NDS
Nutrient Delivery System

Probiotic W-8-CONTROL®

Probiotics for improving the energy metabolism

The link between intestinal flora and obesity.

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Overweight or obese?

Being overweight is usually defined as a BMI between 25 -30 (kg/m2) while having a BMI > 30 is defined as obesity. In the past 30 years or so, the percentage of people who are overweight has grown significantly. The causal links are complex as many genetic factors and lifestyle components, such as eating habits and the level of physical activity, the balance between energy-giving nutrients, individual metabolism and ability to regulate metabolism, all play a part.

In earlier times and throughout human history, intermittent scarcity of food would occur depending on season, population density, wars and natural disasters, so the people who survived the times of scarcity were those who were particularly good at 'storing' when food was plenty. We also know that babies who have been starved as foetuses and are therefore born underweight in relation to the length of the pregnancy, adjust their 'biological regulator' to 'starvation' and are therefore coded to utilise food very efficiently so that when they are given sufficient amounts of food, there will be a greater risk that they will become overweight. This is hitting society like a boomerang now, when most societies in the world have access to energy-dense and nutrient-poor food and industrial development is gaining speed and eliminating the need for the physically demanding activity of earlier eras.

Occurrence: the high level of overweight and obese people is noticeable in many countries, independent of geographical location, ethnic composition of the population, age and gender. Table 1 shows the percentage of people who are overweight (BMI 25-29.9) and obese (BMI +30). The prevalence of both overweight and obesity is high all over the world, and that the only group with a lower prevalence is adults in Asia. This means that there is a serious mismatch between our biological needs and the overall environment that we have created.

Table 1. Occurrence of overweight among adults and children (selected examples)

Country	Overweight, % (adults)	Obese, % (adults)	Obese, % Children aged 5-17 Girls/boys
Lowest occurrence			
India	16	1	
Indonesia	16	1	
Japan	24	3	14.4/16.2
Korea	31	4	19.9/16.2
China	29	2	4.5/5.9
Switzerland	37	8	13.1/16.7
Medium occurrence			
Norway	46	10	14.7/12.9
Sweden	44	10	19.5/17.0
France	38	11	14.9/13.1
Denmark	45	11	15.2/14.1
The Netherlands	47	12	17.9/14.7
Finland	46	16	19.1/23.6
Highest occurrence			
Greece	59	18	37.0/45.0
Hungary	53	19	26.0/25.5
Iceland	60	20	25.5/22.0
United Kingdom	61	25	26.6/22.7
Mexico	70	30	29.0/28.1
USA	68	34	35.9/35.0

Data for adults: OECD-2010 figures
Data for children: International Association for the Study of Obesity (2011).

Probiotics are good intestinal bacteria that create life. Read more about life's bacteria.

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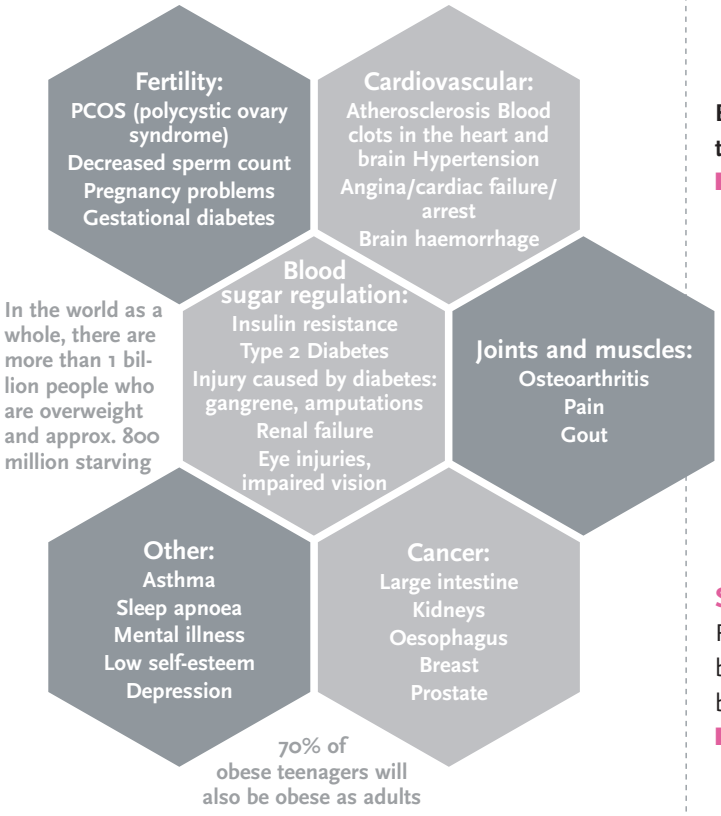
Sadly, the prevalence of obesity in children and teenagers is very high – even in those countries that have traditionally had lower levels of obesity among adults. It has so far not been possible to find a way of reversing this trend, despite intensive research efforts all over the world.

