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THE EFFECT OF NIMODIPINE ON LEFT VENTRICULAR FUNCTION AND HEMODYNAMICS IN THE NEWBORN LAMB. Marcel JJ Albers, Frank van Bel, Robert JM Klautz, Paul Steendijk, Jaap Ottenkamp, Jan Baan. Dept. of Pediatrics and Cardiology, Univ. Hosp. Leiden, The Netherlands.

The calcium-channel blocker Nimodipine (Nimo) may mitigate birth asphyxia-induced brain damage. Many calcium-channel blockers negatively affect left ventricular function (contractility, cardiac output [CO]) and lower blood pressure. Nimo-treatment in asphyxiated newborns may be precluded because of the combination of poor post-hypoxic heart function and cerebral autoregulation. In 8 vagotomized newborn lambs we investigated left ventricular (LV) function and systemic hemodynamics before and shortly after Nimo administration (20 ug/kg/iv). LV contractility and CO were assessed by measuring LV pressure (tip-manometer) and volume (conductance catheter), using inferior caval vein occlusion to obtain slope (Ees) and volume-intercept (V_{10}) of the end-systolic pressure-volume-relationship.

Results: LV-contractility decreased significantly as shown by a decrease in Ees, but CO did not significantly change. Mean blood pressure (MBP), systemic vascular resistance (SVR) and heart rate (HR) decreased.

after vs before Nimo	Ees	CO	MBP	SVR	HR
% change ± SD:	-32 ± 26*	-1.6 ± 19.8	-50 ± 6*	-45 ± 7*	-11 ± 8

*p < 0.05 (paired *t*-test)

Conclusion: Nimo affects LV function and lowers blood pressure in the newborn lamb.
Suggestion: Nimo should be used with caution in the asphyxiated newborn, because the combination of impaired cerebral autoregulation and suboptimal LV function with low systemic blood pressure may aggravate brain damage.

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CONTROLLED CARDIAC REOXYGENATION REDUCES NITRIC OXIDE (NO) PRODUCTION AND OXIDANT INJURY OF HYPOXEMIC INFANT HEARTS. Michael P. Sherman, Gerald D. Buckberg, Kiyozo Morita, Kai Ihnken, and Louis J. Ignarro. Depts. of Pediatrics, Surgery, and Pharmacology. University of California, UCLA Medical Center, Los Angeles, California, U.S.A.

Cardiopulmonary bypass (CPB) is used increasingly to correct cyanotic heart defects during early infancy, but myocardial dysfunction is often seen after surgical repair. This study evaluates whether starting CPB at a conventional, hyperoxic pO_2 causes an uninattended reoxygenation (ReO_2) injury. We subjected 2-week-old pigs to ventilator hypoxemia [FIO_2 = 0.06 & pO_2 = 25 mmHg] followed by 5 min of ReO_2 on CPB before instituting cardioplegia. CPB was begun in hypoxemic piglets by either abrupt ReO_2 at a pO_2 of 400 mmHg [standard clinical practice] or by maintaining a pO_2 = 25 mmHg on CPB until controlling ReO_2 with blood cardioplegic arrest at a pO_2 = 400. Myocardial NO production [chemiluminescence measurements of NO_2^- + NO_3^- in aortic and coronary sinus blood] and conjugated diene (CD) generation [spectrophotometric A_{233} measurements of lipid extracts of blood] were assessed during cardioplegic induction. Thirty min after CPB, left ventricular end-systolic elastance [Ees, catheter conductance method] was used to determine cardiac function. CPB and blood cardioplegic arrest caused no functional or biochemical change in normoxic (control) versus hypoxemic hearts. Abrupt ReO_2 caused a 10-fold rise in NO and CD production by the heart with subsequent depression of myocardial function (Ees = 21±2% of control). In contrast, controlled cardiac ReO_2 reduced NO production by 50%, CD did not rise, and Ees was 83±8% of normal. We conclude controlled ReO_2 when starting CPB to correct cyanotic heart defects may improve myocardial status post-operatively.

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MONITORING CARDIAC FUNCTION IN CHILDREN DURING AND AFTER DOXORUBICIN THERAPY. Cristina Azcona, Jesús García-Foncillas, Carmen Villaizán, Pasual Barona, María J García-Velloso, José Richter, Luis Sierrasesúmaga. Dept. of Pediatrics. University Hospital. University of Navarra. Spain.

