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CNS Speaker and Competition Abstracts Booklet

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Société canadienne de nutrition

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Session Abstracts

Session 1A: Friday, June 6, 2014, 10:45 AM - 12:00 PM
Claude Roy Symposium on Nutrition and Child Health: Nutritional and Surgical Management of Paediatric Intestinal Failure

SPEAKERS:

- **Dana Boctor, MD, FRCP(C), MSc**
- **Paul Wales, BSc, MD, MSc, FRCSC, FACS**
- **Matthew Nosworthy**

ABSTRACT: Cysteinyl-glycine ameliorates intestinal inflammation in neonatal piglets with parenteral nutrition-induced gut atrophy.

Matthew G. Nosworthy & Janet A. Brunton

Department of Biochemistry, Memorial University of Newfoundland, St. John's NL A1B 3X9, Canada

PepT1 is an intestinal dietary peptide transporter also capable of transporting pro-inflammatory bacterial peptides including formyl-methionyl-leucyl-phenylalanine (fMLP). Cysteinyl-glycine competes for PepT1-mediated uptake and has anti-inflammatory potential. We used an in situ model to measure the ileal mucosal inflammatory response to fMLP when delivered with cysteinyl-glycine in piglets with parenteral nutrition (PN)-induced intestinal atrophy. Pigs (n=6, 10 d) received PN for 4 d to induce SI atrophy; littermates (n=6) remained with the sow. Subsequently, five 10 cm loops of the distal SI were isolated and perfused for 3 h with one of: 1) 5 mM each of L-cysteine and glycine (cys + gly) 2) 5 mM cysteinyl-glycine 3) 10 μM fMLP 4) 5 mM cys + gly + 10 μM fMLP 5) 5 mM cysteinyl-glycine + 10 μM fMLP. In both dietary treatments, intestinal segments exposed to fMLP had higher mucosal TNF-α and IFN- compared to unexposed loops ($p<0.001$). IFN- was higher in PN-fed piglets compared to sow-fed pigs ($p < 0.01$). Co-perfusion of fMLP and cysteinyl-glycine resulted in a lower IFN- response in both sow-fed and PN-fed piglets ($p <0.05$), but neither group responded significantly to free cys + gly. Interestingly, free cys + gly reduced the TNF-α response in sow-fed pigs ($p<0.001$), but not in the PN-fed group. Loops exposed to cysteinyl-glycine and fMLP had lower TNF-α concentrations compared to fMLP alone in both diet groups ($p<0.001$) and in sow-fed piglets the response was significantly more abated than with cys + gly ($p < 0.001$). Interleukin-10, an anti-inflammatory cytokine implicated in the regulation of epithelial permeability, was lower in animals undergoing PN compared to sow-fed ($p<0.05$). Morphologically, fMLP exposure did not alter villus height or crypt depth in sow-fed animals; in contrast, intestinal segments from PN-fed piglets exposed to fMLP had reduced villus height compared to unexposed loops ($p<0.05$). Inclusion of cysteinyl-glycine was effective at attenuating a bacterial peptide-induced inflammatory response in the injured SI; this may be due to efficient dipeptide uptake in a situation of impaired free amino acid absorption, and/or competitive inhibition of fMLP uptake. (Funded by CIHR)

Session 1B: Friday, June 6, 2014, 10:45 AM - 12:00 PM
What should be the Dietary Recommendation for Salt/Sodium? (DEBATE)

SPEAKERS:

- **Mary L'Abbé, PhD**
- **Alexandra Kazaks, PhD, RD**

Session 1C: Friday, June 6, 2014, 10:45 AM - 12:00 PM
Biological Activity and Protective Effects of Berries

SPEAKERS:

- **Katherine Gottschall-Pass, PhD**
- **Wilhelmina Kalt, PhD**
- **John T. Weber, PhD**

ABSTRACT: Consumption of berries upregulates antioxidant enzyme expression in animal models of chronic disease

Katherine Gottschall-Pass, PhD

Applied Human Sciences, University of Prince Edward Island

Numerous studies have shown that consumption of fruits and vegetables reduces disease risk. It has been hypothesized that high levels of polyphenols in fruits and vegetables are responsible for this change. Berries in particular contain high levels of these compounds. A common factor in the development of many chronic diseases is the role of reactive oxygen species (ROS). In biological systems, ROS are produced as part of essential metabolic oxidation reactions. The danger of ROS lies in their ability to react with and damage biological macromolecules. Not only do ROS induce lipid oxidation and inactivate enzymes, they damage proteins, tissue and cell membranes. Once begun, oxidative damage can progress like a chain reaction until arrested by antioxidants. When the ratio of oxidant to antioxidant shifts to favour the former and the antioxidant capacity of a cell is surpassed, oxidative stress results. Low levels of oxidative stress may be countered by up-regulation of endogenous enzyme antioxidants; however, in the presence or high levels of ROS, this defense may be insufficient and disease-causing damage may result. Our research explores the role berries play in the upregulation of endogenous antioxidants in models of chronic disease.

ABSTRACT: Anthocyanin metabolites are abundant and persistent in human urine. Might this help to explain berry health benefits?

Wilhelmina Kalt[1], Jane E. McDonald[1], Melinda R. Vinqvist-Tymchuk[1], Sherry A.E. Fillmore[1] and Yan Liu[2]

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2 Institute of Special Economic Animal and Plant Sciences. CAAS, 4899 Juye Street, Changchun, 130112, CHINA

Introduction. Anthocyanin (Acn) pigments impart the blue, purple, and red coloration to the peel and flesh of many fruit crops and are especially abundant in berries such as blueberries, blackberries and black currants. Acn are also flavonoids and possess a variety of bioactivities *in vitro* that support the notion that berries benefit human health. However it remains an enigma how Acn contribute to health when their capacity for digestive absorption is so low. After ingestion, dietary Acn are no longer detectable in plasma after about 6 hr and after < 24h in urine. Typically about 0.1% or less of the ingested dose can be accounted for in plasma. The *ex vivo* Acn concentration typically reported for plasma or urine is far below that used in Acn bioassays *in vitro*.

Study Design and Analysis. Seventeen volunteers consumed daily 250 ml single-strength wild blueberry juice (BJ) after conforming to a 5-day Acn-free diet. On day 0, 7, 14 and 28 just before and for 24 h after drinking BJ volunteers collected samples from each of their voids. Day 28 was followed by a 7-day Acn-free washout, and then on Day 35 intake of one final dose of BJ, followed by a 24h collection. LC-MS/MS (ABSciex QTrap 4000) was used to scan urine samples for specific 'food' Acn and possible phase 2 Acn metabolites following sample cleanup.

Results. With modern mass spectrometric scanning abilities it was possible to reveal for the first time diverse abundance of phase 2 Acn metabolites in urine even after volunteers had abstained from Acn for the previous 5 days. For 24 h following BJ on Day 0 total urinary Acn was only about 13% higher than pre-BJ. In these samples 'food' Acn contributed only 4% while phase 2 Acn metabolites made up the remaining 96%. The great variety and high total concentration of Acn metabolites suggested that dietary Acn were subject to extensive Phase 1 metabolism and enterohepatic recycling *in vivo*. These results may prompt investigations on the relative role of food Acn vs. Acn metabolites in health, and may influence the design of clinical interventions.

ABSTRACT: Chemical analysis and the potential neuroprotective effects of berries

John T. Weber
School of Pharmacy, Memorial University of Newfoundland

Production of reactive oxygen species (ROS) and reactive nitrogen species (RNS) are natural processes occurring in the brain. However, overproduction of ROS and RNS may occur during brain aging and contribute to neurodegenerative diseases (e.g. Alzheimer's disease) as well as disorders such as stroke. Polyphenols, such as anthocyanins, are a large class of phytochemicals that are widespread in the plant kingdom and are known to have antioxidant capacities. We have analyzed extracts from the fruits and leaves of several species of berries that are native to Newfoundland and Labrador, including bilberries, blueberries and lingonberries (partridgeberries). High performance liquid chromatography analysis revealed several polyphenolic compounds in extracts, and biochemical assays indicated that the extracts had high total antioxidant capacity in terms of radical scavenging activity and reducing power. Interestingly, overall antioxidant capacity was much higher in the leaves of blueberries and lingonberries, compared to their fruits. We next tested the potential neuroprotective effects of the extracts using brain-derived cultures of neurons and glia *in vitro*. Cells were either injured using an *in vitro* traumatic injury model, or by glutamate-mediated excitotoxicity, a pathological process by which cells are damaged and killed by excessive stimulation from glutamate, in part by overproduction of ROS and RNS. Cultures that were traumatically injured in the presence of extracts displayed less cell death as measured using a variety of assays. Cell cultures exposed to glutamate (100 μM) for 24 hours demonstrated obvious cell loss and morphological abnormalities. Surprisingly, treatment of cells with extracts from the fruits and leaves of blueberries and lingonberries demonstrated profound protection. These findings suggest that berries or their components may provide protection to the brain from various pathologies. This protective effect may be due to a decrease in oxidative or nitrosative stress, or to other mechanisms. Importantly, the extent to which polyphenols from berries cross the blood brain barrier and achieve good bioavailability is relatively unknown. Appropriate and accurate extrapolation of findings from *in vitro* experiments to biological activity *in vivo* will be discussed. (Supported by the Natural Sciences and Engineering Research Council and the Canada Foundation for Innovation)

Friday, June 6, 2014, 12:45 - 1:45pm

Home TPN: Exploring Management of Central Line Infections and Indications for Intestinal Transplant

SPEAKERS:

- **Stuart Rosser, MD**
- **Yaron Avitzur, MD**
- **Alastair Forbes, MD**

ABSTRACT: **Who Needs Intestine Transplantation? - Referral and Listing Criteria**

Yaron Avitzur, MD

Intestine transplantation is the recommended treatment modality for carefully selected patients with intestinal failure and severe or life threatening complications. The outcome of intestine transplantation has improved over the last decade and now reaches 1 and 5-year patient survival of 70% and 50% respectively. However, patient outcome is hampered by high mortality of listed patients as a result of delayed referrals for transplant assessment and the current organ allocation criteria. Early referral for transplant evaluation of potential candidates is critical and will improve patient outcome. Patients fulfilling one of the following criteria should be referred for transplant assessment: Intestinal failure associated liver disease with bilirubin >80 mmol/L or portal hypertension; Recurrent severe catheter related sepsis; Loss of 50% of conventional central venous access sites; massive resection of small bowel (>75% of bowel); Unresectable benign tumors (desmoid); Massive mesenteric vascular thrombosis with gut or liver impairment; Patients with severely diseased bowel and unacceptable morbidity; unacceptable poor quality of life; and Request of the patient or family.

Following a transplant assessment selected patients will be listed for intestine, liver-intestine or multi-visceral (stomach, small bowel, pancreas and liver) transplantation. The surgical technique and type of transplant is determined based on the patient's etiology and end organ failure (intestine, liver or both). Criteria for listing for transplantation include the following: Progressive Intestinal failure associated liver disease with bilirubin >100 mmol/L, synthetic liver failure or severe portal hypertension; Recurrent severe life threatening episodes of sepsis; Loss of 50% or more of conventional central venous access sites; Unresectable benign tumors (desmoid); Massive mesenteric vascular thrombosis with gut or liver impairment; and unacceptable poor quality of life.

Timely referral and listing for intestine transplantation is critical for improved outcome and survival of patients with intestinal failure. Intestine transplantation is an integral part of the treatment armamentarium for intestinal failure and should be offered for patients who fulfill the listing criteria.

Session 2A: Friday, June 6, 2014, 2:00 PM - 3:15 PM

An Interdisciplinary Approach to Nutrition Screening and Assessment for Patients Admitted to Acute Care Hospitals

SPEAKERS:

- **Khursheed Jeejeebhoy, MBBS, PhD, FRCPC**
- **Dieneke van Asselt, MD, PhD**

ABSTRACT: Subjective Global Assessment: A comprehensive clinical assessment tool

Khursheed Jeejeebhoy MBBS, PhD, FRCPC
Director of Home Nutrition Program, St. Michael's Hospital
Emeritus Professor of Medicine University of Toronto

Nutrition screening is necessary to quickly and efficiently identify patients who require further assessment, however these tools typically only consist of two or three parameters that can misclassify patients, as their sensitivity is typically 70% or below. Nutrition risk and malnutrition require confirmation, but in a busy clinical service this can be elusive as objective parameters have a wide normal ranges and are also influenced by disease (e.g. albumin).[1] Subjective Global Assessment (SGA) and the Patient Generated SGA are the only valid and reliable standardized **assessment** methods that are sufficiently efficient to be used in all patients, or those identified by nutrition risk screening. Based on key symptoms, physical parameters and history (e.g. food intake, functional status, disease status) that influence nutritional status, as well as incorporating the rapidity of change in body mass and function based on disease, this assessment can be quickly done at bedside on a routine basis without measurements of weight/BMI, arm muscle circumference, fat in skin fold thickness and albumin levels. The original validation work showed that it correctly predicted nutrition associated complications[2] and had better sensitivity ans specificiaty than individual traditional parameters in predicting outcome[3]. Detsky el al. [4]found that the use of SGA in evaluating hospitalized patients gives reproducible results and there was more than 80% agreement when two blinded observers assessed the same patient. This presentation will review the components of the SGA, emphasizing its utility in general medicine and surgery patients. Due to the prevalence of malnutrition in acute care, SGA is a valuable tool for confirming nutritional status post screening and should be a part of standardized nutrition care pathways, as it provides a sufficiently efficient but effective assessment process.

