

67

UTILIZATION OF OLEATE AND D-BETA-OH-BUTYRATE (BOHB) AS ALTERNATE ENERGY FUELS IN BRAIN CELL CULTURES OF NEWBORN MICE AFTER HYPOXIA AT DIFFERENT GLUCOSE CONCENTRATIONS. Emilio Bossi, Norbert Herschkowitz, Eva Kohler. University of Berne, Switzerland, Department of Pediatrics.

Can oleate and BOHB substitute for glucose as cerebral energy fuels after hypoxia? Oleate-U-14C or BOHB-3-14C were added to 7 days old cultures after 4 hours preincubation at 0 or 4 mM gluc under normoxia or hypoxia. During 3 hours of incubation of all cultures under normoxia, 14CO₂ was collected. Defining CO₂-production at 4 mM gluc as 100%, CO₂-production at 0 vs. 4 mM gluc was 156±40% in normoxia and 162±24% after hypoxia for BOHB, the corresponding values for CO₂-production from oleate were 218±66 and 261±50% (mean±1 SD, n=15-25, p 0 vs 4 mM gluc < 0.001). CO₂-production after hypoxia was compared with CO₂-production in normoxia both at 0 and 4 mM gluc (100%=CO₂-production under normoxia). After hypoxia, BOHB was significantly less converted to CO₂: 86±28% at 0 (n=15-20, p < 0.005), 86±38% at 4 mM gluc (n=19-21, p < 0.01). Oleate was also less converted to CO₂ after hypoxia at 4 mM gluc (87±34%, n=23-25, p < 0.01). At 0 gluc, however, CO₂-production from oleate was higher after hypoxia than in normoxia (112±46%, n=39-41, p < 0.005). In our system, oleate and BOHB are alternate cerebral energy fuels for glucose in normoxia and hypoxia.

68

CALORIMETRIC BIKINIS FOR THE UNHINDERED, LONGTERM ASSESSMENT OF DRY HEAT LOSS IN NEWBORN INFANTS. Georg Simbruner, Margit-Andrea Glatzl-Hawlik, University of Vienna, Children's hospital, Department Neonatology, Vienna, Austria.

Neither indirect nor direct calorimetry are suitable for assessing metabolic rate in each newborn infant *unhindered* for an *unlimited* period of time. As an alternative, metabolic rate could be assessed as the sum of components of the energy balance equation. Among those, dry heat loss (HL) is the most important component. We investigated, whether dry heat loss determined by 17 heatflux transducers (HL tot) was related to dry heat loss determined from 12 or 8 heatflux transducers and correction factors, a set-up nicknamed calorimetric bikini (HL-bik 12 or HL-bik 8). We studied twenty healthy newborns infants, attached five heatflux transducers to the head, six to the torso and six to the limbs of each infant and determined HL tot from the heatflux and the surface area, it represented, during a half hour period for prone and supine position respectively. The HL-bik 12 and HL-bik 8 correlated statistically significant with HL tot in the infants lying prone or supine (HL tot vs. HL-bik 12: $y = 0.01 + 0.99x$ (Watt/kg), $r = 0.97$, $p < 0.001$ and HL tot vs HL-bik 8: $y = 0.16 + 0.91x$, $r = 0.92$, $p < 0.001$). The mean and 1 S.D. of differences between HL tot and HL-bik 12 or HL-bik 8 were < 1% and < 6.5% of HL tot respectively. In conclusion, dry heat loss can be fairly accurately measured by a few calorimetric elements on the surface of the newborn infant and these calorimetric bikinis are a first step towards a method allowing unhindered monitoring of metabolic rate for an unlimited period of time.

69

FULLTERM NEWBORN INFANTS INCREASE THEIR RESPIRATORY WATER LOSS IN A WARM ENVIRONMENT. Karen Hammarlund, Tomas Riesenfeld and Gunnar Sedin. Uppsala University, University Hospital, Department of Pediatrics, Uppsala, Sweden.

It has not been known whether newborn infants can increase their respiratory water and heat loss when exposed to a warm environment in the same way as many animals can. In order to study this, continuous measurements of respiratory water loss (RWL), oxygen consumption and carbon dioxide production were made in 10 fullterm infants on their first day after birth. The infants were first studied in incubators with a temperature of 32.5 °C and an ambient humidity of 50%. After an interval with stable conditions the incubator temperature was raised to 36.5 °C while the water vapour pressure was kept constant. When body temperature had increased to 37.8 °C or when the infant had reacted with sweating the relative humidity in the incubator was increased to 50%. At the start of the measurements mean RWL was 4.7 mg/kg min. As a mean RWL increased to a maximal value of 6.5 mg/kg min in the warm environment. Mean oxygen consumption increased from 5.5 ml/kg min to 5.7 ml/kg min. This means that when nursed in this warm environment the infants were able to increase their respiratory water loss with around 40% without a significant change in oxygen consumption.