In order to study doxorubucin cardiotoxicity in children affected of malignancies and treated with polychemotherapy without mediastinal radiotherapy, we have assesed cardiac function in 59 children, mean age 16 years (range: 5 to 20 years; 33 males, 24 females) who have received a mean doxorubicin dosage of 340 mg/m^2 (range: 123,5 to 800 mg/m^2), performing serial radionuclide angiocardiographies (RNA) at rest and exercise during and after chemotherapy. The following parameters were studied by RNA: left ventricular ejection fraction (LVEF), LVEF in the first third of the cardiac cycle, as well as the emptying and filling Maximal Rate (e/f-Max Rate), Average Rate (e/f-Avg Rate) and Time to Peak (e/f-T-P). 20 patients have been followed after completion therapy during a mean period of time of 13.6 months (range 3 to 26.4 months). Multivariate Cox model analysis was used to evaluate the doxorubicin cardiotoxicity by RNA. At cumulative dose ranging from 320 to 420 mg/m^2 LVEF at 50% exercise and the emptying and filling Max Rate at 25% exercise decreased significantly (p=0.041, p=0.047 respectively). With doxorubicin dosage greater than 420 mg/m^2 we have found statiscally significant differences in the following parameters: LVEF at rest, 25 % and 50% exercise (p=0.0301, p=0.028 and p=0.032), e/f-Max Rate at rest (p=0.0417, p=0.038) and 25% exercise (p=0.033, p=0.045), e/f-Avg Rate at rest (p=0.042, p=0.031); and e/f-T-P at rest (p=0.037, p=0.038). No changes have been found in these results during a follow-up of 15 months that indicate an improvement in cardiac function.
Serial assesment of LVEF, e/f-Max Rate and e/f-Avg Rate by RNA during doxorubicin therapy may anticipate the diagnosis of congestive heart failure.

CONGENITAL MALFORMATIONS

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MAINZ CONGENITAL BIRTH DEFECT MONITORING SYSTEM
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The two most important aims of the Mainz Congenital Birth Defect Monitoring System were to find "incidence" rates and to look for etiological causes of congenital malformations. All babies born in Mainz underwent a standardized physical and sonographic examination. Anamnestic data of family history, enviromental factors, drug exposure etc. were collected. Using case controll studies we looked for special correlations between morphologic defects and anamnestic data as factors of risk. The relative risk was calculated as odds ratio. Results: In 1990 and 1991 we examinated 8430 newborns. 656 (7,8%) children had major and 2609 (31,1%) minor malformations. Systemic localisation of major defects: Skeletal 2,6%, urogenital 1,8%, cardiovascular 1,3%, nervous 0,6%, digestive 0,5%, chromosomal anomalies 0,3% and others 0,6%. Localisation of minor defects: Simian crease 3,9%, Darwinian tubercle 3,8%, facial haemangioma 3,2%, auricular tag 3,0%, haemangioma 2,7%, auricular pits 2,3% and others 12,2%. Increased relative risks (odds ratios) were found for following factors: Sibling (2,4*)/parent (1,4) with major malformation, alcohol abuse (2,3), medication (1,8*) during pregnancy, consanguinity (1,8), diabetes mellitus (mother; 1,7), placental insufficiency (1,4) etc. (*:statistically significant).
Conclusions: The Mainz Congenital Birth Defect Monitoring System is able to find regional "incidence" rates and represent a further step in the search for new etiological factors. More patients and a longer study period is necessary for in depth evalution. Comparisons with other regional monitoring systems are required.

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TERATOGENIC EFFECTS IN A CASE OF MATERNAL TREATMENT FOR ACUTE LYMPHOBLASTIC LEUKEMIA (ALL)
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Acute lymphoblastic leukaemia (ALL) was diagnosed in a 36-year-old and treated with cytarabin, daunorubicin, doxorubicin and cytarabin, thioguanin, respectively, in an unrecognized pregnancy at conception and at about 35-37 days p.c.. Amniocentesis at 16 weeks of gestation revealed a normal female karyotype.
At delivery, brachycephaly, hypoplasia of supraorbital bony structures and hypotelorism were seen. Hypoplastic nasal root, bilateral choanal atresia and micrognathia caused hypoplasia of naso- and oropharynx. There was also bilateral aplasia of the radius and hypoplasia of the first ray of the hands. Internally, an atrial septal defect II could be demonstrated. The malformations detected are in accord with the timing of teratogenesis. Neurodevelopment is normal at the age of 8 months. Experience with the use of cytotoxic drugs in pregnancy has so far been limited to folate antagonists.

DEVELOPMENTAL NEUROLOGY

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PARENTAL PERCEPTIONS OF VERY LOW BIRTHWEIGHT SURVIVORS' (VLBW) ABILITIES AT 8-10 YEARS OF AGE.
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As part of a population based study the parents of 124 VLBW [<1500g] survivors in mainstream schools, and age/sex matched classmate controls, were asked to assess their children's abilities including aspects of school performance, and objective test scores [BAS and TOMI]. There were significant differences in IQ [p=<0.001], reading [p=<0.02] and number [p=<0.002] age ratios and tomi scores [p=<0.001] between VLBW and control children with VLBW survivors performing less well throughout. The control children's parents' assessments were not significantly different to the teachers' but the VLBW children's parents significantly over-rated their children's performance in 6 of 12 areas assessed. When compared with objective measures the teachers of VLBW and control children were equally accurate in their prediction of overall school performance but the parents of the VLBW children were significantly less accurate than the teachers, or control children's parents. Interestingly however the VLBW parents had insight into their children's co-ordination but not their educational difficulties. Even at 8-10 years of age the VLBW children's parents over-estimate their children's abilities