Dr. Max Nieuwdorp

THE POWER OF HORMONES

The new science of how hormones shape every aspect of our lives

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DR MAX NIEUWDORP

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For my parents(-in-law): Willemijn, Hannah, Matthias and Leah

For a list of the various hormones mentioned, see pages 331–2.

Foreword

> *I was (and am) unsure about how I am related to my old self, or to myself from year to year. The hormonal profile of an individual determines much of the manifest personality. If you skew the endocrine system, you lose the pathways to self. When endocrine patterns change, it alters the way you think and feel. One shift in the pattern tends to trip another.*
>
> Hilary Mantel, *Giving Up the Ghost*[1]

This quote from Hilary Mantel about her endocrine disorder endometriosis highlights the extent to which hormonal changes affect people's self-image. It also captures what I love about being a doctor. In the consulting room, you get a glimpse into a patient's life and the way illness affects their character.

I became a doctor because a lot of my relatives worked in the healthcare sector. Although I was more attracted by a career as a diplomat or historian while I was at secondary school, fate (and the Dutch university system) decided otherwise, and I went off to study medicine in Utrecht, like my relatives before me.

Besides a fantastic student life, where I made friends for life and found the love of my life, this course turned out to be a brilliant move. Contrary to my expectations, medicine encompassed so much more than writing prescriptions or performing operations. I learned how to conduct laboratory tests and was inspired when I saw how they helped doctors understand underlying diseases and their associated symptoms – symptoms we then hear about from patients in our consulting rooms.

It was the interactions with patients and the intimacy of the consulting room that led me to study internal medicine at the end of my course. Science played a role too, because there was still so much to be discovered in the field of hormones and gut bacteria. Spurred on by the fact that virtually my entire family suffers from some sort of endocrine disorder – from diabetes to thyroid disorders and even adrenal gland tumours – I decided to specialise in endocrinology, the study of hormones.

After working in this field for almost twenty years – motivated by questions my patients had asked me over the years and to which I didn't always have an answer – I came up with the idea of writing this book. Not only to make the fascinating endocrine system a bit more accessible to anyone who might be interested, but also to put the power of hormones into perspective.

The title of the original edition, *Wij zijn onze hormonen* (literal translation: 'We are our hormones'), refers to the fact that hormones are the conductor of our body's orchestra. It's also a nod to the fantastic book, *We Are Our Brains*, written by my colleague Dick Swaab. While our brain is central to all the decisions and choices we make, hormones, in turn, influence how the brain functions. A hormonal imbalance can play havoc with both our personality and our day-to-day functioning. I recall, for example, a female patient who became sexually disinhibited as a result of an overactive thyroid and ended up in bed with every male patient. It was only when her thyroid was surgically removed that she gradually returned to her old self.

This book was written in the early mornings and late evenings, because my days were filled with caring for patients, carrying out research and management, as well as meeting the demands of my personal life: a family with young children and a wife who works full-time as a midwife. Despite that, writing proved to be a fantastic source of energy – energy that was badly needed during the COVID-19 pandemic, when I treated people, but also watched them die, on hospital wards.

The Power of Hormones is a mix of history and medicine in the broadest sense of the word. I didn't want to write a medical handbook; rather, I tried to confront pseudoscientific claims about the use of hormones as the answer to common complaints. I certainly don't want to suggest that we are slaves to our hormones (or our brains). There is always an interaction between environment, body and

mind. Hormones might cloud your ability to make decisions, but they cannot absolve you of responsibility for your own actions.

By writing this book, I have gained an even greater respect for our incredible endocrine system. As doctors, we shouldn't mess with it too much, but we shouldn't become complacent either. We must continue to strive for a deeper understanding of these fascinating bodily substances and keep searching for better treatments. Because, as the famous therapist Salvador Minuchin put it so eloquently: 'Certainty is the enemy of change.'

