-HLA ANTIBODY FORMATION IN PRETERM INFANTS.** Alison R Bedford Russell, Rodney PA Rivers\*, Nicholas Davey\*\*. Dept Child Health, St George's Hospital Medical School Cranmer Terrace, London SW17 0RE.\* St. Mary's Hospital, London W2. \*\* Dept. of Immunology, Hammersmith Hospital, London W12.

Leucocyte antigens in whole blood may induce antibody formation in multiply transfused individuals (Human Pathology. 26:228-234, 1980). Babies receiving whole blood transfusions might also produce antibodies to leucocyte antigens eg HLA, although in a previous study of 13 multiply transfused infants no such antibodies were detected (Transfusion 26:419-22, 1986).

Fifty-seven neonates <37 weeks gestation, requiring >2 blood transfusions were studied prospectively for the development of anti-HLA antibodies (aHLAA) after randomisation to receive either whole blood or blood transfused via a leucocyte filter.

Anti-HLAA were measured in Maternal and cord blood and 1ml samples drawn monthly until discharge from hospital. Detection was by lymphocytotoxicity microtitre assay.

Results were obtained in 42 babies, 19 in the filter and 23 in the no-filter group. 15 babies were excluded because of preterm violation or death. No baby receiving filtered blood developed aHLAAs, but 7 babies in the no-filter group developed aHLAAs (p=0.0182, Fisher's exact test).

In conclusion, multiply transfused preterm infants can produce antibodies to HLA, and leucocyte filters may prevent this.

**IRON SUPPLEMENTATION ENHANCES THE RESPONSE TO HIGH DOSES OF RECOMBINANT ERYTHROPOIETIN IN PREMATURE INFANTS.**

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**Introduction:** We have recently reported that early administration of high doses of EPO (1200 IU/kg/wk) in association with iron are effective in reducing blood transfusions in premature infant, although the role of iron supplements during EPO therapy in low birth weight infants is still controversial.

**Aims:** To demonstrate the effect of iron supplements (20mg/kg/wk IV) on the erythropoietic response of premature infants of gestational age (GA) less than 33 weeks and birth weight (BW) less than 1.75 kg receiving prophylactic administration of high doses of EPO (1200 IU/kg/wk).

**Patients and study design:** 36 infants randomly assigned to receive EPO (n:12, BW 1.26±0.26kg, GA 29.3±2.0wk) EPO+IRON (n: 10, BW 1.30±0.29kg, GA 29.6±2.1wk) or no EPO and no iron= CONTROLS (n: 14, BW 1.29±0.23kg, GA 29.4±2.3wk) have completed the study to the present.

Results:	N Transfusions <sup>§</sup>	Hematocrit <sup>°</sup>	Reticulocytes <sup>°</sup>	Ferritin <sup>°</sup>
CONTROLS	3.7±2.0 <sup>§</sup>	42.1±3.3 <sup>°</sup>	0.9±0.5 <sup>°</sup>	720±580 <sup>°</sup>
EPO	1.3±1.9 <sup>°</sup>	41.0±3.1 <sup>°</sup>	3.7±0.8 <sup>°</sup>	32±42 <sup>°</sup>
EPO+IRON	1.0±1.9 <sup>°</sup>	44.7±3.5 <sup>°</sup>	5.9±0.5 <sup>§</sup>	815±470 <sup>°</sup>

<sup>§</sup> data refer to the hospital stay, <sup>°</sup> mean values of weekly determinations from the fourth to the eighth week. Different superscripts indicate differences at a p level less than 0.05.

**Conclusions:** 1) Early administration of high doses of EPO with or without iron supplements reduces the need for blood transfusion. 2) Iron supplement in conjunction with EPO does not further reduce blood transfusions but yields higher reticulocytes and hematocrits after the fourth week of life. 3) Infants treated with EPO alone show signs of reduced iron stores.