REFERENCES

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2 Baker, J., A.S. Detsky, D.E. Wesson, S.L. Wolman, S. Stewart, J. Whitwell, B. Langer and K.N. Jeejeebhoy. Nutritional assessment: a comparison of clinical judgment and objective measurements. N Engl J Med 306: 969-972, 1982.

3 Detsky, A.S., Baker, J.P., Mendelson, R.A., Wolman, S.L., Wesson, D.A., and Jeejeebhoy, K.N. Evaluating the accuracy of nutritional assessment techniques applied to hospitalized patients: methodology and comparisons. JPEN 8:153, 1984.

4 Detsky, A.S., McLaughlin, J.R., Baker, J.P., Johnston, N., Whittaker, S., Mendelson, R.A., and Jeejeebhoy, K.N. What is subjective global assessment of nutritional status? JPEN 11: 8, 1987.

ABSTRACT: The Dutch Approach

Dieneke van Asselt, MD, PhD

Two related topics will be covered in the presentation. First, the approach of Dutch Malnutrition Steering Group (DMSG) to fight malnutrition in ten steps: 1. Install a national multidisciplinary steering group, representing the disciplines involved in screening and treatment of malnutrition and which has authority; 2. Create awareness for the problem of disease related malnutrition by collecting and publishing prevalence data; 3. Provide protocols with tools and treatment plans; 4. Command screening and treatment with the use of compulsory quality indicators by the health care inspectorate; 5. Facilitate and perform research to obtain evidence for tools, treatment and cost-effectiveness; 6. Obtain the Ministry of Health as a key stakeholder to strengthen the message; 7. Implement projects in all health care settings to create a chain for nutrition care; 8. Provide toolkits with tools, ready-to-use presentations and best practices, downloadable, free accessible to everyone; 9. Install multidisciplinary project teams in all institutions; 10. Organize training programs, workshops and symposia. Through these ten steps the prevalence of malnutrition has steadily decreased in all health care settings. Key in the success of the DMSG is the mandatory quality indicators.

The second topic concerns the recently published Dutch guideline for malnutrition in geriatric patients. This guideline covers the definition, assessment, treatment, transmural communication, multidisciplinary roles and responsibilities, and four compulsory quality indicators. In addition, an accompanying app will be presented.

Session 2B: Friday, June 6, 2014, 2:00 PM - 3:15 PM

Beyond BMI: New Approaches to Childhood Obesity and Chronic Disease Prevention

SPEAKERS:

- **Tracey Bridger, MD, FRCP(C)**
- **Geoff Ball, PhD, RD**

ABSTRACT: Beyond BMI: New approaches to childhood obesity and chronic disease prevention

Tracey Bridger and Geoff Ball

Despite years of research and interventions, concerns surrounding childhood obesity rates and the impact of this on the health of children and their risk of chronic disease in adulthood remain. It is clear that most traditional approaches are not effective and many have shown to be quite harmful. Mounting evidence shows that there needs to be a paradigm shift in our approach to childhood obesity and chronic disease prevention. In order to move towards healthier, happier children and adults, we must shift our focus from weight to a more holistc view of health.

This session will review current evidence on what influences the health of children and what risk factors of later chronic disease (including obesity, insulin resistance, inactivity, poor nutrition) start in childhood. We will explore ways to approach and manage these risk factors successfully, without causing harm to the child and family.

Session 2C: Friday, June 6, 2014, 2:00 PM - 3:15 PM
Improving the Way Nutritional Information is Provided on Food Labels!

SPEAKERS:

- **William Yan, PhD**
- **Hasan Hutchinson, PhD, ND**
- **Paula Trumbo, PhD**
- **Mary L'Abbé, PhD**

ABSTRACT: Proposed Amendments to U.S. Nutrition Facts Label

Paula Trumbo
US Food and Drug Administration

The US Food and Drug Administration (FDA) recently published a proposed rule to amend various provisions of the regulations for the Nutrition and Supplement Facts label. Some of the changes include 1) no longer permitting "Calories from fat," 2) caloric values for soluble fiber and sugar alcohols, 3) mandatory listing of vitamins and minerals, 4) mandatory listing of added sugars, 5) updated Daily Values for vitamins, minerals and dietary fiber, 6) a definition for dietary fiber, 7) Daily Values for subpopulations, 8) requirements for record keeping, and 9) the Nutrition Facts label format. FDA also published a proposed rule on serving size. The FDA is currently accepting public comments. Based on the review of public comments and any new relevant information, FDA will publish a final rule to amend the regulations on the Nutrition and Supplement Facts labels, as well as serving size.

ABSTRACT: Health Canada Update on Nutrition Labelling Activities

William Yan, PhD and Hasan Hutchinson, PhD, ND
Health Canada

The Government of Canada's latest Speech from the Throne (October 2013) made a commitment to consult with Canadian parents to improve the way nutritional information is presented on food labels. On January 28, 2014, Health Canada launched the first phase of the nutrition labelling review, which focussed on consulting parents and other consumers on their use, understanding and needs with respect to using food labels to make healthier food choices for themselves and their families. Health Canada plans to publish a report of what was heard from Canadians during face-to-face sessions and from comments submitted through the on-line component of the consultation. Building on the first wave of consultations, Health Canada will be launching the second phase of the nutrition labelling review in the spring, focussing on technical elements of the Nutrition Facts table. To help consumers more easily read food labels and compare products, Health Canada will first consult on proposed new guidelines to help food industry make serving sizes shown in the Nutrition Facts table more consistent between similar foods. This will be followed by consultations on the regulated reference amounts that will form the basis of the serving size guidance, as well as on proposed updating of the daily values (DVs) used in generating %DVs, and possible changes to the list of core nutrients. Results will be used to develop options for testing with consumers and stakeholders in the fall, which will help inform the future direction for improving nutrition labelling in Canada. To further support Canadians in making healthier food choices, Health Canada has developed educational materials and public campaigns about the Nutrition Facts table since its introduction in 2003. The Nutrition Facts Education Campaign (NFEC) was launched in 2010 as a collaborative effort between Health Canada and the food industry, and focussed on raising consumer awareness and understanding of the Nutrition Facts table, and in particular, the % Daily Value. With changes coming to improving the consistency of serving sizes on food labels, Health Canada plans to expand the scope of the NFEC to educating consumers on how to use the serving size in choosing and comparing foods to make healthier choices.

Session 3A: Friday, June 6, 2014, 4:00 PM - 5:15 PM
The Human Microbiome in Health and Disease

SPEAKERS:

- **Eytan Wine, MD, PhD**
- **Remy Meier, MD**

ABSTRACT: Who Are We Really Feeding? Nutrition and Microbes in Health and Disease

Eytan Wine, MD, PhD
Departments of Pediatrics and Physiology, University of Alberta, Edmonton, AB

The critical role of host-microbe interactions in normal development and disease has received much attention over the last few years due to advances in tools assessing microbial composition and development of complex experimental models. Detrimental changes in microbes (termed *dysbiosis*) are now linked to immune-mediated and metabolic conditions, including inflammatory bowel diseases (IBD), allergies and asthma, obesity and metabolic syndrome, and even cancer. Mechanisms for these effects have been thought to mainly relate to establishment and maturation of mucosal immunity and microbes are recognized as an integral part of host defense.

While microbes have been known to assist the gut in nutrition, for example through mediating the availability of otherwise indigestible calories, production of short chain fatty acids, and biosynthesis of vitamins and micronutrients, recent publications have highlighted another aspect of this relationship - the ability of nutrients to change and even control microbes and their effects, presenting the concept of a nutrition-microbe-gut/immune axis. This axis could be manipulated to benefit the host by controlling immune responses and gut physiology through controlled alterations in nutrition, which could revolutionize how we treat patients in the future.

During this presentation I will first provide an overview of the nutrition, microbe, gut/immune axis, highlighting basic observations and mechanisms by which nutrients affect health by altering microbes. Next, I will focus on nutrition and bacteria in early development, describing how infant feeds affect the microbiome, and the evolution of microbes with age, in relation to nutrition. Finally, mechanisms of microbe-induced inflammation will be illustrated, as will examples of how nutrition could change this, to benefit health. Specific examples already in use in patient care include use of complex carbohydrates (*e.g.*, prebiotics) and exclusive nutritional therapy in pediatric Crohn disease. However, these principles could expand into treatment and prevention of many more disease in the future, once extensive research in this evolving filed is completed.

Session 3B: Friday, June 6, 2014, 4:00 PM - 5:15 PM
Advances in Nutrition and Obesity Research in Atlantic Canada

SPEAKERS:

- **Sara Kirk, PhD**
- **Jennifer Taylor, PhD**
- **Brandon Gheller**
- **Shannan Grant, MSc, RD**

ABSTRACT: The Healthy Living Challenge

Sara Kirk, PhD

Canada Research Chair in Health Services Research, School of Health and Human Performance, Dalhousie University

Public policy is a critical component of population health interventions and offers an important opportunity to address the rising public health concerns of child and adolescent obesity. Rates of overweight and obesity have increased over the last two decades and have significant health and economic implications. Current evidence suggests the need for comprehensive, sustainable initiatives to produce a population-level change in childhood weight status and to address the range of factors that have created an "obesogenic" environment. Using data from studies undertaken in Nova Scotia, this presentation will explore the costs and consequences of obesity in children, with a focus on school-based research from the Children's Lifestyle And School performance Study (CLASS). The challenges and opportunities of research to evaluate the impact of healthy public policies for obesity prevention will also be considered.

ABSTRACT: Are school nutrition policies worth the effort? Evaluating the Prince Edward Island Elementary School Nutrition Policy

Jennifer P Taylor, PhD, RD

While school nutrition policies have become the norm across the country, there are only a few studies which have evaluated the impact of such policies on dietary behaviours and weight status. This presentation will provide an overview of the findings of the recently completed five year SNAP (School Nutrition & Activity Project) research project in Prince Edward Island, which evaluated the level of policy implementation and policy impact on children's food intakes at school and at home, as well as weight status using a population based sample of grade 5 and 6 children. Results suggest that, while there were some positive impacts on food and nutrient intakes, rates of overweight and obesity increased over the five years of implementation. Challenges in addressing the poor eating habits and rising obesity rates across the country using healthy public policy will be discussed.

RESEARCH ABSTRACT: **Higher circulating levels of insulin after a dairy snack in children are not determined by insulin secretion as measured by C-peptide but rather reduced levels of hepatic insulin extraction**

Brandon JF Gheller[1], Mary Gheller[1], Athena Li[1], N. Theresa Glanville[1] Younes Anini[2], Nick Bellissimo[3], Jill Hamilton[4], G. Harvey Anderson[5], Bohdan L Luhovyy[1]

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A dairy product provided as a snack has been shown to increase subsequent serum insulin levels and reduce levels of blood glucose in children compared to a non-dairy snack of the same available carbohydrate content and similar energy but lower in protein and higher in fat. Therefore, the objective of this study was to measure serum C-peptide in previously collected samples from normal weight and overweight/obese children to determine if the observed increase in insulin is due to increased secretion or reduced hepatic clearance. Methods: In a repeated measures crossover design, normal weight (5th-85th BMI percentile; n =11, 5 boys and 6 girls) and overweight/obese (>85th BMI percentile; n =7, 7 boys) children (age: 9-14 y), were randomly assigned to consume one of two treatments containing 25 g of available carbohydrates: Greek-style sugar-sweetened yogurt (GY, 198.9 g, 171 kcal, 0 g fat, 26.1 g total carbohydrate, 23.9 g sugar, 1.1 g fibre, 17 g protein) and mini sandwich type cookies (C, 37.5 g, 175 kcal, 7.5 g fat, 26.3 g total carbohydrate, 15 g sugar, 1.3 g fibre, 1.3 g protein). Venous blood samples were collected at 0 min (immediately before the treatment), and at 30, 60, 90 and 120 min. Insulin secretion was calculated from deconvolution of plasma C-peptide and hepatic insulin extraction was calculated as mean C-peptide divided by mean insulin. Results: There was no difference between treatments in baseline C-peptide levels. There was an effect of time ($P<0.001$) but not treatment ($P=0.5221$) or weight status ($P=0.9110$) on mean two-hour concentrations of C-peptide and its area under the curve (AUC). There was no effect of treatment ($P=0.3607$), time ($P=0.1755$) or their interaction ($P=0.3211$) on insulin secretion (C 5.02 $\pm$ 0.42 pmol/kg/min, GY 4.66 $\pm$ 0.35 pmol/kg/min). There was a difference between the treatments in baseline hepatic insulin extraction ($P>0.01$). When expressed as change from baseline, there was an effect of time ($P<0.05$) and treatment ($P<0.01$) indicating less hepatic insulin extraction after GY. Conclusion: The sustained levels of increased circulating insulin in children after consuming a snack high in milk protein are mediated by reduced hepatic insulin clearance. (Supported by an internal grant from Mount Saint Vincent University and Dairy Farmers of Canada)

RESEARCH ABSTRACT: The effect of continuous sipping of a glucose solution on markers of oxidation in men and women

Shannan Grant[1,2], Robert Josse[1,2], Edward Barre[3], and Thomas Wolever[1,2]

