**Anita Kåss: The Immune Mystery**

**(Mamma er en gåte)**

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**Chapter SYNOPSIS**

**Prologue**

Doctor and researcher Anita Kåss is waiting to be welcomed onstage, about to appear on Scandinavia’s biggest talk show. Millions of viewers will hear about how she landed the biggest deal with a global pharmaceutical company in Norwegian history – and has possibly discovered a new treatment for rheumatoid arthritis.

The reader is given an initial insight into how our amazing immune system works, as well as the possible consequences of errors in this system – the autoimmune diseases. These illnesses affect tens of millions of people, and represent some of our biggest health problems. Rheumatoid arthritis, coeliac disease, multiple sclerosis, ankylosing spondylitis, psoriasis and type 1 diabetes are just some of the over one hundred diseases that stem from a misunderstanding within the immune system.

**Beginnings**

Anita is born in Liverpool in 1979, and her birth proves to be the start of years of suffering for Anita’s mother and the family as a whole. The birth triggers rheumatoid arthritis in Anita’s mother, who over the following years becomes increasingly ill. This first chapter describes the tenderness and love of a childhood spent in a home overshadowed by illness.

When Anita is thirteen years old, her mother dies of the disease. At the funeral, Anita stays in the background, taking a volume of the encyclopaedia from the shelf and starting to read about rheumatoid arthritis. She decides to become a researcher in order to find out why her mother became ill.

**The master and a clue**

Anita enrols to study medicine. During her practical training she meets her mentor, Doctor Roger Bucknall, and describes a fumbling start to her studies with blunders and bottomless curiosity. The reader learns a little about the history of rheumatoid arthritis, and just how serious the disease can be.

Over the course of her medical training, Anita meets a number of patients who describe how they became ill after giving birth, just as her mother did. Could the sex hormones be the key to better understanding the disease?

Around this time Anita also meets Robin, a Norwegian man, and the couple soon marry. Then Anita becomes pregnant, which raises the question: is rheumatoid arthritis an inherited disease? Should Anita be nervous now that she is pregnant, since her mother became ill following childbirth? To answer this question, Anita takes us on her childhood travels to India, her parents’ homeland. Using simple examples, she illustrates how autoimmune diseases arise through the interplay between a person’s genes and their environment.

**The lonely researcher**

Anita drives out of Liverpool in an old red VW Golf, with her daughter in the back seat and three suitcases in the boot. She’s on her way to catch the ferry – to Norway and a new life. There, she is offered an irresistible position in an internationally renowned research environment in Oslo, but turns the job down. The position would require her to give up her own project and the pursuit of an answer to the burning question of rheumatoid arthritis – something she is unwilling to do. Her salvation is a small, private hospital just outside the capital, where she starts her daring project, seemingly with little chance of success.

The early stages are difficult, with insufficient funding and many hours spent doing lonely work in a new and unfamiliar country. But suddenly things improve. Anita receives additional funding and throws herself into her work, day and night. But when her mentor from Liverpool, Roger Bucknall, comes to visit, Anita is reminded of just how much she has sacrificed – and the chances that she’s taking with her career.

**The body at war**

Anita provides a pop science introduction to the immune system – the body’s armed forces. The body is home to several hundred billion immune cells, and a system malfunction can be fatal. What is an autoimmune disease, and why do such diseases occur? This chapter provides an accessible overview of the clues followed by researchers.

Anita receives the results of her first study, which come as a surprise. She starts to realise that this might be the start of something big.

**The female diseases**

Around eight out of every ten patients suffering from autoimmune diseases are women. Might the sex hormones be a critical piece of the puzzle? The reader is given a simple introduction to the importance of the endocrine system, before being introduced to the protagonist in in Anita’s research story: GnRH – a tiny hormone in the brain, which despite its modest size is the actually the main hormone involved in ensuring the survival of the human race. Anita wonders whether this hormone might be an important driving force in the significant inflammation caused by rheumatoid arthritis.

At the airport on the way to a conference in the USA, Anita puts a new idea to her boss. She wants to make a bold attempt to trial a medicine that has never before been tested on autoimmune diseases. Should they take a chance on blocking GnRH, a central hormone in the brain, in the hope that this will improve their patients’ conditions?

**Going against the grain**

Anita is met with scepticism from other researchers, and has to battle against her own insecurities. Doubt gnaws away at her. In a last desperate attempt to find encouragement to continue her work, she grabs the phone and calls a Nobel prize winner in medicine.

**A Nobel prize winner answers the phone**

Andrew Schally discovered the brain hormone GnRH in the 1960s – a groundbreaking discovery. This is the hormone Anita wants to block in her patients in an attempt to treat rheumatoid arthritis. Schally received the Nobel Prize for Physiology or Medicine in 1977, and Anita finds out that he is still alive. To her great surprise, the legend answers her telephone call, and this is a turning point for Anita – Schally believes. in her idea.