70

NUTRITION-INDUCED CHANGES IN INSULIN-LIKE GROWTH FACTORS (IGF'S) AND BINDING PROTEINS IN NEONATAL RATS. AF Philipps, K Drackenberg, B Persson, K Hall and V Sara. Univ. of CT Health Ctr, Farmington, CT USA and Karolinska Inst., Stockholm, Sweden

IGF's are potent hormones that may regulate perinatal growth and are found linked to high affinity binding proteins (BP's) in blood and tissues. To investigate the premise that caloric (cal) intake is a determinant of IGF/BP synthesis, 10d rats were milk deprived and given 24 hr infusions of saline (SAL), glucose (GLU), glucose/amino acids (GA), or glucose/amino acids (aa)/lipid (CAL). Acid chromatography was used to separate IGF's and BP in sera and liver cytosols. When compared to controls (CON), fasting (SAL) induced a marked decline ($p < 0.001$) in serum IGF-1 and 2 concentrations [IGF-1,2] as well as liver [IGF-2]. In addition, serum [IGF-2] but not [IGF-1] was restored in CAL rats to near CON levels. BP activity, as measured in untreated specimens by radioreceptor assay (RRA-IGF-2), rose 2-4x above CON in SAL serum and liver. Infusion of aa suppressed the changes in liver BP activity and in pooled data, liver BP was inversely related to serum aa but not to cal intake. Increased liver BP activity appears due to a 40,000 MW BP. In serum, BP activity was inversely related to cal intake but not to [aa]. The fasting induced rise in serum BP activity appears due to a BP of 180,000 MW. Fasting induced changes in IGF & BP may be a protective mechanism to depress growth during cal restriction.

71

NERVE GROWTH FACTOR - AN ENDOCRINE ROLE ? U. Stephani, A. Sutter, A. Zimmermann Universitätskinderklinik Göttingen (W.-Germany) Introduced by F. Hanefeld

Nerve growth factor (NGF) is a molecularly well characterized neurotrophic protein for certain peripheral and central neuronal populations. Further, studies on B- and T-lymphocytes, mast cells and macrophages indicate a function of NGF in immunological, inflammatory and neuroregenerative processes. We have analyzed NGF in serum (S-NGF). One- and two-site immunoassays primarily reflected the presence of NGF binding proteins in serum. However, with a sensitive *in vitro* assay employing embryonic sensory neurons as indicators of NGF bioactivity the presence of S-NGF could be demonstrated. In mice basal S-NGF values (10-50 pM) were independent of sex, age or presence of the submandibular gland. Analyses of S-NGF bioactivity in (pre)mature newborns, infants and older children revealed normal S-NGF levels of 20-100 pM NGF equivalents. The NGF bioactivity exhibited circadian periodicity. In an adolescent with multiple endocrine neoplasia syndrome IIb we observed S-NGF values up to 2 nM NGF equivalents. These data together with reports of the transcriptionally active NGF gene in the pituitary, the thyroid and parathyroid glands strongly suggest an endocrine role of NGF.

72

PROLIFERATIVE AND METABOLIC ACTION OF INSULIN IN A LEUKEMIC CELL LINE DURING THE CELL CYCLE W.Hartmann, R.Goßla and U.Vetter Dep.Pediatrics, University of Ulm, D7900 Ulm

Exponentially growing cells of a AML cell line were separated by counterflow elutriation into subpopulations representing G₀/G₁, S and G₂+M cells without disturbances of cellular metabolism. The separation was followed by DNA-flowcytometry. Specific binding of Insulin could be demonstrated with 20-25000 binding sites in G₀/G₁, 1000 - 2000 in S and 30-50000 in G₂/M cells. The affinity of Insulin binding remained constant over the cell cycle. The specificity could be demonstrated by crosslinking experiments. Glucose transport was stimulated by Insulin independently of the cell cycle. In contrast glycogen synthesis could only be stimulated by Insulin in the G₀/G₁ phase. Insulin stimulated G₁/S transit inducing proliferation and in addition the transit to G₂ and through mitosis was accelerated. It could be demonstrated that these neoplastic cells remained under metabolic control of Insulin which has additionally proliferative action. The cells became independent from classical growth factors.