Nestlé
Good Food, Good Life

Food and Nutrition Communication

April 2006

The Metabolic Syndrome

The Metabolic Syndrome is a collection of health conditions, including fat around the waistline, high blood pressure, insulin resistance and low HDL cholesterol, which, taken together, significantly increase the risk of Type 2 Diabetes and heart disease.

Many people are unaware that their symptoms match the definition of Metabolic Syndrome, even though the American Heart Association estimates that 20–25% of the adult population of the U.S. suffer from this disorder – between 58 and 73 million men and women.

The Diabetes Time-Bomb

Today it is estimated that around 194 million people have diabetes, an alarming 40 percent increase over the 1995 global estimation of 135 million published in a World Health Organization study in 1998. Of these, about 85 percent have Type 2 Diabetes. The prevalence of diabetes is still increasing sharply and is expected to reach almost 333 million by the year 2025. If left unchecked, it promises to exceed the ability of public health services to manage the costs alone.

While the pathogenesis of the metabolic syndrome and each of its components is complex - and not yet fully understood, central obesity and insulin resistance are acknowledged as important causative factors.

There has been much debate as to the definition of this syndrome. Indeed the existence of multiple definitions has caused confusion and made comparisons between data from different studies more difficult. Therefore in April 2005, the International Diabetes Federation (IDF) proposed a consensus definition for use worldwide in both research and clinical practice.

The New International Diabetes Federation (IDF) Definition

For a person to be defined as having the metabolic syndrome they must have:

Central obesity (defined as waist circumference ≥ 94 cm for Europid men and 80 cm for Europid women, with ethnicity-specific values for other groups **plus any two of the following four factors:**

- **Raised TG level:** ≥150mg/dL (1.7 mmol/L) or **specific treatment of this lipid abnormality**
- **Reduced HDL cholesterol:** <40mg/dL (1.03 mmol/L) in men and <50 mg/dL (1.29 mmol/L) in women, or **specific treatment for this lipid abnormality**
- **Raised blood pressure:** systolic BP ≥130 or diastolic BP ≥85m Hg, **or treatment for previously diagnosed hypertension**
- **Raised fasting plasma glucose** (FPG) ≥100 mg/dL (5.6 mmol/L), **or previously diagnosed Type 2 diabetes**

Insulin Resistance

Insulin Resistance is an underlying cause of Metabolic Syndrome. There are many factors that contribute to its presence in the body. In essence, our environment and lifestyles have evolved too rapidly for our bodies to keep pace. We are still genetically "wired" to thrive on the habits of our ancestors, who consumed different, nutrient-rich foods and a diet low in carbohydrates. These ancestors also sustained greater levels of physical activity.

Some people may have a genetic predisposition to Insulin Resistance, while others develop the condition through high stress and unhealthy lifestyles.

Insulin Resistance affects glucose and insulin levels

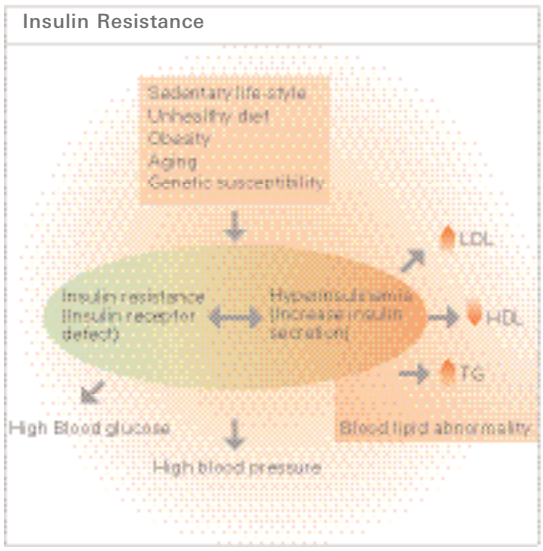
Over time, the above factors damage the complex ability of the body's cells to use insulin correctly in converting glucose into energy. Insulin action is initiated through the binding to and activation of its cell-surface receptor. The receptor then undergoes a series of intra-molecular reactions allowing glucose to enter the cells. Insulin resistance, or reduced insulin sensitivity, involves the disruption of these signalling events downstream of the receptor. With the cell 'door' almost closed to it, glucose remains in the blood stream, causing elevated levels of blood sugar. The body attempts to overcome this defect/resistance by secreting more insulin from the pancreas. The high insulin levels resulting from insulin resistance contribute to abnormalities in blood lipids (cholesterol and triglycerides).

Lipotoxicity

A major contributor to the development of insulin resistance is an overabundance of free fatty acids circulating in the bloodstream. Various complex biochemical reactions during metabolism are responsible for this overabundance.

Low-grade chronic inflammation

Insulin resistance in the liver, muscle and adipose tissue is associated with the abundance of pro-inflammatory cytokines and the relative lack of anti-inflammatory cytokines such as adiponectin. Both adiponectin, the protective cytokine, and the inflammatory types, including interleukin 6, and tumour necrosis factor alpha (TNF-α), are produced in the fat tissue.