**Digging deep in the rubbish**

Anita has to overcome several obstacles in the work to set up a successful study, but she finally has enough patients to get started. Some of them seem notably better following treatment, and the results confirm that Anita is on to something. After her research is widely reported on TV, Anita is contacted by a company that helps Norwegian researchers to commercialise their research. The company makes a bold suggestion – to test the medicine over a longer period of time on a small group of test patients, to see if it has an even greater effect.

**The experiment**

Anita trials the medicine on the first two test patients. The results are astonishing – their inflammation is dramatically reduced. The first patient is able to return to work; the second goes from being bedridden to taking a mile-long cycling trip with friends.

Anita can hardly believe the results. She trials the medicine on other diseases, such as multiple sclerosis and lupus, and here too several patients experience astounding improvements. Anita starts to truly believe that she might have made an important discovery.

**The billion dollar companies arrive**

Lab work is necessary to take the research further, but Anita has no laboratory experience – and no lab, for that matter. Her solution is to create her own lab, in a storage room. Anita borrows equipment worth millions of kroner and starts from scratch. She purchases five chemistry textbooks, watches instructional videos about lab work on YouTube, and for months teaches herself as she goes along – until she finally gets it right.

Then Anita receives the news she’s been longing to hear. A Japanese pharmaceutical company has made a decision – and it’s a deal. The agreement is the biggest licence agreement to be made with a pharmaceutical company in Norwegian history. After years of solitary, lonely work, without the support of a research team, Anita has achieved something that most researchers can only dream of.

**Nothing is black and white**

The biggest pharmaceutical agreement in Norwegian history becomes front page news. Anita finds herself at the centre of a media circus, with journalists calling her around the clock.

Towards the end of the book, Anita asks the question: ‘What if it’s wrong?’. Research in the field is far from complete. Nothing is proven, and there is a long way to go before researchers can say whether the medicine is effective with any certainty. Anita acknowledges that her findings might prove incorrect, but hopes and believes that her work could be the start of an enormous breakthrough – that it will lead to a new treatment for rheumatoid arthritis and other autoimmune diseases. And perhaps prevent other children from experiencing a childhood like her own.

From *The Immune Mystery: When the body attacks itself*

(*Mamma er en gate: Når kroppen angriper seg selv*)

by Anita Kåss and Jørgen Jelstad

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Translated from the Norwegian by Alison McCullough

**Prologue**

I stared at the line on the floor. ‘Just stand here, then walk out when your name is called’, said the man who had positioned me there. He smiled reassuringly as he listened to the message being relayed over his huge headphones. On either side of the TV studio, rows of seats sloped up towards the ceiling. The laughter from the audience faded among the stage lights, and applause took over. It would soon be my turn.

This was not my home turf – I preferred to be sitting in my office full of books and research articles, or to be examining samples under the fancy microscope we had at the hospital. But I was now about to appear on Scandinavia’s biggest talk show. A couple of million viewers were waiting for me out there. What was I doing here?

The past week had been a hectic one, with journalists calling me incessantly and my husband finally having to act as my secretary, fielding their enquiries. I hadn’t the stamina to respond to all of them – sharing my life and work in this way was completely alien to me. Everything I had worked so hard for, over so many years. Now the same questions would be put to me again. About the medicine, about the money. About Mum.

The applause abated. On the round stage a few metres away the talk show host smiled as he looked straight into the camera, took a breath, and said: ‘At a small hospital in Norway, a researcher has been working to develop a treatment for rheumatoid arthritis – and possibly psoriasis, MS and other diseases. Last week, it was announced that the rights for this treatment have been sold for 800 million kroner. Please welcome researcher Anita Kåss!’

I had never been so nervous in my entire life.

As I took those first few steps onto the stage, terrified that I might trip and fall, a hormonal storm was raging within me. In situations involving extreme stress, we all experience the more uncomfortable aspects of having a body. We might sweat or shake; feel slightly nauseous or be struck by tingling sensations. Things happen that are beyond our control, and which affect how we feel, what we’re able to do – even our very sense of who we are. This discomfort is due to hormones, the body’s messengers, working at a frantic pace. They affect cells throughout the entire body, among them billions of faithful soldiers – the army that keeps us alive.

Every day our soldiers go to war. They march and fight, win battles and die – fearless and loyal until their dying breath. To study them under a microscope is to peer into a universe of superheroes, where each and every one has its own special powers and cool costume. This is the immune system – the world’s most sophisticated killing machine.

The body has many systems. The digestive system, consisting of the mouth, oesophagus, stomach and intestines, is easy to understand. Likewise the cardiovascular system, with the heart at its centre and its network of blood vessels; the nervous system, with the brain and its branching nerve fibres. You can point to each of these systems and say: there it is. But where in the body is the army, the immune system, stationed?

