Obesity

What's the problem?
This booklet contains information on all the objects in the exhibition "Obesity - what's the problem?".

The exhibition is about obesity, and what can be done about it.

Don't expect to get tips on how to get a flat stomach. Instead, prepare to get close to obesity treatments, and get ready to meet some of the latest research into why the world seems to be experiencing an obesity epidemic.

The exhibition shows samples from different corners of reality. When they are brought together, surprising connections are revealed. Just take a close look.

Enjoy.
The Genomic Shortcut
NO ONE wants to be obese. Obesity is met with prejudice, stigmatisation and overt discrimination, and can lead to low self-esteem, discomfort, health problems, and increased risk of serious illness and premature death. What's going on?

It is often assumed that obese people have simply eaten too much and moved too little. Anyone can see that they still eat too much and do not exercise enough, or why would they be obese? If they want to lose weight, they should just eat less and move more. How hard can it be?!

But it's just not that simple. At the same time as building up fat, the lean body mass of obese people also increases, speeding up the metabolism. On top of this it also requires more energy to move a heavier body. Although discomfort and pain often prevent obese people from exercising, they still need more energy. Therefore, they eat more.

The energy required for fat storage operations per day is so small - less than 1% of a person's total energy intake - that it's hard for an individual to know when they're eating too much. Even the most sophisticated measurement techniques can't track it. Studies of thousands of people have shown that obesity can develop independently of the amount people eat and exercise at a given point in time – the body can still find extra energy to store as fat. It's a bit like your personal finances: you can
continue adding a little to your account whether you have a large or small income, and whether you have large or small outgoings. However, there is of course a limit to this, and so it is for the metabolism. During periods of enforced diet or famine, when the body is forced to use what reserves it has to stay alive, people of course lose weight, and eating excessive amounts, of course, leads to weight gain. But this proves only that the thermodynamic law of energy balance applies. It doesn’t actually explain what drives the development of obesity. What determines when energy is stored as fat is largely unknown, and is a major challenge for research.

The obesity epidemic is usually thought to be a result of changes in society. Namely, increasing availability of energy-dense foods and beverages and technological changes that make it possible to cope with everyday life with less movement. Nevertheless, the small excess in energy storage that leads to obesity can easily occur in less abundant societies.

"It is often assumed that obese people have simply eaten too much and moved too little.

If they want to lose weight, they should just eat less and move more. How hard can it be?!

But it’s just not that simple."
These social changes, of course, also make it easier to obtain the extra calories that a metabolism increased by fat demands. In the past, more difficult access to food prevented this. During periods of food shortage, obesity rates do not increase, and people lose weight. But careful analysis of epidemiological developments in Denmark has shown that obesity does not neatly track these societal changes, which are usually assumed to cause obesity. Evidence points instead to the crucial factor being something that occurs very early in life, even before birth. But no-one knows what this might be.

Obesity has a large number of well-described effects on health - especially through the so-called metabolic syndrome, which is associated with increased risk of, for example, diabetes, cardiovascular disease, dementia and some cancers.

But there are also some seemingly paradoxical factors in the relationship between fat and health. In fact, fat is
a highly effective and safe way for the body to build up a reserve of energy, and it’s unclear why only some obese people experience health complications.

A current, partially substantiated theory suggests that metabolic problems occur when an individual's fat stores are completely full. This creates a kind of chronic, low-level intoxication condition, with excess free fatty acids (lipotoxicity) that are not being either immediately used as energy or being bound in the inert fat in the body. Cells in adipose tissue and other organs show signs of damage and there is a chronic inflammatory condition associated with metabolic syndrome and type 2 diabetes.

How much fat can accumulate in fat stores before metabolic damage occurs is highly individual, and what determines each person's capacity for fat storage is an open question. The relative contributions of genes, environment, gene-environment interactions, and early life circumstances are being investigated. Which bacterial species dominate in our gut may also play a key role, raising new questions about the impact of the composition of our diet.

