the peripheral blood of adults or neonates showed that of milk monocytes to be significantly lower. Since phagocytosis has been shown to be important ($p < 0.001$) in the lysis of sensitized A, red cells perhaps milk monocytes are not so active because they are loaded with fat granules.

9 KINMONTH, A-L*, and Baum, J.D. University Department of Paediatrics, John Radcliffe Hospital, Oxford. THE EFFECT OF ALTERING THE TIMING OF PRE-BREAKFAST INSULIN INJECTION ON POST PRANDIAL METABOLIC CONTROL OF DIABETIC CHILDREN.

A randomised cross over study was performed on children aged 10-16, at home, to evaluate the effect of varying the time of their morning insulin injection on the post breakfast glycaemic peak. Ethical approval was obtained and consent given by parents and children. After optimisation of diabetic control 9 children injected their insulin 30 minutes (early = 'E') or 5 minutes (late = 'L') before breakfast on two consecutive Saturdays. Blood was sampled over 3.5 hours at 30 minute intervals for estimation of glucose, ketones, pyruvate, lactate, alanine, free insulin and C peptide. Diet, insulin dose and exercise were kept constant on test days. The mean blood glucoses at breakfast time were 10.98 mmol/l (E) and 10.55 mmol/l (L). Subsequent blood glucoses were all lower after the early injection, the mean peak values being 16.75 (E) and 19.35 (L) at 90 minutes after breakfast. Insulin levels rose from 7 mU/l to 11.1 mU/l at breakfast time after the early injection while they were still at 7.6 mU/l after the late injection. C-peptide levels were 1/10 of those expected in normal subjects and changed in parallel with the glucose levels. Total ketones were high and rising before breakfast to peak at 0.1 mmol/l (E) and 0.4 mmol/l (L). By 3 hrs after breakfast they had fallen to normal values of 0.05 mmol/l (E) and 0.07 mmol/l (L). Other metabolites were normal and similar on the two regimes. This study suggests that giving the morning insulin injection before rather than after dressing can significantly improve post prandial metabolic control.

10 F.A.VAN ASSCHE*, L.AERTS* (Intr. by L.CORBEEL) - Dep. Obst.Gynaec.University of Leuven - Is gestational diabetes an acquired condition?

Intravenous injection of 30mg of streptozotocin per Kg. body weight induces a mild diabetes in pregnant rats (first generation); the non-fasting blood glucose is increased and the percentage of endocrine tissue and also the percentage of granulated B cells do not increase. The fetuses of these mildly diabetic pregnant rats have an increased percentage of pancreatic endocrine tissue and there is B-cell degranulation. The modifications of the endocrine pancreas during intrauterine life causes persistent changes in later adult life (second generation), which are not perceptible in basal conditions but become apparent in situations stressing the B cell activity, such as an intravenous glucose load or pregnancy. During pregnancy in the second generation rats have increased non-fasting blood glucose and no adaptation of the B cells is seen. This inadequate adaptation to pregnancy causes changes in the foetal endocrine pancreas of the fetuses of the third generation. From these experiments it may be concluded that gestational diabetes is an acquired condition.

11 GY.SOLTÉSZ*, L.KLUJBER*, D.MOLNÁR*, M.KARDOS*, V.JASZAI* and J.MESTYÁN /Intr. by J.MESTYÁN/ Department of Paediatrics, University Medical School, Pécs, Hungary. Changes in total-, HDL-cholesterol, N-acetyl- β -glucosaminidase in relation to the quality of metabolic control judged by HbA_{1c} in diabetic children.

28 diabetic children were studied. In the fasting blood samples the following substances were measured: glucose, total-cholesterol, HDL-cholesterol, triglyceride, N-acetyl- β -glucosaminidase and HbA_{1c}. The results obtained were the following: 1. Both fasting blood glucose and urinary glucose excretion were found to be positively related to HbA_{1c} / $r=0.77$, $p<0.001$; $r=0.58$, $p<0.001$, respectively/. 2. The positive correlation between HbA_{1c} and total as well as HDL-cholesterol were highly significant / $r=0.51$, $p<0.01$; $r=0.68$, $p<0.001$, respectively/. This relationship demonstrates that poor control of juvenile diabetes is associated with an increased HDL-cholesterol concentration. 3. N-acetyl- β -glucosaminidase, a lysosomal hydrolase was found to be increased in diabetic children and directly related to the percentage of HbA_{1c}, fasting blood glucose and HDL-cholesterol. The present examinations extend the influence of juvenile diabetes on HDL-cholesterol concentration by the observation that the poorer the metabolic control the higher the HDL-cholesterol content in the plasma.

