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When the body doesn't want to lose weight - Interview on obesity and GLP-1 obesity drugs

Obesity increases the risk of numerous secondary diseases such as type 2 diabetes, high blood pressure and mental illness. Prof. Dr. Kerstin Stemmer, Professor of Molecular Cell Biology at the Department of Biochemistry and Molecular Biology at the University of Augsburg, explains the role of genetics in weight loss and the effect of GLP-1 weight loss medication . She is researching the extent to which fat cells can communicate directly with the pancreas in order to stimulate insulin production.

What is obesity?

Obesity is now considered a chronic disease. The body stores too much fat. It is medically diagnosed when the body mass index (BMI) exceeds 30 and represents a serious health problem. It increases the risk of numerous secondary diseases such as type 2 diabetes, high blood pressure, cardiovascular disease and certain types of cancer, as well as joint problems and mental illness. Since 2020, obesity has been recognized as a chronic disease in its own right; previously it was only considered a risk factor for the diseases mentioned.
In 2024, around 43 percent of adults worldwide will be overweight, including 16 percent with obesity. Particularly alarming: since 2022 there have been more obese children and adolescents worldwide than underweight ones for the first time in history.

How did this come about?

Our environment and lifestyle have changed dramatically in recent decades. High-calorie foods are available at all times, physical work is decreasing, exercise is becoming less common - many activities now take place in a sitting position. Energy intake permanently exceeds consumption. At the same time, our body is still programmed to “survive” in times of scarcity: It stores energy in the form of fat and is reluctant to give it back.

What role do genetics play in putting on weight?

Many people think: “You just have to pull yourself together.” But it's not that simple. Genetics play an important role. In most cases, however, there is not a single genetic cause, but a complex interplay of genetics, environmental factors and behavior. Even preferences for certain healthy or unhealthy foods, or whether we like to exercise, lie in our genes. Today, several hundred gene variants are known, i.e. small individual changes in the genes that can have a different influence on body weight. This means that some people gain weight faster than others despite having a similar lifestyle. We can influence our genetic predisposition to a certain extent, for example by trying to change bad eating habits. However, we usually fall back into old patterns after a short time, especially as we live in an environment that strongly promotes obesity.
In very rare cases, there is a genetic defect. Resistance to the hormone leptin, which is also rare, can also promote obesity.

Why is losing weight so difficult - and why does the weight often come back?

Staying slim in the long term therefore requires more than discipline: the body “remembers” the old weight and actively strives to regain it.
It is important to understand that people with a BMI over 30 cannot permanently get rid of their excess weight by dieting. When dieting, the body tries to regain the lost energy - it lowers the resting metabolic rate, i.e. the calorie consumption of the body in a state of absolute rest, and increases the feeling of hunger. This mechanism is deeply rooted in the metabolism and used to be essential for survival. Today, it causes many people to gain weight again after losing weight - sometimes even more than before. This effect is called the yo-yo effect. It often occurs more frequently with so-called crash diets, where you lose a lot of weight in a very short time. Scientific studies have shown that the resting metabolic rate is significantly lower even years later and that those affected therefore quickly gain weight again.

What can the popular GLP-1 obesity drugs do?

A major advance in obesity therapy is drug treatment with so-called GLP-1 receptor agonists such as semaglutide. This medication acts like a natural hormone that is released after eating. It signals to the brain: “You're full.”
Semaglutide works on several levels: It inhibits the feeling of hunger in the brain, and food cravings also become less frequent. It slows down gastric emptying, which also contributes to satiety, and it improves blood sugar regulation after eating
Studies show: With a weekly injection of up to a maximum of 2.4 mg semaglutide, sufferers can lose an average of around 15 percent of their body weight. The effect appears to be stronger with a high BMI than with a low BMI.

Are there side effects?

Yes, as with any medication. The slimming injection may therefore only be taken with a doctor's prescription. The most common side effects are digestive disorders such as diarrhea, vomiting or nausea.
These symptoms usually occur at the beginning and subside over time. More serious side effects are very rare.

How long do you have to take the injection?

The effect only lasts as long as the medication is taken regularly. If it is discontinued, appetite and weight often return. Today we assume that obesity is a chronic disease - in other words, it cannot be cured. This means that many people need long-term or even lifelong treatment.

Are there other new drugs?

Yes. Tirzepatide, another active ingredient, has been on the market since 2024. This combines the effect of GLP-1 with a similarly effective second hormone, GIP. The combination active ingredient suppresses the feeling of hunger but stimulates insulin production even more strongly through GIP. In clinical studies, the effect on blood sugar and weight was stronger than with semaglutide.
Intensive research is also being carried out into combinations with other substances that have a positive effect on fat, energy and sugar metabolism, but these have not yet been approved.

And is the medication by itself enough?