[1]Department of Nutritional Sciences, Faculty of Medicine, University of Toronto; [2]Keenan Research Centre of the Li Ka Shing Knowledge Institute of St. Michael's Hospital; [3]Department of Health Sciences and Emergency Management, School of Professional Studies, Cape Breton University

Acute increases in blood glucose (BG) impair physiological homeostasis by increasing oxidative stress and lowering antioxidants in serum/plasma. This phenomenon has led to the hypothesis that low glycemic index (GI) foods decrease postprandial oxidative stress. Previous studies support this hypothesis, but are limited by lifestyle confounders. We aimed to eliminate these confounders and address the question: Will slowing carbohydrate absorption reduce postprandial oxidative-stress? Participants (n=18) were administered four treatments: Glucose solution as bolus (B), B plus 1g vitamin-C (BC), glucose sipped evenly over 3hr (S), and S plus 1g vitamin-C (SC). Blood samples were drawn at 0, 30, 60, 120, 180, 240, 270, 300 and 360 min. Standard lunch was given after the 240 min blood sample. Total peroxyl radical trapping antioxidant potential (TRAP, primary endpoint), glucose, insulin, free fatty acids (FFA), vitamin-C, C-reactive protein, LDL oxidation and conjugated dienes were measured (results are shown as means $\pm$ pooled SEM). S significantly flattened the BG and insulin curve and reduced FFA rebound ($p<0.05$). TRAP was significantly affected by time, rate of glucose administration, and whether vitamin-C was administered ($p<0.05$). S attenuated TRAP fluctuations. There was no significant change in TRAP after S and SC over the 360 min experimental period. TRAP was significantly higher after SC treatment than B at 300 min (81.7 versus -50.9 $\pm$ 31.1 µmol/L; $p=0.023$). By 360 min, TRAP was significantly less after B than after BC, S, and SC, respectively (-153.1 versus 10.4, 7.9, and 105.9 $\pm$ 32.607; $p<0.05$). Neither rate nor vitamin-C significantly influenced C-reactive protein, LDL oxidation and conjugated dienes. The preliminary results suggest that slowing glucose absorption reduces postprandial oxidative stress to a similar extent as 1g vitamin-C. This work provides additional insight into the mechanism by which low GI foods reduce risk for diabetes and provide rationale for subsequent studies examining the effect of delayed carbohydrate absorption on postprandial oxidative stress. (Supported by Canadian Institutes for Health Research)

Session 3C: Friday, June 6, 2014, 4:00 PM - 5:15 PM
Effective Nutrition Care Process for Canadian Hospitals

SPEAKERS:

- **Johane Allard, FRCPC, MD**
- **Jack Bell, APD**

ABSTRACT: Malnutrition in Canadian hospitals: prevalence, association with length of stay, in-hospital changes and contributors

Johane Allard, FRCPC, MD

Malnutrition is prevalent in hospitals and increases health care resource utilization. We conducted a prospective multicenter cohort study including patients 18 years and older admitted to 18 acute care hospitals across Canada. In the first part of the study we examined the prevalence of malnutrition, pre-admission factors associated with malnutrition and the association between malnutrition at admission and length of hospital stay (LOS). In the second part, nutritional status changes during hospitalization, association between these changes and LOS and factors associated with deterioration of nutritional status were examined. Subjective global assessment (SGA) was the primary measure of nutritional status; malnutrition was defined as SGA B+C. SGA was measured at admission and discharge. SGA at admission was measured in 1015 patients, 45% [95% CI: 42 to 48] were malnourished. Independent factors associated with malnutrition at admission in a multivariate logistic regression model were: Charlson comorbidity index >2, having 3 diagnoses, relying on adult children for grocery shopping and living alone. The multivariate Cox PH model showed that malnutrition was independently associated with prolonged LOS (HR 0.77, CI (0.66, 0.91)). Changes in nutritional status were analyzed in a 693 patients with SGA measured both at admission and discharge. Patients were divided into short stay (<7d) and prolonged stay (≥7d) groups. In the short-stay group, nutritional status deteriorated (SGA A to B/C, or B to C) in 6%, and improved (SGA B to A, or C to B/A) in 11%. In the prolonged-stay group, SGA deteriorated in 20% while it improved in 17%. For the majority of patients nutritional status did not change. Multivariate analyses were based on the group staying >7 days (n=424). In logistic model male gender, having 2 or 3 diagnoses, cancer, low food intake, dissatisfaction with taste of hospital food and pain affecting amount of food eaten were independently associated with deterioration in SGA. In multivariate Cox PH model nutritional deterioration was associated with prolonged LOS (HR 0.56, CI: 0.43, 0.74). Malnutrition at admission and deterioration in-hospital increases LOS. Interventions need to be targeted on risk factors that are amenable to change and can improve food intake.

ABSTRACT: Identifying and Overcoming Barriers to Effective Nutrition Care in Elderly, Multimorbid Inpatients

Jack Bell, APD

Background & aims: Malnutrition is highly prevalent and perceived resistant to intervention following hip fracture. A multiphase, pragmatic, action research based approach to identify and overcome barriers to nutritional care in hip fracture compared the impact of individualised versus multidisciplinary nutritional care on patient and healthcare outcomes.

Setting: A metropolitan hospital acute hip fracture unit.

Methods: Four sequential action research cycles built upon baseline data including 614 acute hip fracture inpatients and 30 purposefully sampled clinicians involved in treating them. Phase I considered nutrition screening and assessment in hip fracture including two diagnostic accuracy studies and a prospective, consecutive case series. Phase II reported a further prospective, consecutive case series investigating protein and energy intakes post hip fracture and inpatient barriers to intake. Phase III built on earlier results including an explanatory mixed methods study and presented additional patient and clinician barriers and facilitators to nutritional care. Subsequent changes to routine clinical practice were developed and implemented by the treating team between Phase III and IV; these were implemented as a new multi-disciplinary, multi-modal nutritional model of care. A controlled before and after study was then used to compare the new model of care to individualised nutrition care. Ethics approvals for all phases were obtained.

Results: Publications resulting from this study highlight novel barriers and facilitators identified across the nutrition care process. Engagement of the multidisciplinary team in a multiphase, pragmatic action research intervention significantly reduced observed and reported barriers, doubled energy and protein intakes, tripled return home discharge rates, and effected a 75% reduction in nutritional deterioration during admission in a reflective cohort of hip fracture inpatients when compared with an individualised nutritional care model. Conclusions: Multidisciplinary nutritional care improves nutrition intake and outcomes in acute hip fracture inpatients. The multiphase, pragmatic action research approach facilitated exploration of the root causes of nutritional barriers and enabled engagement of the multidisciplinary team to develop, implement and evaluate effective and applicable solutions within the constraints of routine clinical practice. Similar pragmatic study designs should be considered in other elderly inpatient populations perceived resistant to nutritional intervention.

Session 4A: Saturday, June 7, 2014, 10:45 AM - 12:00 PM
Protein Provision in Critical Illness: Does One Size Fit All?

SPEAKERS:

- **Rupinder Dhaliwal, RD**
- **Charlene Compher, PhD, RD, FASPEN**

ABSTRACT: Protein in Critical Illness: Evidence and Current Practices

Rupinder Dhaliwal, RD

Despite nutrition therapy being an integral part of standard patient care, evidence surrounding the appropriate amount of nutrition and protein to provide critically ill patients is controversial. Most clinical practice guidelines recommend early enteral nutrition to optimize calorie and protein intake (1, 2, 3) with recent advocates suggesting protein doses as high as 2.5 grams/kg/day (4), yet other guidelines recommend low-dose enteral feeding in the first week of ICU stay (5) . Signals from observational studies of nutrition practices show that better protein intakes are associated with better outcomes in critically ill patients (6, 7, 8), however surveys of current practices show that underfeeding in ICUs still exists and protein needs are not being met (9). Innovative approaches to overcome barriers associated with protein delivery such as the PEP UP Protocol and the use of supplemental PN in high risk patients may help in improving protein intakes in this population.

LEARNING OBJECTIVES:

At the end of this talk, you will be familiar with the

1. Latest evidence behind optimizing nutrition and protein intake in critical illness.
2. Results of the International Nutrition Survey of current protein intakes in critically ill patients.
3. Recent efforts at improving the delivery of protein in ICUs i.e. the PEP UP Protocol & the use of supplemental parenteral nutrition in high risk patients.

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ABSTRACT: Protein in Critical Illness: Dose vs. Diagnosis

Charlene Compher, PhD

While it is widely accepted that protein catabolism is increased in critically ill patients due to the stress of injury or infection, little is known about the most optimal dose of protein intake to achieve optimal clinical outcomes. Some thought leaders suggest that high protein doses are needed (1), particularly in patients with obesity (2). However, others are concerned that cellular autophagy processes may be impaired by high protein feeding (3, 4). Patients with sepsis (5), and those with high nutritional risk (6) have lower mortality with additional protein intake. Clearly, in patients with shock and multi-organ failure, supplemental glutamine should not be given (7,8). This session will demonstrate the evidence behind protein dose in critical illness and attempt to decipher the sources of these contradictions.

LEARNING OBJECTIVES:

At the end of this talk, you will be able to:

1. Describe the importance of protein intake in critically ill patients.
2. Recognize key diagnoses or conditions when protein dose should be modified.
3. Articulate areas of research to follow for future developments.

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Session 4B: Saturday, June 7, 2014, 10:45 AM - 12:00 PM
Interventions to Address Food Insecurity in Canada

SPEAKERS:

- **Valerie Tarasuk, PhD**
- **Sharon Kirkpatrick, PhD**
- **Virginia Lane, RD, MA**

ABSTRACT: Money Matters: policy interventions to reduce food insecurity in Canada

Valerie Tarasuk, Naomi Dachner, Andrew Mitchell, Rachel Loopstra, Herb Emery, Lynn McIntyr

Household food insecurity (i.e., inadequate or insecure access to food due to financial constraints) has risen significantly in Canada in recent years. More than 4 million Canadians lived in households affected by food insecurity in 2012. In this presentation, we weave together insights from several different analyses of data from the Canadian Community Health Surveys (CCHS) to delineate the effects of specific federal and provincial policy decisions on the vulnerability of low-income households to food insecurity and identify future directions for intervention. Findings from a multivariate analysis of data from the 2011-12 CCHS point to the significance of household income in predicting vulnerability, but they also reveal differential patterns of vulnerability depending on main source of income. Compared to households reliant on salaries or wages, those reliant on old-age pensions and retirement benefits are less likely to be food insecure, whereas households on social assistance, Employment Insurance or Workers' Compensation are at much higher risk. Further examination of the apparent protective effect of seniors' incomes suggests that the guaranteed annual incomes provided to Canadians over 65 effectively cut the vulnerability of low-income adults in half (Emery, Fleisch and McIntyre, 2013). While seniors' incomes are primarily a function of federal policy, inter- and intra-provincial comparisons of food insecurity rates indicate that provincial policies are also important determinants of household food insecurity. The prevalence of food insecurity has remained stable or slightly increased in most provinces and territories in recent years, but it dropped significantly in Newfoundland and Labrador between 2007 and 2011. This decline appears in part to reflect the impact of Newfoundland and Labrador's poverty reduction strategy, a finding that highlights the value of policy interventions that target depth of poverty. Both the protection from food insecurity afforded to Canadian seniors through guaranteed annual incomes and the reduction in food insecurity observed in Newfoundland and Labrador argue that policy interventions to improve the adequacy and security of household incomes are an effective strategy to reduce food insecurity in Canada.

ABSTRACT: A between-country comparison of nutritional vulnerability associated with food insecurity: Insights for policy and program responses

Sharon I. Kirkpatrick[1], Kevin W. Dodd[2], Ruth Parsons[3], Carmina Ng[4], Didier Garriguet[5], Valerie Tarasuk[4]

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Household food insecurity is a serious public health problem in need of effective responses. The use of the same metric to monitor food insecurity in different countries provides the opportunity for comparative analyses to interrogate experiences of food insecurity in different contexts and the impact of interventions on this problem. In Canada and the US, food insecurity is measured using the

Household Food Security Survey Module. The most recent statistics indicate that the prevalence of food insecurity in the US is double that observed in Canada. This is despite the fact that, unlike Canada, the US has extensive food programs intended to provide assistance to vulnerable households. Other contextual factors that could influence food security include income support programs, food fortification regulations, and food pricing. Using data from Canada and the US, we conducted a comparative analysis to explore the potential implications of existing policies and programs in mitigating the nutritional manifestations of food insecurity. Drawing upon the 2004 Canadian Community Health Survey and the 2003-2006 National Health and Nutrition Examination Survey, we examined prevalences of inadequate intakes of vitamins A and C, folate, calcium, magnesium and zinc among individuals aged 9 years and older, according to household food security status. The observed prevalences of nutrient inadequacies differed between the two countries irrespective of food security status, with higher prevalences of inadequate vitamin C and magnesium intake in the U.S. compared to Canada. However, food insecurity appeared to take a bigger toll on nutrition in Canada, with higher prevalences of inadequate intakes evident among individuals in food-insecure households compared to their food-secure counterparts for calcium, magnesium and zinc. In the U.S., a significant gap in prevalences of inadequate intakes by food security status was evident only for vitamin A. The results of this study, in combination with contextual information on the policies and programs in place in each country, will inform further work to identify potential interventions to alleviate food insecurity and its effects.