The consequences of being overweight and obese

It is not at all healthy to be very overweight or obese. A modest excess weight of 5-10 kilos has hardly any health consequences if the person lives healthily and is physically active/exercises to raise the pulse, i.e. ensure that the metabolism of the cells is kick-started at least four times a week. High levels of obesity, on the other hand, are dangerous: Long term, the occurrence of a wide range of diseases and physical disability increases significantly both among children and adults. See Figure 1:

Figure 1. Consequences of morbid obesity



Reasons for obesity and their links to intestinal flora

What are the reasons that obesity-related health problems are rising all over the world? Obesity is the largest health problem facing the world today and it has not been possible to find the key to the problem and achieve a definitive outcome:

Many factors are, of course, interacting. These include heredity, nutrition, physical activity, the composition of the intestinal flora, the child's nutritional condition during pregnancy and early childhood and the importance of birth and breastfeeding.

All these areas are being researched, but in the past 5-10 years a great deal of new knowledge has been obtained:

- In 2003, the human genome had been mapped and this knowledge was applied to a wide range of health problems, including obesity, and this new knowledge has been coordinated across disciplines to map complex health problems more precisely.
- The body's microflora explains a larger part of the problem of obesity (80-85%) than our DNA does (55-60%).
- It has been demonstrated that three general microbiome types (Arumugam 2011) exist across geographical conditions, ethnic background, age, social class etc.: **Bacteroidetes, Prevotella and Ruminococcus.** It is not yet known what determines the type people are. It may be blood type. It may be the first microflora the person meets as a baby. It may be diet throughout life. It may be determined by different ways of eliminating excess hydrogen gases.

But we know something about the capabilities of the respective species of bacteria:

- **Bacteroidetes are good at breaking down carbohydrates** and the ratio between Bacteroidetes and Firmicutes (the other large group) is out of balance in overweight or obesity.
- **Prevotella are good at breaking down mucosa in the intestine,** which can result in gut pain. Prevotella in excess are also associated with autoimmune diseases such as arthritis.
- **Ruminococcus help to absorb carbohydrates** and may also be involved in difficulties keeping weight stable and healthy.

Specific findings related to obesity

Research in which genetic analysis of the intestinal flora has been carried out (in order also to map the bacteria that cannot be cultivated in a laboratory) has shown that

- **Obese people have more Firmicutes bacteria** *(consisting of Clostridia, Eubacteria, Lactobacillus, Enterococcus, Strepto- and Staphylococcus and various others)* so that there may be up to 85-90% Firmicutes and maybe only 2-5%. Bacteroides/Bacteriodetes: Slim people have 60-70% Firmicutes and approx. 25-30% Bacteroidetes (Ley, 2006 og Turnbaugh 2009). Others believe that they should be equally represented at about 50% of each main type to maintain a sensible balance. **Laboratories working on stool analysis currently operate with a normal range of max. 80% Firmicutes and min. 20% Bacteriodetes.**
- The composition of the microflora changes as weight is lost, irrespective of the weight loss method. The weight loss can be achieved either with a diet limiting carbohy-

drates or fat. During this process, the microbiota becomes similar to that of a slim person after a year (Ley 2006).

- Children with an intestinal flora consisting of many *Bifidobacterium species* and few *Staphylococcus Aureus* stayed slim during their childhood (Kalliomaki 2008) whereas those children with few *Bifido* and many *Staphylococcus Aureus* gained more weight up to school age.

How does the microflora contribute to the control of metabolism and weight?

The composition of the intestinal flora in the small intestine **affects digestion and energy conversion in the body** by extracting more or less energy from the food. Short chain fatty acids are also created in the large intestine based on otherwise indigestible fibres in the food and these contribute to keeping the intestinal mucosa healthy, as signal molecules and as a source of energy. The former belief that 'fibres are not digested, but just act as a filler', is no longer conclusive, as some energy can be extracted from soluble food fibres if the microbiota is able to do so.

People with a 'far too energy-efficient' intestinal flora, often experience, that they cannot eat the amount of food they 'should be able to' on the basis of their gender, age, weight and physical activity without gaining weight. And vice versa: those people who have a 'not so energy-efficient' intestinal flora can eat `anything' without gaining weight.

