

## Hypoglycemia

## ABSTRACTS

Croset M., 1994. Rat small intestine is an insulin-sensitive gluconeogenic organ.

Geng M.-Y., 1997. Protective effects of pyridoxal phosphate against glucosedepprivation- induced damage in cultured hippocampal neurons.

Houseknecht KL., 1998. Dietary conjugated linoleic acid normalizes impaired glucose tolerance in the Zucker diabetic fatty fa/fa rat.

McCarty M.F., 1996. Chromium and other insulin sensitizers may enhance glucagon secretion: Implications for hypoglycemia and weight control

Mithieux G., 2001. New data and concepts on glutamine and glucose metabolism in the gut.

Pearson S & Shaw S., 1982. Preventing Hypoglycemia.

Ryder JW., 2001. Isomer-specific antidiabetic properties of conjugated linoleic acid. Improved glucose tolerance, skeletal muscle insulin action, and UCP-2 gene expression.

Stumvoll M., 1999. Role of glutamine in human carbohydrate metabolism in kidney and other tissues.

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Cersosimo E., 2000. Renal substrate metabolism and gluconeogenesis during hypoglycemia in humans.

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Chapman IM., 1997. Oral administration of growth hormone (GH) releasing peptide-mimetic MK-677 stimulates the GH/insulin-like growth factor-I axis in selected GH-deficient adults.

Coiro V., 1997. Effect of melatonin on hypoglycemia and metoclopramide-stimulated arginine vasopressin secretion in normal men.

Dennis SC., 1997. Nutritional strategies to minimize fatigue during prolonged exercise: fluid, electrolyte and energy replacement.

Galarza Guzman M., 1997. Effects of coca chewing on the glucose tolerance test.

Kazda A., 1997. A metabolic complications of nutritional support. I. Carbohydrates, amino acids, fats, water, ions, trace elements.

Natah SS., 1997. Metabolic response to lactitol and xylitol in healthy men.

Quevedo-Coli S., 1997. Alterations in circulating fatty acids and the compartmentation of selected metabolites in women with breast cancer.

Shibata S., 1995. Glutathione protects against hypoxic/hypoglycemic decreases in 2-deoxyglucose uptake and presynaptic spikes in hippocampal slices.

**Rat small intestine is an insulin-sensitive gluconeogenic organ.**

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Diabetes 2001 Apr;50(4):740-6

At variance with the current view that only liver and kidney are gluconeogenic organs, because both are the only tissues to express glucose-6-phosphatase (Glc6Pase), we have recently demonstrated that the Glc6Pase gene is expressed in the small intestine in rats and humans and that it is induced in insulinopenic states such as fasting and diabetes. We used a combination of arteriovenous balance and isotopic techniques, reverse transcription-polymerase chain reaction, Northern blot analysis, and enzymatic activity assays. We report that rat small intestine can release neosynthesized glucose in mesenteric blood in insulinopenia, contributing 20-25% of total endogenous glucose production. Like liver glucose production, small intestine glucose production is acutely suppressed by insulin infusion. In the small intestine, glutamine and, to a much lesser extent, glycerol are the precursors of glucose, whereas alanine and lactate are the main precursors in liver. Accounting for these metabolic fluxes: 1) the phosphoenolpyruvate carboxykinase gene (required for the utilization of glutamine) is strongly induced at the mRNA and enzyme levels in insulinopenia; 2) the glycerokinase gene is expressed, but not induced; 3) the pyruvate carboxylase gene (required for the utilization of alanine and lactate) is repressed by 80% at the enzyme level in insulinopenia. These studies identify small intestine as a new insulin-sensitive tissue and a third gluconeogenic organ, possibly involved in the pathophysiology of diabetes.

