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CARBOHYDRATES

THROUGH THE LIFE CYCLE AND ACROSS TISSUES

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A REPORT FROM

The 117th Abbott Nutrition Research Conference

JUNE 21, 2018 • COLUMBUS, OHIO, USA

Dr Hakim Bouzamondo (Abbott Nutrition, USA) opened the 117th Abbott Nutrition Research Conference (ANRC) on carbohydrates with a head-turning question: "*Why is sugar viewed as today's dietary villain?*" This bad-guy reputation of carbohydrates is mostly undeserved and unfair. As highlighted throughout the ANRC 2018 meeting, carbohydrates—including sugar—are nutritionally necessary. There are, however, carbohydrate cautions to be considered when seeking good health through nutrition. The quantity and quality of dietary carbohydrates matter, and so does the balance of carbohydrates with other macronutrients.

This year's research conference featured a faculty of world-renowned experts who summarized state-of-the-art evidence on nutritional roles of carbohydrates across the lifespan—from healthy fetal development to growth of infants, toddlers, children, and adolescents. The program likewise included presentations on carbohydrates for physical performance, brain function, and adult weight management, as well as on metabolic flexibility and nutrigenomics and their roles in next-generation assessment of health status.

ANRC 2018 Faculty
Left to right (front row) Dr Joel Cramer (USA); Dr Suzan Wopereis (The Netherlands); Prof Helen Murphy (UK); Dr Robert Murray (USA); (middle row) Dr Richard Mattes (USA); Prof David Benton (UK); (upper row) Dr John Sievenpiper (Canada); Prof Rafael Salto (Spain)

HIGHLIGHTS OF 117TH ANRC PRESENTATIONS

- Keynote speaker Dr John Sievenpiper (Canada) presented "What I tell my patients when they ask about a healthy diet and carbohydrate intake." Page 3.
- Achieving optimal maternal glucose control for women with gestational diabetes mellitus is paramount for a successful pregnancy and for long-term health of the mother and child. Page 3.
- Breast milk is sweet and fragrant to stimulate avid sucking, but how much sweetness is right for toddlers and older children? Page 4.
- Carbohydrates provide necessary fuel for physical performance in adolescents and adults. Page 5.
- The snacking habit of American adults—is it good or bad? Page 5.
- Together liver, adipose tissue, and skeletal muscle balance carbohydrate fuel use and carbohydrate storage. Page 6.
- The brain must be well fueled for optimal function. So how does carbohydrate consumption influence the way we think? Page 6.
- The future for nutrition and health may be in the new field of nutrigenomics, but what is it? Page 7.

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KEYNOTE ADDRESS: CARBOHYDRATE QUALITY

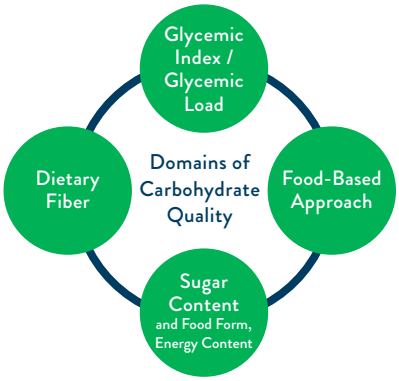
What do I tell my patients?

Keynote speaker Dr John Sievenpiper (Toronto, Canada) is a nutrition scientist at the University of Toronto and staff physician at Li Ka Shing Knowledge Institute at St Michael's Hospital. With recent headlines like 'sugar is the new tobacco' or 'death by sugar,' Dr Sievenpiper recognized a need to take a close and systematic look at the evidence. Does a low sugar or low carbohydrate diet actually decrease weight gain, enhance weight loss, reduce diabetes incidence, or lower risk of heart attack and stroke? He needed this evidence to answer the question, "What do I tell my patients?"

