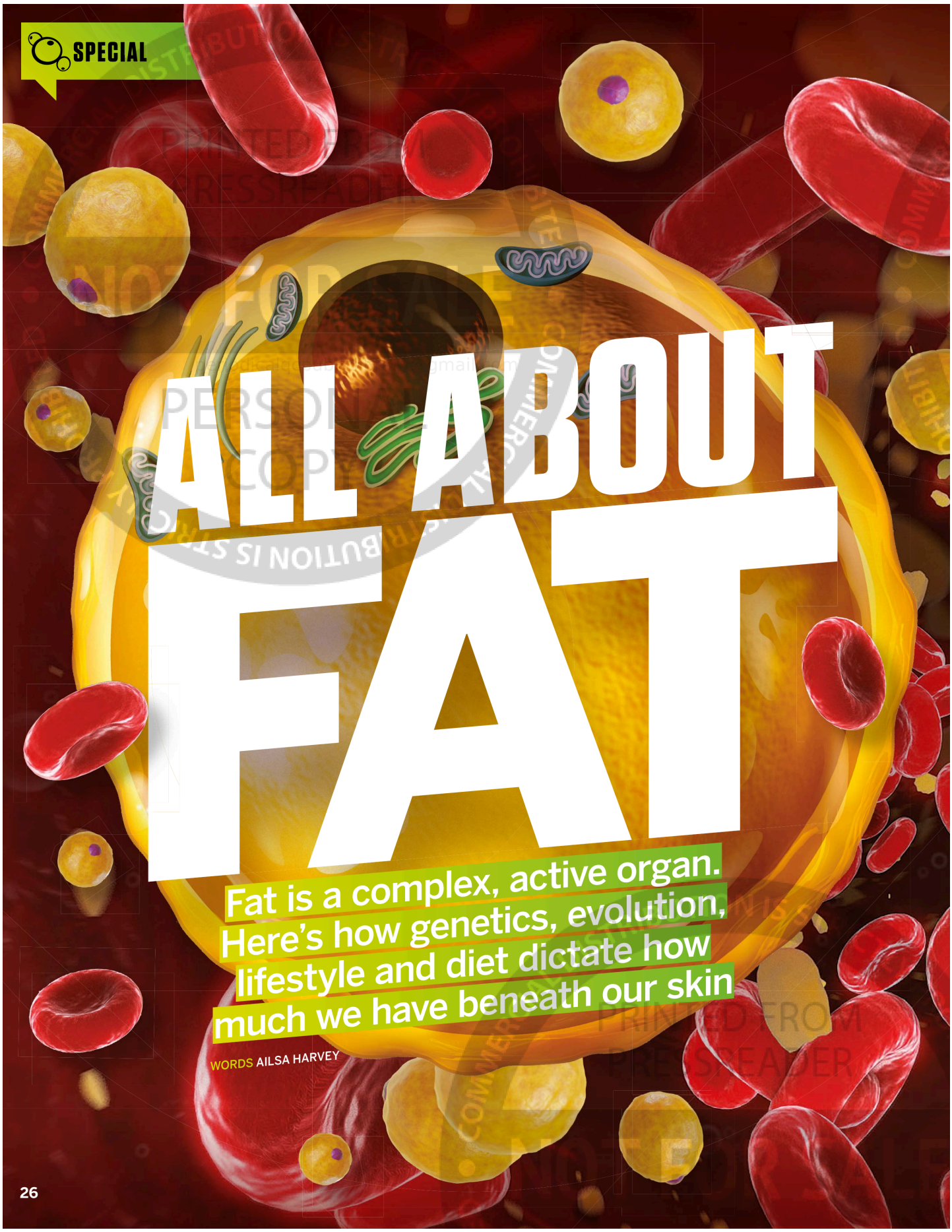
- Cells / Genetics





**DID YOU KNOW?** Around 30 per cent of your diet should consist of fat

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The word 'fat' has become a stigmatised slur, its importance being considered largely aesthetic over its biological purpose. In reality, there's more to fat than meets the eye, and there is much more to understand when considering fat health than just our lifestyle choices. Fat serves our bodies by providing energy to survive when food isn't accessible. Most people today rarely encounter a situation where food is hard to come by. Yet for our early human ancestors, fat tissue beneath the skin was a buffer between survival and starvation. Fat is broken down in the body into fatty acids, releasing energy for all the cells in your body to use. When your energy levels deplete, the body relies on fat as a backup. The organ is also an effective insulator, which helps regulate your body temperature.