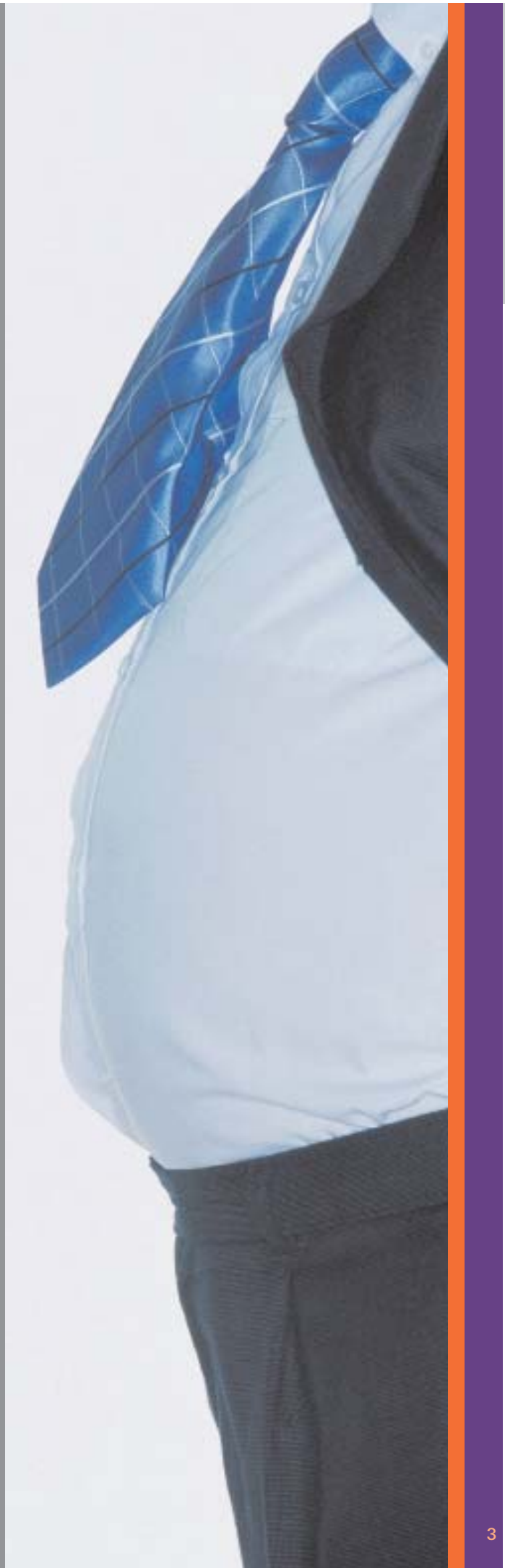


When the amount of body fat is excessive, an added burden is put upon metabolism, upsetting the delicate balance required for insulin to act correctly.

Many factors are involved in the development of insulin resistance and the metabolic syndrome as a whole; insulin and glucose, lipids and lipoproteins, blood pressure, expanded fatty tissue and triglyceride stores, the action of enzymes, and hormones such as leptin.

Much still remains to be elucidated in all of these areas.

The American Heart Association states that the underlying causes of Metabolic Syndrome are overweight, physical inactivity and genetic factors. Studies have shown, for example, an increased link between Metabolic Syndrome and atherosclerosis, which occurs when fatty deposits cling to the interior walls of the arteries, leading to blockages that can cause heart attacks or stroke. People with Metabolic Syndrome are also more prone to developing Type 2 Diabetes, as well as PCOS (Polycystic Ovarian Syndrome) in women and prostate cancer in men.



All these findings substantially show just how serious this syndrome can be, making it even more important that medical practitioners correctly diagnose the condition and inform patients about one of its underlying causes – Insulin Resistance.

Prevalence of Metabolic Syndrome

The International Diabetes Federation (IDF) believes that metabolic syndrome is driving the twin global epidemics of Type 2 Diabetes and cardiovascular disease. The prevalence of metabolic syndrome is estimated to be around 20–25% of the world population *[1]*.

People with metabolic syndrome are three times as likely to have a heart attack or stroke compared to people without the syndrome, and twice as likely to die from either condition *[2]*.

To obtain better epidemiological data, ethnic and gender differences are nowadays measured according to characteristic racial type to see which populations are most affected.

An estimated 15% of the European adult population already have the following combination of obesity-related conditions:

- Impaired glucose regulation or diabetes
- Insulin resistance
- Raised arterial blood pressure: ≥140/90 mm Hg
- Raised plasma triglycerides: ≥1.7mmol/L; 150mg/dL and/or low HDL cholesterol: under 0.9 mmol/L, 35 mg/dL men; <1.0mmol/L, 39 mg/dL women
- Abdominal obesity: men, waist/hip ratio >0.90; women, >0.85 and/or BMI >30

Criteria: World Health Organisation

What is Diabetes?

Diabetes mellitus is a metabolic condition characterized primarily by high blood sugar levels that result from the body's inability to make or use insulin, a hormone produced by the pancreas that plays a vital role in metabolism. Symptoms include increased thirst and urination, hunger, weight loss, fatigue, and blurred vision. Diabetes can lead to debilitating and life-threatening complications including blindness, memory problems, kidney disease, heart disease, nerve damage, and amputations.

Diabetes literally means "the passage of large volumes of urine". Some diabetics pass up to 10 litres of urine per day. This occurs because high sugar in the blood leaches out into the urine, attracting with it water and salt from the blood and tissues through the process of osmosis.

The Different Types of Diabetes

Type 1 Diabetes, formerly called juvenile diabetes, usually develops in childhood. It is caused by the radical inability of the pancreas to produce insulin. Genetic predisposition combined with exposure to viruses are the main risk factors. Treatment includes carefully monitored insulin replacement, typically via needles or a special pump. In Type 1 Diabetes, the immune system destroys the islets of Langerhans in the pancreas. Total insulin deficiency results. The body cells fail to take up glucose. Plasma glucose rises, overflows into the urine taking with it water, and increasing the urine volume. The liver then produces ketones, which eventually acidify the blood. The brain cannot function in an acid medium.

Type 2 Diabetes, previously called adult onset diabetes, is the most common type. It usually develops because the body fails to use insulin properly or resists its action. It occurs in people (including children) who are overweight. Other risk factors include high cholesterol, high blood pressure, ethnicity, and a family history of diabetes. Many patients require daily insulin injections.

In Type 2 diabetes there is resistance to the action of insulin, producing a secondary rise in glucose. The pancreas increases its production of insulin in an attempt to compensate, but over time the pancreas suffers strain and becomes unable to produce enough insulin.

Type 3 Diabetes A small percentage of pregnant women (around 2%) develop gestational diabetes, sometimes labelled Type 3 Diabetes, as a result of changing hormonal levels. Blood sugars often return to normal after the birth, but almost half of the women who experience gestational diabetes develop Type 2 Diabetes later in life.