12 I. DESCHAMPS* and J. HORS* (Intr. by H. Lestrade) Groupe de Recherche sur le Diabète et la Nutrition

chez l'Enfant, Hôpital Hérold 75935 Paris, France. HLA GENOTYPING AND RISK OF DIABETES.

Five different HLA-loci were tested in 53 families with one or more diabetic children. The alleles B15, B18, Cw3, Cw5, B*F1, DRw3, DRw4 were increased in diabetics, and significantly higher frequencies were found for several haplotypes with stronger lin-

kage disequilibrium than in the control population. The strongest associations occurred with the DRw3 and DRw4 alleles, suggesting the existence of several "high risk axes" carrying the diabetogenic gene (s) closely linked to the DR-locus. The excess of HLA-identity in multiple affected siblings of 12 families is in agreement with a recessive transmission. Yet the lack of homozygosity does not support a single-gene hypothesis. Moreover, the highly significant excess heterozygosity DRw3/DRw4 in diabetics (32 %, $p < 0.001$) provides evidence for a pseudorecessive mechanism, two complementary acting genes being linked to each of the DR-alleles. In conclusion, the low frequency of DRw3/DRw4 heterozygotes in healthy siblings of diabetics (10 %) and their absence in controls, attribute the highest risk of diabetes to related as well as unrelated carriers of this combination. (Relative risk = 5.3 and 46.6, respectively)

13 J.L. CHAUSSAIN, P. GEORGES*, D. GENDREL*, A. BRIJAWI* and J.C. JOB. Hôpital Saint-Vincent de Paul, Paris, France.

Interest of the measure of serum branched-chain amino-acids (BCA) in the diagnosis of hyperinsulinism in infancy.

Fasting values of BCA (valine, leucine and isoleucine) were measured by column chromatography in the sera of 27 normal children aged 2 days to 9 years, 14 children with ketotic hypoglycemia (KH) aged 1 to 7 years, and in 12 sera from 5 infants aged 15 days to 2 years with documented hyperinsulinism. In normal and KH children, each individual BCA and their sum were highly significantly negatively correlated with blood glucose (BG) values ranging between 0.11 and 0.92 g/l ($r = 0.61$, $p < 0.001$). In infants with hyperinsulinism BCA concentrations were significantly lower ($p < 0.001$) than in the other groups without correlation with BG values (ranging from 0.13 to 0.51 g/l), and with plasma insulin concentrations (ranging from 9 to 85 μ U/ml). In all the children studied, the sum of BCA was highly significantly correlated with blood beta OH butyrate measured by enzymatic method in the same time ($r = 0.75$, $p < 0.001$). The association low BG-low BCA during fast seems characteristic of hyperinsulinic states, and the measurement of fasting BCA in these infants offers a simple way of diagnosis, avoiding the technical difficulties of beta OH butyrate determination.

14 G.DAHLQUIST*, (St.Görans's Childrens Hospital, S-112 81 Stockholm), J.GENTZ, L.HAGENFELDT*, A. LARSSON*, H.LÖW*, B.PERSSON, R.ZETTERSTRÖM, Stockholm. Ketotic hypoglycemia-a clinical trial of several unifying ethiological hypotheses.

After the informed consent by parents and children we have studied 15 children referred to our clinic because of suspected ketotic hypoglycemia. The patients were investigated according to a program designed to test several hypotheses - old and new postulated to explain the ethiology of ketotic hypoglycemia. The plasma levels of glucose, FFA, glycerol, β -HBA, alanine, cortisol and insulin as well as the urinary excretion of nitrogen, 3-methylhistidine and catecholamines and an i.v. glucose tolerance test were measured before and after a classical ketogenic provocation test. Out of the 15 children 6 will fill the criteria of ketotic hypoglycemia at the time of the study. The most remarkable finding in these 6 children in contrast to the other children studied was that they did not decrease their peripheral glucose utilization (measured as Kg) during starvation. These 6 children seemed to be more "advanced" in their adaptation to ketogenic diet in all other parameters studied. The children with ketotic hypoglycemia did not differ from the other children in plasma level of cortisol or urinary excretion of nitrogen, urea, 3-methylhistidine and catecholamines. - We favour the concept that the children with ketotic hypoglycemia represent the tail of the gaussian curve in the normal physiological development of the adaptation to starvation.