No. The medication helps to get you started - but lifestyle is crucial. To keep the weight off permanently, new, healthy habits must be firmly anchored in everyday life. Above all, this includes a balanced diet and more exercise. However, it is crucial that this change is achieved much more frequently with the help of weight loss injections.

What is your research interest in this field?

Obesity is a risk factor for type 2 diabetes, in which the body initially loses the ability to react to the blood sugar-lowering hormone insulin. As a result, the pancreas releases more insulin to compensate for the declining effect. Since obesity is initially characterized by an increase in fat mass, we in Augsburg were interested in the question of whether fat cells can communicate directly with the pancreas in order to stimulate insulin production. We were able to show that this is indeed possible: fat cells send out so-called extracellular vesicles - tiny bubbles that contain proteins, fats or genetic information. These vesicles can influence the function of the pancreas - for example by increasing or changing insulin production.
The aims of our research are: to develop new therapeutic approaches, e.g. by specifically influencing these extracellular vesicles, to recognize the early signs of diabetes even earlier and more accurately and to better understand the effects and side effects of new obesity and diabetes medications.

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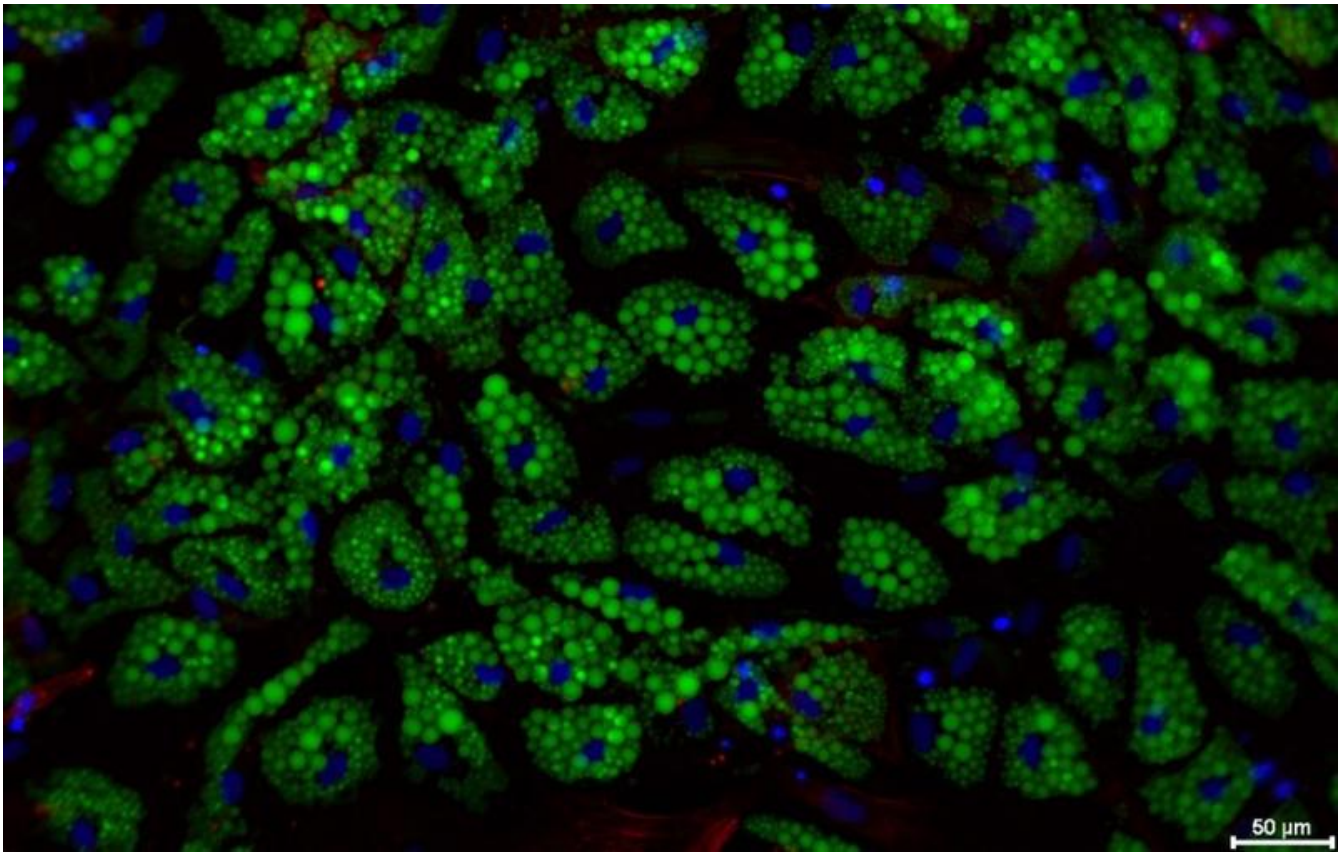

Fat cells under the microscope. These grow in a culture dish. The cell nuclei are shown in blue, the fat droplets in green.
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