The answer is everywhere. In order to defend us against attacks from foreign intruders, this inner army has access to every nook and cranny of the kingdom that is the body. Within this kingdom is everything we need in order to live: energy production, waste disposal, infrastructure and transport, lines of communication and birthing rooms for cells. To get a person through the events of everyday life demands indefatigable efforts from billions of inhabitants on the inside.

The body is a peaceful land surrounded by dangers; all foreign substances are potential enemies. This is why the body has a military academy that puts its soldiers through the toughest of training camps, and only the very best pass the final test. They patrol our borders and monitor alien intruders, checking them against a comprehensive register in order to find out who they are and whether or not it’s safe to let them in.

These soldiers are white blood cells – the cells of the immune system. And although they patrol the entire body, there are certain areas and organs that house large parts of this army. The training camps are located within the bones, bone marrow and a small organ located just above the heart, known as the thymus. Hundreds of outposts – the lymph nodes – are spread around the body, connected by the lymphatic vessels. If the blood vessels are the roads of this country, then the lymphatic vessels are its pavements.

Even with vigilant defences, intruders often manage to sneak past border patrols and outposts. Suddenly the bus station might be set on fire, or a bomb might be detonated by the waterworks. Hostile terrorists might be spawned within the residential areas of a city.

When this happens, local forces quickly launch counter attacks to stop these intruders. Blaring alarms are sounded, and specialist soldiers storm the scene to strike the final blow. When the conflict is over, the inhabitants clear and repair the battlefield. And then life carries on more or less as before. But not always.

This book describes how our spectacular immune system works, and looks at what can happen when things go wrong – how the body’s defences are in fact able to make our existence a chronic nightmare. And how in the most extreme cases, these defences can destroy us, annihilating the very body that keeps them alive.

When the body attacks itself, we call the condition an autoimmune disease. ‘Auto’ means ‘self’. The immune system attacks ‘the self’. Examples of autoimmune diseases include rheumatoid arthritis, psoriasis, multiple sclerosis, type 1 diabetes, Sjögren’s syndrome, coeliac disease, inflammatory bowel disease and ankylosing spondylitis. The list is long – over a hundred diseases are thought to be caused by the body’s own soldiers making disastrous mistakes.

Statistically, if you invite ten of your friends to dinner, one of them will suffer from an autoimmune disease. If you attend a wedding with a hundred guests, one of them will have rheumatoid arthritis. And if you’re among those who have a thousand friends on Facebook, it’s likely that a couple of these will have multiple sclerosis. Autoimmune diseases affect so many people that if you suffer from one yourself, you’ll hardly be alone among family and friends. And if you yourself are not affected, you’re guaranteed to know someone who is. Many tens of millions of people across the world live year upon year with the consequences of a mistake within their immune system. Autoimmune diseases are one of the most significant causes of death among people under the age of 70, and particularly among women.

For the authorities, autoimmune diseases are responsible for some of the largest expenditures in local healthcare budgets. For patients, the cost is in many cases a ruined life.

Why the body attacks itself is one of medicine’s greatest mysteries. It is also the mystery of my mother – a puzzle I have wanted to solve since childhood. The desire to solve this mystery has led me on a long journey, towards something I hope will help to improve the lives of all those who suffer as my mum did.

**Beginnings**

‘Though some things in life are hard to bear

Don’t let it bring you down.’

Paul McCartney, born in 1942 at Walton Hospital, Liverpool, in *Don’t let it bring you down*.

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Mum looked out at the October rain running down the window panes as she passed a hand over her belly. Would tonight be the night? She looked over at Dad and smiled. A new life awaited these two expectant doctors in Liverpool. They would soon be a family.

It wasn’t long before they entered the red brick building that housed the Walton Hospital. A birth was far from Dad’s everyday life as a psychiatrist, and the careful smile his patients had come to know so well now had a slightly nervous look to it. Unease and worry, pain, smiles and tears – some hours in life contain everything. But in Mum’s body, an unexpected storm was brewing.

I was born on a Monday in 1979. Little did my parents know that this would be the start of years of suffering.

They had only married a year ago. Dad’s family had noticed a newspaper advertisement back home in India, and together with one of his brothers, Dad travelled thousands of miles to the industrial city of Kanpur to find out more about the woman in the ad. A woman who had qualified as a doctor, and who was strikingly beautiful in her colourful sari. Mum. After just a single meeting they married in my father’s home town of Chandigarh.

That same year, they packed their belongings into suitcases and moved to Liverpool, England – a common journey for highly educated Indians seeking a better future. There, they found a small house in the suburb of Rainhill, right next to the Whiston Hospital where Dad started work. Mum got a job as a pathologist at Royal Liverpool University Hospital, where she spent her days studying samples for cancer and taking the occasional trip down to the autopsy room as necessary. It wasn’t long before she fell pregnant.

