79 PHYSICAL FITNESS, OBESITY AND ATHEROSCLEROTIC RISK FACTORS

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Treadmill stress testing was carried out according to the Bruce protocol on 43 control (C) and 25 obese (O) children of the same age. Body fat was 11.9+-0.8 and 37.1+-0.7% in C and O, respectively. Fasting plasma insulin (IRI),triglyceride and low density cholesterol (LDL-ch) levels were higher,high density cholesterol (HDL-ch) was lower in O compared to C ($p<0.05$). Exercise duration (ED) (C:749+-18.6, O:529+-22.2 sec) and physical working capacity (PWC-170/kg LBM) (C:3.5+-0.2, O:2.2+-0.2W/kg LBM) were decreased in the O ($p<0.001$).The relationship of anthropometric and atherosclerotic risk parameters (IRI and lipoprotein-ch classes) with the above fitness factors was investigated using multiple regression analysis. The relationship of blood pressure, ECG and atherosclerotic risk factors was also studied.The variation of ED was mainly influenced by rel.bw.(R=0.77) and by IRI and LDL-ch (R=0.7).LBM (R=0.53) and IRI and LDL/HDL-ch (R=0.59) accounted for the variation of PWC-170/kg LBM.It is suggested that beside body composition IRI level and LDL/HDL-ch ratio are important factors related to physical fitness.

80 VITAMIN SUBSTITUTION IN OBESE CHILDREN AND ADOLESCENTS DURING WEIGHT REDUCTION.

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In children and adolescents rapid weight reduction results in a considerable decline of serum vitamin A and E levels. In order to evaluate whether these "biochemical" vitamin deficiencies can be prevented by oral supplementation (30.000 IE vit A, 78.4 g/d vit E/d) we measured vit A, E and their transportproteins in 39 male obese children and adolescents: group I (n=20, mean+SD; 12.3+0.3 yrs, 68+12 % overweight) group II (n=19, 12.4+0.3 yrs, 71+10% overweight). Both goups received a hypocaloric diet (700 kcal/d), group II was vit supplemented. Vit.A and E were determined by HPLC, lipoproteins by ultracentrifugation and polyanionprecipitation. Weight loss after 3 weeks was 6.7+1.0 kg in I and 6.4+0.7 kg in II.

Results

mean+SD, mg/dl

	vitamin A	ß-carotine	vitamin E	LDL-C
I begin	449+90 *	228+110	8.8+2.1 *	154+23
I end	252+44	241+118	6.1+1.6	132+19
II begin	485+77 *	230+98	9.3+1.3	149+20
II end	259+60	236+84	9.0+2.5	131+23

* $p < 0.001$, (diff.begin and end) # $p < 0.001$, (diff.I and II)

Substitution of vit A did not reveal any effect on serum vitamin concentrations, in both groups serum vit A levels declined. However, vit E levels decreased only in group I. Thus the vitamin E substitution prevented a decline of serum vit E inspite of decreased LDL-C levels (which acts as the main transport vehicle). From our results it is concluded that vit A serum levels can not be influenced by oral vit supplementation, which suggests the exixtence of other transportprotein independent vehicle functions.

81 SERUM IMMUNOREACTIVE ERYTHROPOIETIN IN NORMAL CHILDREN

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To provide reference data for normal children, serum immunoreactive erythropoietin (siEp) was estimated by radioimmunoassay in samples from 130 healthy children, 57 girls and 73 boys, with ages between 1 month and 16 years. The children were referred either for minor complaints or for elective surgery. In 128 of the children the (geometric) mean estimate of siEp was 15.8 mIU/ml with 95% range (the range within which 95% of the observations are predicted to fall) 9.1-27.6 mIU/ml. The remaining two children, both girls aged 9.5 and 9.8 years, had estimates of siEp >256mIU/ml. In both Hb and PCV were normal and we have no explanation for these atypical findings. Children in the youngest age group, 0.9 to 2.0 months (n=4), had the lowest estimates of siEp, mean 8.0 with range 4-13 mIU/ml. This was lower than the estimates in children aged 2.8 to 3.5 months (n=6), in whom mean siEp was 17.6 with range 12-38 mIU/ml (Wilcoxon rank sum test, $p=0.019$). Otherwise there was no relation between siEp and the variables Hb, PCV, age and sex. Estimates of siEp in the 128 children were not significantly different from those in 22 normal adults investigated simultaneously (mean 16.2 mIU/ml, 95% range 11.2-23.3 mIU/ml).