There is a need for continued research if we are to combat what threatens to be one of the biggest future health problems for the world's population.

THORKILD I.A. SØRENSEN, professor, physician, dr. with. Novo Nordisk Foundation Center for Basic Metabolic Research & Institute of Preventive Medicine.
Open abdominal surgery

Retractor
→ Early 1900s

Simple retractor. Used only to hold apart the abdominal skin, as the sharp teeth would damage the fragile organs inside the abdomen.

Logothetopulos’ self-retaining retractor
→ Early 1900s

Wound retractor that can be tightened and locked into position. Used to hold the abdominal skin apart during the operation, creating a large enough opening for the surgeon to work in.

Payr’s stomach resection forceps
→ Invented around 1916

Designed for operations on the stomach such as removing an ulcer. The forceps clamp the tissue together, and simultaneously close off the blood vessels, preventing bleeding. The use of forceps in stomach operations is crucial to prevent gastric acid spilling out when excess tissue is cut away.
**Graser's resection forceps**
→ Early 1900s

Forceps for clamping together the stomach. The groove in the middle was added to help the surgeon sew as close as possible to the forceps.

**Petz' gastric stapler**
→ Invented in 1921

Stapling is faster than sewing with a needle and thread and more effective at preventing the stomach contents from flowing into the abdominal cavity. In this early model the staples had to be individually loaded by hand.

**Intestinal shield**
→ Early 1900s

The shield can be unfurled like a fan inside the abdomen, keeping the intestines and organs in place so they don't interfere when the abdomen is sewn back together. Just before the opening is closed completely, the leaves are folded back together, and the shield can be pulled out.
A small hole is cut in the abdominal wall, and the trocar is pushed through into the stomach.

The white tip is then removed, leaving a port through which instruments can be inserted.

During 'gastric bypass' surgery, trocars are used to make five ports into the abdomen, through which instruments can be passed: one for the camera, one for the liver holder and three for the operation, usually performed by two surgeons.

Films surgery in the abdomen. Before the camera is passed through the port, it is warmed up in water kept at body temperature, to stop the lens fogging up.

This automatic suturing instrument is used in gastric surgery to create a smaller stomach. The disposable head inserts two rows of staples and cuts the stomach inbetween them.
| **Ultrasonic Harmonic Scalpel with generator**  
Ethicon-Endo Surgery, Harmonic ACE, Johnson & Johnson → 2009 |
<table>
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<tr>
<td>Ultrasonic scalpel used to burn through the adipose tissue and intestinal walls, emitting a beeping noise as it goes.</td>
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| **Handle for laparoscopic instruments**  
Karl Storz → 2000s |
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<td>The surgeon's tools are mounted on the end of long thin rods. A good grip is important for precise movements.</td>
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| **Endo Stitch**  
Covidien → 2000s |
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<tr>
<td>Automatic disposable suturing device. The Endo Stitch has two needles at the tip, and the thread can jump between the two, minimizing the need for twisting movements.</td>
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| **Laparoscopic grasper**  
Karl Storz → 2000s |
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<tr>
<td>Can grab and hold onto the intestine, so that it can be moved around. The rounded serrations prevent damage to the intestine.</td>
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| **Suturing grasper**  
Karl Storz → 2000s |
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<td>Grasper used to hold the needle and thread during stitching.</td>
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| **Laparoscopic scissors**  
Karl Storz → 2000s |
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<td>Used to cut suturing thread.</td>
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| **Wound closure sutures**  
Covidien → 2011 |
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<tr>
<td>The green thread dissolves in the body, and has little barbs that hold the stitches in place instead of knots. The blue thread is not absorbable.</td>
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| **Skin stapler**  
Covidien → 2012 |
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<tr>
<td>The ports in the abdominal skin are closed with skin clips (agrafer), which are removed after the wound has healed.</td>
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Gastric band
Johnson & Johnson → 2012

Invented in 1978, grounded in the principle of restriction. The band is tightened around the top of the stomach so that the patient can’t eat as much. It can be removed, but can leave scar tissue on the stomach.
Therapy of morbid obesity
Sahlgrenska Interactive Education.
Bariatric surgery workshop → 2012

Booklet for demonstration of tools developed for Roux-en-Y gastric bypass.

