

## Abstracts from a conference on healthy eating, aspartame, and chronic non-communicable disease. Beijing, and Shanghai, 1994

### Preventive nutrition and health: an Asia-Pacific perspective

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The economics and socio-demography of the Asia-Pacific region are changing rapidly. With these changes come changes in the food supply, food intake and related health advantages and problems. The nexus between protein-energy malnutrition in the young is being replaced by a nexus between nutrient excess, with associated food component deficiencies, and non-communicable disease in an ageing population. A food supply which is abundant, refined and fatty characterises the present situation. The early expressions of abdominal fatness, with its attendant metabolism dysfunctions and health sequelae, are indicative of the transitional health problems. These include cardiovascular disease,

diabetes, certain cancers, osteoporosis and immune deficiency. Urbanisation and population pressures will be eased by innovations in food production and food technology, with attention to the full risk-benefit equation for individuals and the need for an environmentally sustainable food supply. Prevention will depend on how well the region manages each of these dimensions.

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### Nutrition transition in China: the growth of affluent diseases with the alleviation of undernutrition

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### Studies on the relationship between changes in dietary patterns and health status

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### Diabetes mellitus: classification, therapeutic aspects, interventions and complications

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Diabetes mellitus is a major cause of morbidity and mortality and is increasing in prevalence in many populations around the world. The most common form of diabetes is non-insulin dependent (NIDDM or Type II) diabetes, comprising over 90% of cases. Gestational diabetes mellitus (GDM) and impaired glucose tolerance (IGT) may be forerunners of NIDDM and when they are diagnosed appropriate interventions should be taken to prevent or delay progression to NIDDM.

Although the pathogenesis of NIDDM is not fully understood, at least three factors are important: a genetic predisposition, the presence of insulin resistance, and a defect in pancreatic B-cell function. Conditions associated with the development of insulin resistance increase the risk of NIDDM greatly. Chief among these are obesity, advancing age and decreased physical activity. Moderate degrees of weight reduction and increased physical activity are associated with decreases in plasma insulin, improved insulin sensitivity and lower plasma glucose levels. Appropriate diet, weight reduction and exercise programs are the first step in the prevention and treatment of NIDDM. If these are

unsuccessful, oral hypoglycaemic agents or insulin therapy should be used to achieve blood glucose levels as close to normal as possible.

The Diabetes Control and Complications Trial has demonstrated conclusively that improved glycaemia in patients with insulin dependent diabetes (IDDM) is associated with a marked reduction in the development and progression of retinopathy, nephropathy and neuropathy as well as improved lipid profiles. It is logical to assume that these beneficial effects of improved glycaemic control will also apply to patients with NIDDM. Since many patients with NIDDM are not diagnosed, it is important to increase awareness of this disease, identify high risk populations and previously undiagnosed cases and implement life style changes in diet and physical exercise that will reduce the risk of developing NIDDM or provide effective treatment.

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## The epidemiology of diabetes mellitus

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Diabetes Mellitus is associated with external and internal factors. External factors include diet, nutrition, virus infection, urbanisation, immigration from industrial countries, intellectual profession and chemical agents. Internal factors are inheritance, race, obesity, ageing, and immune and neuro-endocrine status. About 10% (12 million) of the world's 120 million diabetics live in China and more than 90% of Chinese diabetics have Type II (NIDDM) diabetes. China's diabetic population is the second largest in the world (after the US). Incidence in China is climbing rapidly; onset increases after age 40 and peaks in the seventh decade. There is no gender difference; males and females are affected equally. The incidence of diabetes is 3-40 times greater in persons with a diabetes-positive family history. Even though the prevalence rate in China is low, a large reservoir of known and unknown diabetics exists. About a three quarters of China's diabetic population remain undiagnosed because many (around 50%) remain asymptomatic. Treatment of diabetes is improving but complications occur and many patients die from complications rather than the disease. Complications increase with age and they include microvascular disease, ketoacidosis, and neuropathy.