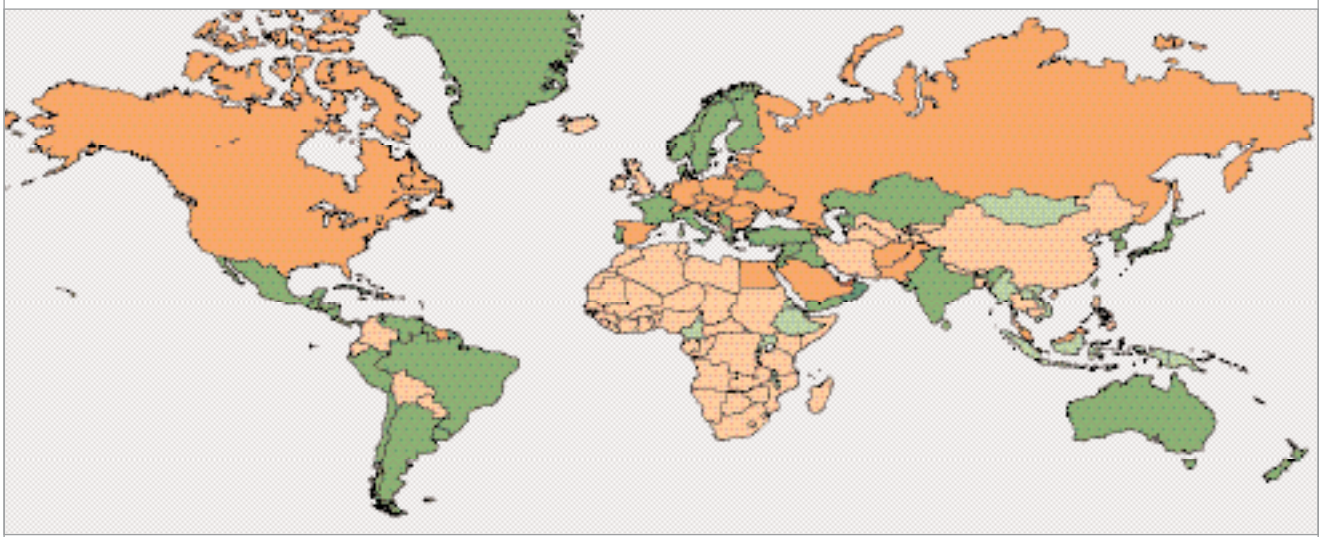
Complications of Diabetes

One of the potential consequences of inappropriate glycaemic control in diabetics is the development of micro- and macro- lesions of blood vessels and nerves. In tandem these degenerative changes can have very serious consequences on an individual's health. They can ultimately lead to the amputation of a foot or limb, reduced vision or blindness.

The real world – Diabetes in New York City

As always, the beds at Montefiore Medical Center in the Bronx are filled with people suffering from a host of afflictions related to one single illness: diabetes. Room after room, floor after floor: diabetes. On any given day, hospital officials say, nearly half the patients are there for some trouble precipitated by the disease. An estimated 800,000 adult New Yorkers - more than one in every eight - now have diabetes, and city health officials describe the problem as a true epidemic. Diabetes is the only major disease in the city that is growing; both in the number of new cases and the number of people it kills. And it is growing quickly: faster than heart disease.

Prevalence estimates of diabetes, 2003



Source: Diabetes Atlas, International Diabetes Federation

Why and How Diabetes Affects the Feet

Poor glycaemic control and chronic hyperglycaemia provide conditions where glucose, and other reducing sugars, spontaneously attach to proteins in a process called "nonenzymatic glycosylation", which alters the structure and function of tissue proteins and the tissues themselves. When this occurs in nervous tissue, it is referred to as *neuropathy*. Several types of neuropathy can occur in diabetes: *sensory, motor* and *autonomic*, and all may play a role in the development and severity of foot lesions experienced by diabetics. Of the three neuropathies *sensory neuropathy* predominates, and results in the loss of "the gift of pain" in the extremities. With the inability to feel pain, temperature or touch, the foot is particularly vulnerable to many accidental lesions caused by stones, nails, burns or wrong shoe size, which will go unnoticed. Untreated lesions rapidly develop into ulcers, which heal slowly or not at all, due to an altered blood supply. Tissue death (gangrene) may follow.

Leg and foot ulcers develop when several risk factors occur together:

- Poor diabetes management
- Nerve damage
- Impaired blood supply
- Inadequate footwear
- Foot injury
- Lack of or low quality foot care

Prevention:

- Follow a healthy eating plan *(see guidelines page 11)*
- Be active – at least 30 minutes a day
- Take diabetic medicines at the same times each day
- Check and record blood glucose every day
- Check feet every day for cuts, blisters, sores, swelling, redness or sore toenails
- When choosing shoes, feet should be measured. Do not rely on touch and pressure sensations to obtain a "good fit".
- Do not smoke

Motor neuropathy causes wasting or loss of muscle tissue and deformities in the feet such as "claw toes" or "hammer toes", which results in a redistribution of the areas of the foot that take the most pressure when standing or walking. The autonomic nervous system supplies nerves to all organs of the body including the skin and sweat glands. In *autonomic neuropathy* sweat gland secretion is reduced or nonexistent, the skin becomes dry and prone to cracks and fissures, which in turn present sites for infection. Additionally *autonomic neuropathy* influences blood flow to the limbs and skin by dilating arteries and arterioles. Although this increases blood flow, the condition is associated with arteriovenous shunting, which means that blood passes from the arteries to the veins without passing through the capillary circulation that provides nutrients and oxygen to the tissues. Neuropathy on its own does not cause ulceration but allows injuries to go unnoticed.

Diabetic patients are also more susceptible to *peripheral vascular disease* than non-diabetics, due to a build-up of atherosclerotic plaque in the blood vessels supplying the feet and legs. This commonly involves the tibial and peroneal arteries but not those in the foot. Atherosclerotic narrowing of the arteries reduces blood supply to the tissues and in consequence nutrients, oxygen and protective immune cells. Reduction of both arterial and capillary blood flow increases tissue susceptibility to injury, reduces resistance to infection and delays or prevents tissue healing during treatment *[3]*.