This procedure was developed as obesity surgery in 1960, inspired by ulcer patients who lost weight after a similar procedure on the intestine.

EndobARRIER
GI Dynamic → 2011

New technology that mimics the effect of 'gastric bypass'. A "sock" is fixed at the bottom of the stomach, so that food passes through the upper intestinal tract without coming into contact with the intestinal wall.

Used both for obesity and type-2 diabetes treatment, but can only stay in place for up to one year.
Early apparatus for administering anaesthetic gases such as ether and nitrous oxide. Anaesthesia is maintained through a complex combination of inhaled gas, barbiturate injection, and other substances.

Newer apparatus in which anaesthetic gases are dispensed via an evaporator, making it easier to control the gas flow and ensure the correct dose.
**Servo Ventilator 900**
Siemens-Elima → 1970s

Electronically controlled ventilator. The first respirator that could automatically monitor breathing and alert medical staff if there was anything irregular.

**Respirator Type A**
Bang & Olufsen → 1950s

This respirator was developed for patients who could not breathe on their own for a longer period of time. With this device, it was recommended to deliver the oxygen through a hole in the neck (tracheostomy). Oxygen can also be provided by passing a plastic tube through the mouth and into the windpipe (intubation), or via a mask.

**Heart-lung machine**
Melrose N.E.P. → 1955

The first heart-lung machine in Denmark, purchased by Rigshospitalet. During heart surgery the oxygenator takes over the function of keeping the blood oxygenated. Blood flows out of the body, is pumped through the oxygenator, and back into the body again.
A typical individual weighing scale can take up to 150 kg. How would you measure a body weight of 220 kg? One solution might be to use two scales.

A typical tape measure is 150 cm long. A patient at Hvidovre Hospital with a BMI of 65.6 measured 138 cm round the waist, 190 cm round the hip and 42.5 cm round the neck.

Clinical guidance for general practice: Detection and treatment of obesity in adults
Danish College of General Practitioners in collaboration with the Health Protection Agency → 2009

Plastic laminated sheets to help General Practitioners diagnose obesity, including instructions for how to measure and interpret Body Mass Index (BMI) and how to locate and measure the waist.
The DEXA scan can measure bone mineral density, but can also measure muscle mass and fat mass. Used mostly in the research context and not in common diagnosis of obesity.

Fact sheet no. 311: Obesity and overweight
World Health Organization (WHO) → 2012

"Overweight and obesity are defined as abnormal or excessive fat accumulation that may impair health"

It is controversial whether obesity should be classified as a disease, or if it should be understood as a maladaptive response to a complex mix of lifestyle factors and environmental conditions. The WHO fact sheet collects current knowledge, definitions, statistics, and advice on obesity.

Danish Obesity in Numbers
Magazine of the Danish Dental Association → March 2012.

Key figures on obesity in Denmark from the Danish Dental Association’s member magazine. This issue focused on the potential role of dentists in the treatment and prevention of obesity.
Dieting

Slim in the right way
Johanne Christiansen → 1938

The author was a doctor and had a large practice with many female patients. She wrote dieting advice books very similar to those on sale today.

Eat, drink, and be slim → 1950
Food for slimming → 1951/1957
Edward Clausen and Knud Lundberg

The authors explain that the title “Food for slimming” is nonsense – there is no food that will make you slim. “Eat, drink, and be slim” was written in Danish, but also published in English. The books contain recipes with calorie counts, and tables with calorie allowance adjusted for age, weight and level of daily physical work.