Amsterdam, August 2022

Introduction

In 2001, I worked in a rural hospital in Pretoria, South Africa. Pregnant women from the townships – out-of-town suburbs left over from the time of apartheid – would come to the rudimentary maternity hospital in the early stages of labour. Lying on flattened cardboard boxes on the grass outside the building, they would ride out their contractions until the time came to swap the boxes for hard beds hidden behind flimsy curtains inside and delivery could begin. On average, there were about twenty women under my care. Several children would be born each night and I would spend my time dashing between the rooms. One of the children, a girl called Muna, was brought to see me in the outpatient clinic a short while later with stunted growth. She barely responded to attempts to communicate with her and had a puffy face and delayed reflexes. The thyroid hormone in her blood was extremely low, so I decided to give her thyroid hormone tablets immediately to address the deficit.

When I visited the same maternity hospital years later while back in South Africa for a conference, a nurse told me that Muna was severely disabled and cared for at home by her grandmother. Muna's first few months of life without any treatment had taken their toll. She would never be able to live independently and had an increased risk of premature death due to pneumonia or bedsores.

Muna's story shows how important hormones are for our development. We simply cannot do without these substances our bodies make that direct organs and tissues, via the bloodstream, to regulate all sorts of bodily functions. At first, an unborn child is dependent on its mother's hormones. Only after three months in the womb does a foetus develop the cells and organs needed to effectively

produce hormones itself. The thyroid is formed in the first trimester of the pregnancy, which illustrates just how crucial this organ is for our existence; indeed, the thyroid hormone is involved in many of our bodily processes.

Due to a dysfunction in the first phase of pregnancy, Muna's thyroid gland failed to develop and she ended up with a congenital deficit of thyroid hormones known as congenital hypothyroidism (CH). In the Netherlands, approximately eighty children are born with this disorder each year. It is not easy to diagnose this condition in newborn babies, and there can be major consequences if it is diagnosed too late, as was the case with Muna. This insight led Hans Galjaard, who was an emeritus professor of human genetics at Erasmus University Rotterdam, to put routine screening for congenital conditions in the Netherlands on the political agenda. Thanks to his efforts, Dutch hospitals and maternity units have been taking blood samples from all newborn babies since 1974 by means of a heel-prick test. Partly motivated by the fact that his brother died of a congenital condition at a young age,[1] Galjaard kickstarted these tests, which now screen for thirty-two congenital diseases, after exhaustive political lobbying. As Galjaard put it: 'Better to prevent than not be able to cure.'

As a result, thousands of children have been spared Muna's fate. I see them in my clinic as lively thirty-somethings, whose lives have been changed for ever thanks to that one thyroid tablet per day (and Galjaard's forward-looking view).

A brief history of hormones

The term 'hormones' was coined by the British physiologist Ernest Starling and his brother-in-law William Bayliss in 1902. They studied how our digestive system works and how food can be broken down and absorbed by certain substances in the intestine.[2,3]

Two years later, their Russian colleague, Ivan Pavlov, won the Nobel Prize for Physiology or Medicine for his research into the digestive system.[4] Pavlov, chiefly known for his research into conditioning and after whom the acclaimed Pavlovian response is named, used experiments to demonstrate the role of the nervous system in our digestion. But Bayliss and Starling found that digestion also took place in laboratory animals with damaged nervous systems due to the release of

special substances into the blood from neighbouring glands. One of these substances was what they called *secretin* (from the verb 'to secrete') – the first of a now extensive group of substances that control our lives in invisible yet far-reaching ways.

It was also Bayliss and Starling who proposed the term *hormone* – Ancient Greek for 'impetus' or 'to set in motion' – as a collective name for these substances. Hormones are signalling molecules created by endocrine (hormone-producing) glands. These molecules travel via the blood and other bodily fluids to their destination – specific cells or organs – where they carry out their work. Most hormones have a central regulatory function; they can either set processes in motion or inhibit them. They also interact with each other.

Our endocrine system's headquarters are found in the centre of the brain, right behind our eye sockets. That's where the hypothalamus and the pituitary gland are located, the size of a strawberry and a pea respectively. Both groups of specialised nerve cells form part of our emotional brain, the limbic system (which you will read more about in Chapter 5). They control both our nervous and our endocrine systems like army generals, keeping a close eye on all the troops.