When two cells merge and start to develop into a person, there is a system that the body must hold in check – the immune system. The patrolling cells of this system quickly notice if anything foreign suddenly appears in their hunting grounds, and a growing foetus might be regarded as an intruder, a potential hazard.

Over millions of years, the body’s defences have developed to attack everything that may pose a threat. But our survival as a species is equally dependent on mothers being able to carry children who are genetically different from themselves. This is the immunological paradox of pregnancy. The immune system is technically incompatible with having children, but something tells it that the foetus must be left alone; without these finely tuned control mechanisms, none of us would have been born. For over fifty years, researchers have tried to find out exactly what happens during these nine months, but we still don’t have all the answers as to how the female body controls the cells of its immune system during pregnancy.

Might this paradox help us to understand how autoimmune diseases arise? For Mum, this is exactly where it started – with pregnancy and birth, when something tipped her immune system out of balance. What is it that triggers this self-destructive cascade that causes such pain and suffering – and in some cases, even death?

Six weeks after my birth, Mum could no longer hold me – the pain in her fingers had become too great. After nine months with the brakes on, her immune system was starting to return to business as usual. Cells capable of killing came back to life, and a howling wind of hormones began to blow in new directions.

As Mum’s immune system returned to its normal functioning, some error triggered a chain reaction of destruction that spread through her body, year after year. Her fingers and toes became contorted beyond all recognition; complete exhaustion rendered her bedridden, and she was unable to walk. Her body slowly collapsed – she had developed rheumatoid arthritis. The cells of her immune system were confused, tricked into thinking that completely healthy parts of her body were foreign enemies. They were mutineers in her body’s vital defences.

As Christmas approached, Mum had to leave it to others to pick me up whenever I needed comfort. ‘It’ll pass’, said Dad – but uncertainty hung in the air. Mum was a doctor. Perhaps she already feared that something was seriously wrong. That the infinite duty of care she felt for me, her newborn daughter, would be swallowed up by the darkness of a disease where everything is turned upside down. Where I would have to take care of her.

I never got a sibling. Over the course of my childhood, Mum faded away before my eyes.

*Touch*

I held Mum’s hand carefully, so as not to hurt her strange, swollen fingers; as if I was handling a baby bird. We would sometimes take short walks together, sauntering through the neighbourhood, but Mum didn’t walk like other mothers. There was no skipping or running or games – everything happened in slow motion. These are my earliest memories.

In the 1980s, Liverpool, in north-west England, was a city deeply affected by the collapse of the labour market for industrial workers and dockers. These were bleak economic times, but football fans were at least partly cheered by the fact that this was the golden age of Liverpool FC. One in every six of the city’s employable inhabitants was out of work and money was a constant concern for many, but in my family it wasn’t financial problems that coloured our everyday activities. What I remember most is Mum’s illness.

When I was around eight years old, we moved from the suburb of Woolton to a much larger house on the other side of the city, in Blundellsands. ‘She needs more open space’, everyone said to me. In the new house, my mother sat in a chair by the big living room window, as if keeping watch. She was either there, or in bed – I hardly ever saw her anywhere else. Her disease was a heavy burden to carry, but she was always good to me, although she said little – she was more of a loving presence.

My childhood centred around two things. I went to school and was a diligent student, then came home and was a dutiful daughter. In the mornings I would enter the dark of the bedroom, where Mum would be dozing. In my hand I carried a bowl of Weetabix, the cereal sloshing around in cold milk.

If Mum was awake I would whisper ‘hello’ before carefully setting the bowl on the bedside table. On a good day, she might give me a cautious smile. Her skin was shiny, like a balloon on the edge of bursting. Scars ran across her thighs, like millipedes; both her knees had prostheses. Her toes were pulled out into an unnatural V-shape, as if they had been cracked apart. On the times she sat in the living room and there were other people around I made sure to keep a close eye on her – her toes were a forbidden zone. If anything touched them, she writhed in agony.

When I got home from school, I would go straight in to see her again; the crispy bricks of Weetabix now reduced to a soft, sludge-like porridge. The sores in her mouth made all food seem like sandpaper, so she was often unable to eat. I would carry the tepid mixture down to the kitchen. A daily defeat.

Mum couldn’t sleep alone, so on the nights my father needed a break I would lay in bed beside her. We would stand and turn her during the night, tentatively moving her frail, ever more emaciated body. One wrong move or a hand that gripped too hard and she would groan with pain.

In the half-dark of the bedroom, Mum’s thin arms lay stretched out along the sides of the bed. They ended in red, swollen finger joints, her fingers permanently bent, like the neck of a swan.

My father was strict, and the importance of doing well at school was impressed upon me from a young age. Helping me to learn was Dad’s way of showing how much he cared about me. He taught me how to read when I was three years old, and at school I became one of the best students in my class. I felt this was the only way of making Dad happy.