Consolation for the chubby
Dieting in theory and practice
Claus Brenøe → 1977

The back cover reads "This book offers a sober judgement of the chances of the overweight person". The author was a chemical engineer with a desire to dig deeper than the numerous dubious diets but also to show respect for people who might not wish to lose weight.
The diet pyramid was developed by the Danish co-operative "Brugsen" in 1970. It circulated widely, but never became the official government recommendation.

Brugsen's (the Danish co-operative) diet book 1 + 2 The Pyramid Plan → 1989

Jars containing human fat could be found on any European pharmacy shelf in the 1600s-1700s, used as a powerful ingredient for treatments for both external and internal use.

Axungia Hominis (Latin for human fat) → 1600s -1700s

The fat would probably come from executed criminals, as executioners had the right to sell the bodies.

Cambridge Weight Plan → 2012

Very-Low-Calorie-Diets (VLCD) such as the Cambridge Cure and the Danish Nupo Cure appeared in the 1970s and 1980s.

The idea is to replace meals with low-calorie, high-protein products such as soups, beverages and bars.
Diet pills

Dexedrine
Smith Kline & French Laboratories → 1964

Diet pills with amphetamine as the active ingredient were popular in the 1940s-60s. They inhibited the appetite and had an exhilarating effect, but were also addictive and put a strain on the heart.

Recipe for 'Tablettæ dinitrophenolin'
National Pharmaceutical Composition Council (DAK) → 1935

Normally, energy from food is converted into other forms of energy that can then be used to build cells or stored in fat deposits. Dinitrophenol (DNP) stops the process of oxidative phosphorylation, meaning that all energy is converted to heat. DNP therefore has a slimming effect, but even in small doses causes dangerous overheating of the body. DAK gave the recipe for Tablettæ dinitrophenolin to the Danish pharmacies. Today the substance is strictly prohibited in Denmark, but foreign websites claim to offer it for sale.

Ponderal
A/S Alfred Benzon → 1970s -1980s

Appetite-inhibiting remedy containing the substance fenfluramine. Was developed in an attempt to find a substance with the appetite-inhibiting effect of amphetamine, but without its dangerous side effects. However, it turned out that fenfluramine had a soporific effect and increased the risk of depression. Ponderal was on the market until the late 1980s.

Tablettæ Thyroidini Vermehren
Alfred Benzon → 1930s

The thyroid gland was linked to the regulation of metabolism in the 1890s. Several brands of powdered thyroid extract were launched, and up until the 1970s they were widely used for treating obesity when the cause was suspected to be "something metabolic". But overdosing can lead to heart problems, so these pills are no longer used for obesity treatment.

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**Mirapront**
Novo Industri A/S → 1970s -1990s

Appetite-inhibitor containing fentamin. Belongs to the group of central nervous system stimulating sympathomimetic amines, which also includes amphetamine and fenfluramine. Mirapront is no longer for sale in Denmark.

**Letigen**
Nycomed → 1990-2002

Pill combining ephedrine with caffeine, which both inhibits appetite and increases fat metabolism.

Was taken out of production in 2002 when it lost its approval in Denmark due to a suspected risk of blood clots in the brain.

**Regenon**
Temmler-Werke → 1970s

An appetite-inhibiting sympathomimetic amine, which can still be purchased in Denmark with a prescription.