> *"All carbohydrates are under attack, but sugar is the poster child."*
>
> **Dr John Sievenpiper**
> *Physician-scientist, Toronto, Canada*

Evaluating effects of varying carbohydrate quality and quantity requires comparing different dietary strategies. Dietary carbohydrate quantity is measured by total intake (a low-carb diet contains only 20-60 g carb/day). Good carbohydrate quality is assessed in terms such as: (1) a diet featuring foods with low glycemic index (GI) or glycemic load (GL); (2) a diet high in fiber; (3) a food-based approach that emphasizes specific carbohydrate-containing foods (whole grains, pulses, or fruit); and (4) a low-sugar diet with the caveat that any effect depends on the food form and energy content.

In his systematic review of evidence, Dr Sievenpiper considered large meta-analyses of trials and other recent randomized, controlled trials of diets with varying macronutrient profiles.[1-5] Comparative studies found no between-diet differences in weight loss; all were effective. As well, various markers of high carbohydrate quality were associated with decreased weight gain, diabetes incidence, and cardiovascular disease incidence and mortality. Irrespective of the carbohydrate content, the most important determinant of success in these trials was adherence to the diet program and clinic attendance.[1]



According to Dr Sievenpiper, too narrow a focus on avoidance of dietary sugar or even carbohydrates may unintentionally overlook big-picture strategies that promote a healthy diet. Based on a recent burden-of-disease assessment of dietary factors and their effects on health, researchers found that 6 factors accounted for the highest health risks—diets high in sodium, low in vegetables, low in fruit, low in whole grains, low in nuts and seeds, and low in seafood omega-3 fatty acids. Such results suggest that a dietary policy focusing only on limiting sugar or fat might have a comparatively smaller effect than a policy that promotes eating more vegetables, fruit, whole grains, nuts and seeds, and omega-3-containing seafoods.[6]

To sum up for his patients, especially those with diabetes and overweight or obesity,[7] Dr Sievenpiper advised, "Good eating is more about including nutrient-rich foods and following healthy dietary intake patterns than about avoiding certain macronutrients."

CARBOHYDRATES THROUGH THE LIFE CYCLE

Gestational diabetes mellitus: interventions for best outcomes

Prof Helen Murphy (London, England, UK) is a Professor of Women's Health at King's College London, a researcher in the area of diabetes in pregnancy, and a practicing clinician. She firmly believes that achieving optimal maternal glucose control during pregnancy is important both for a successful pregnancy outcome and for better long-term health of both mother and child.

Today 1 in 6 live births occurs in a woman with diabetes; gestational diabetes mellitus (GDM) accounts for most of these cases.[8] With GDM, elevated levels of blood glucose in the mother stimulate fetal pancreatic insulin secretion, in turn leading to fetal growth acceleration, increased fetal fat accumulation, and newborns large for gestational age (LGA, birthweight > 90th percentile). Mothers of LGA infants are at risk of giving birth prematurely, having operative deliveries, and delivering stillborn infants. LGA infants are predisposed to developing insulin resistance, obesity and type 2 diabetes, thus perpetuating an intergenerational cycle of cardiometabolic disease.[9]

RISK FACTORS FOR GDM

- Pre-pregnancy BMI > 30 kg/m^2
- Previous GDM pregnancy
- Previous LGA infant or infant > 4.5 kg
- Family history of T2D
- Ethnic origin with high prevalence of T2D (eg, South Asian, Hispanic, Middle-Eastern, Afro-Caribbean)
- PCOS, infertility, IVF

GDM=gestational diabetes mellitus, BMI=body mass index, LGA=large for gestational age, T2D=type 2 diabetes, PCOS=polycystic ovary syndrome, IVF=in vitro fertilization

Prof Murphy and colleagues recently performed a systematic review and meta-analysis demonstrating that dietary interventions (in addition to routine clinical advice) can further optimize maternal glycemia and reduce newborn adiposity.[10] While trial results did not specifically support superiority of any specific diet during pregnancy, attention to nutrition definitely yielded benefits. The take-home message was that any culturally acceptable dietary intervention that helps control glycemic status and limit excessive weight gain in pregnancy is likely to be effective. Many professional organizations also recommend 30 minutes of moderate daily exercise throughout pregnancy.