15 CORNILLIE F.*, LAUWERYS J.*, CORBEEL L., BOEL M.*, ECKELS R.* VAN DE WALLE J.* (Departments of Pathology, Pediatrics and Anesthesiology, University of Leuven). Acquired ultrastructural abnormalities of bronchial cilia in recurrent airway infections and bronchiectases as compared with the findings in Kartagener syndrome.

Electron microscopic studies revealing a lack of the dynein arms of the microtubular doublets of bronchial cilia and sperm tails suggest that Kartagener syndrome is a special manifestation of a hereditary disease, now referred to as the immotile cilia syndrome (Eliasson et al. N Engl J Med 297: 1, 1977). Anomalies of the bronchial cilia were observed in 5 patients with recurrent pulmonary infections. Patient 1 had Kartagener syndrome and an absence of the outer dynein arms in most ciliae, although occasional shortened and even normal arms were seen. Patient 2 and 3 had unilateral bronchiectases without family history of Kartagener syndrome. Serial studies of the bronchial epithelium showed a bilateral lack of the inner dynein arms and incomplete outer arms. These abnormalities persisted after recovery from acute pulmonary infection. In patients 4 and 5 with recurrent pulmonary infections without bronchiectases, many shortened outer dynein arms were observed, but these anomalies disappeared after recovery. In all 5 patients additional striking ciliary anomalies were found: megacilia, fused cilia, nude cilia and completely disorganized axo-

nemes. These defects were more numerous in the patients without bronchiectases. Our observations suggest that anomalies of the bronchial ciliary microtubular system may not only be congenital but also acquired, and could be an important factor explaining some cases of repeated airway infection and bronchiectases.

16

K. SCHOPFER*, B.J. WILKINSON* and K. BAERLOCHER. Children's Hospital, St. Gallen Switzerland and Department of Biological Sciences, Illinois State University, Illinois 61761 USA. Characterisation of antistaphylococcal IgE antibodies in patients with recurrent *S. aureus* infection, eczema and hyperimmunoglobulinemia E.

Antistaphylococcal IgE antibodies have recently been demonstrated in patients with recurrent staphylococcal infections, eczema and hyperimmunoglobulinemia E. The formation of these IgE antibodies may be a manifestation of an aberrant immunological response to *S. aureus* infection and may be related to the undue susceptibility of staphylococcal infections in these patients. In an attempt to further investigate this immunological disorder the IgE antibody binding site within the staphylococcal cell wall was studied. Cell walls from various staphylococcal strains were purified and IgE binding was measured using a solid phase radioimmunoassay. Binding occurred only to purified cell walls (PCW) from *S. aureus*. Since the glycan backbone and the peptide subunit of the peptidoglycan (PG) of the PCW tested are believed to be identical it is concluded that the IgE antibodies are directed to the interpeptide bridge or an unknown antigenic site within the PG of *S. aureus* cell walls. This hypothesis is further studied using synthetic analogues of PG interpeptide bridges.

17

R. SEGER*, P. JOLLER*, J. WUEST*, D. GARZONI*, A. RAPP* and G. DUC. Department of Paediatrics and Institute of Medical Microbiology, University of Zurich. Unmasking of the Thomsen-cryptantigen in necrotising enterocolitis (NEC): Bacteriological and immunological findings.

Clostridial infections have been associated with neonatal NEC. Neuraminidase, produced by *Cl. perfringens* and other clostridial species, cleaves neuraminic acid from the red blood cell glycoprotein and thus exposes a hidden receptor, the so-called Thomsen cryptantigen (T-Ag). Clostridial infection in NEC can thus be recognised by demonstration of the T-Ag on the patient's red blood cells. Among 22 cases with clinical signs of NEC 7 revealed T-antigen-positive erythrocytes. In one of those circulating neuraminidase was detectable for a short period. In 2 cases clostridial species were isolated from blood or peritoneal fluid cultures. The filtrates of these cultures were able to expose the T-Ag on normal red blood cells. Commercially available purified neuraminidase from *Cl. perfringens* unmasked the T-Ag on normal neutrophils and impaired function as measured by their killing of staphylococcus aureus. Our data indicate that screening of patients with NEC for the presence of T-Ag allows to delineate a subgroup of patients infected with neuraminidase-producing microorganisms. They also suggest that in this subgroups non-specific defense may be impaired.