When I came home from school, I would usually sneak a few minutes of children’s TV; as soon as I heard Dad’s car come up the driveway I would turn the TV off and make a start on my homework. Mum cared little for school or success – she only wanted me to be happy. Perhaps living with an illness makes other things in life seem more important than good grades and careers.

Our house eventually functioned like a nursing home. We had domestic help, and relatives often visited to help out – aunts and cousins living with us for months at a time to reduce the strain on Dad and me. Our home life meant that I never had friends over – it wasn’t that I didn’t have friends, but I had no desire to bring my primary school classmates home to a hospital.

I accepted the situation. Children who experience such challenges early in life often take on a lot of responsibility. I even cared about and looked out for the other children at school – to my teachers I was probably the perfect student. A mature and conscientious little girl.

Our family situation changed my father. As the years passed, he put more and more distance between himself and what was happening at home. I remember feeling that he’d given up, and that even more of the burden was then transferred to me.

Mum sank deeper into the darkness that surrounds all serious illnesses. She seemed depressed. Her social life vanished – family friends mostly stopped by to check that everything was ticking over, not to chat about what had happened over the past week. Her helplessness also embarrassed her. The few visitors who came to the house were forced to go into the dark bedroom to greet her, and she eventually tried to avoid this as much as possible. The days became a repetitive affair, filled with pain and melancholy.

I come from a family of doctors, and since Mum was also a doctor, she understood better than most just how bad her situation was. She was suffering from a serious case of a disease she knew would only worsen with time, and so I don’t think it was long before she stopped fighting it. In the early 1980s there were few medicinal treatments available, so hope of a better future was as good as non-existent. My parents never spoke to me about these things; we rarely spoke at all. Our main focus was on getting Mum through one day at a time.

Luckily, memory is a sorting machine that generally wants what’s best for us, and one of my most vivid memories of Mum is a happy one. It was our last journey together – a trip to London to meet the most famous woman in the world.

*A last smile*

She’s so tall, I thought as I walked across the stage towards her. Princess Diana held out her hand to me; I took it with my clammy one. ‘Congratulations’, she said, a word she had uttered countless times in her role as a member of the royal family.

She was elegant, as always, in a blue skirt and red buttoned jacket, her earrings oversized and shining yellow spheres. But even to a thirteen-year-old it was clear that she wasn’t completely present. This Saturday, 10 February 1993, marked two months since she and Prince Charles had officially separated. She was in the middle of the world’s most talked-about divorce.

Alongside 150 other children from all across the UK, I received the Child Achievement Award at a prestigious ceremony held at the Queen Elizabeth II Centre in Westminster, London. The prize was awarded to children who had excelled in various areas, and not even royal relationship problems could dampen the joy and excitement felt by those of us who attended. My dutiful life – in which I juggled being good at school with being a carer at home – had been acknowledged.

The room was full of children, parents, celebrities and other guests. Among them, Mum sat in her wheelchair. She was wearing a red jacket and round, wobbly gold earrings. The thirteen-year battle against her illness was evident in her face – she had the characteristic moon face, a well-known side effect of years spent taking anti-inflammatory medications. The rest of her body was skin and bone. She was so proud that day. Her face broke into the genuine but cautious smile I had barely seen in years.

The trip to London was like a holiday – we rarely left our suburb of Liverpool. Staying in a hotel together was fantastic – even my dad was in a good mood. To have two happy parents seemed like a miracle at the time. They saw that recognition could also be paid to people who had been dealt a poor hand in life. Maybe it gave my mother hope to know that something good had come out of it all – something that gave meaning to the meaningless pain.

Five weeks later her condition worsened, and she had to go into hospital. We were used to this – she was continually being admitted with complications. But this time she didn’t return home.

‘She stayed alive so she could be at your award ceremony’, said a friend of the family. Maybe she did, for all I know. And perhaps painful experiences can also give people drive. The drive to create meaning in their life’s story.

*Release*

‘Anita, you have to come, your mother is very sick.’ I glanced towards the door of the classroom where a family friend was beckoning to me. My heart sank. Despite Mum’s countless admissions to hospital, I had never been collected from school. The day before she had been in good spirits, sitting up in the hospital bed and seemingly alert, even cheerful. I’ve since heard the same said of cancer patients – that their condition often seems to improve slightly, just before they die.

The tiles on the floor of the hospital corridor were diamond shaped; children also look at the floor when concerned or afraid. Outside Mum’s room were several familiar faces, people who had come to say their goodbyes. Some of them bowed their heads; others looked at me with shining eyes. Nobody said anything, but I understood the looks they gave me. Those looks carried silent voices that said: ‘we’re sorry.’

I took a deep breath and entered the room. It was silent. Beside the bed, nurses stood administering glucose to Mum from cotton buds, to prevent her mouth from drying out. It was as if she was already gone.