The effects of these important signalling substances had, however, already been observed fifty years before Starling and Bayliss. In an experiment carried out in 1849, the German scientist Arnold Berthold compared castrated male chickens (capons) with their non-castrated brothers, and found that the first group experienced physical and behavioural changes.[5] For example, the capons were unable to crow. What was striking was that when the testes were restored (by re-implantation or transplantation), and thus the production of the hormone testosterone, the chickens were able to crow again. Similar experiments continue to capture the imagination of writers and scientists to this day, not least because they allude to the existence of an elixir for 'eternal' youth.

The opera *A Dog's Heart* by the composer Alexander Raskatov is a wonderful example of this. Inspired by a novella by Mikhail Bulgakov from 1925,[6] the opera tells the story of the street dog Sharik, who is implanted with the pituitary gland and testicles of a notorious criminal. The animal then turns into Sharikov, a vulgar, destructive human whose behaviour and choices fall prey to his hormone-

driven urges. Only a second operation is able to offer salvation to this testosterone-riddled dog...

References to hormones can be found in older literature too, if we read between the lines – for instance, in the Old Testament. Although techniques to demonstrate the presence of hormones in blood did not exist in those days, their 'momentum' is described: 'the life of flesh is in the blood' (Leviticus 17:11). Certain characters in the Bible probably had congenital hormonal conditions, such as the giant Goliath, who likely had excessive growth hormone. The Egyptian god Bes's dwarfism and Cleopatra's irritability and great energy could also very well have been caused by abnormal thyroid glands.

Let's return to the fascination with the male hormone for eternal youth. In 1889, the 72-year-old Mauritian-French neurologist Charles Brown-Séquard injected himself with testicular extracts from animals to see what would happen.[7]

> I have made use, in subcutaneous injections, of a liquid containing a small quantity of water mixed with the three following parts: first, blood of the testicular veins; secondly, semen; and thirdly, juice extracted from a testicle, crushed immediately after it has been taken from a dog or a guinea-pig.

Although the professor was relatively healthy for his age, before he began experimenting on himself he regularly complained of fatigue after a hard day's work, suffering from heartburn and painful joints and muscles. The latter was likely wear and tear as a result of osteoarthritis, which is very common among older people.

In May and June of that year, Brown-Séquard injected himself as many as ten times every day. Almost immediately, the vitality and energy seemed to return to his body; he felt stronger and could run upstairs again. His biceps seemed to increase significantly in circumference, he no longer felt fatigued and he is said to have regained his virility. Testosterone (more about this in the following chapters) is, however, a fat-soluble hormone, and given the fact that Brown-Séquard's injections were water-based, it is perfectly possible that a placebo effect was at play here.[8]