**Protective effects of pyridoxal phosphate against glucosedepprivation- induced damage in cultured hippocampal neurons**

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Journal of Neurochemistry (USA), 1997, 68/6 (2500-2506)

When hippocampal cultures were deprived of glucose, massive release of lactate dehydrogenase (LDH), an indicator of neuronal death, occurred via NMDA receptor activation. Addition of pyridoxal phosphate (PLP; 1 and 10 microM) inhibited this LDH release in a concentration-dependent manner. Prior exposure to PLP evoked more potent inhibitory effects on LDH release compared with those treated at the onset of glucose deprivation. Furthermore, PLP inhibited the reduction of intracellular content of pyruvate induced by glucose deprivation, which was accompanied by the reversal of intracellular ATP depletion. A noteworthy elevation of extracellular glutamate in response to glucose deprivation was completely reversed by addition of PLP. Aminooxyacetic acid, a potent inhibitor of PLP-dependent enzymes, antagonized the effects of PLP on LDH release, pyruvate production, and ATP formation. These results suggest that PLP protects neurons from glucose deprivation-induced damage by enhancing the formation of energy-yielding products and relieving extracellular load of glutamate. The observed phenomena further indicate that PLP might be used prophylactically against neuronal death induced by metabolic disorders.

### **Dietary conjugated linoleic acid normalizes impaired glucose tolerance in the Zucker diabetic fatty fa/fa rat.**

Houseknecht KL, Vanden Heuvel JP, Moya-Camarena SY, Portocarrero CP, Peck LW, Nickel KP, Belury MA. Department of Animal Sciences, Purdue University, West Lafayette, Indiana 47907, USA.

Biochem Biophys Res Commun 1998 Jun 29;247(3):911

Conjugated linoleic acid (CLA) is a naturally occurring fatty acid which has anti-carcinogenic and anti-atherogenic properties. CLA activates PPAR alpha in liver, and shares functional similarities to ligands of PPAR gamma, the thiazolidinediones, which are potent insulin sensitizers. We provide the first evidence that CLA is able to normalize impaired glucose tolerance and improve hyperinsulinemia in the pre-diabetic ZDF rat. Additionally, dietary CLA increased steady state levels of aP2 mRNA in adipose tissue of fatty ZDF rats compared to controls, consistent with activation of PPAR gamma. The insulin sensitizing effects of CLA are due, at least in part, to activation of PPAR gamma since increasing levels of CLA induced a dose-dependent transactivation of PPAR gamma in CV-1 cells cotransfected with PPAR gamma and PPRE X 3-luciferase reporter construct. CLA effects on glucose tolerance and glucose homeostasis indicate that dietary CLA may prove to be an important therapy for the prevention and treatment of NIDDM.

### **Chromium and other insulin sensitizers may enhance glucagon secretion: Implications for hypoglycemia and weight control**

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Medical Hypotheses (United Kingdom), 1996, 46/2 (77-80)

Increased pancreatic beta-cell secretory activity usually is associated with decreased alpha-cell activity; stimulated beta-cells release gamma-aminobutyric acid, which hyperpolarizes alpha-cells, inhibiting glucagon release. Thus, insulin secretion and glucagons secretion are usually inversely coupled. This suggests that chromium and other insulin-sensitizing modalities, by down-regulating beta-cell activity, may increase glucagons secretion. Such an effect might play a role in the documented therapeutic activity of supplemental chromium and biguanides in reactive hypoglycemia, and might also be of benefit to dieters.

### **New data and concepts on glutamine and glucose metabolism in the gut.**

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Curr Opin Clin Nutr Metab Care 2001 Jul;4(4):267-71

Both glutamine and glucose are highly utilized by the small intestine in various animal species. They are, however, very partially oxidized, the major known fate of glucose being lactate and alanine, and that of glutamine being citrulline or proline. At variance with the current view that only the liver and kidney are gluconeogenic organs, because both are the only tissues to express the glucose-6 phosphatase gene, this gene is also expressed in the small intestine in rats and humans, and is strongly induced in insulinopenic states, such as fasting and diabetes. Under the latter conditions, the small intestine contributes 20-25% of whole-body endogenous glucose production. The main small intestine gluconeogenic substrate is glutamine and, to a lesser extent, glycerol. Accounting for these fluxes, the phosphoenolpyruvate carboxykinase gene is strongly induced in insulinopenia and, although up to now it had been considered absent from this tissue, the glycerokinase gene is expressed in the small intestine. The production of glucose by the

small intestine may be acutely blunted upon insulin infusion. These new data also emphasize the central role of alanine aminotransferase in the coupling of glutamine and glucose metabolisms in the small intestine.