I sat on the chair beside the bed. Her mouth was half open, her breathing heavy, as if every breath was a struggle. In retrospect, as a doctor, I know that my mother had sustained an embolism in her lungs that made it difficult for her to breathe. Perhaps they decided to let nature run its course because she was so ill, choosing instead to focus on ensuring that she would feel as little pain as possible at the end.

A hoarse whisper came from her mouth: ‘Parny… Parny…’ The word for ‘water’ in her native tongue – was she thirsty? Her words were difficult to interpret; perhaps merely the restlessness of a consciousness slipping away.

Suddenly I saw my best friend, Suneet, in the doorway. One of the neighbourhood kids, a sweet Indian boy with caramel brown eyes, always neat and well-dressed. I smoothed down my hair and smiled shyly. What was he doing here? ‘Hi, Anita’, he said, cautiously. He pulled up a chair, sat beside me, and placed a hand on my shoulder. ‘Hi’, I answered. There wasn’t much more to say. We were children, and death felt so grown up.

Watching a parent die – the experience becomes permanently etched in one’s memory. Everyone at the hospital that day knew it was the end. But nobody told thirteen-year-old me that Mum was about to leave forever.

I’d never thought that she might die of her disease – we were supposed to always be together, remain a family. I used to imagine future scenarios, playing them out in my mind, problems we might have to solve. What if another world war broke out? How would she get to safety if she couldn’t walk? Death had never seemed an option to me until later that day, when my father and I sat in the car on the way home from the hospital.

‘Do you think Mum’s going to die?’ I asked.

‘Yes’, Dad answered. He didn’t cry – or at least, never in front of me. But later my cousin told me that my father had cried that day.

We went into the house. Mum’s never coming home, I thought to myself.

I had never experienced the feeling of a happy home. Anyone who has lived with someone who is ill over an extended period of time knows that this creates a special kind of atmosphere. The constant presence of disease carries with it an aura of grief. I noticed how relaxed I became when visiting the homes of friends, which were just like a home should be. Our house had a shadow cast over it. Sometimes, it was like entering someone else’s house. Now the shadow had withdrawn – Mum was dying. It was a relief.

‘I’ll get us take out’, said Dad. It was a kind of tradition – whenever Mum was in the hospital, we bought fish and chips from the local chip shop. For me this was synonymous with taking a break from sickness, in a home free from shadows.

At nine o’clock the next morning, a Saturday, the telephone rang. She was dead.

I walked down the hospital corridor at Dad’s side – he came to work here every day, but this was anything but the same old everyday routine. I thought it must be strange for him. He was always so controlled; we didn’t rush down the corridor, there was no drama. It could have been just another ordinary day. I’d never seen a dead person before, and I was apprehensive. Dad’s silence didn’t help much.

Saturday mornings at the hospital were quiet. A nurse passed us and gave us a sympathetic nod. Then we were standing at the door to death itself. Dad slowly opened the door and went in. I peered hesitantly through the opening, then crept into the room. Her eyes were closed, her mouth wide open, as if she was still trying to breathe. She didn’t look dead. Were they sure? I thought I heard sounds coming from deep within her. ‘Yes, she’s dead’, said Dad. Sounds were normal. Mum was gone.

‘Feel how soft her hands are’, said Dad, stroking and squeezing her fingers. He was right – her hands were soft. I thought that was a nice thing to say. All the pain was gone. Dad leaned towards her face and touched her cheek. ‘I’ll look after Anita’, he said.

I wondered how things would be from now on. We had never had a normal life, had always been different – life’s daily routines had always centred around Mum. I thought of all the times I’d slept in the bed beside her at night. How that was all over now.

At home a few days later, an open casket lay in the large, sun-filled hall. Mum was dressed in a beautiful pink sari – one of her favourites. The extra rouge and lipstick made her look a little strange, but she looked pretty. I glanced down at my new, black shoes; they had small heels. For the first time, I felt like a grownup.

The house was full of Indian friends and a number of my father’s colleagues from the hospital. It felt good to feel the warmth of the people who were there to support us. The room was full of low voices and compassion. An unfamiliar atmosphere for a family isolated by illness.

I was unable to feel sad – I’d already processed my grief over several years. Instead, I felt an overwhelming sense of relief. No more suffering for Mum. No more suffering for us. I was unable to put on any kind of act, and so tried to remain in the background. Taking my place among the large group of mourners didn’t come naturally to me – I was already looking ahead, towards a new chapter in my life. A chapter free from illness.

In a quiet moment, I went across to the hall bookshelf. With my mother as the only witness, I took down volume R of the Encyclopaedia Britannica, its brown cover smelling of leather. I sat down, opened the book, and turned the pages until I found the entry for rheumatoid arthritis. And then I began to read.

A sense of meaning began to seep into me as my eyes worked their way through the words. Joints, pain, genes, inflammation, T-cells. All that had gone on in Mum’s body; an entire world I knew nothing about. Why does it happen? I thought. All the unanswered questions sparked off new trains of thought, which curiously seemed to bring me closer to Mum. In the background I heard low voices from the hall, but they didn’t reach me. This was my world alone.