Glucose provides the body with energy. Glucose in the blood binds to a carrier protein which facilitates transportation and passage across cell membranes. It moves from areas of higher (extracellular) to lower concentrations (intracellular). Insulin controls glucose passage into the cell. When extra- and intracellular concentrations are equal, passage

does not occur. Glucose in the cell is phosphorylated by hexokinase to glucose-6-phosphate (G-6-P) and little intracellular glucose remains free. G-6-P cannot exit the cell; it remains until metabolised to pyruvate or lactate (depending on oxygen levels). The final metabolic step is conversion via the tricarboxycyclic acid cycle to carbon dioxide and water. If G-6-P in the cell increases, glucose phosphorylation slows, and free glucose builds up in and outside the cell. Normally, unused glucose is stored as glycogen, mainly in liver and muscle. When glycogen capacity is exceeded, glucose is converted to triglycerides and stored in adipose tissue.

Aspartame, a sweetener 200 times sweeter than sugar, does not affect blood glucose homeostasis. It is safe for persons with chronic renal failure and diabetes. It has been approved for use in the general population, including pregnant women and children. It has no effect on plasma concentrations of insulin, cortisol, growth hormone and prolactin. The FDA and regulatory agencies of over 100 countries have approved its use.

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## Weight loss in severely obese subjects prevents type II diabetes and reverses insulin resistance and early type II diabetes

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Obesity is associated with several disease states: diabetes, hypertension, abnormal cholesterol levels, and insulin resistance. Insulin resistance occurs when normal amounts of body insulin produce inadequate physiologic responses. Insulin resistance is common in type II (adult-onset) diabetes where it is associated with Syndrome X (hyperinsulinemia, hypertension, hypertriglyceridaemia, and atherosclerosis), possibly due to under compensation. Higher insulin concentrations for given glucose levels suggest the presence of insulin resistance and a glucose (mg/dl)/ insulin (p/ml) ratio lower than 6 (the SIMPDEX) is diagnostic. SIMPDEX investigations may be of value in evaluating insulin resistance in both non-obese and obese individuals. Since insulin resistance induces many metabolic derangements, special diets, exercise and weight loss need to be initiated in its management.

Impaired glucose tolerance (IGT), which affects 11-22% of the adult US population is also associated with obesity. Restricting caloric intake reduces IGT and lowers plasma glucose concentrations in the short-term. Dieting and weight loss may prevent or delay the onset of type II diabetes. One of our studies indicates that type II diabetes, a genetic condition of unknown genotype, can be reversed or improved by weight loss. At present there is no effective drug for the treatment of insulin resistance, so weight loss and improved fitness remain the cornerstones of treatment.

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## HLA gene and clinical study of insulin dependent diabetes mellitus (IDDM) in Chinese individuals

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## Dietary intervention to reduce body weight in obese individuals: the usefulness of aspartame

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As China becomes more westernized, the incidence of obesity and diet related disease will increase. One strategy frequently used in treating obesity is to consume nutrient-modified foods. This study investigated the effect of using nutrient-modified foods containing the high-intensity sweetener aspartame on long-term control of body weight. Specifically, we evaluated whether the addition of foods and beverages containing aspartame to a multidisciplinary weight control program would improve weight loss and long-term control of body weight. One hundred sixty three obese women aged 20 to 60 years were placed on a 19-week balanced deficit diet (1000 + 200 kcal/d) and randomly assigned to either consume or abstain from aspartame-sweetened foods and beverages during the active weight loss (AWL) phase. Participants were encouraged to continue to consume or abstain from aspartame during the 2.6 year maintenance phase. Data were collected at 19, 71, and 156 weeks from baseline.