RESEARCH ABSTRACT: Unpacking the health and nutritional risks of newcomer children

Virginia Lane, Hassan Vatanparast

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Newcomers are usually healthy when they arrive in Canada, but subsequently experience health declines shortly thereafter. It is important to understand the health and nutrition issues of newcomer children as dietary patterns are established early in childhood and impact the development of chronic disease. This study evaluates the health/nutritional status of newcomer children through a cross-sectional analysis of 299 participants aged three to thirteen years who have been in Canada for less than five years. Questionnaires evaluate socio-demographics, food security, and physical activity. Participants' diets are assessed through serial 24 hour recalls. Physical measurements include total body bone mineral content (TBBMC), blood pressure, serum vitamin D, total cholesterol, and glucose. Half of refugees (43%) and one quarter of immigrants (26%) were low income. Given the prevalence of low income, it is not surprising that 40% of refugees and 24% of immigrants experienced food insecurity, which is higher than the prevalence of food insecurity previously observed among immigrants (13%) in the Canadian Community Health Survey 2008. Young children in food insecure households tend to consume an energy dense diet that contributes to the establishment of unhealthy eating patterns and leads to obesity and chronic diseases. There was a higher rate of overweight/obesity among immigrants (32%) compared to Saskatchewan-born children (28%), while refugee children were at reduced risk (22%). Dietary assessments revealed that newcomers do not consume sufficient servings of milk/alternatives, and have low intakes of vitamin D (92%) and calcium (81%). Inadequate zinc intake was common among participants (38% girls versus 22% boys). Newcomer children's TBBMC was similar to the Canadian-born; however, 44% of refugees and 38% of immigrants had low TBBMC. 72% of refugee and 53% of immigrant children were vitamin D deficient or had inadequate levels to support optimal development, which is greater than the Canadian–born. In addition, 28% of refugees and 8% of immigrants had high blood cholesterol. Overall the study results indicate that newcomer children are at risk for food insecurity, vitamin D deficiency and poor dietary practices; while immigrants are at increased risk of obesity; and refugees are at risk for high cholesterol. (Supported by the Saskatchewan Health Research Foundation)

Session 4C: Saturday, June 7, 2014, 10:45 AM - 12:00 PM
One-Carbon Metabolism: Perspectives from Newfoundland and Ireland

SPEAKERS:

- **Anne Molloy, PhD**
- **John T. Brosnan, DPhil, DSc, FRSC**
- **Mary Ward, RD, PhD**

ABSTRACT: **One-carbon metabolic profiling in a genetically homogeneous young adult population**

[1]Anne M. Molloy, [2]Faith Pangilinan, [3]Barry Shane, [4]Per M. Ueland, [5] Cheryl D. Cropp, [5]Yoonhee Kim, [5]Joan E. Bailey-Wilson, [5]Alexander F. Wilson, [6]Peadar N. Kirke, [7]John M. Scott, [8]James L. Mills, and [2]Lawrence C. Brody.

[1]School of Medicine, Trinity College Dublin, Ireland, [2]Molecular Pathogenesis Section, Genome Technology Branch, NHGRI, [3]Nutritional Science and Toxicology, University of California, Berkeley CA, [4]Section of Pharmacology, Institute of Medicine, University of Bergen and Haukeland University Hospital, [5] Inherited Disease Research Branch, NHGRI; [6]Child Health Epidemiology Division, Health Research Board, Dublin, [7] School of Biochemistry and Immunology, Trinity College Dublin, [8] Division of Intramural Population Health Research, Eunice Shriver NICHD, Bethesda, MD.

To fully understand the role of the one-carbon network in health and disease conditions, the interactions between multiple factors that constitute the system – genes, metabolic intermediates, nutrients and environmental influences - must be considered. Studies of candidate SNPs and genes have been an important starting point but the discovery of other functional SNPs and new biomarkers remains an important objective. Knowing the most important genetic determinants of the one-carbon metabolic network in healthy individuals is a particularly relevant goal because it will help to interpret changes in flux through this metabolic network in disease conditions.

With the primary aim of understanding genotype –phenotype interactions within the one-carbon network, we recruited approximately 2,500 healthy, ethnically homogeneous (Irish) individuals within the narrow age range of 18 and 28 years old (termed the Trinity Students' Study; TSS). Information on age, gender, height, weight, medical conditions, smoking, dietary habits, consumption of fortified foods, supplements and alcohol was collected. Participants donated a blood sample which was used to extract DNA and for profiling of one-carbon metabolites and other relevant parameters including liver, kidney function and hematology markers. We then carried out a genome-wide association study (GWAS) on the cohort.

High density genotyping was performed with the Illumina 1M HumanOmni1-Quad chip. After quality control assessment, 2232 unrelated individuals and 757,533 SNPs were retained for association testing of 38 metabolites. Tests of association were performed with univariate linear regression, regressing each marker on each trait and assuming an additive genetic model as implemented in PLINK v1.0.7. Locus-specific heritability (h^2) for the effect size of each SNP on phenotypic variation was calculated using R v2.12.1.

Associations reaching genome-wide significance were observed for 22 metabolites. These associations included several previously published SNP associations. New associations were observed for a number of metabolites providing new candidate genes/regions. The GWAS provides data for further targeted studies in determining the genetic factors that influence the one carbon metabolic network.

ABSTRACT: Formate, new kid on the block in one-carbon metabolism.

John T. Brosnan and Margaret E. Brosnan, Memorial University of Newfoundland.

Formate has emerged as a major player in one-carbon metabolism. We now appreciate that the greater part of the body's one-carbon groups are derived from mitochondrially-produced formate. Genetic ablation of mitochondrial formate production is embryologically lethal, the embryos displaying neural tube defects; this may be partly rescued by providing formate in the dams' drinking water. We will report on new work that measured *in vivo* production of formate in rats. We conclude that formate is a major, though unappreciated end-product of amino acid metabolism. The only intermediate of the folate cycle to be found in plasma, formate measurements can provide novel information into intracellular events. Plasma formate is markedly elevated in folate- and vitamin B_{12}-deficiency. It is also elevated in situations of rapid growth, including rat pups, fetal sheep and pregnant women. We will also report the first measurements of formate in a number of human cohorts. (Supported by RDC and CIHR).

ABSTRACT: Riboflavin, the *MTHFR* 677TT genotype and hypertension

Mary Ward, JJ Strain and Helene McNulty

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Convincing evidence has emerged in recent years to support an association between hypertension and a common polymorphism in the gene encoding the folate-metabolising enzyme, methylenetetrahydrofolate reductase (MTHFR). Riboflavin (vitamin B2) in the form of FAD acts as a cofactor for MTHFR and molecular studies have indicated that the decreased activity associated with the variant enzyme appears to result from an increased propensity to dissociate from FAD. Previous work from our centre demonstrated that supplementation with low-dose riboflavin can stabilise MTHFR activity *in vivo* in homozygous individuals. More recently we reported that CVD patients with the *MTHFR* 677TT genotype (compared to CC or CT genotypes) had significantly higher blood pressure, and that blood pressure was highly responsive to riboflavin intervention, specifically in the TT genotype group. Further investigations confirmed this gene-nutrient interaction in hypertensive patients (with and without overt CVD), and furthermore showed that the blood pressure lowering effect of riboflavin in the TT genotype group was independent of the number and type of antihypertensive drugs that they were taking. We have also recently investigated the role of the *MTHFR* TT genotype on blood pressure throughout adulthood in a representative sample of Irish adults.

Although the precise mechanism linking this polymorphism to hypertension remains to be established, it would appear that the biological perturbation that leads to higher blood pressure in individuals with the MTHFR 677TT genotype is modifiable by correcting the variant MTHFR enzyme through enhancing riboflavin status. Given that the prevalence of the TT genotype ranges from 3-32% worldwide the findings that this genetic predisposition for hypertension is correctable by riboflavin have considerable clinical and economic implications.

Sessions 5A/6A: Saturday, June 7, 2014, 2:00 PM - 3:15 PM
ESPEN Lifelong Learning: Nutrition in GI Disease

SPEAKERS:

- **Remy Meier, MD**
- **Alastair Forbes, MD**

Session 5B: Saturday, June 7, 2014, 2:00 PM - 3:15 PM
Omega-3 Fatty Acids in Health: Marine vs. Plants

SPEAKERS:

- **Marc Surette, PhD**
- **Philip Calder, PhD, DPhil, RNutr, FSB, FAfN**
- **Jennifer Monk**
- **Kaitlin Roke**

ABSTRACT: **Marine omega-3 fatty acids in health**

Philip Calder, PhD, DPhil, RNutr, FSB, FAfN
Faculty of Medicine, University of Southampton, Southampton, UK

Omega-3 fatty acids (O3FA) are a family of polyunsaturated fatty acids that contribute to human health and well-being. Functionally the most important O3FA appear to be eicosapentaenoic acid (EPA) and docosahexaenoioc acid (DHA) found in oily fish and in supplements, but roles for docosapentaenoic acid (DPAn-3) are emerging. Because of their source EPA, DPAn-3 and DHA are sometimes referred to as marine O3FA. Intakes of EPA and DHA are typically low and much below recommended intakes. Increased intakes are reflected in greater incorporation into blood lipid, cell and tissue pools. Increased content of EPA and DHA can modify the structure of cell membranes and also the function of membrane proteins involved as receptors, signaling proteins, transporters and enzymes. EPA and DHA also modify the production of lipid mediators and through effects on cell signaling can alter patterns of gene expression. Through these actions EPA and DHA act to alter cellular responsiveness in a manner that seems to result in more optimal conditions for growth, development and maintenance of health. The effects of O3FA are evident right through the life cycle. EPA and DHA have a wide range of physiological roles which are linked to certain health or clinical benefits. A number of risk factors for cardiovascular disease are modified in a beneficial way by increased intake of EPA and DHA: these include blood pressure, platelet reactivity and thrombosis, plasma triglyceride concentrations, vascular function, cardiac arrhythmias, heart rate variability, and inflammation. As a result of these effects, increased EPA and DHA intake is associated with a reduced risk of cardiovascular morbidity and mortality. Thus, there is a key role for these fatty acids in prevention and slowing progression of cardiovascular disease. Furthermore, some supplementation studies with EPA and DHA have demonstrated reduced mortality in at risk patients, such as post-myocardial infarction, indicating a therapeutic role. A number of other, non-cardiovascular, actions of EPA and DHA have also been documented, suggesting that increased intake of these fatty acids could be of benefit in reducing the risk of (i.e. protecting from) or treating many conditions. For example, they have been used successfully in rheumatoid arthritis and, in some studies, in inflammatory bowel diseases, and may be useful in other inflammatory conditions like asthma, chronic obstructive pulmonary disease, and psoriasis. EPA and DHA may also have a role as part of cancer therapy; some recent studies show that they improve the effectiveness of some chemotherapeutic agents. DHA has an important

structural role in the eye and brain, and its supply early in life when these tissues are developing is known to be of vital importance in terms of optimizing visual and neurological development. For this reason it is very important that pregnant and breast feeding women have adequate DHA intake. Recent studies have highlighted the potential for EPA and DHA to contribute to enhanced mental development and improved childhood learning and behaviour and to reduce the burden of psychiatric illnesses in adults, although these areas of possible action require more robust scientific support. There may also be a role for EPA and DHA in preventing neurodegenerative disease of ageing. The effects of EPA and DHA on health outcomes are likely to be dose-dependent, but clear dose response data have not been identified in most cases. Also in many cases it is not clear whether both EPA and DHA have the same effect or potency and therefore which one will be the most important for a particular indication. Finally, there is increasing evidence that O3FA metabolism, status and function are determined partly by genetic variations among individuals. This suggests that different genetic sub-groups of the population will have different needs for exogenous O3FA and will respond differently to a certain intake of O3FA.

ABSTRACT: **Plant seed oils as dietary omega-3 fatty acids**

Marc Surette, PhD
Université de Moncton

Omega-3 fatty acids form a family of essential polyunsaturated fatty acids (PUFA) that are preferentially enriched in tissue phospholipids following their consumption. The most common dietary sources of these PUFA are fatty fish and some plant seed oils. The molecular mechanisms by which dietary omega-3 PUFA affect health involve the enrichment of cellular membranes with long chain 20- and 22-carbon omega-3 PUFA that impacts tissues by altering membrane protein functions, cell signaling and gene expression profiles. The consumption of the long chain family members, EPA, DPA and DHA that are typically found in marine oils, is associated with their efficient enrichment in tissues. Seed oils on the other hand are typically enriched in the 18-carbon precursor of all omega-3 PUFA, alpha-linolenic acid (ALA). Mammals have the capacity to convert dietary ALA into the longer chain omega-3 PUFA, however in humans this conversion is typically very poor mainly due to the limited capacity to catalyze the delta-6 desaturation of ALA into stearidonic acid (SDA). Thus dietary ALA has very little impact on tissue EPA, DPA and DHA content. Since positive health outcomes are mainly linked with the enrichment of tissues with EPA and DHA, the consumption of omega-3 PUFA from plant seed oils is largely thought to have a lesser impact on health than that of marine oils. Because the supply of omega-3 PUFA from marine sources is limited and may not be sustainable, there has been considerable effort to produce seed oils that are more capable of enriching tissues in long chain omega-3 PUFA following their consumption than ALA-enriched oils. Transgenic plants that can produce oils enriched in EPA and DHA have been developed; however their commercial production may be years away. Other plant-derived sources of omega-3 PUFA like SDA-enriched soy oil from genetically modified soybeans and Ahiflower oil from *Buglossoides arvensis* seeds that are naturally enriched in SDA have been developed and show promise to become sustainable and effective sources of dietary omega-3 PUFA.