## **Preventing Hypoglycemia**

Durk Pearson and Sandy Shaw

Anti-Aging News, January 1982 Vo.2, No. 1 pg 6-7

Cysteine is a strong reducing agent (it can prevent oxidation of some other substances). In fact, it has been found that too much cysteine in a cell culture medium can inactivate the hormone insulin contained in the medium. The insulin molecule contains three disulfide bonds, at least one of which can be reduced by cysteine. When this happens, the insulin molecule can no longer maintain the proper shape to function normally in stimulating the metabolism of sugar. In hypoglycemia attacks, there is too much insulin and too little sugar in the blood stream. Cysteine can inactivate insulin, thereby allowing the sugar level to begin to rise again. We and others have used the combination of vitamins B1, C, and cysteine to successfully abort severe attacks of hypoglycemia. A reasonable dose for a healthy adult is 5 grams of C, 1 gram of B1, and 1 gram cysteine. Although cysteine is a nutrient, its use on a long-term basis should be considered experimental. Start with a low dose (250 milligrams per day) and work your way up. Always use at least three times as much Vitamin-C as cysteine. Be sure to consult with your physician and have regular clinical tests of basic body functions, especially liver and kidney. Diabetics should not use cysteine supplements due to its anti-insulin effects.

## **Isomer-specific antidiabetic properties of conjugated linoleic acid. Improved glucose tolerance, skeletal muscle insulin action, and UCP-2 gene expression.**

Ryder JW, Portocarrero CP, Song XM, Cui L, Yu M, Combatsiaris T, Galuska D, Bauman DE, Barbano DM, Charron MJ, Zierath JR, Houseknecht KL. Department of Clinical Physiology, Karolinska Institute, Stockholm, Sweden.

Diabetes 2001 May;50(5):1149-57

Conjugated linoleic acid (CLA) isomers have a number of beneficial health effects, as shown in biomedical studies with animal models. Previously, we reported that a mixture of CLA isomers improved glucose tolerance in ZDF rats and activated peroxisome proliferator-activated receptor (PPAR)-gamma response elements in vitro. Here, our aim was to elucidate the effect(s) of specific CLA isomers on whole-body glucose tolerance, insulin action in skeletal muscle, and expression of genes important in glucose and lipid metabolism. ZDF rats were fed either a control diet (CON), one of two CLA supplemented diets (1.5% CLA) containing differing isoforms of CLA (47% c9,t11; 47.9% c10,t12, 50:50; or 91% c9,t11, c9,t11 isomers), or were pair-fed CON diet to match the intake of 50:50. The 50:50 diet reduced adiposity and improved glucose tolerance compared with all other ZDF treatments. Insulin-stimulated glucose transport and glycogen synthase activity in skeletal muscle were improved with 50:50 compared with all other treatments. Neither phosphatidylinositol 3-kinase activity nor Akt activity in muscle was affected by treatment. Uncoupling protein 2 in muscle and adipose tissue was upregulated by c9,t11 and 50:50 compared with ZDF controls. PPAR-gamma mRNA was downregulated in liver of c9,t11 and pair-fed ZDF rats. Thus, the improved glucose tolerance in 50:50 rats is attributable to, at least in part, improved insulin action in muscle, and CLA effects cannot be explained simply by reduced food intake.

## **Role of glutamine in human carbohydrate metabolism in kidney and other tissues.**

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Kidney Int 1999 Mar;55(3):778-92

Glutamine is the most abundant amino acid in the human body and is involved in more metabolic processes than any other amino acid. Until recently, the understanding of many aspects of glutamine metabolism was based on animal and in vitro data. However, recent studies using isotopic and balance techniques have greatly advanced the understanding of glutamine metabolism in humans and its role in glucose metabolism in the kidney and other tissues. There is now evidence that in postabsorptive humans, glutamine is an important glucose precursor and makes a significant contribution to the addition of new carbon to the glucose carbon pool. The importance of alanine for gluconeogenesis, viewed in terms of the addition of new carbons, is less than previously assumed. It appears that glutamine is predominantly a renal gluconeogenic substrate, whereas alanine gluconeogenesis is essentially confined to the liver. As shown recently, renal gluconeogenesis contributes 20 to 25% to whole-body glucose production. Moreover, glutamine has been shown not only to stimulate net muscle glycogen storage but also to stimulate gluconeogenesis in normal humans. Finally, in humans with type II diabetes, conversion of glutamine to glucose is increased (more so than that of alanine). The available evidence on the hormonal regulation of glutamine gluconeogenesis in kidney and liver and its alterations under pathological conditions are discussed.

