43 CARDIO-RESPIRATORY COMPLICATIONS OF DIAZOXIDE TREATMENT IN NESIDIOBLASTOSIS

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In 6 infants (3 males, 3 females) with histologically proven nesidioblastosis (ranges blood glucose, blood insulin and insulin glucose ratio of 9-35 mg/dl, 8-68 mU/l and 0.5-5.2 resp.), the cardiorespiratory effects of diazoxide treatment was studied. All infants were free from heart disease; birth weight range 3640-5020 g.
Diazoxide (12-25 mg/kg/day) and chlorothiazide with continuous i.v. infusion of glucose (15-25 mg/kg/min) were given to all patients (7 times) before pancreatectomy and to 3 post pancreatectomy under daily control of weight change, fluid intake, respiratory and heart rate (RR and HR), heart and liver size and heart murmurs.
Cardio-respiratory toxicity symptoms occurred in 7 of 10 instances. The failure symptoms were not related to fluid overload, neither to the diazoxide dose alone but rather to diazoxide dose in relation to the severity of the disease. We expressed this relationship as Toxicity Index (TI) by multiplying the diazoxide dose by the insulin/glucose ratio.
All infants with TI $\geq$ 10.2 developed toxicity: significantly ($p < 0.005$) increased RR and HR, hepato- and cardiomegaly, heart murmur. TI (total range 1.4-78.5) was significantly higher in infants with than in those without toxicity: 30.2±23.6 (x±SD) vs 2.8±1.5, $p < 0.05$. TI can be used for estimating the potential risk of cardio-respiratory failure and for calculating a safe diazoxide dose in infants with nesidioblastosis.

44 HIGH VITREOUS HUMOUR HYPOXANTHINE (HX) LEVEL IN SUDDEN INFANT DEATH SYNDROME (SIDS) INDICATES PROLONGED CEREBRAL HYPOXIA

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HX levels were measured, in vitreous humour in 19 SIDS cases. The results were compared with levels found in adults who died from trauma, hanging, myocardial infarction (MI) or intoxication (1). The HX levels in SIDS were significantly higher ($p<0.05$) than in the cases with immediate deaths from trauma, hanging or MI, but similar to those obtained in persons who died from drug intoxication (Table).

Table

Cause of death	No of cases	HX level µmol/l Median	Range
SIDS	19	350	180 - 660
Intoxication	13	345	60 - 800
Trauma	24	105	0 - 500
Hanging	10	120	0 - 300
MI	19	110	0 - 500

Death from drug intoxication often follows a period of prolonged hypoxemia. Since HX is elevated in hypoxia the increased levels of HX in SIDS thus favours the theory that SIDS is associated with prolonged cerebral hypoxia. Conversely the finding is contradictory to the hypothesis that acute reflectory death mechanisms are involved in SIDS.

1. Saugstad OD, Olaisen B. Post-mortem hypoxanthine levels in the vitrous humour. Forensic Sci. Int. 1978, 12, 33-36

45 EFFECT OF ATRIAL NATRIURETIC PEPTIDE ON THE HORMONE RELEASE IN SUPERFUSED RAT PITUITARY CELLS.

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Atrial natriuretic peptide (ANP) is the most potent endogenous natriuretic/diuretic substance described to date. Recent immunohistochemical studies and tests based on radioimmunoassays indicate that ANP is present in the central nervous system. In our studies, we investigated the effect of ANP in a superfused rat pituitary cell system. When ANP was administered at increasing concentrations (10^{-8} M to 10^{-6} M), it caused a significant, dose related stimulation of the release of luteinizing hormone (LH) and follicle stimulating hormone (FSH). The lowest effective dose of ANP in our system was $3x10^{-8}$ M. When ANP and luteinizing hormone-releasing hormone (LH-RH) were administered together, the response was prolonged and had the characteristics of ANP stimulated LH and FSH release. In contrast with some previous reports, ANP in high concentration (10^{-6} M) consistently induced a small but significant stimulation of the release of corticotropin. ANP did not influence the basal release of prolactin, growth hormone and thyrotropin.