RESEARCH ABSTRACT: n-3 polyunsaturated fatty acids derived from fish oil and flaxseed oil reduce chemotactic and inflammatory cross-talk between co-cultured adipocytes and CD8+ T cells

Jennifer M. Monk[1,2], Anna A. De Boer[1], Danyelle M. Liddle[1], Krista A. Power[1,2], David W.L. Ma[1], Lindsay E. Robinson[1]

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Production of obesity-associated adipose tissue (AT) inflammatory adipokines has been largely attributed to paracrine interactions (cross-talk) between adipocytes and macrophages; a process mitigated by n-3 polyunsaturated fatty acids (PUFA). However, other AT-infiltrating immune cells, in particular CD8+ T cells, precede AT macrophage accumulation, contribute to early inflammatory adipokine production, and therefore, could be a target for n-3-PUFA anti-inflammatory effects. Purified (positive selection) splenic CD8+ T cells from C57Bl/6 mice consuming one of two isocaloric diets: 7% w/w safflower oil + 3% w/w menhaden oil (marine n-3 PUFA) or 10% w/w safflower oil (control), were co-cultured in direct-contact with 3T3-L1 adipocytes at a physiologically relevant ratio of CD8+ T cells to adipocytes that reproduces the degree of CD8+ T cell infiltration reported in obese AT (10% of the stromal vascular cellular fraction). Co-culture conditions were: unstimulated (CD8+ T cells + adipocytes alone), stimulated with lipopolysaccharide (LPS, 10 ng/ml: dosage that mimics obese circulating endotoxin levels), or through the T cell receptor (TCR, 5µg/ml anti-CD3 + 20µg/ml anti-CD28) for 24 h. With LPS-stimulation, adipocytes co-cultured with n-3 PUFA-enriched CD8+ T cells had reduced mRNA and secreted protein levels of IL-6, TNFα and MCP-1 compared to control ($P<0.05$). Additionally, secreted protein levels of the macrophage chemotactic mediators MIP-1α, MIP-1β, MIP-2 and MCP-3 were all reduced by n-3 PUFA ($P<0.05$). Lastly, n-3 PUFA reduced TCR-stimulated MCP-1 mRNA and secreted protein ($P<0.05$). In a separate study, splenic CD8+ T cells co-cultured as above, from mice fed a 3.5% w/w flaxseed (FS) oil diet (plant n-3 PUFA) corroborated the beneficial effect marine n-3 PUFA had on the inflammatory paracrine cross-talk between these cell types. In unstimulated cell co-cultures, FS oil reduced mRNA expression of the inflammatory mediators IL-6, IL-1β, TNFα, MCP-1, and RANTES ($P<0.05$). Moreover, under both LPS and TCR stimulation, FS oil reduced IL-6, IL-1β, TNFα and MCP-1 mRNA expression versus control ($P<0.05$). Collectively, these data demonstrate a reproducible anti-inflammatory and anti-chemotactic effect of n-3 PUFA on CD8+ T cell/adipocyte cross-talk, irrespective of source (i.e. marine versus plant), and highlight a novel mechanism of n-3 PUFA action in obesity.

RESEARCH ABSTRACT: The role of FADS1/2 polymorphisms on cardiometabolic markers and fatty acid profiles in young adults consuming fish oil supplements

Kaitlin Roke and David M Mutch

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High intake of n-3 fatty acids (FAs), specifically eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), are associated with cardiometabolic health benefits. While the typical Western diet has little to no EPA or DHA, these FAs can be obtained by consuming fish oil supplements. Evidence suggests that single nucleotide polymorphisms (SNPs) in the fatty acid desaturase 1 and 2 gene cluster (FADS1/2) may influence an individual's response to fish oil supplements. The objectives of this study were to determine the impact of fish oil supplements on clinical markers of cardiometabolic health and FA levels in serum and red blood cells (RBC). We also explored whether SNPs in FADS1/2 influenced the aforementioned endpoints. Young healthy adults consumed supplements (providing 1.8 g EPA and DHA / day) for a period of 12 weeks, followed by an 8 week washout period. FAs were analyzed in serum and RBC using gas chromatography. Two SNPs (rs174537 and rs174576) in FADS1/2 were genotyped. During the supplementation period blood triglyceride and glucose levels decreased significantly (-12.7% and -10.9%, respectively), but returned to baseline levels during the washout period. EPA and DHA levels increased significantly in serum (+250% and +51%, respectively) and RBC (+132% and +18%, respectively) within the first two weeks of supplementation and remained elevated throughout the 12 week period. After the washout, EPA and DHA remained significantly elevated in RBC, but returned to baseline levels in serum. Minor allele carriers for both SNPs experienced greater increases in EPA levels in serum and RBC during supplementation. This study demonstrated that fish oil supplements can reduce blood triglyceride and glucose levels in young adults, but that these cardiometabolic benefits are quickly lost once supplementation has stopped. Minor allele carriers of common SNPs in FADS1/2 showed a greater enrichment of EPA in serum and RBC compared to major allele carriers, highlighting that genetic variation at this locus can influence an individual's response to fish oil supplements. (Research supported by NSERC (DMM) and OGS (KR))

Session 5C: Saturday, June 7, 2014, 2:00 PM - 3:15 PM
New Ways of Influencing Dietary Changes in 2014 and Beyond

SPEAKERS:

- **Laura M. O'Connor, PhD**
- **Jess Haines, PhD, RD**

ABSTRACT: Dairy Product Intake and Incident Type 2 Diabetes

Laura O'Connor, PhD

Career Development Fellow, MRC Epidemiology Unit, University of Cambridge School of Clinical Medicine, Institute of Metabolic Science, Cambridge Biomedical Campus, Cambridge, United Kingdom

The global prevalence of type 2 diabetes continues to rise together with the increasing burden of its adverse health consequences to both individuals and health care systems. While the potential benefits of overall healthier diets in the prevention of type 2 diabetes have been demonstrated in clinical trials, there is lack of clarity on the role of specific foods in free-living populations.

Dairy products can serve as important sources of high-quality protein, vitamins, and minerals, but there has been concern about their relatively high saturated fat content. Evidence has emerged that overall dairy product consumption may be related with a lower risk of developing type 2 diabetes, but there has been insufficient information on the association of sub-types of dairy products in relation to diabetes risk.

This presentation describes recent work undertaken to explore associations between intakes of total and sub-types of dairy products and the risk of new-onset type 2 diabetes. It focuses on evidence from a large prospective study in the United Kingdom that made use of a detailed 7-day food diary to assess dietary intakes. This enabled the examination of the contribution of low- and high-fat dairy products, milk, yoghurt, cheese, and fermented dairy products intake to diabetes risk.

ABSTRACT: Parents and Tots Together: Adaptation of a family-based obesity prevention intervention to the Canadian context

Jess Haines, PhD, RD

Assistant Professor, Department of Family Relations and Applied Nutrition, University of Guelph

Formative research shows that parents of young children are enthusiastic about learning general parenting skills, but less interested in nutrition and physical activity. To capitalize on this enthusiasm, Parents and Tots Together (PTT) was designed to embed strategies to improve child weight-related behaviors within a general parenting program. PTT has been tested using a randomized controlled design among 110 families in Boston, MA. However, it is unknown whether PTT is feasible and contextually appropriate for Canadian families. This presentation will describe the formative work to adapt PTT to the Canadian context, compare process and outcome data from the US and Canadian trials of the PTT program, and describe key lessons learned.

Session 6B: Saturday, June 7, 2014, 4:00 PM - 5:15 PM
Functional Insights into Nutritional Lipids

SPEAKERS:

- **Ken Stark, PhD**
- **Richard Bazinet, PhD**
- **Kayode Balogun**
- **Mélanie Plourde, PhD**

ASBTRACT: Omega-3 Blood Biomarkers: What do they say about Diet, Metabolism and their Potential Impact on Function?

Ken Stark, PhD
University of Waterloo, Waterloo, ON

The fatty acid composition of blood can provide information about dietary habits and the metabolic state. While full fatty acid profiles are the most informative, blood "markers" of omega3 polyunsaturated fatty are desirable to simplify interpretation and to enable clinical utility. Various factors can influence levels of omega-3 blood biomarkers and include; sample collection and handling, specimen chemical preparation, gas chromatography analysis, and data processing. Interpretation of omega-3 biomarkers is greatly influenced by the type of blood sample (ex. venous vs. erythrocytes), dietary situation (ex. steady state vs. dietary modification), and metabolic interplay between fatty acid synthesis, oxidation and incorporation into complex lipids. The end use of the biomarker (as a marker of disease vs. a marker of dietary intake) should also be considered. The response of different omega-3 blood biomarkers to different intake levels of eicosapentaenoic and docosahexaenoic acid over time, and the relationships between the blood biomarkers will be examined. Specifically, the use of omega-3 blood biomarkers to confirm dietary adherence in clinical studies will be examined. Insights on metabolism and the relationship between blood and tissue levels based on rodent models will also be presented that will include an examination of hepatic expression of genes involved in fatty acid. Future directions, including the potential application of lipidomic analytical techniques, will also be discussed.

RESEARCH ABSTRACT: Dietary omega-3 polyunsaturated fatty acids differentially alter brain docosahexaenoic acid and neurotrophins levels in weaning and adult C57BL/6 mice

Kayode A. Balogun and Sukhinder K. Cheema
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Omega-3 (n-3) polyunsaturated fatty acids (PUFA) and neurotrophins such as brain-derived neurotrophic factor (BDNF), and nerve growth factor (NGF) are crucial for the proper functioning of the brain. A decrease in brain n-3 PUFA and /or expression of neurotrophins positively correlates with an increased predisposition to neurological disorders. The development of the brain happens during perinatal period; the question arises whether there is an effect of age on the accretion of dietary n-3 PUFA and neurotrophin signalling in the brain? Female C57BL/6 mice were fed semi-purified diets (20% w/w fat) containing 10% (high) and 2% (low) n-3 PUFA before mating, during pregnancy, and until weaning. Male offspring (n=6 per group) were studied at weaning and 16 weeks postweaning on their mother's designated diet. Cerebral cortical phospholipids fatty acids were measured by gas chromatography. The mRNA expressions of BDNF, NGF, TrKB (BDNF receptor), and cAMP response element binding protein (CREB), the regulator of BDNF were measured using quantitative real-time PCR. Means were compared using two-way ANOVA to determine main effects of diet and age. There was an independent

effect of diet ($p<0.0001$) and age ($p<0.0001$) on cortical accretion of docosahexaenoic acid (DHA) and total n-3 PUFA; this positively correlated with the mRNA expressions of BDNF, NGF, and TrKB. There was a significant effect of diet ($p<0.05$) and age ($p<0.05$) on the mRNA expression of NGF. There was a significant effect of diet ($p<0.01$) on the BDNF gene expression; high n-3 PUFA diet increased the expression compared to the low n-3 PUFA diet. The mRNA expression of TrKB was higher ($p<0.0001$) at 16 weeks in the high n-3 PUFA group compared to the low n-3 PUFA group; however, no difference was observed at weaning. There was no effect of diet on the gene expression of CREB; however the activated form of CREB, phosphorylated CREB was higher in the high n-3 PUFA group compared to the low n-3 PUFA group ($p<0.05$). Our findings show for the first time that n-3 PUFA directly regulate neurotrophin signalling and that the neuroprotective effects of the accretion of dietary n-3 PUFA is age dependent. (Supported by NSERC).

RESEARCH ABSTRACT: **Apolipoprotein epsilon 4 genotype and docosahexaenoic acid metabolism: data from mice and humans**

Mélanie Plourde, PhD

Centre de recherche sur le vieillissement, Institut Universitaire de Gériatrie de Sherbrooke, Université de Sherbrooke, Sherbrooke, Canada

Background: Over the last five years, our group investigated imbalance in the metabolism of docosahexaenoic acid (DHA) in humans and in transgenic mice carrying human apolipoprotein E epsilon 4 (APOE4+) genotype. One of our hypotheses is that rebalancing DHA metabolism could contribute to lower the risk of cognitive decline in APOE4+. Objective: To overview evidences collected from human and mice studies on disturbed DHA metabolism in APOE4+ compared to APOE4-. Results: In 2009, data obtained from clinical trial showed that in APOE4+, DHA concentration in plasma triglycerides was higher than APOE4-, but after a n-3 fatty acid supplementation, increase of DHA was lower than APOE4-. Using 13C-DHA, APOE4+ had 31% lower 13C-DHA in postprandial compared to APOE4-. However, we recently performed additional analysis from the SATgene studies and reported no differences in DHA of APOE4+ compared to APOE4-, potentially because of the younger age of the participants compared to our first studies. Our recent results in 4 and 13 month-old transgenic mice carrying human APOE4+ showed that brain uptake of 14C-DHA was 24% lower in APOE4+ than APOE2 but cortex DHA was significantly lower in 13 month-old mice only. Plasma DHA was significantly higher in APOE4 mice than APOE2 suggesting that lower brain uptake was not because of lower availability of DHA in plasma. Recently, we fed a diet containing 0.5 g/100g DHA to APOE4+ mice and found that cognitive deficits were absent compared to other genotypes but when feeding a control or a high fat diet, APOE4+ mice had spatial and visual cognitive deficits compared to other genotypes. Conclusion: Disturbed DHA metabolism in APOE4+ seems highly age-dependant. However, a diet rich in DHA seems to prevent cognitive deficits in APOE4+ mice and is therefore a potential promising way for prevention of cognitive decline in this population.