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Infants and children need carbohydrate fuel for growth and development

Dr Robert Murray (Columbus, Ohio, USA) is a highly respected pediatric educator and recent past director of the Center for Healthy Weight and Nutrition at The Ohio State University School of Medicine. His presentation focused on the importance of carbohydrates, especially sugars, in the diets of infants and children. He opened, "Nutrition supports the remarkable rate of growth of infants and toddlers, including weight gain, linear growth, and development of organs and systems."

Brain volume doubles in the first year of life,[11] and at least half of an infant's energy intake fuels brain growth and function. Breast milk is sweet and fragrant to stimulate avid sucking, nature's way of ensuring intake of necessary nutrients, including the milk sugar lactose, for this early growth spurt. Breast milk provides complete nutrition until around 6 months of age when the infant's needs for energy, iron, and zinc require complementary foods.

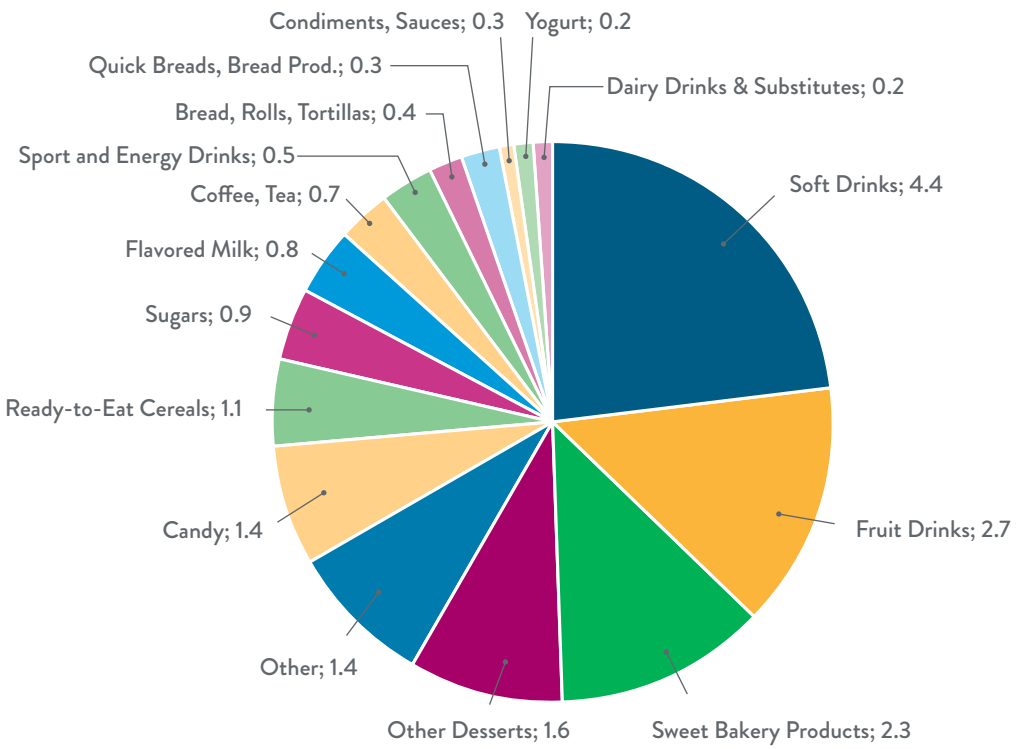
The introduction of complementary foods is an opportunity to establish healthy eating patterns for older infants, toddlers, and young children. The sensory and motor experiences associated with first foods—variety, timing, colors, flavors, smells, and textures—all contribute to lifelong food preferences. While sugar remains an important fuel, dietary supplies can come from highly nutritious foods, such as fruits and healthy cereals or breads.[12]

Childhood diets, like those of US adults, contain too much sugar. The main foods contributing sugars to childhood diets are sweetened beverages and sweet bakery products.[13,14] Candy and other desserts (eg, ice cream) are added to intake by children and adolescents. To help build healthy eating patterns, Dr Murray instead recommends adding sugars wisely as a way to promote intake of nutrient-rich foods, such as lightly sweetened fruits.