**Xenical**
Roche → 1999 -

Pill containing orlistat, which reduces fat absorption by inhibiting the intestinal enzymes that break down fat. It can cause severe diarrhea. A non-prescription version called Alli was pulled from the market in the summer of 2012, allegedly due to the absence of the active ingredient orlistat.
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<th>#</th>
<th>Question</th>
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<tr>
<td>1</td>
<td>Does obesity surgery extend life?</td>
<td>The &quot;Swedish Obese Subjects Study&quot; is one of the main sources of data on the life-prolonging and weight loss effects of obesity surgery.</td>
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<td>2</td>
<td>What impact does obesity surgery have on weight in the long term?</td>
<td>Study of weight loss after different types of obesity surgery compared to a control group which has received treatment, but no surgery.</td>
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<td>4</td>
<td>How many people have obesity surgery in Denmark?</td>
<td>The number of obesity operations by year, hospital region and type, and type of operation, 2007-2011. From Statens Serum Institut, National Patient Registry → May 2012.</td>
</tr>
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|   | Why is it dangerous to be fat? | Complications of obesity. Danish Health and Medicines Authority → 2012 | The Danish Health and Medicines Authority explains: "The relative risk (RR) shows how many times the risk of having the complication is increased if you are obese (BMI > 30) compared to if you are of normal weight (18.5 < BMI < 25)."
|   | Does obesity kill you? | Mortality of overweight and normal weight conscripts. From “Lifelong doubling of mortality in men entering adult life as obese”. International Journal of Obesity → 2011 | How dangerous is it to be overweight? A study of Danish men taking the examination for military service born between 1943 and 1977 found that the mortality rate for those with BMIs between 31 and 51 is double as high as that for a control group with a BMI between 15 and 30.
|   | How have obesity rates changed over time in Denmark? | The prevalence of obesity between 1930 and 1980 (left) and between 2002 and 2009 (right) in Danish men taking the examination for military service, according to year of birth. From “The leveling off of the obesity epidemic since the year 1999 - a review of evidence and perspectives”. Obesity reviews → 2010 | These graphs raise many questions. The prevalence of obesity increased for men born during two periods; between 1940-1950 and 1970-1980, and now appears to be leveling off (as suggested by the graph on the right). These graphs offer no explanation, but pave the way for hypotheses that can lead research in new directions.
|   | Putative contributor to obesity epidemic | Prevalence of putative contributors against the increasing prevalence of obesity. From “Ten Putative Contributors to the Obesity Epidemic”. Critical Review in Food Science and Nutrition → 2009 | Hormone-disrupting chemicals (PBDEs) in breast milk, sleep deprivation and increasing maternal age were among ten hypotheses tested in a large study investigating possible explanations for increasing levels of obesity, other than the amount people eat and exercise. |
# Early metabolism research

**Poster with dietary guidelines**
Danish Propaganda Ministry → 1942

Government dietary guidelines during a time when under- and malnutrition were the major threat to health, especially for children.

**Experimental set-up with a cycle ergometer inside an air chamber. From "The relative value of fat and carbohydrate as sources of muscular energy"
Biochemical Journal → 1920**

This experimental setup allows researchers to control how hard the subject works, whilst making precise measurements of metabolism.

**Measurement of hard physical work**
Rockefeller Institute → 1930s

The subject is hanging by a weight while working on a bicycle ergometer wearing a rubber suit. The suit picks up his sweat. The set-up is from a series of experiments that examined respectively fats and carbohydrates as fuel for the human body in heavy muscular work.

**August Krogh's Bicycle Ergometer → 1911**

This bicycle was developed to allow researchers to control exactly how hard the subject worked. The bicycle’s resistance was controlled by electromagnets that could be turned up and down, allowing for groundbreaking accuracy.
Apparatus for measuring a wide range of physiological parameters at rest and during exercise. By measuring the consumption of oxygen and production of carbon dioxide the device can calculate metabolism under different conditions. The subject is connected to the apparatus with a mouthpiece, a mask, or a hood.

Visual Analogue Scale (VAS)
to measure appetite

In physiological studies of metabolism, appetite is measured using a scaled questionnaire that asks subjects to rate their feelings of hunger and satiety.

Respiration Hood for Oxycon Champion
Jaeger → 1998

This hood is used for respiration measurements when the subject is lying down. It is designed not to interfere with the subject's breathing.