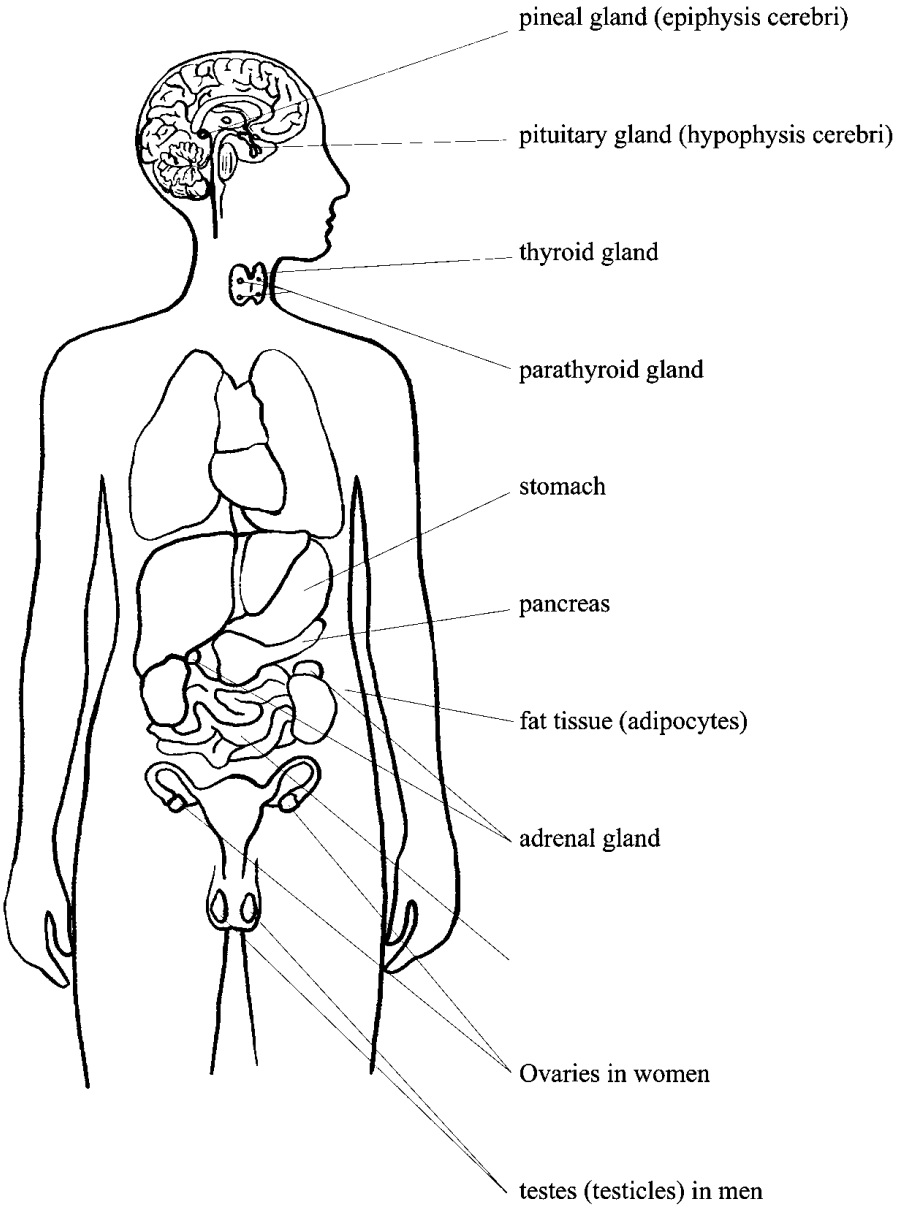
This and other cases have greatly accelerated our understanding of hormones over the past century. Thanks to technological progress, hormones can be

extracted from animal material and injected into humans and other animals to observe their effects. This has not only led to many new, important insights for medical science – resulting in several Nobel Prizes between 1920 and 1930 for the discovery of today's best-known hormones oestrogen (female hormone), testosterone (male hormone) and progesterone (which plays an important role in the implantation of the embryo in the lining of the womb) – but it has also had major social, societal and economic effects. The development of the contraceptive pill in the 1950s, for example, had a tremendous impact on the emancipation and empowerment of millions of young women. Successful hormone treatments for numerous conditions have reduced the general burden of disease and simultaneously led to huge opportunities for the pharmaceutical industry.

Unfortunately, our hormone helpers haven't always cut a good figure. Since the publication of Rachel Carson's *Silent Spring* in 1962 – in which the American biologist drew attention to the disastrous impact of agricultural pesticides on the environment, the quality of our food and our own bodies – we have a better understanding of the extent to which these toxins can interfere with our hormonal balance.[9] To cite one unfortunate example: injecting patients with growth hormone taken from the brain glands of human corpses resulted in many of them contracting the infectious and fatal Creutzfeldt-Jakob disease (the human equivalent of mad cow disease).[10] The medication DES, a synthetic oestrogen widely prescribed to pregnant women in the Netherlands in the 1950s and 1960s to prevent miscarriages, also had major consequences for the health of their daughters, including an increased risk of cancer and infertility; it was found to even potentially lead to abnormalities in their grandsons.[11]