Session 6C: Saturday, June 7, 2014, 4:00 PM - 5:15 PM

Protein Quality Assessment of Food – Recent Advances and in Vivo Assessment in Humans

SPEAKERS:

- **James House, PhD**
- **Rajavel Elango, PhD**

ABSTRACT: Defining the Quality of Dietary Proteins

James D. House, PhD

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The quality of a protein for the human diet is generally influenced by two primary factors: 1) the relative proportions of the indispensable (essential) amino acids plus dispensable nitrogen in the food in relation to human amino acid/protein requirements; 2) the extent to which the dietary protein is digested, absorbed and made available for metabolic purposes (ie: protein synthesis). The latter factor can be influenced by the presence of anti-nutritive factors in the food that depress digestibility, and by processing steps (ie: heat in the presence of reducing sugars) that can reduce metabolic availability. While numerous methods have been developed and implemented for the assessment of protein quality, two methods are used internationally for estimating protein quality for regulatory purposes: 1) The Protein Efficiency Ratio (PER), and 2) The Protein Digestibility-Corrected Amino Acid Score (PDCAAS).

The PER method is an *in vivo* rat bioassay that measures weight gain per unit of protein consumed, with casein used as a reference. In Canada, the PER method serves as the official method for establishing protein claims, and is used in calculating the Protein Rating. In the United States, protein quality is evaluated by the 1990 WHO/FAO/UNU established PDCAAS methodology. With this method, the amino acid composition of the food is determined and related to a reference protein pattern, based on human amino acid requirement estimates. The resultant amino acid scores are evaluated and those less than 1.0 are limiting relative to the requirement pattern, with the lowest score serving as the final amino acid score value for the protein. The PDCAAS attempts to measure the overall quality of a protein as the product of the digestibility of the protein and its amino acid score. Values approaching 1.0 or greater are considered the highest quality proteins. For measuring protein digestibility, the use of the true fecal nitrogen digestibility method, using the rat bioassay, is required. In 2013, a new method called the Digestible Indispensable Amino Acid Score (DIAAS) was positioned to address limitations of the existing PDCAAS methodology. An understanding of the strengths and limitations of each method, and their inherent differences is important for both the nutrition community and food industries in order to best position the quality of dietary proteins.

ABSTRACT: Application of Stable Isotope Based Techniques to Measure Amino Acid Availability from Foods

Rajavel Elango

University of British Columbia, Vancouver, BC

Dietary protein forms an essential component of a healthy diet in humans. To meet the metabolic demands in the body, an adequate quantity and quality of protein is necessary. The quality of dietary proteins is ultimately related to the amount of metabolically available amino acids provided at the cellular level (termed "bioavailable") for the various functions that protein and amino acids serve in maintaining normal growth and health. In other words, protein quality is a combination of the amino acid content in foods and the bioavailability of those amino acids. Traditionally, bioassays using growing rats were the preferred approach to assess the nutritional value of proteins for humans. These methods have several shortcomings, but primarily they are estimates of whole body protein utilization, and do not provide much information on individual amino acid availability. Using the minimally invasive stable isotope based indicator amino acid oxidation (IAAO) technique developed to determine amino acid requirements in humans, we have recently developed a new method to estimate the whole body bioavailability, termed "metabolic availability", of essential amino acids from dietary protein sources. The IAAO is inversely proportional to the rate of protein synthesis. Therefore, at a given amino acid intake, the relative difference in the IAAO rate between test and reference proteins will be proportional to the whole body metabolic availability of the test amino acid for protein metabolism, and thus account for all losses of dietary amino acids during digestion, absorption, and cellular metabolism. The IAAO method has been applied to determine the availability of methionine from casein and soy protein isolate, and lysine from cooked white rice. The technique is relatively non-invasive and holds great potential for the evaluation of protein quality of foods directly in humans.

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Nestlé Graduate Student & Trainee Competition Finalists

PTGS1 (COX1) polymorphisms are associated with plasma phospholipid arachidonic and docosapentaenoic acids after an omega-3 polyunsaturated fatty acid supplementation

Hubert Cormier[1], Iwona Rudkowska[1,2], Simone Lemieux[1], Pierre Julien[2], Patrick Couture[2] and Marie-Claude Vohl[1,2]

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Prostaglandin-Endoperoxide Synthase 1 (PTGS1), commonly referred to as COX1 gene, is a gene encoding for a protein involved in the cyclooxygenase pathway, a key enzyme in prostaglandin biosynthesis. The preferential substrate of COX-1 is mainly arachidonic acid (AA), which is less abundant in plasma phospholipids after an omega-3 (n-3) supplementation due to the competition between omega-6 and n-3 for the same sets of enzymes, directly impacting the fluidity of the membrane. Recent studies showed that an eicosapentaenoic acid (EPA) supplementation decreased COX-1 metabolites and a docosahexaenoic acid (DHA) supplementation also reduced COX-dependent AA metabolites, but to a greater extent, concomitant with an increase in lipoxygenase metabolite production. Aim: To test whether PTGS1 gene single nucleotide polymorphisms (SNPs) are associated with differences in plasma phospholipid concentrations of AA, EPA and/or DHA. Methods: 210 subjects completed a 2-wk run-in period followed by 6-wk supplementation with 5g/d of fish oil (1.9-2.2g/d of EPA + 1.1g/d of DHA). Plasma phospholipid fatty acid profiles were obtained by gas chromatography pre- and post-supplementation. Genotyping of 7 SNPs, covering 100% of the common PTGS1 genetic variation, was performed using TaqMan technology (Life Technologies Inc., Burlington, Canada). Results: After the 6-wk supplementation with n-3 PUFA, AA levels decreased by 11.2$\pm$10.0% while EPA and DHA levels increased respectively by 330.0$\pm$214.1% and 46.2$\pm$27.4% ($p<0.0001$, for all). In a general linear model adjusted for the effects of age, sex, BMI and baseline fatty acid levels, rs8046 was significantly associated with post-supplementation AA levels (β-estimates: A/A=-0.4062 and A/G+G/G=0, $p=0.03$) while rs5788 was significantly associated with post-supplementation DHA levels (β-estimates: C/C=0.2754 and A/C+A/A=0, $p=0.02$). None of the PTGS1 gene SNPs was associated with post-supplementation EPA levels. Conclusions: PTGS1 gene SNPs may modulate AA and DHA levels measured in plasma phospholipids post-n-3 PUFA supplementation possibly leading to reduced COX-dependent metabolites. [Supported by CIHR MOP-110975]

Long-chain n-3 fatty acids decrease M1 macrophage polarization, antigen presenting co-stimulatory molecule expression and inflammatory mediator secretion in an ex vivo murine adipocyte macrophage co-culture model

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Chronic inflammation in obesity is generated, in part, by paracrine interactions between adipose tissue (AT) adipocytes and macrophages, and subsequent adaptive immune responses driven by adipocyte and/or macrophage major histocompatibility complex (MHC)-mediated antigen presentation to T cells. Dietary strategies to mitigate such inflammation include long-chain n-3 polyunsaturated fatty acids (LC n-3 PUFA), such as docosahexaenoic (22:6 n-3, DHA) and eicosapentaenoic (20:5 n-3, EPA) acids, although the mechanisms are not well established. We utilized an ex vivo model designed to mimic the ratio of macrophages:adipocytes in obese AT, whereby murine 3T3-L1 adipocytes were co-cultured with splenic CD11b+-enriched macrophages isolated from adult C57Bl/6 mice fed either a LC n-3 PUFA-rich (10% fat w/w as 3% menhaden-oil +7% safflower-oil) or a n-6 PUFA-rich (10% w/w safflower-oil) isocaloric control diet for 3 weeks (n=6/diet). Co-culture conditions tested the effect of soluble mediator-driven mechanisms (trans-well system) and/or chronic inflammation (low-dose LPS adipocyte pre-treatment; 10 ng/mL) on cellular cross-talk after 24 h. We hypothesized that co-cultures containing LC n-3 PUFA-enriched macrophages would reduce polarization toward a pro-inflammatory M1 phenotype and subsequent expression of inflammatory mediators. Confirming our previous findings in an in vitro co-culture model, secreted IL-6 protein and mRNA expression of iNOS, a M1 macrophage marker, were decreased ($p \leq 0.05$) in co-cultured n-3 PUFA-enriched macrophages under LPS-stimulated conditions (-36%, -48%, respectively, compared to control). Further, mRNA expression of key antigen presentation genes were increased (MHCI: β2M; +20%, MHCII: CD74; +55% and CIITA; +43%), while CD86, a key co-stimulatory molecule, was decreased (-44%) in co-cultured n-3 PUFA-enriched macrophages with LPS stimulation ($p \leq 0.05$, versus control). Our findings suggest that LC n-3 PUFA reduce inflammatory M1 macrophage polarization, while decreasing macrophage expression of a critical co-stimulatory molecule, suggestive of a semi-mature antigen presenting phenotype unable to stimulate naïve T cell-driven adaptive responses. Thus, LC n-3 PUFA may decrease the intensity of adipocyte-macrophage inflammatory cross-talk and subsequently supress the potential to fully activate an adaptive immune response. Our work emphasizes a beneficial role of LC n-3 PUFA in attenuating obesity-related inflammation through potential direct and indirect modulation of innate and adaptive immune responses, respectively. (Funded by NSERC)

Immune development is dependent on the amount and form of choline in the maternal diet

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The maternal requirement for choline increases during lactation to meet the needs of the infant. Lactation is a critical period for immune system development; however, there is limited research on maternal choline intake and immune development in the offspring. The objective of this study was to examine the effect of feeding different dietary amounts and forms of choline to suckling rats on immunity in the offspring. Lactating dams were fed nutritionally complete, isocaloric, high fat (20% w/w) diets of similar fatty acid compositions, containing either 0 g/kg choline (D, n=9), 1.0 g/kg choline as free choline (C, n=20) or 1.0 g/kg choline as phosphatidylcholine (PC, n=9). At 3 weeks, 2-3 suckled pups from each dam were euthanized and the mean of the pups of each dam combined to determine the effect of diet on the types of immune cells present in spleen and mesenteric lymph nodes (by flow cytometry) and the ability of splenocytes to produce cytokines (via ELISA) in response ex vivo to mitogens. The D pups had lower final body and liver weight and lower number of splenocytes, but no change in the relative percent of the major types of cells in immune tissues, compared to C pups. When stimulated with T cell mitogen Concanavalin A (ConA), splenocytes from D pups produced less IL-2 (22%) and less TNF-α (47%) compared to the C pups ($P<0.05$). When stimulated with B cell mitogen Lipopolysaccharide (LPS), splenocytes from D pups produced similar amounts of IL-6, IL-1 and TNF-α cytokines and more IL-10 ($P<0.05$). There was no difference in growth or the relative proportion or number of immune cell types between C and PC pups. However, splenocytes from PC pups produced more IL-6 (163%) and more IFN-γ (106%) with ConA and more IL-6 (110%) and TNF-α (43%) with LPS compared to C pups ($P<0.05$). In summary, both the amount and form of choline in the maternal diet influence immune system development in the offspring. (Supported by NSERC, Alberta Innovates Bio-Solutions, Alberta Livestock and Milk Association and WCHRI)

The dietary methyl donors folate, betaine and choline have a significant impact on the partitioning of methionine in the neonatal piglet

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The metabolism of the essential amino acid methionine is critical during development. It is incorporated into protein and, via the methionine cycle, it synthesizes >50 critical nutrients and contributes to epigenetic regulation. Three major processes can summarize the methionine cycle, transmethylation (TM) which transfers methyl groups to nutrient precursors and DNA, transsulfuration (TS), the irreversible oxidation of demethylated methionine to cysteine, and remethylation (RM) which reforms methionine using the methyl donors folate and choline (via betaine). Intakes of folate, betaine, choline and methionine are highly variable in infant diets. We hypothesized that dietary methyl donors significantly impact the partitioning of methionine in neonates. We fed 4-8 day old piglets a low-methionine diet that was either deficient (MD-) or replete (MS+) in methyl donors. MD- diet was verified by low plasma concentrations of methyl donors. We measured methionine partitioning among the major TM products in liver using [3H-methyl] methionine. The MD- group lowered creatine synthesis by ~20% ($p<0.02$) and enhanced the synthesis of phosphatidylcholine by ~70% ($p<0.03$) to compensate for low dietary choline; DNA methylation was unchanged. The [3H] incorporation into liver protein was unaffected, however muscle protein synthesis was significantly lower in the MD- vs. MS+ animals ($p<0.02$). Further, whole-body protein synthesis was lower in MD- piglets ($p<0.05$) as measured by [13C] phenylalanine oxidation; however, this was balanced by a concomitant decrease in protein breakdown ($p<0.05$). Next, we measured the effect of methyl donors on the rates of TM, TS, and RM using a dual-labeled [13C, 2H-methyl] methionine infusion. Rates of RM and TM were reduced by ~75% in the MD- group ($p<0.02$). In order to evaluate the impact of individual methyl donors, we then rescued MD- animals with betaine, folate or both. The rate of RM and TM increased by ~2-fold after rescue with folate and folate/betaine ($p<0.05$); however, betaine alone could not restore RM. Methyl donors have a significant impact on the partitioning of methionine during development in neonates and need to be considered when establishing methionine requirements.