ADDED SUGARS IN CHILDREN'S DIETS

National Health and Nutrition Examination Survey (NHANES) 2007-2010, 2-18 years of age

VALUES ARE TEASPOONS PER DAY EQUIVALENTS



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Carbohydrates for performance in adolescents and adults

Dr Joel Cramer (Lincoln, Nebraska, USA) is a leader in sports nutrition and performance nutrition.[15] *Sports nutrition* specifically focuses on improving sports performance in athletes, eg, marathon runners and gymnasts, who perform better when strategically fueled. In contrast, *performance nutrition* addresses performance of the human body, especially skeletal muscle, as used for everyday physical activities like walking, playing, swimming, or gardening. Experts like Dr Cramer have acquired critical knowledge of skeletal muscle performance through sports nutrition research, and they can advise how to apply this knowledge to the broader goals of performance nutrition.

In a quick review of biochemistry, Dr Cramer noted that when carbohydrates are consumed, all metabolic pathways ultimately lead to glucose—some by breakdown of complex carbohydrates to constituent sugars and some by conversion of simple sugars (eg, fructose and galactose) to glucose. In skeletal muscle, glucose is either stored as glycogen, or metabolized by glycolysis to produce energy for muscle work.

Athletes participating in events with very high energy demands—such as marathon running, distance swimming, or multi-event tournaments—can benefit from fueling or refueling with ready supplies of glucose.[16] For everyday activities, Dr Cramer noted that adolescents and adults are better off consuming foods that supply sustained release of glucose. Such intake promotes release of glucose from stored supplies, and avoids potentially harmful glucose spikes that can lead to obesity and other bad health consequences.

As a good first step toward improving general skeletal muscle health and lowering risk for other metabolic diseases, Dr Cramer specifically advised avoiding sweetened beverages.

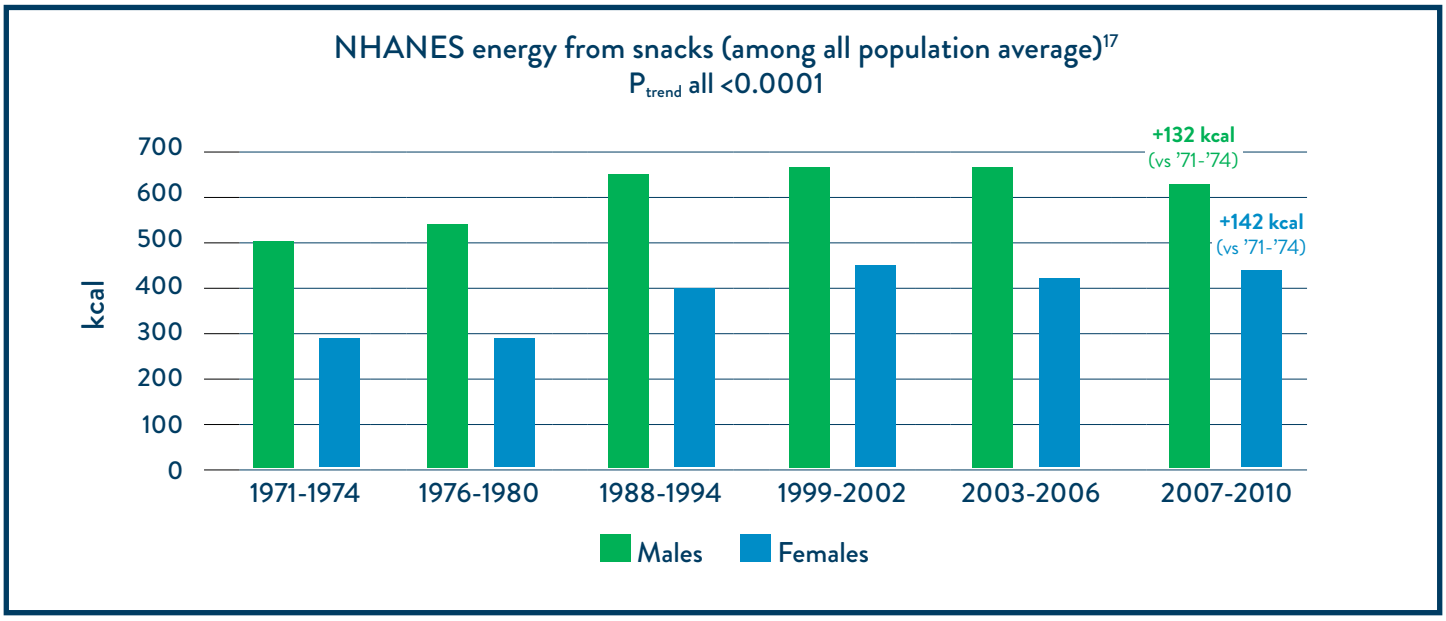
Snacking for adults: is it good or bad?