**Did you know?**
Just 1 in 340 people carry the MC4R gene

Fat cells don't just remain passive, waiting for their moment of glory. Every day, fat tissue works to control essential biological functions. There are two types of fat: essential fat – which makes up the membranes of our bodies' cell building blocks – and non-essential, or storage fat. Storage fat is the fat referred to when acknowledging weight gain, as this tissue is stored beneath the skin. But storage fat also holds essential functions, such as releasing chemical messengers called hormones to interact with other organs. In doing this, the fat itself is responsible for managing its own levels. When you have eaten too much, fat sends a message to the brain that you don't need any more food, preventing too much extra body fat being added.

More than a billion people in the world live with obesity. By taking a closer look at the function of fat, the causes of fat gain and the pitfalls of unhealthy fat tissue, scientists can get closer to understanding the complexities of this organ and the broader causes of the obesity epidemic.

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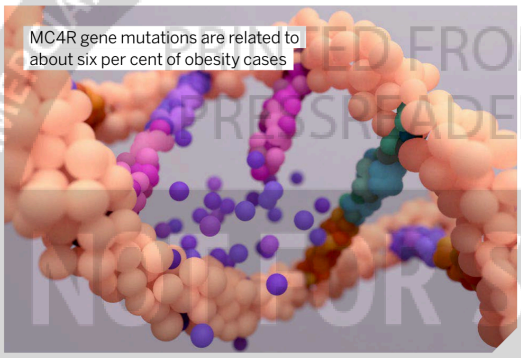
SPECIAL


MC4R gene mutations are related to about six per cent of obesity cases

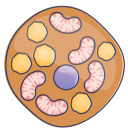
# DO YOUR GENES PLAY A PART?

Gaining and losing body fat isn't the same process for all people. Around half of the factors that result in excess fat storage and obesity are due to genetics. One of the genes that partly dictates the level of hunger a person feels is the FTO gene. This gene can either hold a high or low-obesity risk variant.

Research shows that if someone inherits a high-risk variant from each parent, their chance of developing obesity increases by 70 per cent. In the body of someone with the high-risk variant, a hunger hormone called ghrelin – responsible for telling your brain you're hungry – circulates at higher levels for longer after eating. Thus a person is more likely to continue eating and not feel as full.

Mutations in a gene called Melanocortin 4 Receptor (MC4R) also increase a person's fat storage. MC4R is responsible for producing a protein that informs the brain of how much fat has been stored. But when the gene isn't working as it's meant to, the brain interprets that the body hasn't stored enough fat when it has. This can make a person hold onto more fat than is required and healthy.

## TYPES OF FAT CELLS



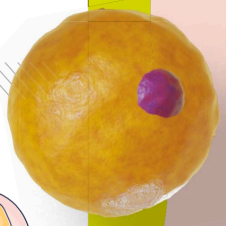
**BROWN**
Brown fat cells convert chemical energy into heat energy. They have more mitochondria, which are responsible for generating the energy to power cells.



**BEIGE**
A combination of white and brown fat. White cells become beige due to cold exposure or in the presence of certain hormones. As they become beige, the fat cells begin to burn more energy.



**WHITE**
These cells convert excess energy from food into molecules called triglycerides to store as fat under the skin.





## IMPACTING ORGANS

Where is fat stored and which type is harder to lose?

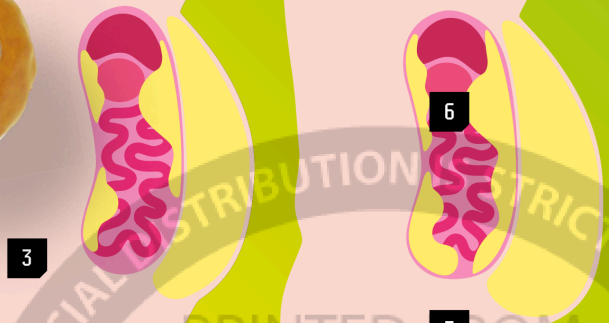
**1 HEALTHIER BODY**
In a healthy body, levels of visceral fat, which is stored around vital organs, are low. Usually, ten per cent of body fat is visceral fat.

**2 FATTY ORGANS**
Visceral fat is potentially harmful at higher levels. It's metabolically active, releasing hormones that impact the body's regular internal functions.




**3 OVERWEIGHT**
The body has begun to change shape due to subcutaneous fat. Visceral fat has accumulated, and this can cause issues such as insulin resistance – the hormone regulating blood sugar levels.