My first taste of discovery. A moment I constantly return to – the start of my journey into the mysteries of the immune system. Right then, I decided that I would become a researcher. All questions have an answer. It’s simply about looking in the right place.

Those first years after Mum’s death were a chaotic mix of rebellion and teenage angst; a reaction to all that needed to come out, an overcompensation for an isolated childhood. I went from being a straight A student to a rebel who ended up with Ds and Fs. But at a certain point, I ran out of things to lash out at. I left home at 17, returned to my studies, and ended up in the newspaper as one of the students with the best exam results in England.

I had an aim in sight – medical school. There, I became completely obsessed with the body’s defences – the immune system. The very same cells that had stolen my mother’s life.

**The body at war**

(pp. 85–97)

‘The immune system has enormous power to protect us from the ravages of infection through its ability to kill disease-causing microbes or to eliminate them from the body. But the power of the immune system is a double-edged sword. Its power to destroy infectious agents, if it goes wrong, can have devastating effects on the body.’

William E. Paul, in *Immunity*

A

The immune system consists of a range of cells with different functions, and the birthing rooms for these cells are found in the bone marrow, inside the bones. Both red and white blood cells are born here – and this is a maternity ward that’s always busy. Every second, the bone marrow creates more than two million red blood cells, which transport oxygen around the body. Each of us is also home to billions of white blood cells, which must be continually replaced with new ones. These white blood cells are the cells of the immune system.

The cells of the immune system are the body’s soldiers, and protect us against attack. The classic invaders are bacteria – group A streptococcal infections are some of the most common to affect us, and cause various illnesses such as throat infections and impetigo. The bacteria are shaped like strings of pearls, and enter the body through bodily fluids or contact with the skin. The immune system would prefer to stop all enemies at the door, but should any force their way in, the system’s job is to prevent them from spreading. In order to succeed with their invasion, streptococcal bacteria must therefore overcome a number of sophisticated obstacles and deadly attacks.

The body is like a country, with a military that protects its borders against invasion. The first obstacle that the bacteria must overcome is the fortifications – the physical structures that shield us from the surrounding environment. It’s often believed that the skin is the most important barrier here, but this is actually only a small part of the body’s surface that requires protection. The largest area is the mucous membranes, which cover the digestive system, respiratory system and genitals. If we were to lay it out flat, the skin would cover a couple of square metres, but the internal surfaces of the mucous membranes would cover an area of around 400 square metres in total.

Mucous, saliva and tears help to wash away unwelcome guests. But streptococci might be able to sneak past these first-line defences – and so on the other side, the border patrol will be waiting for them.

*The home guard*

The body’s border patrol has to be able to distinguish between dangerous enemies and the friendly substances that can be let in. Vital nutrients from food and drink are also alien substances – but eating a hamburger or an apple shouldn’t trigger all-out war. It’s therefore important to have smart guards at the border.

The most body’s most well-known border guard is the macrophage. ‘Macro’ means ‘large’, while ‘phage’ comes from the Greek word for ‘eat’ – in other words, a macrophage is a ‘big eater’. For any streptococcus that has managed to make it past the body’s fortifications, the monster macrophage must be a terrifying sight. It stretches out its tentacles and greedily devours the streptococcus as if at an all-you-can-eat buffet. Inside the macrophage, a cocktail of poisons is administered to the bacteria to kill it. There are also several other cells that operate as border patrol guards and assist the macrophages in their work, and an armada of deadly proteins are an important part of these first-line defences. This is known as the complement system.

If the situation becomes too much for the border defences to handle alone, the guards call for help by sending emergency signals through the blood, where numerous foot soldiers known as neutrophil granulocytes are out on patrol. The body produces around one hundred billion of these foot soldiers every day, and they storm to the battlefield the instant they detect an emergency signal. Like the macrophages, they eat the enemy – but with even greater effectiveness. They can even make their own cobweb-like substances, which trap and kill the bacteria. But there can be life-threatening consequences if these foot soldiers are allowed to rage around the body over an extended period of time, and so they don’t live long. Just a few days after they are born, they die.

There are several types of border patrol guards and foot soldiers, all with different roles. But the purpose of each and every one is the same – to ensure that the body can react quickly, with a broad spectrum of defences. These rapid response soldiers make up the innate immune system, much of which is already in place when we are born. This is the body’s home guard, which can be rapidly mobilised but doesn’t possess the most sophisticated weaponry. This type of defence can be found in all plant and animal life – it is an ancient system. Similar mechanisms probably existed in the first multicellular organisms to arise.