Dr Richard Mattes (West Lafayette, Indiana, USA) tried to answer the difficult question, "Is snacking a good or bad practice for adults?" First, he reviewed the definition of a "snack." Common definitions are based on when the eating event occurs (eg, mid-morning, mid-afternoon, evening), type of food consumed (eg, sweet and salty, single-serve, convenience items), energy content (eg, researcher-defined and fixed-amount intake that is less than a meal), or some combination of these definitions. As well, some studies define snacks as consumer-reported eating events.

Regardless of the definition used, there is unequivocal evidence that snacking and eating frequency have increased over time for US adults. In fact, a rate of 2.25 snacking events per day has been reported.[17] Further, data from a large national study indicated that snacks contribute approximately 600 kcal/d for males and 450 kcal/d for females, reflecting a steady increase since the mid-1970s. Indeed, the increment in snacking energy has outpaced the energy contributed by meals.[17] Snacking is therefore prevalent, increasing in frequency, and responsible for approximately 20-25% of daily energy intake in the US.

With the high prevalence and severe consequences of obesity now well established, attention is focused on total energy intake. Total intake is determined by how much energy is consumed in each eating event and how frequently eating occurs.[18] While obesity has been attributed to increased portion size in recent years, growing evidence suggests that higher total intake resulting from increased eating frequency is likely more problematic for weight gain.[18,19]

Dr Mattes concluded by viewing snacks from another perspective. He advised, "Snacks may present opportunities to improve nutrient intake and overall health." In many ways, healthy snacks make good sense.



CARBOHYDRATE USE IN ORGANS AND TISSUES

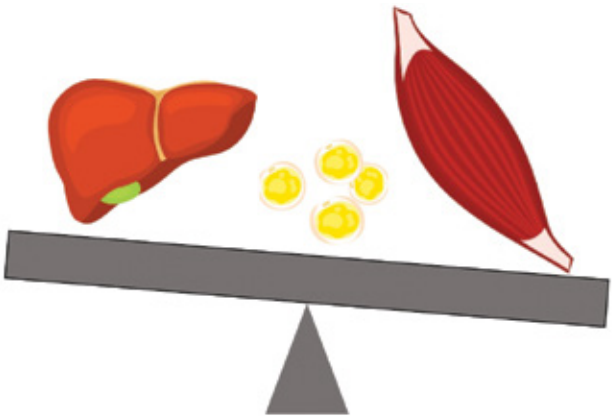
Flexibility of fuel use by liver, adipose tissue, and skeletal muscle

Prof Rafael Salto (Granada, Spain) introduced the concept of metabolic flexibility, ie, the body's ability to respond or adapt metabolically to conditions such as different diets, and exercise or rest.[20] Carbohydrates and fats fuel body metabolism, and 3 organs work synergistically to balance fuel use and storage—liver, adipose tissue, and skeletal muscle.