As with Muna, the baby who ended up with intellectual and physical disabilities as a result of defective thyroid hormone production, our health and that of our offspring is highly dependent on the right hormonal balance. In this book, I will explain the influence of the various hormones and the relationship between them throughout the different stages of life – from the cradle to the grave. I will also delve deeper into the consequences of a lack or excess of hormones and the sometimes destructive effect of these powerful endogenous

substances on our mental and physical well-being. I hope, like me, you will become fascinated by the wonderful role that hormones play in our bodies and our lives.


pineal gland (epiphysis cerebri)
pituitary gland (hypophysis cerebri)
thyroid gland
parathyroid gland
stomach
pancreas
fat tissue (adipocytes)
adrenal gland
Ovaries in women
testes (testicles) in men

Our endocrine glands and their functions

Pituitary gland (hypophysis cerebri) – our body's conductor; quantity: 1, size 1 × 1 cm; looks like: a pea. Produces growth hormone, prolactin, luteinising hormone (LH), follicle-stimulating hormone (FSH), adrenocorticotropic hormone (ACTH) and antidiuretic hormone (ADH), also known as vasopressin. Function: instructs other glands to produce hormones.

Pineal gland (epiphysis cerebri) – quantity: 1, size 0.5 × 0.5 cm; looks like: a pine cone. Produces melatonin. Function: determines circadian rhythm and sleep quality, inhibits the production of sex hormones until puberty.

Thyroid gland – quantity: 2, size 5 × 3 cm; looks like: the wings of a butterfly. Produces T4 and T3 (via TRH and TSH from the pituitary gland); controls metabolism, heart rate and body temperature.

Parathyroid gland – quantity: 4, size 0.5 × 0.5 cm; looks like: a grain of rice. Produces parathyroid hormone (PTH), important for bone quality and calcium regulation.

Stomach – quantity: 1, size 30 × 10 cm; looks like: an inverted pear. Produces ghrelin (the hunger hormone) and gastrin. Function: digestion.

Pancreas – quantity: 1, size 14 × 3 cm; looks like: a flat pear. Produces insulin and glucagon. Function: controls sugar level and fat metabolism.

Fat tissue (adipocytes) – present throughout the body, especially abdominal area, size varies; looks like: semolina pudding. Produces leptin and oestradiol (from testosterone). Function: energy supply, elasticity of the skin.

Adrenal gland – quantity: 2, size approx. 1 × 1 cm; looks like: a thimble. Produces aldosterone, cortisol, oestrogen, DHEA (dehydroepiandrosterone) and testosterone under the influence of CRH (corticotropin-releasing hormone) from the hypothalamus and ACTH from the pituitary gland. Important for: blood pressure, maintaining sugar and salt levels, immune system and libido. The adrenal medulla produces (nor)adrenaline, important for the stress response.

Ovaries in women – quantity: 2, size 5 × 3 cm; look like: almonds. Produce oestrogen, progesterone and testosterone under the influence of GnRH (gonadotropin-releasing hormone), FSH and LH via the pituitary gland. Function: menstrual cycle, breast development, reproduction, bone mass and bone quality.

Testes (testicles) in men – quantity: 2, size 4 x 5 cm; look like: eggs. Produce testosterone. Important for: sperm, reproduction, sexual desire, muscle mass, beard growth, bone mass and bone quality.

Duodenum – quantity: 1, size 20 x 25 cm; looks like: a bicycle tyre. Produces cholecystokinin (CCK), serotonin, glucagon-like peptide (GLP-1). Function: digestion.

1

First the Egg, Then the Chicken

Pregnancy and Birth

Today I am seeing Anna, an elegant 35-year-old woman, in my outpatient clinic. Anna and her boyfriend have come for a consultation because she is struggling to get pregnant. She hasn't had a period for two years either, even though she hasn't had a coil for any of that time. Her menstrual cycle was normal during puberty but became irregular when she started her law studies in her late teens. Other doctors such as her gynaecologist haven't found any abnormalities and the psychiatrist ruled out anorexia nervosa as a possible cause. Anna looks slightly embarrassed when she tells me she's a high achiever: a perfectionist, but with low self-image. She often feels inferior to other women and compensates for this by throwing herself into her work. She has been seeing a psychologist for the past year, but doesn't feel this is helping much.