## **SUGGESTED READING**

## **Renal substrate metabolism and gluconeogenesis during hypoglycemia in humans.**

Cersosimo E, Garlick P, Ferretti J. Department of Medicine, State University of New York at Stony Brook, 11794-8154, USA.  
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Diabetes 2000 Jul;49(7):1186-93

To examine the potential contribution of precursor substrates to renal gluconeogenesis during hypoglycemia, 14 healthy subjects had arterialized hand vein and renal vein (under fluoroscopy) catheterized after an overnight fast. Net renal balance of lactate, glycerol, alanine, and glutamine was determined simultaneously with systemic and renal glucose kinetics using arteriovenous concentration differences and 6-[2H<sub>2</sub>]glucose tracer dilution. Renal plasma flow was measured by para-aminohippurate clearance and was converted to blood flow using the mathematical value (1-hematocrit). Arterial and renal vein samples were obtained in the postabsorptive state and during a 180-min hyperinsulinemic period during either euglycemia or hypoglycemia. Insulin increased from 49 +/- 14 to 130 +/- 25 pmol/l (hypoglycemia) and to 102 +/- 10 pmol/l (euglycemia). Arterial blood glucose decreased from 4.5 +/- 0.2 to 3.0 +/- 0.1 mmol/l during hypoglycemia but did not change during euglycemia (4.3 +/- 0.2 mmol/l). After 150 min, endogenous glucose production reached a plateau value that was higher during hypoglycemia (10.3 +/- 0.6 micromol x kg<sup>-1</sup> x min<sup>-1</sup>) than during euglycemia (5.73 +/- 0.6 micromol x kg<sup>-1</sup> x min<sup>-1</sup>), P < 0.001). Hypoglycemia was associated with a rise in renal glucose production (RGP) from 3.0 +/- 0.7 to 5.4 +/- 0.6 micromol x kg<sup>-1</sup> x min<sup>-1</sup> (P < 0.05), although glucose utilization remained the same (2.0 +/- 0.8 vs. 2.1 +/- 0.6 micromol x kg<sup>-1</sup> x min<sup>-1</sup>). As a result, net renal glucose output increased from 1.0 +/- 0.3 to 3.3 +/- 0.40 micromol x kg<sup>-1</sup> x min<sup>-1</sup>. Elevations in net renal uptake of lactate (2.4 +/- 0.5 to 3.5 +/- 0.7 vs. 2.8 +/- 0.4 micromol x kg<sup>-1</sup> x min<sup>-1</sup>), glycerol (0.6 +/- 0.3 to 1.3 +/- 0.5 vs. 0.4 +/- 0.2 micromol x kg<sup>-1</sup> x min<sup>-1</sup>), and glutamine (0.7 +/- 0.2 to 1.1 +/- 0.3 vs. 0.1 +/- 0.3 micromol x kg<sup>-1</sup> x min<sup>-1</sup>) during hypoglycemia versus euglycemia (P < 0.05) could account for nearly 60% of all glucose carbons released in the renal vein during hypoglycemia. Our data indicate that extraction of circulating gluconeogenic precursors by the kidney is enhanced and responsible for a substantial fraction of the compensatory rise in RGP during sustained hypoglycemia. Increased renal gluconeogenesis from circulating substrates represents an additional physiological mechanism by which the decrease in blood glucose concentration is attenuated in humans.