In terms of carbohydrate quality, foods in a diet can be categorized as having a high or a low GI. GI is a ranking of food carbohydrates according to how they affect blood glucose levels; foods are ranked relative to pure glucose, which has a GI of 100. Carbohydrates with a low GI value (55 or less) are more slowly digested, absorbed or metabolized and cause a lower and slower rise in blood glucose and, therefore usually, insulin levels. Eating carbohydrate-containing foods with a high GI (greater than 70) causes blood glucose to spike and then drop. Vegetables, many fruits, and most dairy products have low GI values, while breads and cakes have high GI values. GL is obtained by multiplying the quality of carbohydrate in a given food (GI) by the amount of carbohydrate in a serving of that food. GI is thus a measure of carbohydrate quality, while GL reflects both quality and quantity.

High GI diets (and high GL too) have the capability to produce long-lasting changes in metabolism leading to metabolic inflexibility. In the liver, consumption of a high GI food leads to increased glycogen storage and increased triglyceride accumulation.[21] When fed high GI diets, muscles depend on glucose as the main fuel instead of fatty acids (FA), with the consequence of less energy production and limits on muscle performance during exercise. In fact, high GI foods increase glucose uptake and release of non-esterified FA, leading to increased adipose tissue mass and decreased insulin sensitivity. All of these high GI changes are reversed with consumption of low GI diets.

Prof Salto cited recent evidence that diets of foods with low GI (and low GL) can improve glycemic status in people with diabetes, can lessen risk of excess adiposity in infants of pregnant women, and may lower risk for metabolic syndrome in adults who are at risk.[22-24]



Glucose and the brain

Prof David Benton (Swansea, Wales, UK) is a behavioral psychologist who has spent 30 years studying relationships between food, mood, and cognitive function. Prof Benton highlighted the brain's role as the command center of the body, thus making the brain a hub for mediating nutritional effects on behavior. The brain has high energy needs and limited reserves, and it lacks the ability of other organs to function on a range of fuels. The brain represents 2% of body weight, yet estimates indicate it consumes about 20% of basal metabolic energy.[25] The brain runs primarily on glucose, and its glucose supply is exhausted in less than 10 minutes if it is not continually replenished.

While brain functions of memory and behavior control are complex, recent clinical evidence reveals fascinating links to consumption of carbohydrates, especially glucose. Consider the following clinical findings:

- To fuel brain function, children need more glucose per gram brain tissue than do adults. In a study with 9- to 10-year-old children, a glucose-containing drink or a placebo was given in the afternoon of alternating days. On the days children received the glucose, they spent more time attending to their schoolwork, also with positive impacts to memory.[20]
- In fasted young and older adults, simply giving a drink containing glucose can have positive impacts to episodic memory.[26] Episodic memory is the recall of events associated with time, place, and context (contrasting with semantic memory of factual information that lacks context).
- People who experienced higher-than-normal blood glucose levels subsequently had reduction in the size of the hippocampus, the brain region responsible for memory.[27]
- In older adults, higher glucose concentrations in brain tissue and lower rates of brain glycolysis (glucose metabolism) corresponded with severity of Alzheimer's disease pathology and with expression of disease symptoms.[28]
- Adults with type 2 diabetes had a 60% greater chance of developing dementia than did those with normal glycemic control, leading researchers to call this type of dementia type 3 diabetes.[29]

Putting all this information together, Prof Benton concluded that glucose intake per se is not a problem for learning and memory; the real problem is the elevated glycemia associated with insulin resistance (type 2 diabetes) or with excessive intake of foods with high GI/GL.