Oxycon Champion
Jaeger → 1998

Apparatus for measuring a wide range of physiological parameters at rest and during exercise. By measuring the consumption of oxygen and production of carbon dioxide the device can calculate metabolism under different conditions. The subject is connected to the apparatus with a mouthpiece, a mask, or a hood.
The pancreas is kept alive after the mouse is sacrificed. The substance of interest is then sprayed into the pancreatic veins and flows naturally through the organ, and is then collected for testing.

Perfusion of pancreas in mouse → 2012

The set-up is similar in principle to the heart-lung machine in the operating room. In both cases pump, oxygenator and heat regulation ensure that the organs can be kept alive. This set-up is testing how the hormone GLP-1 behaves in a living pancreas.


A perfusion model is used to investigate the effect of hormones on the pancreas. For pig experiments, the organ is isolated from the rest of the body but kept alive with the help of machines.

Pancreas from a pig → 2012

After the GLP-1 hormone was discovered and its chemical structure described, its apparent role in diabetes was explored by testing its effects on pig pancreas.
This scientific article reported a study following the outcomes of 'gastric bypass' patients, and showed that the surgery could cure type-2 diabetes. As the title of the article suggests, it was a big surprise that an obesity operation could act as a treatment for a medical condition.

Containers for a solvent are seen at the top left. This is pressed through the system by pumps. At the injection point the solvent is mixed with the sample under investigation.

The mixture of solvent and sample is pressed through columns filled with granulated material. Then the fraction collector at the bottom collect the purified sample of the chemical substance, for instance GLP-1.
Treating patients with the pure form of the intestinal hormone GLP-1 proved impossible. Its chemical life is too short, and the necessary dose would be so high that diabetics would struggle to handle the medication regime.

The rapid decomposition of GLP-1 is caused by the enzyme dipeptidyl peptidase. A group of drugs including Januvia inhibit this enzyme and thus boost GLP-1 levels.
One strategy led to the development of GLP-1-analogues: drugs whose molecular structure and behavior resemble GLP-1 but with greater stability.

**Victoza**  
Novo Nordisk → 2009

**Byetta**  
Lilly → 2005

One example, Victoza, is based on a modified version of GLP-1 called liraglutide.

Byetta was developed from an enzyme found in the skin of the Gilamonster lizard.
As soon as the snippet is pulled out of the stomach through the laparoscopic opening, small samples are excised and put on ice. Normally the remainder of the gut tissue is discarded, but here two such pieces have been preserved for the collection of the museum.

The drawing shows a stomach that has not undergone surgery on the left and a stomach that has undergone 'gastric bypass' surgery on the right. The points A, B, and C indicate the points from where sample are taken 6 to 9 months after the operation. The samples are taken with an endoscope i.e. a camera on a flexible tube that is inserted through the mouth.

Sections of tissue (biopsy) from small intestine of a 'gastric bypass' patient. It is stained with immunohistochemistry, so you can see GLP-1 hormone as small luminous spots in the intestine.
GLP-1 is produced in the intestine by L-cells. Here intestines of rats that have undergone ‘gastric bypass’ surgery are investigated for the presence of L-cells. The investigation increases our understanding of the causes behind the increased production of GLP-1 after ‘gastric bypass’ surgery.

A gut hormone was injected into the rat’s brain, in a region believed to be involved in appetite-regulation.

Zucker rats is a strain of rats bred with a gene defect that means that they burn less fat and develop a greater appetite. They are bred for the purpose of obesity research and can be fed up to twice the weight of a normal rat. The fat is deposited around the organs – in this case the small intestine – exactly as is the case in humans.

The brain and the intestine interact in ways we are far from understanding completely. The interaction between the intestinal hormones and nerve impulses is the object of intense research.
Bead Chips for genotyping
Illumina → 2011

650 'gene chips' used in a Danish-Chinese research project (www.lucamp.org) in which 17,000 Danish individuals were genotyped in order to identify novel genetic variations that lead to increased risk of common metabolic disorders, such as obesity, type 2 diabetes, and hypertension.
What's the problem?

Obesity