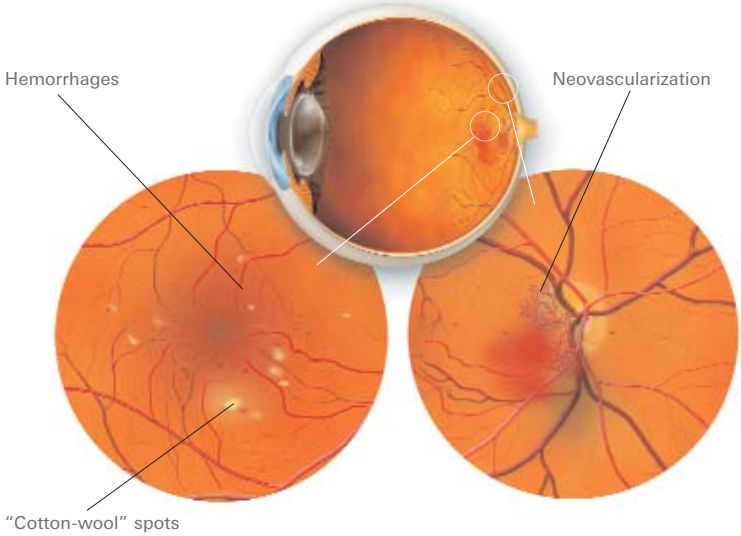
Why and How Diabetes Affects the Eyes

Glycosylation of proteins, due to chronic hyperglycaemia, can damage the blood vessels of the eyes and lead to the development of *diabetic retinopathy*. Everyone who has diabetes, particularly those who have had diabetes longer, may be at risk of developing diabetic retinopathy, but not all diabetics do. Thickening of the capillary basement membrane may cause transcapillary leakage of large protein molecules and fluid, or even bleeding. In early-stage diabetic retinopathy, called non-proliferative or background retinopathy, the retina swells and small dot-like haemorrhages form, accompanied by decreased vision.

With time, areas of the retina become ischemic or deprived of oxygen and new vessels develop in an attempt to supply the retina with oxygen. These fragile vessels haemorrhage easily and blood may leak into the retina and vitreous humor - the clear gel that occupies the posterior chamber of the eye between the crystalline lens and the retina - causing spots or floaters that accompany the diminished vision. As the disease progresses abnormal vessel growth and scar tissue may cause retinal detachment and glaucoma.

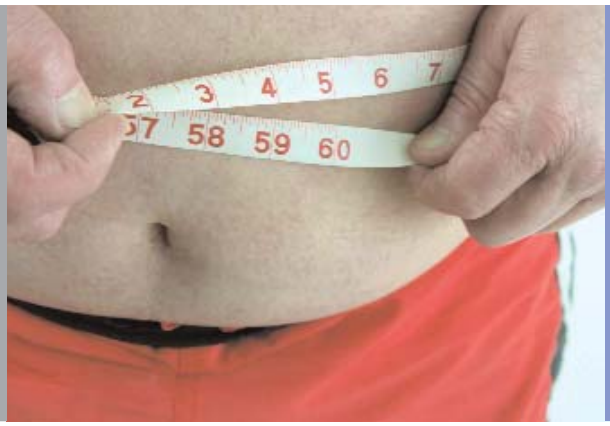
Other eye problems

Cataracts and glaucoma also develop in non-diabetics with age; however, diabetics develop them more often and at a younger age.
With age structural changes in the lens cause it to become opaque (cataract) and vision becomes "cloudy". In this condition the lens is removed and replaced by an artificial plastic lens.
Glaucoma is the result of increased pressure within the eye, which over time can damage the optic nerve and initially cause loss of peripheral vision. It can usually be treated with eye drops that lower the pressure in the eye.



Background Diabetic Retinopathy **Proliferatve Diabetic Retinopathy**

Photo source: www.theretinasource.com/conditions/diabetic_retinopathy.htm



Obesity

Currently, at least 300 million of the world's one billion overweight adults are clinically obese and obesity rates have risen three-fold or more since 1980 in many areas of the globe. Humans vary in their genetic predisposition to become overweight in response to particular environmental surroundings in the same way as the tendency to become diabetic. Hence, each individual requires a specific dietary strategy tailored to his or her metabolism to prevent and reduce the impact of obesity and diabetes.

The obesity epidemic has been described as a chronic, relapsing, neurochemical disease produced by the interaction of environment and host *[4]*. However it can also be argued more simply that most modern obesity is a highly predictable biological response to our new environmental conditions and is not an abnormal pathology.

Direct Metabolic Regulation in Skeletal Muscle and Fat Tissue by Leptin

In recent years, adipose tissue has emerged as an important endocrine organ. It is now recognized that besides storing energy, the adipocytes (fat cells) also secrete several bioactive peptides, collectively called adipocytokines. Among these, leptin, the product of the *ob* gene, has been extensively investigated over the last decade. Skeletal muscle and adipose tissue, two major tissues involved in the regulation of glucose and fatty acid metabolism, are directly affected by leptin. By binding to its receptors located in skeletal muscle and fat cells, leptin promotes energy dissipation and prevents fatty acid accumulation and 'lipotoxicity' in these tissues. On the other hand under conditions of peripheral leptin resistance such as observed in obese humans, the activation of pathways involved in fatty acid oxidation may be impaired. This leads to intracellular accumulation of lipid intermediates and causes insulin resistance *[5]*.

Energy Expenditure

The average yearly weight gain of adults in the US is equivalent to an excess energy storage of 3,400–7,400 kcal or only around 15 kcal every day. This is a very small amount of energy, equivalent to eating two bites of food too much or walking 0.5 km too little per day! In order to recommend a public health goal to all those gaining weight and make some allowance for the efficiency with which energy is being stored as adipose tissue, a more prudent proposal estimates that a negative energy balance of 100 kcal per day could prevent weight gain in most of the US population. This could be achieved by a combination of reductions in energy intake (a few fewer bites at each meal) and increases in physical activity (15 minutes more walking per day) *[6]*).