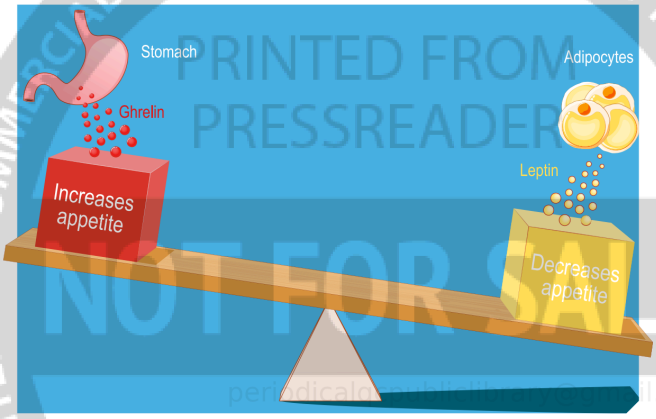
**4 SUBCUTANEOUS FAT**
This fat is stored directly under the skin. It is insulating, cushioning and a slow-burning energy reserve.




**5 OBESE BODY**
There is a high volume of subcutaneous fat, impeding mobility, and high visceral fat, impacting organs and increasing the risk of chronic diseases.

**6 ORGAN IMPACTION**
Excess fat around organs causes chronic inflammation and hormonal imbalances, preventing vital organs from functioning properly.

**DID YOU KNOW?** In 2022, one in eight people worldwide were obese




# HORMONAL INFLUENCE

Hormones are signalling molecules in the body that direct organs to carry out biological processes. This means they play a crucial role in fat storage and controlling how much and where fat is stored in the body. Some of the key players include insulin, leptin, ghrelin, adiponectin and cortisol.

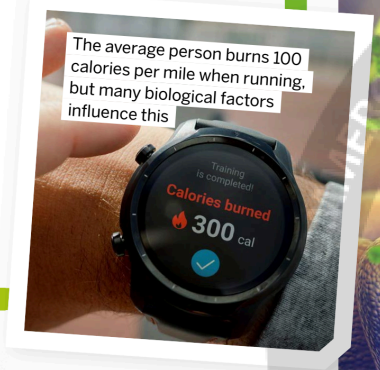
Insulin promotes fat storage. It's released when there are high glucose levels in the blood to signal the body to convert glucose into fat. The hormone glucagon, which is also released in the pancreas, works when glucose levels are low. It causes fatty acids to be released from fat tissue and converted into glucose for energy.

A hormone released by the fat tissue itself is leptin. This informs the brain of how much fat is stored, to reduce or increase your appetite accordingly.

In the stomach, ghrelin is released in higher volumes when the stomach is empty to make you feel hungry. Cortisol is a stress hormone that can result in more fat being stored in the abdominal area, while adiponectin works to break down fat. Adiponectin makes the body more sensitive to insulin, increasing the efficiency of breaking down fatty acids.

## ALL ABOUT ENERGY

**The central factors controlling fat levels in the body are your calorie intake and basal metabolic rate. Calories are units of energy which the body acquires through food consumption. The number of calories you eat directly impacts fat gain. Your basal metabolic rate is the number of calories your body needs to keep your body functioning. If you consume more calories than are used, you're in a calorie surplus. This means you have more energy than can be used. The extra is stored as fat. When you consume less calories than are demanded by the body, this causes the body to use up stored energy. It accesses calories from the fat carried on the body. Having some fat on the body serves as an essential energy reserve. Hormones help maintain an energy balance by creating feelings of hunger when energy is needed, giving you a desire for food.**



The average person burns 100 calories per mile when running, but many biological factors influence this





## FAT-CONTROLLING MICROBES

Microbes live throughout your body, from the surface of your skin to the inside of your gut. This army of microbes is called the microbiome, and it helps keep your body healthy. These microscopic organisms fight harmful germs, produce essential compounds like vitamins and break down food in the gut. Studies have shown that it also plays a significant role in regulating your metabolism and fat storage.

The prevalence of different beneficial microbes is influenced by your diet. For example, the more fibre you eat from fruit and vegetables, the more beneficial gut bacteria there are in the microbiome. These bacteria produce short-chain fatty acids to support the metabolism by burning fat and decreasing fat storage. Bacteria called firmicutes in the microbiome break down complex carbohydrates in food efficiently and result in more calories being extracted from food. Eating processed foods causes the microbiome to become imbalanced and ineffective, such as by producing too many firmicutes. High sugar and fat diets cause firmicutes to grow, extracting much more energy for the same consumption of food and encouraging excess fat storage.