18

F. LAURENTI*, R. FERRO*, G. ISACCHI*, F. MANDELLI*, G. BUCCI. Depts. of Pediatrics and Hematology-Univ. of Rome, Italy. Granulocyte transfusion in very premature infants with sepsis.

In premature infants with sepsis several defects of PMN function have been documented, suggesting that these infants can be equated to neutropenic patients. We, therefore, evaluated the effectiveness of PMN transfusion in 11 very premature newborn infants with sepsis (b.w. 820-1200 g; g.a. 25-29 wks). The diagnosis of sepsis was established according to clinical signs and to blood picture, and was always confirmed by blood cultures. Transfusion of packed PMNs (0.5×10^{10} cells in 20 ml, obtained by leukafiltration of ABO/Rh compatible blood) was given after sepsis was ascertained and repeated in the subsequent days. Group A (6 cases) received a mean of 1 unit per 2.2 symptomatic days, whereas Group B (5 cases) received a mean of 1 unit per 6 symptomatic days. The mortality rate was significantly lower in Group A than in Group B (17% vs. 100%; $p < 0.02$). No side effect was observed. The present results suggest that PMN transfusion may represent a substantial improvement in the treatment of these infants. Adverse effect of the treatment needs further evaluation, but at present possible risks seem to be reasonably low. (CNR grant no. 78.00563.83).

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L. CORBEEL, R. ECKELS*, G. VAN DEN BERGHE*, H. DEVLIEGER*, J. JAEKEN*, P. BRACKE* (Dept. of Paediatrics, University of Leuven), and L. HUE*, B. LEDERER*, T. de BARSY* (Dept. of Biochemistry, University of Louvain and I.C.P., Brussels, Belgium). Clinical and biochemical findings before and after portacaval shunt (PCS) in type Ib glycogen disease (GSD).

An 11-year-old girl with statural age of 5 yrs. and hepatomegaly (15cm) had fasting hypoglycaemia, acidosis, increased serum cholesterol, triglycerides and uric acid, and increased liver glycogen (7.5%). There was no rise in blood glucose after i.v. galactose or fructose but glucagon gave a delayed response. Type Ib GSD was suggested by the normal activity of glucose-6-phosphatase (G-6-Pase) and of other glycogenolytic enzymes in frozen liver. After PCS, at 12 6/12 yrs., height increased by 29cm in 3 yrs. Serum cholesterol decreased from 620 to 230mg/dl and triglycerides

from 2400 to 200mg/dl. At oral GTT peak values for glucose (mg/dl) and insulin (U/l) were respectively 210 and 50 before, 290 and 90 after PCS. Higher than normal utilisation of (2-³H,U-¹⁴C)-glucose was shown by a ³H/¹⁴C ratio of 24% after 60 min. (mean $\pm$ S.E.M.: $59\% \pm 7$ in normals and $92\% \pm 3$ in type Ia GSD) and can be explained by peripheral hyperinsulinism. Assay of G-6-Pase in a fresh liver homogenate prepared in 0.25 M-sucrose revealed only 29% ($96\% \pm 11$ in 3 controls) of the enzyme activity as compared with an homogenate in H₂O. The latter finding may be in favour of the hypothesis of Narisawa et al. (Biochem. Biophys. Res. Comm. 83: 1360, 1978) postulating a defect of the microsomal G-6-trans-port system in type Ib GSD, but is difficult to reconcile with the isotopic data.

20

M. ODIEVRE*, H. BISMUTH*, P. DOUILLET*, N. MOATTI*, M. BRIVET* and C. BAUSSAN*. Unité de Recherche d'Hépatologie infantile, INSERM U 56. Clinique de Pédiatrie, Université Paris-Sud. Unité de Chirurgie Hépatobiliaire, Villejuif & Laboratoire Central de Biochimie, Hôpital de Bicêtre, 94270 Bicêtre, France. Portal diversion in glycogen storage disease (GSD): studies in 11 cases.