Traditionally, most of the energy expended by man was used in an effort to provide food, survive and reproduce, and there was a direct relationship between the amount of food consumed and the amount of work needed to obtain that food. In the days of the hunter-gatherer, the relationship between energy in and energy out concerned a relatively short interval of days or weeks, since little food could be stored, whereas in pre-industrial society, the in-out relationship extended over entire agricultural cycles. As described by Prentice and Jebb *[7]* in these situations adipose tissue is periodically utilized and redeposited, as nature intended, as a buffer to allow for temporary imbalances between energy needs and energy intake. On average, appetite control mechanisms could detect errors in balance with precision. Today, energy turnover has decreased below a sensitivity threshold where homeostasis can no longer operate properly. Food shortage is an exception in many countries and food can be 'harvested' with as little effort as is required to drive to the supermarket or to open the fridge door. Even the work of chewing is reduced to a minimum.

How can we increase energy expenditure and restore the control of energy balance?

Stimulating thermogenesis is an avenue currently investigated in the food industry. Caffeine, alone or in combination with other food grade herb extracts has been found to increase energy expenditure by up to 100 kcal per day *[8]*. However these

components can only be present in a limited number of foods which themselves contribute calories. They are not without possible side effects and the regular consumption of large amounts of them can hardly be justified merely for the sake of body weight maintenance. Once again voluntary physical activity is the only component of energy expenditure over which we have some direct command, and is the most promising way to regain control of weight and prevent the development of obesity. This might take only 15–30 minutes of moderate-intensity physical activity per day for many individuals. Most data suggest that there would not be any significant increase in energy intake to compensate for this amount of physical activity.

There are clear health advantages of including regular exercise in the daily routine:

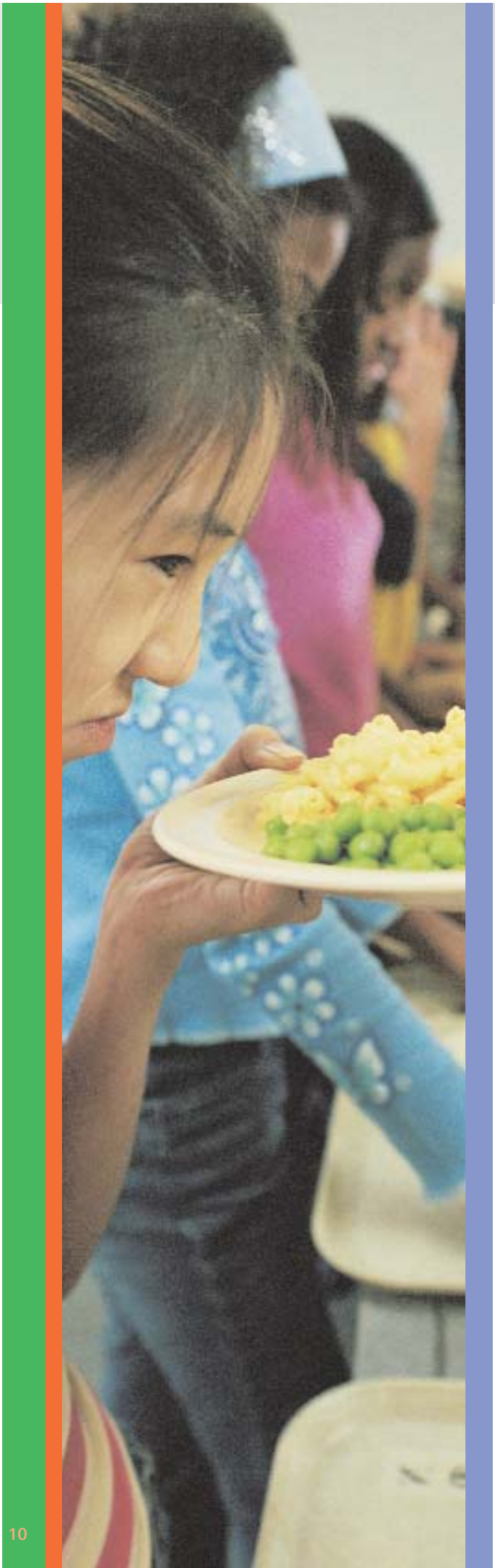
1 Exercise will improve cardio-respiratory fitness;

2 Well-designed exercises, including strength components increase muscle mass. Even though weight loss may not be greater than with dietary restriction alone, energy balance is improved because some of the fat is replaced by lean tissue;

3 The increase in lean body mass and periodic stimulation of the sympathetic nervous system favour an elevation of the basal metabolic rate;

4 Brisk exercise curbs appetite in the short term and is not necessarily accompanied by compensatory increases in energy intake;

5 The resulting enhanced energy turnover through regular exercise will restore the metabolic sensitivity necessary to enable energy homeostasis.



Appetite and Satiety

Appetite and satiety are not isolated processes within the body. These sensations result from the complex interactions of signals, including sensory perceptions, stomach distension, hormonal and neural messages sent from the gastro-intestinal tract to the brain, and messages sent from the brain to the rest of the body. This complex network of signals is responsible for the regulation of food intake. Learned behaviours, eating patterns and external signals, namely the cues to which people are exposed, (sometimes unknowingly), such as the sight of food, work or home environment and personal relationships, are also very significant.

The interplay of neuronal and hormonal signals may translate into feeling full, deprived, pleased or rewarded when eating certain foods and this is what tunes appetite control.

If we focus on the sensorial properties of foods, those that smell and taste delicious are powerful enough to override our innate satiety signals *[9]*. As anyone who has eaten a whole bar of chocolate will confirm, these signals seem to disrupt appetite regulation.

Recent research suggests that fat and sugar-rich foods enhance the expression of hunger signals, blunt the response to satiety signals and activate the reward system (one of the factors that leads to the pleasure of eating). Thus the powerful palatability of high fat and high sugar foods could lead to "passive over-consumption" i.e. unrelated to hunger.