The latest research is mapping the substances that contribute to these processes. The microbiota regulates the Angiopoietin-like protein 4 or ANGPTL4 which, in turn, regulates the body's ability to metabolise fat in both muscles and adipose tissue.

The other important area where the microbiota is involved in weight regulation is **regulation of inflammation and insulin resistance.** Chronic low-grade inflammation is an essential component of metabolic syndrome, i.e. reduced insulin sensitivity and thus reduced ability to convert carbohydrates to energy in a healthy way.

All metabolic systems are functionally interacting molecularly with the immune system, so that an increase in pro-inflammatory cytokines such as TNF-α (typical for obesity) results in insulin resistance. The microflora can both initiate and maintain insulin resistance (Hotamisligil 1996 og 2008).

The effect of the microflora on inflammation is initiated by lipopolysaccharides from the breakdown of bacterial cell walls. Lipopolysaccharides are a strong, but 'bad' immunostimulants as they keep the immune cells in a state of 'high resting burst' which results in both increased inflammation and reduced immunity in the same cocktail. Lipopolysaccharides activate a toll-like receptor 4, TLR4, and this cascade may contribute to increased weight, even when the energy intake is not increased (Cani 2007).

Diet is also important as a high consumption of fat in itself contributes to

- increased absorption of lipopolysaccharides due to leaky gut syndrome (Ghosal 2009). Lipopolysaccharides being absorbed with the fat in the lymph system and subsequently into the blood.
- Increases the *Firmicutes bacteria* which must be held in check/reduced, to prevent or treat weight problems.
- Reduces the amount of *Bifidobacterium species* which otherwise contribute to improving sugar tolerance, reducing inflammation, improving the barrier function (reducing leaky gut) and reducing the absorption of lipopolysaccharides (Cani 2009).

Hormonal communication routes are also involved through the formation of GLP1 and GLP2 which contribute to satiety regulation, gastric emptying rate and the maintenance of the barrier function of the mucosa.

Product information: NDS® Probiotic W-8 Control®

NDS® Probiotic W-8 Control® consists of especially selected strains of the following bacteria:

For the establishment and maintenance of an intestinal flora that contributes to a healthy metabolism in both children and adults.

- **Bifidobacterium Breve M/13**
- **Bifidobacterium Bifido**
- **Bifidobacterium Infantis**
- **Bifidobacterium Lactis**

A total of 20 billion CFU per daily dose

The strains in NDS® Probiotic W-8 Control® have been selected to work preventively and therapeutically in six areas:

1. **Improving metabolism** in converting both fat and carbohydrates, upregulating genes that convert fats and produce beneficial prostaglandins, damping of genes related to stress, improving blood sugar and blood glucose (clinical studies in humans and mice, Kondo 2010 and 2013, and manuscript in preparation, 2014).
2. **Reducing inflammation,** both by increasing the formation of the anti-inflammatory cytokine, IL-10, attenuating the pro-inflammatory, C-reactive protein, CRP, and by helping to break down lipopolysaccharides.
3. **Improving several physiological functions** related to the reduction of stress in the liver (improvement of several liver function tests) (Kondo 2010 og 2013).
4. **Improving barrier function** (as shown by TEER for one strain and analysis of proglucagon in mice for another), protecting against side effects of antibiotic therapy.
5. **Reducing total cholesterol** (Kondo 2010).
6. **Antioxidant effect** and mast-cell stabilising.

Table 2	Improve blood sugar regulation and reduce insulin resistance	Regulation of genes related to fat and carbohydrate metabolism	Barrier function	IL-10 production	Mast cell stabilising	Other	Breakdown of lipopoly-saccharides
Bifidobacterium Breve M/13	++++	++++	++++			Reducing total cholesterol	
Bifidobacterium Bifido			++++	++++	++	Anti-oxidant	++
Bifidobacterium Infantis				+++	++		
Bifidobacterium Lactis						Protects against side effects from antibiotics Fewer sick days Improves sluggish bowel function	
All the strains are viable during production and storage at room temperature for up to two years. They tolerate gastric acid and bile exposure and are harmless. Bifidobacteria do not form D-lactate. NDS® Probiotic W-8 Control® also **inhibits** the growth of specific unwanted bacteria such as **E. Coli, Salmonella, Shigella, Pantoea Agglomerans (previously Enterobacter A), Staphylococcus Aureus, Clostridium Difficile and Clostridium toxin formation.**							

Probiotics play a role, not only in the gut, but in the health of the body as a whole, including blood glucose, satiety and weight control and should be part of a holistic, integrated treatment model for all complex health problems involving the interaction between the gut and energy metabolism in muscles, liver and adipose tissue.