Successful treatment of GSD by portal diversion was reported with subsequent improvement in growth and return to normal dietary habits. An end-to-side portacaval shunt has been performed in 11 patients aged 7 months to 11 1/2 years (6 with type I and 5 with type III GSD). In 10 patients, patency of the anastomosis was confirmed. In 9 of them, a dramatic improvement of physical activity was observed in spite of persistent hypoglycemia and hyperlactacidemia. Liver size decreased in 7. A threefold decrease in blood cholesterol level (m 164 mg/dl vs. 415 peroperatively) was observed in 8 patients and a tenfold decrease in blood cholesterol level (m 170 mg/dl vs. 1548) in 6 out of 7 tested patients. Uricemia, increased in 4 cases, returned to normal. An increased linear growth rate (m 0.66 cm/month vs. 0.27) was noted in only 5 patients. Two type I patients died, 2 years (thrombosis of the anastomosis) and 6 months (intercurrent infection) after surgery. These results show that the most important benefits of surgery are improvement of general condition and normalization of lipids and uric acid metabolism.

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FARRIAUX JP*, RIBET M*, DHONDT JL*, ARDOUIN P*, (Intr. by Corbeel L.) - Service de Génétique et Maladies Hépatobiliaires du Métabolisme-LILLE (F) - Portacaval shunt (PCS) in type IIa hypercholesterolemia: results from three cases. 3 cases of type IIa hypercholesterolemia (homozygous LDL receptor negative type) were treated with PCS. Follow-up is 46, 23 and 3 months respectively (cases 1, 2, 3). 1) clinical and biological tolerances were good (no hepatic nor cerebral abnormality); cutaneous xanthomas slowly decreased. 2) cholesterolemia decreased (pre-operative levels: respectively 20.6 - 23.2 and 25.8 mmol/l; post-operative levels: 10.3, 15.5 and 12.9 mmol/l). 3) insulin and glucagon levels progressively increased (present basal insulin level: 20 µU/ml, glucagon: 500 pg/ml in case 1); results were normal in the 3rd case 2 months after shunt (insulin: 6 µU/ml, glucagon: 34 pg/ml). 4) in case 2, PCS thrombosed during the post-operative period; 18 months later a mesoiliac shunt was as efficient as PCS. 5) in cases 1 and 2 coronarography showed no change of coronary lesions, however; stabilization might be considered as favourable. 6) a diet low in lipids and cholesterol, inefficient before PCS became indispensable in the post-operative period. An increase of 30% of blood cholesterol occurred when the patient returned on a free diet. Continuous nocturnal gastric drip feeding (with a follow-up of 12 months in case 1) did not give better results than a well controlled diet. 7) a decrease of blood cholesterol during total parenteral feeding in the pre-operative period was a good index of the success of the PCS in the 3 cases.

22

Th. ANGERPOINTNER*, O. LINDERKAMP, H. STALLINGER*, J. STRUCK*, K. RIEGEL; Pediatric Surgical Hospital and Dept. of Neonatology of the Children's University Hospital, Munich. The effect of hypoxia on cardiac performance in newborn piglets - evaluation by the electromagnetic method. Tolerance of hypoxia differs among species and with age. Within age groups there is considerable individual variation which is as yet poorly understood. In response to hypoxemia cardio-circulatory adaptation plays a central role. We studied the changes of cardiac performance in artificially ventilated piglets aged 8 to 42 hours (n=10) under fluothane-N₂O₂-anaesthesia. After a stable control period arterial Po₂ was lowered from 60-90 mmHg to 30-40 mmHg (hemoglobin-oxygen-saturation 70-90%) by lowering FiO₂ at otherwise constant conditions. Mean heart rate rose continuously by +38% at 111 $\pm$ 85 min hypoxia time ($p < 0.001$). However, cardiac output, stroke volume, cardiac power, mean aortic blood pressure, aortic peak flow reached their maxima (+11 to +32%; $p < 0.01$), and vascular resistance its minimum (-17%; $p < 0.01$) already during the first 30 min. They subsequently fell below (-60 to -90%) or surmounted (+45%) control levels. These changes were accompanied by increasing metabolic acidosis. Average survival time was 188 $\pm$ 98 min. Survival time depended exclusively on the animals' ability to increase its heart rate ($K=0.83$). It was shorter in piglets, who started with heart rates above the average control level (133 $\pm$ 61 min) than those with heart rates below it (227 $\pm$ 104 min). It is to be concluded that newborn piglets are unable to compensate sustained hypoxemia of such degree by means of cardiac performance longer than 30 min.