## **Renal glucose production during insulin-induced hypoglycemia in humans.**

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Diabetes 1999 Feb;48(2):261-6

We investigated the effects of hypoglycemia on renal glucose production (RGP) and renal glucose uptake (RGU) using arteriovenous balance combined with tracer technique in humans. Our 14 healthy subjects had arterialized hand veins (artery) and renal veins (under fluoroscopy) catheterized after an overnight fast. Systemic and renal glucose kinetics were measured with infusion of [6-(2)H<sub>2</sub>]glucose, and renal plasma flow was measured by para-aminohippurate clearance. After a 150-min equilibration period, artery and renal vein samples were obtained between -30 and 0 min, and subjects received a 180-min peripheral insulin infusion (0.250 mU kg<sup>-1</sup> x min<sup>-1</sup>) with a variable infusion of [6-(2)H<sub>2</sub>]dextrose adjusted to maintain plasma glucose at either approximately 60 mg/dl (hypoglycemic clamp) or approximately 90 mg/dl (euglycemic clamp). Blood samples were obtained between 150 and 180 min during the study period. Insulin increased from 49 +/- 14 to 130 +/- 25 (hypoglycemia) and to 102 +/- 10 (euglycemia) pmol/l. Glucose decreased from 5.32 +/- 0.11 to 3.58 +/- 0.07 micromol/ml during hypoglycemia, but it did not change during euglycemia (5.20 +/- 0.19 vs. 5.05 +/- 0.15 micromol/ml). Endogenous glucose production decreased (9.30 +/- 0.70 vs. 5.65 +/- 0.50) during euglycemia but not during hypoglycemia (9.80 +/- 0.50 vs. 10.25 +/- 0.60 micromol x kg<sup>-1</sup> x min<sup>-1</sup>). During hypoglycemia, net renal glucose output increased from 0.54 +/- 0.30 to 2.31 +/- 0.40, RGP increased from 1.88 +/- 0.70 to 3.65 +/- 0.50 (P < 0.05), and RGU did not change (1.34 +/- 0.50 vs. 1.34 +/- 0.60 micromol x kg<sup>-1</sup> x min<sup>-1</sup>). During euglycemia, renal glucose balance switched from a net output of 0.72 +/- 0.20 to a net uptake of 1.70 +/- 0.92, RGP decreased from 2.31 +/- 0.50 to 1.20 +/- 0.58, and RGU increased from 1.59 +/- 0.50 to 2.90 +/- 0.70 micromol x kg<sup>-1</sup> x min<sup>-1</sup> (P < 0.05). During hypoglycemia, arterial glucagons increased from 105 +/- 6 to 129 +/- 8, epinephrine increased from 116 +/- 28 to 331 +/- 33, norepinephrine increased from 171 +/- 9 to 272 +/- 9 (all P < 0.05), and renal vein norepinephrine increased from 236 +/- 13 to 426 +/- 50 (P < 0.001). These data indicate that, in addition to counterregulatory hormones, activation of the autonomic nervous system during hypoglycemia stimulates glucose production by the kidney, which may represent an important additional component of the body's defense against hypoglycemia in humans.

## **Oral administration of growth hormone (GH) releasing peptide-mimetic MK-677 stimulates the GH/insulin-like growth factor-I axis in selected GH-deficient adults.**