82 RECOMBINANT HUMAN ERYTHROPOIETIN IN THE TREATMENT OF ANAEMIA IN CHILDREN WITH END-STAGE RENAL FAILURE MAINTAINED BY HAEMODIALYSIS

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6 children maintained on chronic haemodialysis (4M, 2F age range 3y 11m-14y 10m) have been entered into a study to establish the efficacy and safety of recombinant human erythropoietin (rHuEPO) in the treatment of anaemia due to end-stage renal disease (ESRD).

rHuEPO has been given in an escalating dose regimen, 3x weekly by IV injection at the end of each dialysis. Efficacy has been assessed by 3x weekly blood counts including reticulocytes (retics), monthly determinations of HLA antibodies and assessments of cardiovascular status and quality of life before commencing rHuEPO and 4 weeks after reaching target haemoglobin (Hb). Biochemical profiles have been checked weekly and iron status assessed monthly.

The first 2 patients studied have responded with increased retic counts and Hb levels. (Pt 1, baseline values; mean Hb 6.3gm/dl, % retics 0.72%, absolute retics $15x10^9$/l; 7th week of rHuEPO; mean Hb 7.4gm/dl, retics 3.05%, absolute retics $72x10^9$/l. Pt 2, baseline values; mean Hb 7.5gm/dl, % retics 1.83%, absolute retics $40x10^9$/l; 7th week of rHuEPO; mean Hb 8.3gm/dl, retics 2.49%, absolute retics $79x10^9$/l). These preliminary results indicate that rHuEPO is effective in correcting anaemia in children with ESRD & will be of benefit.

83 EFFECTS OF RECOMBINANT HUMAN ERYTHROPOIETIN (rhEPO) DURING CORRECTION OF RENAL ANEMIA (RA) IN EXPERIMENTAL UREMIA.

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To get information on other effects of rhEPO than correction of RA we have run a controlled randomized study in young(100g) rats looking for following parameters: food intake(FI), weight gain(WG), growth(G), organ masses (heart, liver, spleen, kidney - corrected for body weight), blood pressure(BP), thrombocytes(T), and potassium(K). 20 animals were subtotally nephrectomized and received either 4 IU rhEPO sc/d or solvent for 4 weeks with free access to food(urea 21.5 mmol/l). 20 sham-operated pair fed and 20 ad lib fed animals with and without rhEPO respectively, served as controls(urea 5.9 mmol/l). Although RA could be prevented by rhEPO (Hct 51 vs 44%, $p<0.05$), it did neither affect FI nor WG,G,T and K. However, BP was slightly increased in the rhEPO treated uremic animals(135+10 vs 121+7 mm Hg, $p<0.05$) as was the spleen weight whereas the other organ masses remained unaffected by rhEPO which could not prevent myocardial hypertrophy.Data suggest that treatment with rhEPO will not ameliorate uremia induced stunting and myocardial hypertrophy and usually leads to hypertension which must be regarded as the most serious side effect.

84 IMMUNOREACTIVE ERYTHROPOIETIN AND ERYTHROPOIESIS STIMULATING FACTOR(S) IN PLASMA FROM HYPERTRANSFUSED NEONATAL AND ADULT MICE.

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The objective was to study whether the high erythropoietic stimulatory activity in plasma from neonatal mice is erythropoietin (Ep) alone or Ep in combination with other factors. Plasma from hypertransfused (hy.tr.) neonatal (20d) and adult (13-20w) WLO-mice were compared by a RIA and a cell culture assay for Ep. The bioassay reflects erythropoiesis stimulating factor(s) (ESF), defined as the net activity of Ep and other stimulatory and possible inhibitory factors. The RIA determines immunoreactive Ep (iEp). There was no difference between the mean iEp levels of hy.tr. neonatal and adult animals ($P>0.3$). ESF was not detectable in hy.tr. adult mice, while significant levels were found in neonatal animals. Thus, the mean ESF level of hy.tr. neonatal mice was significantly above that of adult animals ($P<0.001$). The data show that plasma from hy.tr. neonatal mice contain one or more erythropoietic stimulatory factors not detected by the RIA for Ep. It is concluded that part of the high erythropoietic stimulatory activity in plasma from neonatal mice is due to non-Ep factors.