Anna explains that she is under 'some' pressure in her job as a lawyer in Amsterdam's business district. She works twelve-hour days during the week and usually works one full day over the weekend too. It is therefore hardly surprising that she isn't sleeping well – just four to five hours a night. Because she wants to maintain her lean figure and look good, she hits the gym hard five times a week under the guidance of a personal trainer.

My examination doesn't bring up any particular issues, so during a subsequent consultation I unfortunately have to tell her that I don't have an immediate

solution to her absent menstruation. However, Anna and her boyfriend haven't been sitting around doing nothing. After searching online, they decided to register with a fertility clinic to have Anna's eggs frozen. This will put them in a better position to plan a potential pregnancy.

In the medical world, we refer to cases like this as 'unexplained infertility', probably caused by the psychosocial stress of our western lifestyle with its high efficiency and pressure to achieve. Unexplained infertility is a source of despair for many couples. If stress is the issue, the simple solution is: eat more (i.e. maintain a normal weight) and relax more (reduce stress).

Much has been written about this subject online and this phenomenon has been known about in the animal world for some time. Female mammals that play a subordinate role within the group may fail to ovulate.[1] Research has shown that the status of a female mammal and the resulting stress experienced significantly affects her fertility. High-ranking female chimpanzees not only have more infants, but those infants also have a better chance of survival, probably as a result of better access to good nutrition.

The American primatologist Sarah Blaffer Hrdy studied langur monkeys in the north-west of India.[2] In temple gardens, people serve this species the most delicious meals. Compared with their counterparts in the Indian jungle, these privileged langurs have twice as many young, a surprising number of which are twins.[3] Having offspring is a costly exercise that requires a lot of energy, so nature will only permit this if enough food is available over a sustained period of time. It's as if the species has 'learned' when it is safe to have twins – a subconscious process.

Less is known about how this process works in humans, but we do know, for example, that more girls than boys are born after a period of high mortality in women. The cause of this imbalance between the sexes is unclear, but environmental factors likely play a role. It has been known for a long time in the field of economic sciences, for example, that relatively more male babies are born during a war, probably to restore the balance between the sexes.[4] In short, the interplay between environment, nutrition, psychosocial stress and the functioning

of our reproductive organs is complex. And although I wouldn't like to compare Anna to a chimpanzee, her story also shows that our physical and mental health are closely intertwined – a good starting point to demonstrate how our hormones work.

In this chapter you will read about the role hormones play in pregnancy and birth: in the development of egg and sperm cells, in getting pregnant, in the baby's sex and the mother's immune system, and in both the physical and mental well-being of the mother during and after childbirth. And finally, about hormonal changes in expectant fathers.

Hormones, reproduction and environment

Hormones play a key role in the creation of new life. This is probably the single most important function hormones have in our existence; there is no new life without hormones. They work together meticulously – and miraculously – in a complex network of substances that stimulate and inhibit each other. By doing so, they not only ensure that egg and sperm cells are created, but also that the meeting between the egg and sperm happens at the right place and the right time. This process doesn't only take place low down in the abdomen. The endocrine system controls our body from deep within our brain – much like a mobile network with several transmission masts.

Reproduction therefore starts in your brain; the pituitary gland and the hypothalamus are the control centres of your endocrine system (as well as your nervous system). From puberty onwards, the hypothalamus in men *and* women produces GnRH (gonadotropin-releasing hormone).[5] This causes the other endocrine gland, the pituitary gland, to produce FSH (follicle-stimulating hormone) and LH (luteinising hormone). LH triggers ovulation and enables a fertilised egg to implant in the uterus. Both hormones enter your bloodstream, after which they travel to your gonads (testes or ovaries). Here, they stimulate the production of sex hormones that help make reproduction possible.