46 SUPEROXIDE DISMUTASE IN THE VITREOUS BODY OF DIABETIC PATIENTS WITH PROLIFERATIVE RETINOPAHY (PRP)

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In diabetic retinopathy the vessels become fragile and the permeability over the blood-retinal barrier (BRB) increases. Decreased levels of superoxide dismutase (SOD) in the retina of long-term diabetic rats and rabbits have been reported recently. A possible consequence of this could be that generated superoxide is not removed, allowing it to react with the unsaturated fatty acids of the cell membranes.
We have examined the SOD concentrations of posterior vitreous body in 6 patients with PRP aged 36-74 years undergoing vitrectomy and in 23 non-diabetic subjects aged 37-88 years post mortem. The total SOD concentration was (median and 95% conf interval) 14.4 U/ml (8.7-39.4) and 110 (65.5-138.5) U/ml respectively, $p<0.01$. The SOD level of posterior vitreous body of one diabetic subject with PRP examined post mortem was 6.50 U/ml.
The decreased SOD levels of posterior vitreous body in diabetic patients with PRP support that decreased SOD-activity is one possible mechanism for retinopathy.

47 ABSENCE OF A NOVEL NEURONAL CELL ANTIGEN IN HIRSCHSPRUNG'S DISEASE

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A major obstacle to the understanding of pathophysiology of aganglionosis has been the lack of specific markers for various neuronal cell types that may be affected in this condition. Recently, with the availability of polyclonal and in particular monoclonal antibodies it has become possible to identify more precisely the innervation patterns in normal and aganglionic colon. We have produced a monoclonal antibody D_7 which recognises a subset of axonal antigen which are distributed throughout the wall of normal rectum and colon.

Immunohistochemical scanning of the entire resected specimen of colon from 3 children with Hirschsprung's disease at 0.5 cm intervals, demonstrated large numbers of D_7 immunoreactive nerve bundles in the circular muscle of the ganglionic colon, few fibres in the transitional zone and no immunoreactive fibres in the aganglionic segment. Comparative studies with anti-neuropeptide antibodies and with anti-neuronal cell antibodies suggest that D_7 identifies a 52 kD antigen associated with a subset of axonal fibres distributed throughout the entire nervous system. These findings indicate that fundamental pathology in Hirschsprung's disease is not only the absence of ganglion cells of the myenteric and submucous plexuses but also the absence of D_7 immunoreactive fibres in the circular muscle of the colon.

48 ENZYME REPLACEMENT THERAPY WITH YEAST SACCHAROMYCES CEREVISIAE IN CONGENITAL SUCRASE-ISOMALTASE-DEFICIENCY (SID).

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In an 11 year old girl with SID, treatment with fresh bakers yeast resulted in a dramatic clinical improvement. Therefore we have started a study on saccharolytic enzymes in yeast in vivo and in vitro. In vivo H_2 breath tests (HBT) were performed in 8 patients with SID upon sucrose loading (2 g/kg, $\bar{x}$ = 41 g) with and without the addition of 0.3 g lyophilized Saccharomyces cerevisiae (LSC). H_2 values were corrected for atmospheric contamination and fasting levels. In addition to clinical improvements half of the patients showed a normalization of the HBTs and the remainder a clear decrease of the H_2 areas under the curves by administration of yeast (average H_2 reduction by 70 %). In a control group of 5 patients with the adult form of lactase deficiency neither clinical symptoms nor HBT after the lactose loading were changed by the yeast therapy. - The sucrase activity in LSC as well as in fresh bakers yeast was very high (6.2 and 24 mmol/min/g protein respectively) but the isomaltase and lactase activities were relatively low (isomaltase 0.91 ± 0.01 and 0.28 ± 0.03 resp., lactase 0.06 ± 0.005 and 0.2 ± 0.03 resp.). Dried brewers yeast showed only a very low sucrase activity (0.14 mmol/min/g protein). - In contrast to the fecal flora, yeast did not release any hydrogen from carbohydrates under anaerobic conditions in vitro. - In conclusion, patients with SID and difficulties in keeping a sucrose free diet will benefit from a small amount of viable yeast cells after a sucrose rich meal. -

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