Phosphorylation of hormone sensitive lipase occurs in response to endocannabinoid treatment of 3T3-L1 adipocytes

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The endocannabinoid (EC) system, which consists of several fatty acid-derived endogenous ligands operating through two G protein-coupled receptors, CB1 and CB2, has a role in metabolic homeostasis based on evidence that elevated EC levels promote weight gain by stimulating hunger. As a result, chronic blockade of the CB1 receptor leads to weight loss in humans and rats. The EC system is generally thought to influence body weight through the neuronal CB1 receptor, however, whether ECs can also affect metabolism through peripheral tissues such as adipose remains unclear. This is an area of interest since CB1 receptor antagonists have beneficial actions on obesity, yet have deleterious effects on the central nervous system. The purpose of this study was to determine the effect of the EC 2-arachidonoyl-glycerol (2-AG) on lipid metabolism in adipocytes. 3T3-L1 adipocytes were grown and allowed to differentiate for 8 days until fully mature. They were then treated with various concentrations (1.32 nM-13.2 nM) of 2-AG for 48 hours in the absence or presence of the CB1 antagonist AM281 (1 nM). Cell lysates were analyzed via Western blotting for changes in protein levels and phosphorylation state. Hormone sensitive lipase (HSL) was examined since it regulates lipolysis through the release of free fatty acids for beta-oxidation and energy production in peripheral tissues. After the 48 hour incubation, 2-AG treatment resulted in an increase in HSL phosphorylation at both serine 563 and serine 565. This increase in phosphorylation was attenuated with AM281, which suggests that 2-AG works through the CB1 receptor in adipocytes. Since S565 suppresses activation of HSL via PKA-mediated S563 phosphorylation, this dual phosphorylation of the serine sites likely blocks lipolysis. In conclusion, we have been able to show that the EC system can directly affect lipid metabolism in adipocytes (peripheral tissue), specifically by inhibiting HSL activation. These data suggest adipose tissue CB1 receptors may be a suitable target for anti-obesity therapy. Further research is needed to understand how the dietary fatty acid profile may influence synthesis of 2-AG. (Supported by ARDI, NSERC, MHRC, MICH).

A single dose of DHA causes heart contractile deficits and decreased susceptibility to myocardial ischemia-reperfusion injury after 24 hours

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The intake of docosahexaenoic acid (DHA, 22:6n-3) in humans tends to be sporadic, while rodent studies examining heart function typically use regular chronic feeding designs. The purpose of this study was to examine the effect of acute DHA treatment on rat heart function and susceptibility to ischemia-reperfusion injury. Standard chow fed male and female Sprague-Dawley rats (3-4 months of age, n=14) were gavaged with a single dose of oil. The treatments were either algal-derived high DHA oil providing 0.4 mg DHA/g body weight (0.339 mg DHA/μL oil) or an equivalent volume of soybean oil as a control. Following gavage, rats were returned to their cages and had ad libitum access to food and water for 12h and were then fasted for an additional 12h. Animals were then anaesthetized with intra-peritoneal sodium pentobarbital, sacrificed, and excised hearts were rapidly instrumented in an ex vivo isolated heart perfusion model (Langendorff). Isolated hearts were allowed to equilibrate for a baseline period of 30 minutes followed by 30 minutes of global (no flow) ischemia, and then 90 minutes of reperfusion. Heart function was continuously measured using a left ventricular balloon catheter and infarct size was determined by 2,3,5-triphenyltetrazolium chloride staining. At baseline, DHA treatment was associated with reduced left ventricular systolic pressure (80.7$\pm$23.0 vs. 107.7$\pm$28.3 mmHg, P=0.015), contractility (73.9$\pm$22.8 vs. 102.2$\pm$27.9 mmHg, P=0.013) and rate of relaxation (1314$\pm$387 vs. 1920$\pm$593 mmHg/s, P=0.008). During the reperfusion period, DHA treatment was associated with approximately 25% reduced contractility compared with controls, starting at 15 minutes after ischemia and persisting to the end of the protocol (P<0.05). DHA treatment was also associated with an approximately 23% increase in heart rate from 60 minutes of reperfusion onward (P<0.05). Infarction size was reduced in the hearts from DHA treated rats as compared with controls (29.3$\pm$4.3 vs. 35.2$\pm$5.9 % of total tissue volume, P=0.043). These results suggest that an acute dose of DHA affects isolated heart function at 24 hours after ingestion, and appears to reduce infarction size following induced ischemia-reperfusion injury.

Dilution of plasma deuterated N-tau-methylhistidine as an alternative isotopic method to measure muscle protein breakdown.

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Debilitating muscle loss due to aging and cancer cachexia could be due to impaired action of insulin in suppressing protein breakdown (PB). Current in vivo techniques to measure muscle PB are either imprecise or too invasive to use in frail subjects. N-Tau-methylhistidine (Nτ-MH) is an irreversible metabolite of actin and myosin released during PB. We tested the suppressing action of insulin on myofibrillar PB by measuring the release of Nτ-MH in the plasma using an isotopic tracer dilution approach. Eight healthy men (age 24-±1y; BMI 22.3-±1.7 kg/m2) received primed constant intravenous infusions of [2H3]Nτ-MH to measure myofibrillar PB and [1-13C]leucine for whole-body PB. Protein kinetics were calculated during the fasted state followed by a 3h-hyperinsulinemic (1.25 mU/kg leanbody mass (LBM).min), euglycemic (5.5mmol/L), isoaminoacidemic clamp to assess responses to insulin. [2H3]Nτ-MH and [1-13C]leucine plasma enrichment and amino acid concentrations were measured by LC-MS/MS. During the hyperinsulinemic clamp, plasma branched-chain amino acids (BCAAs) were maintained within 8% of individual fasting levels (total BCAA: 292±26 vs. 263±14 µmol/L, NS). Plasma Nτ-MH concentrations did not change following insulin infusion (2.21± 0.20 vs. 2.44±0.23 µmol/L, NS). Endogenous Nτ-MH release decreased from 0.64±0.06 to 0.46 ±0.04 µmol/kg LBM/h ($p<0.0001$) indicating a decrease in myofibrillar PB by 28±1.5%. Whole body PB was reduced by 31±2.8% (Pre: 105.7±4.9 vs. Post: 64.9±4.5 µmol/kg LBM/h, $p=0.0026$). Myofibrillar PB represented 48-52% of whole-body PB during both fasting and hyperinsulinemia. In conclusion, physiological hyperinsulinemia significantly reduced myofibrillar PB in healthy men. Dilution of plasma deuterated Nτ-MH may be a reliable and sensitive alternative method to measure PB, applicable under various conditions, without the need for muscle biopsies in frail subjects. (Supported by CIHR and MUHC Research Institute)

Mechanism of cholesterol-lowering effect of barley β-glucan

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The cholesterol-lowering effect of barley β-glucan has been documented in a number of animal and human studies. Inhibiting cholesterol absorption and interrupting bile acid metabolism are the mainly proposed mechanisms of action. However, these mechanisms have not been studied adequately. This study was designed to examine the potential mechanisms of the cholesterol-lowering property of β-glucan. In a controlled, four phase crossover trial, mildly hypercholesterolemic but otherwise healthy subjects (n=30) were randomly assigned to receive barley breakfast containing 3g high molecular weight (MW), 5g low MW, 3g low MW barley β- glucan or a control diet, each for 5 weeks. Cholesterol absorption was determined by assessing the enrichment of 13C-cholesterol over 96 hours following oral administration; bile acid synthesis was determined by measuring the level of serum 7α-hydroxy-4-cholesten-3-one (7αHC). Compared with control, 3g high MW resulted in a greater total cholesterol reduction (-0.60 mmol/l vs. -0.30 mmol/l, p = 0.044), a higher level of 7αHC production (14.13ng/ml vs. 10.96 ng/ml, p=0.047), but not low MW β-glucan, even at the high dose of 5g/day. No difference in cholesterol absorption was observed between barley β-glucan and control diet (p =0.26). In summary, daily consuming 3g high MW but not 5g low MW or 3g low MW β- glucan lowered serum cholesterol concentrations. More importantly, these data suggest that the increased bile acid synthesis rather than inhibition of cholesterol absorption may be the mechanism responsible for the cholesterol-lowering effect of barley β-glucan. (Supported by Growing Forward Agriculture and Agri-Food Canada)

Poster Competition Finalists

Dietary omega-3 polyunsaturated fatty acids differentially alter brain docosahexaenoic acid and neurotrophins levels in weaning and adult C57BL/6 mice

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Omega-3 (n-3) polyunsaturated fatty acids (PUFA) and neurotrophins such as brain-derived neurotrophic factor (BDNF), and nerve growth factor (NGF) are crucial for the proper functioning of the brain. A decrease in brain n-3 PUFA and /or expression of neurotrophins positively correlates with an increased predisposition to neurological disorders. The development of the brain happens during perinatal period; the question arises whether there is an effect of age on the accretion of dietary n-3 PUFA and neurotrophin signalling in the brain? Female C57BL/6 mice were fed semi-purified diets (20% w/w fat) containing 10% (high) and 2% (low) n-3 PUFA before mating, during pregnancy, and until weaning. Male offspring (n=6 per group) were studied at weaning and 16 weeks postweaning on their mother's designated diet. Cerebral cortical phospholipids fatty acids were measured by gas chromatography. The mRNA expressions of BDNF, NGF, TrKB (BDNF receptor), and cAMP response element binding protein (CREB), the regulator of BDNF were measured using quantitative real-time PCR. Means were compared using two-way ANOVA to determine main effects of diet and age. There was an independent effect of diet ($p<0.0001$) and age ($p<0.0001$) on cortical accretion of docosahexaenoic acid (DHA) and total n-3 PUFA; this positively correlated with the mRNA expressions of BDNF, NGF, and TrKB. There was a significant effect of diet ($p<0.05$) and age ($p<0.05$) on the mRNA expression of NGF. There was a significant effect of diet ($p<0.01$) on the BDNF gene expression; high n-3 PUFA diet increased the expression compared to the low n-3 PUFA diet. The mRNA expression of TrKB was higher ($p<0.0001$) at 16 weeks in the high n-3 PUFA group compared to the low n-3 PUFA group; however, no difference was observed at weaning. There was no effect of diet on the gene expression of CREB; however the activated form of CREB, phosphorylated CREB was higher in the high n-3 PUFA group compared to the low n-3 PUFA group ($p<0.05$). Our findings show for the first time that n-3 PUFA directly regulate neurotrophin signalling and that the neuroprotective effects of the accretion of dietary n-3 PUFA is age dependent. (Supported by NSERC).

Dietary creatine-supplementation in rats influences hepatic lipid and carbohydrate metabolism

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Non-alcoholic fatty liver disease (NAFLD) encompasses a wide spectrum of liver damage including steatosis, non-alcoholic steatohepatitis (NASH), fibrosis and cirrhosis. Insulin resistance often accompanies NAFLD and both of these phenomena are hallmarks of the metabolic syndrome. Recently, we reported that creatine supplementation prevents hepatic steatosis, lipid peroxidation and insulin resistance in rats fed a high-fat diet. To investigate the potential mechanisms that underlie these observations, we employed McArdle RH-7777 rat hepatoma cells treated with oleic acid as a model of hepatocyte lipid accumulation. Lipid analysis as well as mRNA expression were measured. We found that cells cultures with creatine had a dose dependent reduction in cellular TG accumulation. Using radiolabeled tracers we have demonstrated that incubation of McArdle RH-7777 cells with creatine increases fatty acid oxidation and decreases both fatty acid and TG synthesis. In-line with increased fatty acid oxidation, analysis of mRNA from McArdle RH-7777 cells showed that cells treated with creatine had increased expression of PPARα and its targets CPT1a and LCAD. Interestingly, we have also found that creatine treated McArdle RH-7777 cells have a 343% increase in expression of the phosphoenolpyruvate carboxykinase and a 135% increase in expression of pyruvate kinase. In addition, preliminary data suggests that rats fed a creatine supplemented high-fat diet have significantly improved insulin sensitivity, as assessed by a glucose tolerance test, as compared to high-fat diet fed control animals Taken together, these data strongly suggest that creatine influences carbohydrate metabolism as well as lipid metabolism. (This work is funded by a grant from the CIHR)