Chapman IM; Pescovitz OH; Murphy G; Treep T; Cerchio KA; Krupa D; Gertz B; Polvino WJ; Skiles EH; Pezzoli SS; Thorner MO  
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To determine the effect of the GH releasing peptide (GHRP)-mimetic, MK-677, on the GH/insulin-like growth factor-I (IGF-I) axis in selected GH-deficient adults, we studied nine severely GH-deficient men [peak serum GH concentration in response to insulin-induced hypoglycemia of  $1.2 \pm 1.5$  micrograms/L, mean  $\pm$  SD (range 0.02-4.79)], age 17-34 yr, height  $168 \pm 1.5$  cm, body mass index  $22.6 \pm 3.3$  kg/m<sup>2</sup>, who had been treated for GH deficiency with GH during childhood. In a double-blind rising-dose design, subjects received once daily oral doses of 10 or 50 mg MK-677 or placebo for 4 days over two treatment periods separated by at least 28 days. Four subjects received placebo and 10 mg/day MK-677 in a cross-over fashion in periods 1 and 2. Five subjects received 10 mg and then 50 mg/day MK-677 in a sequential, rising-dose fashion in periods 1 and 2, respectively. Blood was collected every 20 min for 24 h before treatment and at the end of each period for GH measurement using an ultrasensitive assay. The drug was generally well tolerated, with no significant changes from baseline in circulating concentrations of cortisol, PRL, and thyroid hormones. Serum IGF-I and 24-h mean GH concentrations increased in all subjects after treatment with both 10 and 50 mg/day MK-677 vs. baseline. After treatment with 10 mg MK-677, IGF-I concentrations increased  $52 \pm 20\%$  ( $65 \pm 6$  to  $99 \pm 9$  micrograms/L, geometric mean  $\pm$  intrasubject SE,  $P < \text{or} = 0.05$  vs. baseline), and 24 h mean GH concentrations increased  $79 \pm 19\%$  ( $0.14 \pm 0.01$  to  $0.26 \pm 0.02$  microgram/L,  $P < \text{or} = 0.05$  vs. baseline). Following treatment with 50 mg MK-677, IGF-I concentrations increased  $79 \pm 9\%$  ( $84 \pm 3$  to  $150 \pm 6$  micrograms/L,  $P < \text{or} = 0.05$  vs. baseline) and 24-h mean GH concentrations increased  $82 \pm 29\%$  ( $0.21 \pm 0.02$  to  $0.39 \pm 0.04$  microgram/L,  $P < \text{or} = 0.05$  vs. baseline), respectively. Serum IGF binding protein-3 concentrations increased with both 10 mg ( $1.2 \pm 0.1$  to  $1.7 \pm 0.1$  micrograms/L,  $P < \text{or} = 0.05$ ) and 50 mg MK-677 ( $1.7 \pm 0.1$  to  $2.2 \pm 0.2$  micrograms/L,  $P < \text{or} = 0.05$ ). The GH response to MK-677 was greater in subjects who were the least GH/IGF-I deficient at baseline; by linear regression analysis the increase in 24-h mean GH concentration was positively related to both baseline 24-h mean GH concentration ( $r = 0.81$ ,  $P = 0.009$ ) and baseline IGF-I ( $r = 0.79$ ,  $P = 0.01$ ) for 10 mg MK-677. IGF-I responses were not significantly related to any baseline measurement. Fasting and postprandial insulin and postprandial glucose increased significantly after MK-677 treatment, and the clinical significance of these changes will need to be assessed in longer term studies. Oral administration of such GHRP-mimetic compounds may have a role in the treatment of GH deficiency of childhood onset.

#### **Effect of melatonin on hypoglycemia and metoclopramide-stimulated arginine vasopressin secretion in normal men.**

Coiro V; Volpi R; Caffarri G; Capretti L; Marchesi C; Giacalone G; Chiodera P Department of Internal Medicine, School of Medicine, University of Parma, Italy. *Neuropeptides (Scotland)* Aug 1997, 31 (4) p323-6

The present study was performed in order to establish whether melatonin (MEL) plays a role in the regulation of arginine vasopressin secretion (AVP) in normal human subjects. For this purpose, the effects of an oral administration of 6 or 12 mg MEL on basal and metoclopramide (MCP)- or hypoglycemia-stimulated AVP secretion was tested in 18 normal men. MCP was given at a dose of 20 mg as an intravenous (i.v.) bolus; hypoglycemia was induced with an i.v. bolus injection of 0.15 IU/kg body weight of insulin. In addition, in view of the well-known inhibitory effect of MEL on the growth hormone (GH) response to hypoglycemia, GH levels were measured during the insulin tolerance test (ITT), as an independent index of MEL activity. MEL did not produce any change in AVP secretory patterns in basal conditions or during the MCP test. In contrast, the mean peak AVP response to hypoglycemia was 2.33 times higher than baseline in the control ITT, whereas it was only 1.77 times higher than baseline in the ITT plus MEL tests. Also, the GH response to hypoglycemia was significantly lower in the presence than in the absence of MEL. For both AVP and GH, the inhibitory effect of MEL during ITT was similar, when either 6 or 12 mg MEL was given. These data indicate an involvement of MEL in the control of the AVP response to hypoglycemia, but not of basal and MCP-induced AVP secretion. In addition, the similar effects of MEL on GH and AVP secretions during ITT suggest that similar neuroendocrine mechanisms underlie these hormonal responses to hypoglycemia.