Returning to intuitive eating habits, that is to say: *listening to body signals for hunger and satiety*, is being proposed as one possible therapy for obesity to avoid the detrimental side effects of diet cycling.

Inflammation

It is now clear that obesity is not just a matter of excess weight, because fat cells do not merely store fat. They send out bioactive molecules with powerful effects throughout the body. Some of these are low-molecular-weight proteins that induce inflammation, now considered a major cause of cardiovascular disease.

For example, tumour necrosis factor-α (TNF-α) activates inflammatory changes in vascular tissue that promote the adhesion of monocytes, which are a type of white blood cell, to the thin lining of the blood vessels. When a monocyte stuck to the blood vessel penetrates the lining, it becomes a macrophage that feeds on low-density lipoproteins in the plasma. The accumulation of macrophages begins an atherosclerotic plaque. TNF-α also interferes with insulin signalling and causes insulin resistance.

Research

A current focus of Nestlé research is on finding ways of increasing satiety while reducing energy consumption. A recent study comparing the relative effects of meals high in protein, fat or carbohydrate found that these diets influenced the rate at which calories were burned, but they had no direct impact on how much was eaten or how satiated the person felt. On the other hand, added fibre and the amount of water in food seem to play more decisive roles.

The energy-density approach to weight control is one of the approaches to weight loss with the most scientific support. It aims at increasing short-term fullness (satiation) and between meal fullness (satiety) by increasing the proportion of water- and fibre-rich foods in the diet, i.e. reducing the energy density of the diet. When applied under dietetic supervision, this approach is successful. The only problem with this type of diet is ...commitment! People used to highly palatable foods may not stick to the vegetable soup, water and low-fat dairy approach with sufficient regularity, or they may reward themselves too often for good nutritional behaviour with high-fat high-sugar items from their past eating habits.

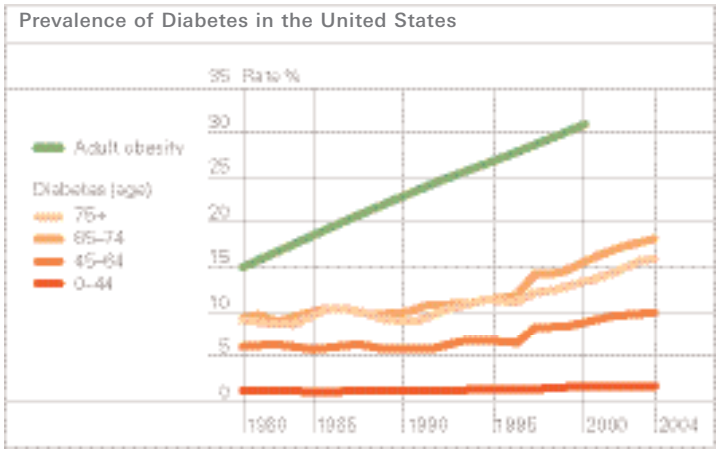
Dietary Guidelines

In general terms, dieticians recommend that food choices should centre on complex carbohydrates, increasing consumption of fibre from pulses, whole grains and plenty of fruit and vegetables. Five portions of fruit and vegetables per day is a good rule. Low fat does not mean no fat at all. Fats from sources of polyunsaturated and monounsaturated fatty acids, such as fish, nuts, and vegetable oils should be present in the diet. Regular protein intake should be neither excessive nor insufficient. (As a rough visual guide, an adult portion of meat or fish should not be larger than a pack of playing cards) Intake of trans-fatty acids, dietary cholesterol, added refined sugars, salt and alcohol should be kept as low as possible without depriving the individual of a little pleasure from time to time. In this respect the recommended daily upper limit on alcohol is at present a moderate 2dl wine per day for women and 3dl for men (or equivalent in other alcoholic drinks).

A Nestlé Branded Active Benefits BG-3 can help people feel satisfied longer. Added to products like cereal bars, dietary fibres such as those used to develop BG-3 bring the benefit of slow intestinal absorption, especially of glucose. This is very useful for diabetics and those interested in reducing the glycaemic index of the foods they eat.

Effect of Protein on Satiety

Food science research also concentrates on finding solutions in which palatability is preserved while satiation and satiety are still enhanced. Increasing the amount of protein in the diet without eliminating carbohydrates, has been shown to be effective for weight loss when carried out under medical supervision. Surprisingly, the effect of protein on satiety seems independent of the hunger hormone, ghrelin, and the satiety hormone, leptin. However, many other satiety hormones and gut peptides, such as cholecystokinin (CKK) and the glucagon-like peptide 1 (GLP-1) are



This graph shows the comparative evolution of diabetes (orange lines) and adult obesity (green line) in the USA suggesting that obesity has about a 10-15 year time lead, with diabetes now on a parallel upsurge.

also secreted in response to nutrients present in the intestinal tract. It will be extremely interesting to discover how these signals are regulated and how they potentiate each other's effects under a high protein diet.

In order to lose weight, a reduction in daily intake of approximately 500 Kcal is required over an extended period. To keep the weight from returning, an increase in daily physical exercise is also required. This dual approach is essential.

Whatever dietary strategy is adopted to avoid weight gain, it should always be in line with current dietary recommendations and contain reasonable amounts of all nutrients, i.e. carbohydrates, fats, and proteins. Weight gain is not inevitable. It depends largely on lifestyle and moderation.

Recommendations for Treatment of the Metabolic Syndrome

Once diagnosed with metabolic syndrome, the patient must realize that uncompromising efforts have to be made to reduce the risk of cardiovascular diseases and Type 2 Diabetes. Patients should have a complete cardiovascular risk assessment (including smoking status), try to avoid stress, and consider the following course of action:

Healthy Lifestyle

- Moderate calorie restriction (to achieve a 5–10% reduction in body weight in the first year)
- Moderate increase in physical activity
- Change in composition of regular diet

For people at high risk who need more than the lifestyle changes above, drug therapy may be required. There is no pharmaceutical magic bullet to treat the whole syndrome, but individual components of it can be treated with a view to lowering non-HDL cholesterol, raising HDL-c , and reducing LDL-c. Options include the use of *Statins* and *Fibrates*.