Creatine de novo synthesis and methionine metabolism in neonatal piglets

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Arginine and methionine are indispensable amino acids in neonates that have a metabolic role in creatine synthesis. Arginine transfers its amidino group to glycine to form guanidinoaceticacid (GAA) which is then transmethylated to creatine. Methionine is the primary methyl donor for transmethylation reactions via S-adenosylmethionine (SAM). SAM is demethylated to S-adenosylhomocysteine (SAH) and transfers its methyl group to synthesize creatine, phosphatidylcholine (PC) and methylated DNA. Determining the partitioning of methionine into these metabolic products was the aim of this study. Thirty-four 7-10 day old piglets were fed one of five elemental diets with: 1) arginine and methionine slightly below requirement (Base), 2) Base diet supplemented with GAA equivalent to the creatine requirement (Base-GAA), 3) Base diet supplemented with creatine (Base-CRE), 4) Arginine and methionine in excess (High Arg/Met) or 5) 100% GAA with excess methionine (GAA/High Met). At the end of five days of experimental diet, animals received a constant infusion of L-[methyl-3H] methionine for 6 h. The rate of 3H-methyl incorporation (RMI) to creatine, PC and protein was measured using specific radioactivity. Hepatic SAM: SAH concentration ratio was higher ($p < 0.0001$) in High Arg/Met and GAA/High Met groups, suggesting more precursors were available for transmethylation. Hepatic creatine concentration was higher only in GAA/High Met, suggesting more dietary methyl groups from methionine were needed to methylate GAA. RMI to creatine was lower in Base-CRE ($p <0.05$) suggesting dietary creatine down regulated creatine synthesis and did not lead to more hepatic creatine. RMI to PC was higher ($p < 0.05$) in High Arg/Metand GAA/High Met compared to other groups suggesting PC synthesis was prioritized over creatine synthesis when methyl supply was expanded with added dietary methionine. RMI to hepatic protein was not affected by diet, demonstrating that hepatic protein synthesis was conserved over transmethylation reactions when methionine was limited; sparing methionine with creatine or supplementing methionine led to more PC synthesis but not protein. Therefore, creatine levels in neonatal piglets can be maintained by de novo creatine synthesis but is enhanced by GAA only with an increased availability of methionine. (Supported by Evonik Industries AG, Germany and NSERC)

Natriuretic peptide and other cardio-protective genes are stimulated by vitamin A (retinoic acid), preventing apoptosis and fibrosis in obese-diabetic mice heart

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Aim: In hypertensive rodents, vitamin A as retinoic acid (RA) prevents adverse cardiac remodeling and improves myocardial infarction outcome, but its role in obesity-diabetes related changes of cardiac tissue are unclear. We hypothesized that RA treatment will improve the cardio-protective oxytocin-natriuretic peptides (OT-NPs) system, preventing abnormal cardiac remodeling in the ob/ob mice, a model of obesity and insulin resistance. Methods: Female 9-week-old B6.V-Lep/J ob/ob mice (n=16) were divided in two groups, a group (n=8) treated with 100 µg of all-trans RA dissolved in 100 µl corn oil (vehicle) delivered daily (~ 2µg/gbw/day) by stomach intubation for 16 days, and a group (n=8) receiving the vehicle alone. A group of non-obese, non-diabetic littermate mice (n=9) served as controls. Genomics, proteins and histology analyses were performed. Results: ob/ob mice exhibited obesity, hyperglycemia and down-regulation of cardiac OT-NPs system, including the transcription factor GATA4, OT receptor mRNA, BNP (brain natriuretic peptides) mRNA and the endothelial nitric oxide synthase (eNOs) protein expression. Hearts from ob/ob mice also demonstrated increased apoptosis and collagen accumulation. RA treatment induced weight loss and decreased adipocytes diameter in the omental fat, thus reducing visceral obesity which is associated with a high risk for cardiovascular disease. RA treatment was associated with a reduction in fasting hyperglycemia and a normalization of the OT-NPs system expression in the hearts of ob/ob mice. Furthermore, RA treatment prevented apoptosis and collagen accumulation in hearts of ob/ob mice, two risk factors for abnormal cardiac remodeling and functions. Conclusions: The present study indicates that RA treatment was effective in restoring the cardio-protective oxytocin-natriuretic peptides system and in preventing apoptosis, collagen accumulation and abnormal cardiac remodeling in ob/ob mice. Key words: Natriuretic peptides, retinoic acid, obesity, diabetes, cardiac remodeling. Note: Authors are proud to mention, a full article including a large part of this work was just submitted (Jan. 2014) and is presently in reviewing for publication with the CNS Journal: The Applied Physiology Nutrition and Metabolism APNM-NRC Press. (Supported by CIHR, FRQS, FESP/NUT-Université de Montréal)

Elementary school home packed lunches: comparison of foods packed and eaten in the traditional vs. balanced school day schedule

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The Balanced School Day (BSD) was created as an alternative to the well-established Traditional Schedule (TS), and has been implemented in many Canadian schools. The BSD consists of two breaks dividing three 100-minute teaching blocks, with a 20-minute eating period during each break. The purpose of this study was to utilize a valid and reliable direct observation methodology to identify if there is a difference between the BSD and TS, according to type and quantity of foods children are bringing and consuming while at school. Grade 3 and 4 students (n=321), ages 7-10 years, from 9 BSD schools (n=153) and 10 TS schools (n=168), were observed during all eating periods of a school day. For the purpose of this study, snacks were defined as non-entrée, non-beverage, non-fruit or vegetable, sweet or savory items. The mean SD servings of food items packed in BSD lunches were significantly higher than the TS for milk and alternatives (M+A; 0.69$\pm$0.70 vs. 0.47$\pm$0.49, respectively, p=0.02), sweetened beverages (SB; 0.91$\pm$1.24 vs. 0.59$\pm$1.00, respectively, p=0.02), and snacks (2.21$\pm$1.44 vs. 1.75$\pm$1.30, respectively, p<0.01). Regardless of school schedule, only 41% of students had vegetables in their lunch, while 87% had a snack packed. When comparing mean servings of foods eaten, SB's and snacks remained significantly higher in the BSD (0.74$\pm$1.02 vs. 0.49$\pm$0.85, p=0.04; 1.87$\pm$1.33 vs. 1.50$\pm$1.19, p=0.01, respectively). M+As were no longer significant as school milk programs were available in 67% of BSD and 100% of TS schools. The mean proportion of children whose consumption met one-third of CFG recommendations for vegetables and fruit was poor in both schedules (16% BSD, 23% TS). Moreover, the mean percentage of uneaten vegetables was 30% in the BSD and 20% in the TS, while only 11% of snacks were left uneaten in both schedules. These findings suggest the BSD may have unintended negative consequences on the school food environment, which could impact weight status and contribute to future health risks. Support provided to families when switching to the BSD should focus on encouraging more vegetables and fewer SB and snacks in packed lunches. (Supported by CIHR grant to Dworatzek: POH-123776)

Methionine availability for protein synthesis is affected by transmethylation and remethylation rates in neonatal piglets

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Methionine is an essential amino acid which, in addition to protein synthesis, can be converted to S-adenosylmethionine, the universal methyl donor in over 50 transmethylation reactions including creatine synthesis. Following TM, homocysteine is formed which can be converted to cysteine or remethylated to methionine by receiving a methyl group from folate or betaine (synthesized from choline). Infant diets are highly variable in creatine, folate, choline and methionine and the neonate must maintain methionine availability for not only protein synthesis, but also for the expansion of transmethylation product pools. Our objective was to determine whether increasing demand for transmethylation reactions or limiting remethylation flux can limit methionine availability for protein synthesis. The methylation of guanidinoacetate (GAA) to form creatine is the most quantitatively significant transmethylation reaction as the neonate must synthesize 75% of its creatine requirement, a demand that is further increased if creatine is not provided in the diet. To determine the effect of increasing demand for creatine synthesis, we performed an acute intraportal infusion of either GAA or saline (n=5) followed by a bolus infusion of [methyl-3H]methionine to measure the hepatic protein and creatine synthesis. Infusion with GAA led to a ~180% increase in methyl-3H incorporation into creatine which limited methionine availability for protein synthesis, which was ~40% lower when GAA was infused ($p < 0.05$). In another study, we wanted to determine the contribution of folate and betaine to methionine availability when dietary methionine is limiting. We supplemented folate, betaine or a combination of both (n=6) to piglets adapted to low-methionine diets devoid of these methyl donors, and measured 13C-phenylalanine oxidation pre- and post-supplementation as an indicator of protein synthesis. Post-supplementation, phenylalanine oxidation was ~30% lower ($p < 0.05$) with either methyl donor with no difference among groups, demonstrating the capacity for both nutrients to increase methionine availability for protein synthesis. Because increasing the demand for creatine synthesis can lower methionine availability and dietary provision of folate and/or betaine can increase methionine availability, these nutrients need to be considered when defining the dietary methionine requirement in the neonate. (CIHR)

Cysteinyl-glycine ameliorates intestinal inflammation in neonatal piglets with parenteral nutrition-induced gut atrophy.

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PepT1 is an intestinal dietary peptide transporter also capable of transporting pro-inflammatory bacterial peptides including formyl-methionyl-leucyl-phenylalanine (fMLP). Cysteinyl-glycine competes for PepT1-mediated uptake and has anti-inflammatory potential. We used an in situ model to measure the ileal mucosal inflammatory response to fMLP when delivered with cysteinyl-glycine in piglets with parenteral nutrition (PN)-induced intestinal atrophy. Pigs (n=6, 10 d) received PN for 4 d to induce SI atrophy; littermates (n=6) remained with the sow. Subsequently, five 10 cm loops of the distal SI were isolated and perfused for 3 h with one of: 1) 5 mM each of L-cysteine and glycine (cys + gly) 2) 5 mM cysteinyl-glycine 3) 10 μM fMLP 4) 5 mM cys + gly + 10 μM fMLP 5) 5 mM cysteinyl-glycine + 10 μM fMLP. In both dietary treatments, intestinal segments exposed to fMLP had higher mucosal TNF-α and IFN- compared to unexposed loops ($p<0.001$). IFN- was higher in PN-fed piglets compared to sow-fed pigs ($p < 0.01$). Co-perfusion of fMLP and cysteinyl-glycine resulted in a lower IFN- response in both sow-fed and PN-fed piglets ($p <0.05$), but neither group responded significantly to free cys + gly. Interestingly, free cys + gly reduced the TNF-α response in sow-fed pigs ($p<0.001$), but not in the PN-fed group. Loops exposed to cysteinyl-glycine and fMLP had lower TNF-α concentrations compared to fMLP alone in both diet groups ($p<0.001$) and in sow-fed piglets the response was significantly more abated than with cys + gly ($p < 0.001$). Interleukin-10, an anti-inflammatory cytokine implicated in the regulation of epithelial permeability, was lower in animals undergoing PN compared to sow-fed ($p<0.05$). Morphologically, fMLP exposure did not alter villus height or crypt depth in sow-fed animals; in contrast, intestinal segments from PN-fed piglets exposed to fMLP had reduced villus height compared to unexposed loops ($p<0.05$). Inclusion of cysteinyl-glycine was effective at attenuating a bacterial peptide-induced inflammatory response in the injured SI; this may be due to efficient dipeptide uptake in a situation of impaired free amino acid absorption, and/or competitive inhibition of fMLP uptake. (Funded by CIHR)

Arachidonic acid has a dominant regulatory effect on adipogenic and lipogenic genes in 3T3-L1 adipocytes compared to omega-3 polyunsaturated fatty acids

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Triglyceride stores in adipocytes are in constant flux and are regulated by dietary status. Studies have shown individual effects of omega (n)-3 and n-6 polyunsaturated fatty acids (PUFA) on triglyceride homeostasis in adipocytes; however these fatty acids are generally consumed together in our diet. We investigated the individual and combined effects of n-3 and n-6 PUFA on the metabolic regulation of adipocytes. Fully differentiated 3T3-L1 adipocytes (Day 8) were treated with 100μM of either docosahexaenoic acid (DHA), docosapentaenoic acid (DPA), eicosapentaenoic acid (EPA) or arachidonic acid (AA); and also a 1:1 combination of DHA+AA, DPA+AA, EPA+AA complexed with bovine serum albumin (BSA). Control cells were treated with BSA alone. After 48h of treatment, total RNA was extracted for gene expression analysis, and lipids were extracted for fatty acid analysis. Statistical analysis was performed using student's t-test. Treatment with individual or a combination of n-3 PUFA and AA significantly ($P<0.05$) increased the gene expression of peroxisome proliferator activated receptors-γ (PPAR-γ) and adiponectin compared to control cells. Interestingly, treatment with EPA had no effect on adiponectin mRNA expression, however treatment with AA+EPA significantly ($P<0.05$) increased the adiponectin gene expression compared to control cells. Treatment with AA increased the mRNA expression of acetyl-CoA carboxylase 1 (ACC1) ($P<0.05$), while decreasing stearoyl-CoA desaturase (SCD1) gene expression ($P<0.01$) compared to control cells. N-3 PUFA had no effect on the gene expression of ACC1 or SCD1. A combination of AA+DHA and AA+DPA inhibited SCD1 gene expression ($P<0.05$), however AA+EPA showed no change in SCD1 expression compared to control cells. A combination of AA+EPA increased the gene expression of ACC1 ($P<0.05$), while AA+DPA and AA+DHA had no effect compared to control cells. These findings demonstrate that AA has a dominating regulatory effect on the expression of adipogenic and lipogenic genes in adipocytes. Furthermore, the fatty acids analysis of adipocytes showed a higher incorporation of AA compared to n-3 PUFA. Thus, our data suggest that the dominating effects of AA on adipogenic and lipogenic genes are due to higher incorporation of AA in mature adipocytes. (Canadian Institutes of Health Research)