#### **Nutritional strategies to minimize fatigue during prolonged exercise: fluid, electrolyte and energy replacement.**

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*J Sports Sci (England)* Jun 1997, 15 (3) p305-13

While the presence of palatable (20 mmol l<sup>-1</sup>) concentrations of NaCl in drinks containing carbohydrate consumed during intense exercise would not be expected to promote absorption or significantly help maintain fluid balance, there is no doubt that athletes should ingest some form of carbohydrate (other than fructose) during moderate-intensity exercise lasting > 90 min. As only approximately 20 g of ingested carbohydrate is oxidized in the first hour of exercise, athletes should probably consume 100 ml every 10 min of a dilute (3-5 g 100 ml<sup>-1</sup>) carbohydrate solution and thereafter increase the carbohydrate concentration to approximately 10 g 100 ml<sup>-1</sup> to match the peak (approximately 1 g min<sup>-1</sup>) rates of plasma glucose oxidation. Drinking more than those amounts of carbohydrate may increase muscle glycogen oxidation by attenuating the fall in plasma insulin concentration and thereby delaying fat mobilization, especially at relatively low (55% of peak oxygen consumption) intensity exercise. As carbohydrate ingestion does not slow the rate of glycogen utilization in working muscle, it is also advisable for endurance athletes to start exercise with an adequate supply of muscle glycogen, irrespective of whether or not they ingest carbohydrate during

exercise. While carbohydrate ingestion 'spares' conversion of liver glycogen to plasma glucose and prevents hypoglycemia, it does not delay the fatigue associated with a low (approximately 20 mmol kg<sup>-1</sup>) glycogen content in working muscle. Conversely, increases in glycogen content of working muscle at the start of exercise have no effect on the rates of plasma glucose oxidation. Higher initial rates of glycogen utilization by active muscles in 'carbohydrate-loaded' subjects decrease the indirect oxidation (via lactate) of non-working muscle glycogen, rather than the conversion of liver glycogen to plasma glucose. Hence, athletes should ingest carbohydrate during endurance exercise even if they have 'carbohydrate-loaded' before exercise.

### **Effects of coca chewing on the glucose tolerance test**

Galarza Guzman M; Penaloza Imana R; Echalar Afcha L; Aguilar Valerio M; Spielvogel H; Sauvain M Laboratorio de Bioquimica, Instituto Boliviano de Biología de la Altura, Facultad de Medicina, Universidad Mayor de San Andrés, Orstom, Bolivia.

Medicina (B Aires) (Argentina) 1997, 57 (3) p261-4

The effects of coca chewing on the glucose tolerance test were measured. The subjects were 14 habitual coca chewers and 14 non-chewers. All were of Aymara ancestry and came from a rural community from the "Altiplano" close to the city of La Paz. The coca users chewed coca leaves during 3 1/2 hours of the test. The non-chewers showed a significant hypoglycemia at 120 minutes of the test. This effect was not observed in the coca chewers. The hormonal counter-regulation response to hypoglycemia worked perfectly in non-chewers, since glucose levels reached normal values at 180 minutes of the test. These results suggest that coca chewers, at high altitude do not present hypoglycemia, due to an antagonistic action of coca metabolites on insulin; allowing a greater availability of glucose in the organism. This would have a positive effect on metabolism in an environment of hypobaric hypoxia, known to lead to situations of hypoglycemia.

### **A metabolic complications of nutritional support. I. Carbohydrates, amino acids, fats, water, ions, trace elements**

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Klinicka Biochemie a Metabolismus (Czech Republic) 1997, 5/4 (251-257)

The paper discusses the metabolic complications described in relation to intake of carbohydrates, amino acids and fats as compounds is parenteral nutrition (PN). Also, the symptoms of possible deficiencies of these nutrients during PN are mentioned. Attention is paid to the dysbalances of selected ions, above all magnesium and phosphate. The significance of trace elements in nutritional support is particularly stressed with respect to metabolism of free radicals. The laboratory monitoring of zinc, and selenium, clinical signs of their deficiency and supplementation during PN are presented. Intoxications described during parenteral supplementation of chromium and manganese are described.