Lowering cholesterol levels

Various medications can lower blood cholesterol levels. These are prescribed only when dietary intervention fails or other health factors coexist alongside high cholesterol. ***Statins***, which block cholesterol synthesis by the liver, are the most potent cholesterol lowering drugs. They can lower the "bad" (LDL) cholesterol by 30–50%. Although less effective in lowering LDL, ***fibrates*** improve HDL and triglyceride levels, and seem to improve insulin resistance when the dyslipedemia is associated with other features of the metabolic syndrome (hypertension and Type 2 Diabetes). ***Phytosterols***, also known as plant sterols, are natural, and essential components of plant cell membranes. They are found in in vegetable material, but are relatively higher in the oils especially corn, sunflower, safflower, soybean and olive oils.

Plant sterols help to protect against coronary heart disease by lowering serum low-density lipoprotein cholesterol (LDL cholesterol), but they have no effect either on high density lipoprotein cholesterol (HDL cholesterol) or triglyceride levels.

The mechanism by which plant sterols lower LDL-cholesterol is through inhibiting the absorption of cholesterol from the gastro-intestinal tract.

The reduction in LDL cholesterol is dose-dependent, with a dose of 2g/day being effective in most people.

Nestlé's Branded Active Benefit ActiCol now enhances products such as soya milk with the effects of plant sterols.

Lowering blood pressure

Losing weight and increasing physical activity can lower blood pressure. When more intervention is needed, anti-hypertensive drugs are prescribed. There are many classes of anti-hypertensives, which lower blood pressure in a variety of ways. A major class of these drugs are the inhibitors of the ACE (angiotension-I-converting enzyme) enzyme in blood vessels. Interestingly natural inhibitors of ACE have been identified in a variety of food proteins. In particular, milk proteins contain ACE inhibitory peptides that can be released by enzymatic hydrolysis either during digestion within the gastrointestinal tract, or during food processing. Nevertheless futher research is needed to demonstrate the hypotensive effects of consuming specific milk protein based ingredients and products.

Omega 3

Omega-3 fatty acids are essential fatty acids, which means that they must come from the diet because the body cannot manufacture them. Although some vegetable oils provide omega-3 fatty acids, the best dietary source is from fish and fish oils.

The precise mechanisms of action by which omega-3 fatty acids can help to protect against coronary heart disease is not clear. However, scientific evidence points to a number of different cardioprotective effects, namely antiarrhythmic, antithrombotic, antiatherosclerotic, anti-inflammatory action, improvement in endothelial function, reduction in blood pressure and reduction in triglycerides.

Nestlé 's Branded Active Benefit Omega 3:6, available in certain milk products provides a balanced ratio of omega-6 to omega-3 fatty acids, combining enhanced nutritional value with excellent organoleptic properties.

Insulin Resistance and Hyperglycaemia

People with Type 2 diabetes often have lifestyles that contribute to their problem. The modification of nutritional and physical habits has been shown to be an effective way of controlling glycaemia in patients with diabetes. Indeed, several trials have shown that exercise or low calorie diets can improve glycaemic levels in diabetic patients and can also reduce the incidence of diabetes in overweight subjects with impaired glucose tolerance *[10]*. Increasing protein consumption while decreasing carbohydrate intake can also reduce hyperglycaemia in diabetic patients by increasing insulin sensitivity *[11]*. Physical activity plus lower calorie intake can bring about the beneficial effects both of lower body weight and greater insulin sensitivity. Interestingly, these straightforward lifestyle modifications have in some cases proved more effective for preventing Type 2 diabetes than treatments with a glucose-lowering drug such as Metformin.

Chromium

Earlier in vitro studies have shown that chromium picolinate supplements could enhance insulin sensitivity by improving receptor signalling. A new study *[12]* is the first to use in vivo animal models to demonstrate the mechanism. This animal study is significant because it suggests a more detailed mechanism of action for chromium in improving insulin sensitivity in muscle, a major insulin-sensitive tissue, according to its author Dr Willian Cefalu from the Pennington Biomedical Research Center, Louisiana.

Medications

Although lifestyle change is very effective for preventing diabetes in population at risk, it demands a high level of discipline for the patients. Once a patient has developed diabetes, lifestyle modifications alone can only control blood glucose in a minority of cases. At this stage, supplementary pharmaceutical measures are generally needed. Suitable medications can be proposed according to the degree of the disease:

- In "pre-diabetic" subjects, who are insulin resistant but have normal glycaemia, drugs recently developed for reducing body weight can prevent Type 2 diabetes. Orlistat and Rimonabant *[13 and 14]*, two anti-obesity agents mentioned in our previous edition, were demonstrated to reduce the incidence of Type 2 diabetes in obese subjects. Thiazolidinediones, which improve insulin sensitivity, could also reduce diabetes development in population at risk.

- At the early stage of diabetes development agents reducing liver glucose production or glucose absorption such as Metformin or Arcabose, respectively, are usually used for controlling glycaemia. The sulfonylurea class of drugs, which increase pancreatic insulin secretion could be associated to the previous medications to enhance insulin effectiveness. Thiazolidinediones could be also added to this treatment to improve glucose utilization by tissues. A new class of drugs stimulating insulin secretion through a process used by the gut peptide GLP-1 is currently being developed and appears very promising.

- In diabetic subjects with severe impairment of insulin secretion, insulin injections represent the only way to control glycaemia. New, patient-friendly ways of administering insulin, notably through nasal sprays, are being developed.

Bariatric surgeries, which reduce the absorption capacity of the stomach and intestines, are usually performed in severely obese patients for reducing body weight. This radical surgery can be a rapid and durable treatment for Type 2 diabetes in seriously overweight patients.