**Did you know?**
Fat has around nine calories per gram


The human gut microbiota weighs 200 grams

© Alamy / Shutterstock

## 5 FACTS EXTERNAL FACTORS FOR GAINING FAT

**1 DIET AND NUTRITION**
Eating foods with high fibre, protein and healthy unprocessed fats helps regulate your metabolism and avoids excessive fat storage.

**2 PHYSICAL INACTIVITY**
You use energy when active. This reduces the chances of excess energy being stored as fat. Building strong muscles through physical activity also helps increase your basal metabolic rate.

**3 SLEEP PATTERNS**
Inadequate sleep can lower your metabolism and disrupt the balance of hormones that regulate appetite.

**4 STRESS LEVELS**
Being stressed increases cortisol levels, increasing fat accumulation. Stress can also cause you to crave calorie-dense and processed foods.

**5 AFFORDABILITY**
Processed foods, which are treated to be edible for longer, are usually cheaper. Higher accessibility to unhealthy foods increases their prevalence in people's diets.



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SPECIAL

**Did you know?**
Obesity has doubled since 1990

# CIRCULATION AND DISTRIBUTION

How does fat from your meal end up in adipose tissue?

**1 FOOD CONSUMPTION**
After swallowing food, the stomach churns the contents with digestive juices to begin to break down fat.

**2 EMULSIFICATION**
In the small intestine, bile salts are released from the gallbladder. The salts mix with the fat to break it into small droplets.

**3 LIPASE BREAKDOWN**
Digestive enzymes work on the fat droplets, reducing them to component fatty acids and monoglyceride – molecules containing one fatty acid and glycerol.

**4 INTESTINAL MUCOSA**
Fatty acids and monoglycerides are absorbed into the cells of the intestinal walls. Here the molecules are rearranged into triglycerides, molecules of three fatty acids.

**5 CHYLOMICRON**
When in the intestinal cells, triglycerides are combined with the waxy substance cholesterol and proteins called apolipoproteins to form fat-carrying particles.

**6 LYMPHATIC NETWORK**
The particles leave the intestine and enter the lymphatic system. This network of vessels transports fats to the bloodstream.

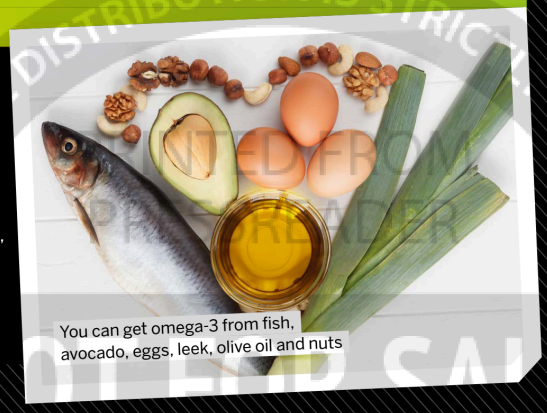
**7 BLOOD TRANSPORTATION**
In the bloodstream, chylomicron particles can be pumped in the blood to access tissue throughout the body. Here, the protein lipase breaks down the particles into fatty acids and glycerol again.

**8 CONVERSION AND STORAGE**
As fatty acids, the fat can be taken up by fat tissue. In the tissue cells, fatty acids are combined again to make triglycerides so that they can be stored until energy is required.

# HOW DO ORGANS USE FAT?

Fat is often associated with poor health and obesity. But obesity only concerns the excess stored fat. The body also contains essential fat that is mandatory to a healthy body. The brain, for example, is about 60 per cent fat, and those who try to cut out fat from their diet can do more harm than good. The brain relies on fats such as omega-3, omega-6 and other fatty acids to keep brain cells healthy and insulated.

The small intestine in the digestive system uses fat to make the digestive fluid bile, while the liver processes and stores fat and the heart uses fatty acids as a primary energy source to keep its muscles contracting and pumping blood around the body.



You can get omega-3 from fish, avocado, eggs, leek, olive oil and nuts

**DID YOU KNOW?** Fat is the main source of energy for a baby in the womb

# MALE AND FEMALE DISTRIBUTION

How is fat stored differently in men and women's bodies?



**1 MALE**

Active men's bodies have between 14 and 17 per cent body fat. Men are more likely to store fat in the abdomen and waist areas. While women have a higher percentage of subcutaneous fat, men are more likely to develop visceral fat in the abdomen area, which can feel firmer as it is located further from the surface.