### **Metabolic response to lactitol and xylitol in healthy men.**

Natah SS; Hussien KR; Tuominen JA; Koivisto VA Helsinki University Central Hospital, Department of Medicine, Finland.

Am J Clin Nutr (United States) Apr 1997, 65 (4) p947-50

Sugar alcohols are used in food products, yet their metabolic effects in humans are poorly known. We examined plasma glucose, insulin, and C-peptide responses and changes in carbohydrate and lipid oxidation after the ingestion of 25 g lactitol, xylitol, or glucose. Eight healthy, nonobese men were studied after an overnight fast. After the ingestion of lactitol or xylitol, the rise in plasma glucose, insulin, and C-peptide concentrations was less than after the ingestion of glucose ( $P < 0.02$ ), with no difference between the two polyols. With the glycemic index of glucose as 100, the indexes of xylitol and lactitol were 7 and -1, respectively. A reactive hypoglycemia was observed 3 h after glucose ingestion, but not after the ingestion of sugar alcohols. There were no significant changes in the carbohydrate or lipid oxidation as determined by indirect calorimetry after the ingestion of sugar alcohols. After glucose ingestion, the rise in carbohydrate oxidation was nearly significant ( $P = 0.07$ ). In conclusion, lactitol and xylitol cause smaller changes than does glucose in plasma glucose and insulin concentrations and thermogenic response. A small hormonal response and the lack of a thermogenic effect may be beneficial when these sugar alcohols are used in food products. The small glucose and insulin responses also suggest that lactitol and xylitol are suitable components of the diet for diabetic patients.

### **Alterations in circulating fatty acids and the compartmentation of selected metabolites in women with breast cancer.**

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Biochem Mol Biol Int (Australia) Jan 1997, 41 (1) p1-10

The presence of the tumor in women with breast cancer provokes a profile of biochemical change characterized by hypoglycemia, hyperuremia and high levels of free fatty acids and ketone bodies in plasma. The total circulating levels of amino acids and lactate are slightly higher in patients with breast cancer. Moreover, alterations in the circulating levels of free and total fatty acids are associated with enhanced levels of total free fatty acids and significantly lower levels of esterified arachidonic acid. This profile may indicate a state of moderate catabolic activation in breast cancer patients and may also be associated with a slight mobilization of proteins and fatty acids by some of the peripheral tissues in order to cover the needs of the host and the tumor. However, the alteration in the distribution of different fatty acids (saturated, mono-unsaturated and poly-unsaturated) and the different behaviour of the free and esterified fractions may be the result of a greater release of only specific fatty acids by tumor or other host tissues, rather than a higher release of the whole spectrum of free fatty acids. Thus, it is proposed that some of the alterations may be directly related to localized tumor activity.

### **Glutathione protects against hypoxic/hypoglycemic decreases in 2-deoxyglucose uptake and presynaptic spikes in hippocampal slices.**

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The effects of glutathione, its analogue: YM737 (N-(N-gamma-L-glutamyl-L- cysteinyl) glycine l-isopropyl ester sulfate monohydrate), a monoester of glutathione, and N-acetyl-L-cysteine on hypoxia/hypoglycemia-induced decreases in CA1 presynaptic fiber spikes and 2-deoxyglucose uptake were investigated using rat hippocampal slices. The drugs were added to normal medium for 30 min before the incubation under hypoxic/hypoglycemic conditions (20 min), and, after a 3-h washout, presynaptic potential or 2-deoxyglucose uptake in hippocampal slices was measured. Treatment with glutathione, YM737 and N-acetyl-L-cysteine produced an attenuation of the hypoxia/hypoglycemia-induced decrease in presynaptic fiber spikes and 2-deoxyglucose uptake. The order of potency for neuroprotective action was YM737 > or = N-acetyl-L-cysteine > glutathione. The present results suggest a role for glutathione in improving hypoxia/hypoglycemia-induced dysfunction of hippocampal regions.

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