Nestlé Nutrition has developed several nutritional healthcare products for diabetes patients. Among these are Nutren Diabetes: a powdered product, suitable for sip feeding and tube-feeding, for Asian and Latin American countries.

Clinutren G: Sip feed developed for Europe. Sondalis Diabetes: Tube-feeding also for Europe, and Glytrol: a ready-to-feed product for sip feeding and tube-feeding, available in the United States and Canada.

In Conclusion

In the January 2006 edition of Food and Nutrition Communication we looked into the challenge of treating and limiting the obesity pandemic. Obesity can and does bring with it morbidity and mortality from diabetes. Existing diabetes drugs are only partially effective and some cause weight gain. Patients' expectations of novel drugs are very high, but regulatory hurdles are challenging. The market opportunities for truly ground breaking new products in this therapeutic area are exceptionally good.

Prevention of the Metabolic Syndrome and its development into diagnosed Type 2 Diabetes and/or heart disease depends to a large extent on the adoption of a healthy lifestyle. The dietary advice is relatively simple in theory, but it needs a lot of willpower to put it into practice. For contemporary society, the great challenge is to re-introduce physical activity simply and effectively into the daily life of the population. While waiting for a panacea to appear on the pharmaceutical horizon to deal with all the components of the Metabolic Syndrome, the healthy diet and lifestyle approach is the best option we have. Nestlé research and development will be at the forefront of the challenge, putting nutrition, health and wellness into action.

References

1 Dunstan, D.W,, Zimmet, P.Z., Welborn, T.A., de Courten, M.P., Cameron, A.J., Sicree, R.A., Dwyer, T., Colagiuri, S., Jolley, D., Knuiman, M., Atkins, R., Shaw, J.E. *The rising prevalence of diabetes and impaired glucose tolerance. The Australian Diabetes, Obesity and Lifestyle Study.* Diabetes Care, **25**, 829–834 (2002)

2 Isomaa, B., Almgren, P., Tuomi T., Forsén, B., Lahti, K., Nissén, M., Taskinen, M-R., Groop, L. *Cardiovascular morbidity and mortality associated with the metabolic syndrome*. Diabetes Care, **24**, 683–689 (2001)

3 Boulton, A.J.M., Diabetic Neuropathy. In "The high-risk foot in diabet es mellitus", (ed) Frykberg, R,D., Churchill Livingstone, New York, 49–59 (1991)

4 Bray, G.A., Champagne, C.M., *Beyond Energy Balance: There Is More to Obesity than Kilocalories*, J. Amer. Diet Assoc. **105**, S17-S23 (2002)

5 Ceddia, R.B., *Direct metabolic regulation in skeletal muscle and fat tissue by leptin: implications for glucose and fatty acids homeostasis*, Int. J. Obesity, **29**, 1175–1183 (2005)

6 Hill, J.O., Wyatt, H.R., Reed, G.W., Peters, J.C., *Obesity and the Environment: Where Do We Go from Here?* Science, **299**, 853–855 (2003)

7 Prentice A & Jebb S., *Energy Intake/Physical Activity Interactions in the Homeostasis of Body Weight Regulation*, Nutr. Rev. **62**, S98-S104 (2004)

8 Acheson, K.J., Campbell, I.T., Edholm, O.G., Miller, D.S., Stock, M.J., *A longitudinal study of body weight and body fat changes in Antarctica*, Am. J. Clin. Nutr. **33**, 972–977 (1980)

9 Blundell, J.E., Macdiarmid, J.I., Fat as a risk factor for overconsumption, :satiation, satiety and patterns of eating. J. Am. Diet .Assoc. **97**, S63–S69 (1997)

10 Goldhaber-Fiebert ,J.D., Goldhaber-Fiebert, S.N., Tristan, M.L., Nathan, D.M., *Randomised controlled community-based nutrition and exercise intervention improves glycemia and cardiovascular risk factors in type 2 diabetic patients in rural Costa Rica*. Diabetes Care, **26**, 24–29 (2003)

11 Knowler, W.C., Barrett-Connor, E., Fowler, S.E., Hamman, R.F., Lachin, J.M., Walker, E.A., Nathan, D.M., *Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin*. N Engl J Med. **6**, 393–403 (2002)

12 Wang, Z.Q., Zhang, X.H., Russell, J.C., Hulver, M., Cefalu, W.T., *Chromium Picolinate Enhances Skeletal Muscle Cellular Insulin Signaling In Vivo in Obese, Insulin-Resistant JCR:LA-cp Rats*, J. Nutrition, **136**, 415-420 (2006)

13 Torgerson, J,S., Hauptman, J., Boldrin, M.N., *Sjostrom Xenical in the prevention of diabetes in obese subjects (XENDOS) study: a randomized study of orlistat as an adjunct to lifestyle changes for the prevention of type 2 diabetes in obese patients*. Diabetes Care, **27**,155–161 (2004)

14 Van Gaal, L.F., Rissanen, A.M., Scheen, A.J., Ziegler, O., Rossner, S., *Effects of the cannabinoid-1 receptor blocker rimonabant on weight reduction and cardiovascular risk factors in overweight patients: 1-year experience from the RIO-Europe study*. Lancet, **365**, 1389–1397 (2005)

Forthcoming congress

The 19th World Diabetes Congress of the IDF will be held from 3–7 December 2006, in Cape Town, South Africa.

Nestlé
Good Food, Good Life

This periodic bulletin on nutrition and health topics is written and edited by the Corporate Wellness Unit with NRC scientific support.

The Corporate Wellness Unit thanks:
Drs. K.Acheson, J. Decombaz, E. Almiron Roig, C. Macé, C. Darimont, H.Green, NRC, and
Dr. Ian Horman (Visualizing Complexity, S.à.r.l., Blonay), for their contributions to this edition

Writing, Editing and Production
Veronica Roy (Corporate Wellness Unit)

Design:
Christian Stuker, Lausanne

Images:
Getty Images, Corbis, Prisma; p. 7: JirehDesign.com

Printing:
Presses Centrales Lausanne S.A.