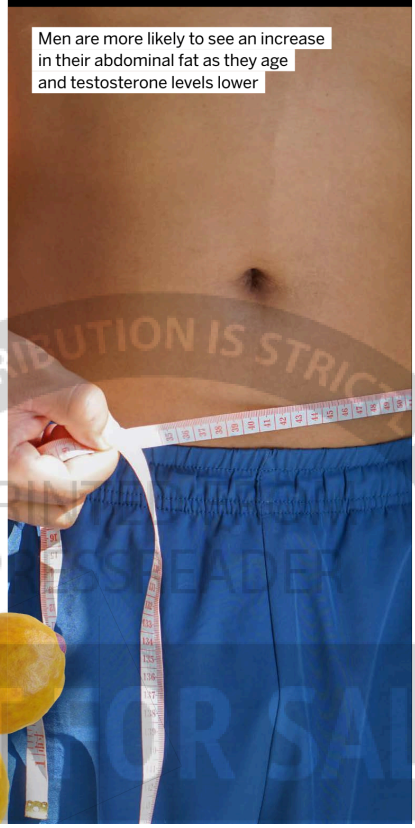
**2 FEMALE**

An active woman has around 21 to 24 per cent body fat. This is largely to serve reproductive purposes. When a woman becomes pregnant, she needs extra fat reserves to provide energy to a growing baby. To support this role, more fat is stored in the buttocks, hips, lower abdomen and thighs than in men's bodies. When losing body fat, these are the last areas to use up their energy.

## SHAPED BY HORMONES

The difference in male and female fat distribution is mostly dictated by the primary sex hormones released in their bodies. Both men and women produce the hormones testosterone and oestrogen, but women have higher levels of oestrogen, compared with men who have higher levels of testosterone. Testosterone reduces belly fat but favours the accumulation of abdominal fat over thigh fat in men. The hormone also helps build muscle mass. With more muscle mass, men require more energy to maintain fat tissue, reducing the levels of excess fat that are stored.

Meanwhile, in women oestrogen directs fat storage to the lower body, resulting in a 'pear-shaped' body. This hormone also encourages the body to store fat below the skin, rather than around organs. During pregnancy, this makes fat more readily available.



Men are more likely to see an increase in their abdominal fat as they age and testosterone levels lower

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## WHEN DO YOU NEED MORE FAT?

From childhood to late adulthood, the human body undergoes many physiological changes and hormonal variations. As a result, how and where the body stores fat tissue changes throughout the course of your life. When you are born, your infant body needs a higher percentage of body fat as it rapidly grows and develops, relying on these energy stores. By six months old, babies can have between 20 and 25 per cent body fat.

Some of the significant changes in later life include puberty, when hormone levels are drastically altered. This is when testosterone and oestrogen begin to alter body fat distribution. For women during pregnancy, more progesterone is released. This hormone increases appetite and increases the fat content in breasts, thighs, hips and the abdomen. Later, when adults age, they generally develop a lower metabolic rate. This causes people to gain fat more easily from their late 30s.



40 per cent of a one year old baby's calories should be from fat



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SPECIAL




# BIOLOGY OF OBESITY

How does obese fat tissue compare to normal fat tissue?

**1 T CELL**
These immune cells are present to prevent infection and keep tissue functioning healthily.

**2 NORMAL FAT TISSUE**
Generally, normal fat tissue is balanced in structure, with smaller fat cells and fewer immune cells.

**3 OBESE FAT TISSUE**
Here, the number and size of fat cells increases and the tissue becomes inflamed.

**7 NEUTROPHILS**
More of these cells create further inflammation. They are white blood cells that serve as the first responders of the immune system.

**5 M2 MACROPHAGE**
These cells lower inflammation by repairing fat tissue.

**4 T CELL INCREASE**
In obese tissue, more T cells are present as the enlarged cells cause stress in fat tissue. The T cells instigate inflammation.

**8 NECROTIC TISSUE**
The high stress and inflamed environment increase the abundance of dead cells and cell turnover.

**"More than a billion people in the world live with obesity"**

**6 MULTIPLE MACROPHAGES**
There are many more M2 macrophages in obese tissue to counteract inflammation. But too many can cause an excess of fibrous connective tissue to form, affecting insulin sensitivity.

**9 B CELLS**
Inflammation attracts more antibody-producing white blood cells in obese tissue. Antibodies are protein markers that target stressed cells and foreign substances in obese tissue.