Women in both treatment groups lost a mean of 10% of body weight (10 kg) during the 19 weeks of AWL. Among participants in the aspartame group, aspartame consumption was positively associated with weight loss ( $p=0.05$ ). During maintenance (week 71), participants in the aspartame group had a 3.1% weight regain, while those in the non-

aspartame group regained an average of 4.9%. By week 156, participants in the aspartame group had regained an additional 2.4% (net weight loss from baseline of 5.1%) compared with a gain of 5.4% (net weight loss from baseline of 0.3%) in the non-aspartame group. Using multivariate analysis, the aspartame group retained significantly less weight during maintenance week 71 ( $p=0.05$ ) and week 156 ( $p=0.01$ ) than the non-aspartame group.

Among individuals consuming aspartame during a 19-week weight loss program, consuming more aspartame was associated with a greater weight loss. At weeks 71 and 156 of maintenance, participation in a multidisciplinary maintenance program that incorporated aspartame-sweetened products was associated with better long-term control of body weight. These results suggest that the high-intensity sweetener aspartame may aid in the long-term control of body weight and should be considered by the Chinese as a strategy for the treatment and prevention of obesity.

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## NutraSweet: an overview of metabolism, safety, and usefulness

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NutraSweet brand sweetener (L-aspartyl-L-phenylalanine methyl ester), known generically as aspartame, provides the clean, sweet taste of sugar to products but without the calories. NutraSweet is unique among high-intensity sweeteners because it is metabolised by enzymes in the gastrointestinal tract to three naturally-occurring dietary components - aspartic acid, phenylalanine, and methanol. NutraSweet provides very small amounts of these components to the everyday diet compared with common foods.

Prior to its approval by regulatory agencies around the world, the safety of NutraSweet was demonstrated by extensive metabolism, pharmacology, and toxicology studies in animals. In addition, studies were done in healthy humans, including both adults and children, as well as in special subpopulations, including obese individuals, diabetics, lactating females, and individuals who have an impaired ability to

metabolise amino acids, such as individuals for the genetic disease, phenylketonuria, and individuals with renal and liver disease. The results of these studies demonstrated that NutraSweet is a remarkably safe sweetener.

In addition, since NutraSweet provides the sweetness of sugar without the calories, it may be a useful part of a diabetic meal plan, and it has been shown to be useful in promoting body weight control. As there are greater cross-cultural exchanges, including dietary patterns, both from East to West and West to East, this may be especially important to the Chinese people to help prevent the development of diseases associated with diet in the Western culture.

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## High-intensity sweeteners: overview of safety and toxicology

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Bulk sweeteners are generally carbohydrates, providing energy (calories) and bulk to food. On the other hand, high-intensity sweeteners possess a sweet taste, but are non-caloric and provide essentially no bulk to food. There are several different high-intensity, low-calorie sweeteners. Some of the sweeteners are naturally-occurring, while others are artificial or synthetic. The chemical formulas of the different sweeteners vary considerably, but generally they are relatively low molecular weight substances. They may range from simple dipeptides (eg, aspartame) to complex organic molecules (eg, stevioside). Most of the more commonly available high-intensity sweeteners and/ or their metabolites are rapidly absorbed in the gastrointestinal tract. For example, acesulfame-K and saccharin are not metabolised and are excreted unchanged by the kidney. Sucralose, stevioside, and cyclamate undergo degrees of metabolism, and their metabolites are readily excreted. Gastrointestinal flora may, in part, assist in the metabolic breakdown depending on the parent compound. Unlike the other high-intensity sweeteners, aspartame is not

absorbed intact but is metabolised in the gastrointestinal tract to naturally occurring dietary components.

The potential toxicity of a particular high-intensity sweetener varies. None of the more highly used high-intensity sweeteners are mutagenic, but large doses of cyclamate or saccharin in rodents have been associated with the production of bladder tumours. There is no evidence of the available high-intensity sweeteners being teratogenic or embryotoxic. High-intensity sweeteners are often non-cariogenic-- they do not support growth of oral cavity micro-organisms, and hence may be useful in preventive dentistry. Thus, the use of safe, high-intensity sweeteners in food products provides the Chinese people the opportunity to enjoy sweetness of sugar without the extra calories or cariogenic potential.

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