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THE FUTURE OF NUTRITION AND HEALTH

Nutrigenomics as the key to personalized diet and health

Dr Suzan Wopereis (Zeist, The Netherlands) addressed the topic of nutrigenomics, the study of how a particular food, food component, or diet affects health by combining classic clinical markers with novel genomics technologies such as metabolomics, transcriptomics, genetics, proteomics, and metagenomics. In practice, the field of nutrigenomics aims to determine whether it is possible to study health outcomes in a more holistic way by understanding biological mechanisms.

Since the impact of nutrition on health can be subtle and long-term, Dr Wopereis and her research team sought ways to detect beneficial or harmful effects of nutrition. First of all, they had to define health, and secondly, they had to find a way to measure nutrition-related health changes. The research team began by recognizing that health depends on the ability of our body to face daily-life challenges, and they noted that physiological adaptations allow us to cope with stressors. Challenges such as physical exercise, infections, and mental stress can be met with healthy adaptive changes, ie, *phenotypic flexibility*.[30] Following a physiological challenge, phenotypic flexibility also facilitates a healthy return to baseline. As a first step toward measuring phenotypic flexibility, they looked for processes and biomarkers that reflected health and were related to diet; they identified 26 biological processes distributed over 7 organs and represented by a total of 132 different markers.[30] Once biomarkers were defined, they developed the PhenFlex nutritional stress test—a high-fat, high-calorie drink containing 60 g palm olein, 75 g glucose, and 20 g dairy protein in a total volume of 400 mL.[31, 32] In testing, PhenFlex discriminated between overweight people who would respond to calorie restriction versus those who would not.[33]

> *"In the near future, we expect to build individual lifestyle advice by combining personal health data with science-based models to link a person's biology and behavior with diet, lifestyle, and environment to improve health outcomes."*
>
> **Dr Suzan Wopereis**
> *The Netherlands*

Dr Wopereis proposed, "In the near future, we want to determine whether it is possible to improve health outcomes by personalizing a diet according to the person's phenotype and genotype. We expect to build individual lifestyle advice by combining personal health data with science-based models to link a person's biology and behavior with diet, lifestyle, and environment to improve health outcomes."

CONFERENCE VIDEOS AND PROCEEDINGS AVAILABLE AT ANHI.ORG

Left to right: Dr José María Lopez Pedrosa, Prof Rafael Salto, Dr Ricardo Rueda, Dr Suzan Wopereis

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Opening Keynote

Carbohydrate Quality: What Do I Tell My Patients?
John L. Sievenpiper, MD, MSc, PhD, FRCPC
University of Toronto
Li Ka Shing Knowledge Institute at St Michael's Hospital
Toronto, Ontario, Canada

Carbohydrates Through the Life Cycle

Carbohydrates for Performance Across Adolescence and Adulthood
Joel T. Cramer, PhD, FACSM, FNSCA, FISSN
University of Nebraska-Lincoln
Lincoln, Nebraska, USA

Gestational Diabetes Mellitus: Latest Research and Guidelines
Prof Helen R. Murphy, MBBChBAO, FRACP, MD
University of East Anglia, Norwich
King's College London
London, England, United Kingdom

Savoring Sweet: Carbohydrates in Infant, Toddler, and Child Nutrition
Robert Murray, MD
The Ohio State University
Columbus, Ohio, USA

Metabolic Flexibility and Carbohydrates Across Tissues

The Role of Dietary Carbohydrates on Metabolic Flexibility in Liver, Adipose Tissues and Skeletal Muscle
Prof Rafael Salto, PhD
University of Granada
Granada, Spain

Phenotypic Flexibility as a Measure of Health Through the Life Cycle
Suzan Wopereis, PhD
Netherlands Organisation for Applied Scientific Research (TNO)
Zeist, The Netherlands

Carbohydrates, Mood and Cognition
Prof David Benton, PhD, DSc
Swansea University
Swansea, Wales, United Kingdom

Closing Keynote

Snacking and Energy Balance
Richard D. Mattes, MPH, PhD, RD
Purdue University
West Lafayette, Indiana, USA

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