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**DID YOU KNOW?** The average man needs 2,500 calories daily, and a woman 2,000

Did you know?
450 grams of fat has a larger volume than muscle

# ENERGY STORAGE EVOLUTION

How human lifestyle changes have impacted how our bodies deal with fat



### FOOD SCARCITY (2.5 MILLION TO 12,000 YEARS AGO)

Early humans lived as hunter-gatherers, making food availability inconsistent. Fat was stored to be used as a reserve of energy during periods with no food.



### AGRICULTURAL REVOLUTION (12,000 YEARS AGO)

As communities developed farmland and grew their own food, there was more control over food availability. More consistent food and less active means of acquiring it caused increased fat storage.



### EARLY CIVILISATIONS (5,000 YEARS AGO)

As people began to trade goods, there was more diversity in foods available for those who could afford it. Class systems in societies facilitated both obesity and famine at the top and bottom.



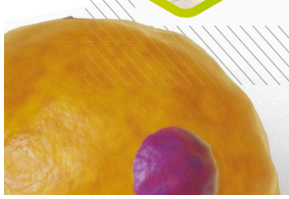
### INDUSTRIAL REVOLUTION (18TH CENTURY)

This led to the rise of more processed foods, while machinery reduced the physical activity needed to secure food. This was the beginning of cheaper, calorie-dense foods.



### MODERN LIFESTYLE (20TH CENTURY TO THE PRESENT)

Today there is an overabundance of processed foods, feeding the current obesity epidemic.





# LIESBETH VAN ROSSUM

Internist-endocrinologist van Rossum of Erasmus University Medical Centre and the European Society of Endocrinology explains the complexity of causes behind the obesity epidemic



© Liesbeth van Rossum

**Why do you think fat is misunderstood?**
Many people do not know it's an organ communicating with your brain and other systems. This organ of fat can be sick, just like a liver or a heart can be sick. If you understand the function of fat, then you can understand why it's bad to have too much or too little. Obesity is about sick fat mass. One of the painful things about this is that the lack of knowledge also leads to stigma. I see my patients suffer a lot from discrimination based on weight.

**How does obesity impact your body after losing weight?**
After weight loss, some immune cells are still different. It's like a scar in the immune system. It's called metabolic memory and it's when your body knows that you once had obesity, and after weight loss it will try to regain fat to reach your older, higher weight somehow.

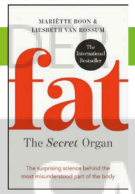
**How long does metabolic memory last?**
There are studies that show only short-term disturbances of just a couple of weeks, then there have been studies showing that even more than a year after stopping a diet these hormones are still disturbed. We don't know whether it's ever restored, but there are indications that some of the systems are being disturbed long term.

**Why do we choose unhealthy foods?**
If you're stressed, you're much more prone to chase chocolate, although you know a salad will be better. We make many food decisions a day. About 20 minutes after eating, you start to produce satiety hormones and they give you a sense of fullness. Your hedonic system concerns other hormones. That makes room for dessert when you're full. And that's because your reward system releases feel-good hormones. The third system to decide your food choice is your cognitive system. That's very conscious, but a lot of your food choice isn't about self discipline, it's about unconscious systems. There are many ultra-processed foods, so we are already prone to eating more chocolate, for example, then you see the advertisements about chocolates, and your biological systems do respond to that.

**How do you think endocrine research can benefit the obesity epidemic?**
I'm fascinated by all the hormones that are produced by fat cells and other organs that all influence each other. All over the world there are new discoveries about the role of hormones being produced by fat mass and other organs that have influence on fat mass. We need a lot more research to really understand all the processes, but what we do understand is that too much fat can be a hormonal disease. Hormones don't always induce it, but the hormones, genes and lifestyle combination induces obesity. Often we try to treat all the hormonal systems fat mass disturbs, but we should treat the fat mass itself. We also know there are endocrine-disrupting chemicals in products like the coffee cups we drink from, children's toys, furniture and cosmetics. People with obesity are more vulnerable to them because these chemicals love fat. They can enter fat easily and stay there, and this may impair weight loss. The more we know about the complexity of fat, the more effective we can be at treatment at an individual level. And when we want to solve the whole epidemic, we need to work on prevention too. If you know how hard it is to lose weight, then you know how important it is to prevent people from becoming overweight and obese.

## Fat: the Secret Organ

**In van Rossum and Mariette Boon's book, the authors break down some of the most recent scientific findings about fat. The book, which has been translated into 11 languages, explores more fat misconceptions and contains expert advice to understand your fat health better.**

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