Probiotics, consisting of specific metabolic strains of friendly intestinal bacteria, are therefore a valuable tool in the prevention and treatment of blood sugar and weight-related problems. It can be used for an unlimited time period.

Dosage

Mix 1 teaspoonful of NDS® Probiotic W-8 Control® in lukewarm water. Let the mixture stand for at least 5 minutes, preferably 10-15 minutes, and drink on an empty stomach, preferably in the morning or just before bedtime. Probiotics also survive well in milk, soy milk, rice milk or similar non-acidic drinks, but should not be mixed with juice or acidic drinks.

References

Manimozhiyan Arumugam et al, **Enterotypes of the human gut microbiome,** Nature 473,174–180, (12 May 2011) doi:10.1038/nature09944

Ley RE, Turnbaugh PJ, Klein S, Gordon JI. **Microbial ecology: human gut microbes associated with obesity.** Nature 2006; 444:1022–1023.

Turnbaugh PJ, Hamady M, Yatsunenko T, et al. **A core gut microbiome in obese and lean twins.** Nature 2009; 457:480–484.

http://www.uspharmacist.com/content/d/featured%20articles/c/16901/#sthash.TmFfGZEv.dpuf

Hotamisligil GS, Erbay E. **Nutrient sensing and inflammation in metabolic diseases.** Nat Rev Immunol 2008; 8:923–934.

Hotamisligil G, Peraldi P, Budavari A, et al. **IRS-1-mediated inhibition of insulin receptor tyrosine kinase activity in TNF-alpha-and obesity-induced insulin resistance.** Science 1996; 271:665–670.

Cani PD, Amar J, Iglesias MA, et al. **Metabolic endotoxemia initiates obesity and insulin resistance.** Diabetes 2007; 56:1761–1772.

Ghoshal S, Witta J, Zhong J, et al. **Chylomicrons promote intestinal absorption of lipopolysaccharides.** J Lipid Res 2009; 50:90–97.

Cani PD, Possemiers S, Van de Wiele T, et al. **Changes in gut microbiota control inflammation in obese mice through a mechanism involving GLP-2-driven improvement of gut permeability.** Gut 2009; 58:1091–1103.

Data on file regarding clinical studies on B. breve M/13

Safety profile

In Europe, strains of probiotic bacteria are regarded as safe if they have QPS status. This stands for Qualified Presumption of Safety[5]. All probiotic strains in the NDS® Probiotics range have QPS status and the product has been manufactured under the regulations for food production.

The NDS® Probiotic range also includes these specific multi-strain products:

NDS® Probiotic Panda® 1 & 2 are used in the prevention and treatment of allergies in both children and adults. Also suitable for pregnant or breastfeeding women, who are concerned, that their child may develop an allergy.

NDS® Probiotic Classic® for excess growth of unwanted bacteria, fungi or parasites in the gastrointestinal tract.

NDS® Probiotic I.L.D.® for use in inflammatory gastrointestinal diseases such as Crohn's disease, ulcerative colitis and other related diseases.

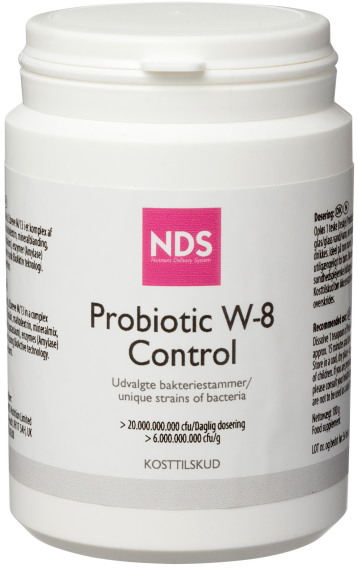
NDS® Probiolax® for constipation/sluggish bowel in people of all ages (children + 1 y old).

NDS® Probiotic Barrier® for the healing of the intestinal mucosa in many kinds of stress, hypersensitivities, mood disorders, depression.

NDS® Probiotic Performance® for balancing intestinal function in exercise- and sport-related stress/loose stools/ diarrhoea, sensitivities with diarrhoea and e.g. demanding treatments, that provoke diarrhoea.

NDS® Probiotic S-60-Nrg® as a help in instances of serious stress.

NDS® Probiotic W8-Control® as a support to balance the gutflora to help improve the energy metabolism and increase weigthloss.



It's all about biology

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