In the book *How the Immune System Works*, I found a telling example of just how important it is that the body’s first-line defences can respond with lightning speed. A single bacterium is able to divide itself into more and more bacteria, and so the bacteria double in number all the time. It’s like the legend about chess, in which the game’s inventor is offered a reward by his master for his wonderful creation. The inventor says that he would like a grain of rice for the first square on the chessboard, two for the next, then four, eight, sixteen, and so on – a doubling of the number of grains of rice for each square. A chess board has sixty-four squares, and so the inventor ends up with a mountain of rice – larger even than Mount Everest. The story illustrates the power of growth based on doubling.

Bacteria multiply in the same way. If a single bacterium enters the body and doubles every half an hour, this will result in hundreds of billions of bacteria over the course of a day – the body will be overrun. Without our built-in immune system, none of us would survive for very long.

The armed troops of the home guard put an end to many hostile attacks, and the immune reaction then stops with them. But what if this bacterial trouble-maker, streptococcus, fights its way past this first line of defence? Luckily, the body’s armed special forces are ready and waiting.

*The special forces*

Evolution has fine-tuned our specialist line of defence, known as the adaptive or acquired immune system – the body’s special forces. Our body isn’t equipped with these forces at birth, but trains them throughout our childhood and youth.

If streptococci manage to fight their way through the border defences, several immune system cells sound the alarm. These cells rip the face off the nearest streptococcus and rush off to show the special soldiers, exclaiming ‘this is what the enemy looks like!’ An alien intruder that triggers an immune response is called an antigen, and in this case, the face of the streptococcus is the antigen.

The body’s special forces are mainly divided into two groups: T-cells and B-cells. These soldiers are so specialised that they only attack enemies they have been trained to recognise. A tremendous number of antigens exist out in nature – bacteria, viruses, parasites and various other junk – and the body trains special soldiers for each and every one of these. This is the only way the body can ensure it will be able to defend itself against all possible threats.

Put simply, the body has B-cells and T-cells for every possible intruder that exists on earth – or Mars, for that matter, should we ever go there. Over the course of a human life, only a tiny percentage of these enemies will ever actually make their way into the body. Most of our special soldiers therefore never meet their antigen and remain inactive throughout their entire lives, like a Superman flying restlessly around without ever meeting his arch-enemy, Lex Luthor.

At any given time, the body contains around 300 billion T-cells and three billion B-cells, but only a tiny fraction of these are trained to recognise streptococcus. These few specialist soldiers are unable to defeat the enemy alone, and so they have a trick up their sleeve. When the alarm reaches the right T-cells and B-cells, something dramatic happens. The streptococcus killers mass-produce exact copies of themselves, and soon an army of clones is mobilised – each and every one of them capable of sniffing out and exterminating streptococcus. Thousands of clones can be produced in less than a week – and then they go to war.

T-cells and B-cells operate in different ways. When the enemy is a bacterium, such as a streptococcal infection, attack by the B-cells is most central. The B-cells produce a weapon known as antibodies, which act like tracker dogs sniffing out the target they have been trained to attack. When one of these tracker dogs discovers a streptococcus, it clings onto it. It can then call in other cells able to kill the bacterium, or hold it prisoner, rendering it harmless.

As for the T-cells, there are several types. One of these is a death squad, which attacks infested cells and destroys them. Viruses attack in a different way to bacteria – they have to hijack one of the body’s cells in order to make it produce copies of the virus. The death squad can see when a cell has been hijacked by a virus, and then eliminate it. These T-cells are therefore vital in preventing a virus from spreading.

We also have a group of cells known as T-helper cells, which act as captains and give orders to help the other cells of the immune system coordinate their attack. If these helper cells are put out of action, things can quickly take a turn for the worse. One example is AIDS, where the HIV virus destroys the helper cells. Without treatment, the patient will die because the immune system collapses.

The last group consists of the regulatory T-cells, which ensure that the armed forces don’t go overboard with their attack. Like a peace corps, they storm in to tell everyone that the danger has passed and it’s time to stop fighting. Without the peace corps, wars can get out of control, and so this group of cells plays a central role in preventing autoimmune diseases.

The rare IPEX syndrome illustrates just how badly things can go when the regulatory T-cells fail to function. The syndrome only affects boys, and is the result of a mutation on a gene that is critical to the normal development of these cells. In individuals with IPEX syndrome, the regulatory T-cells fail to act as they should, and the result is a number of autoimmune attacks. Children who do not receive treatment usually die within two years.

The dramatic effects of a defective peace corps indicate just how important it is to prevent autoimmunity. This is also why the body’s specialist soldiers must graduate from a brutal military academy – and be prepared to pay with their lives.

*The training camps*

The special forces can go berserk and start mistakenly attacking the body – this is the price we pay for developing T-cells and B-cells that are able to recognise every possible intruder. The enormous variation involved means that some cells might be incorrectly programmed to attack our body, and to prevent this, they require thorough training. The training camps are located in the thymus and the bone marrow, and this is where the T-cells and B-cells get their names: T for thymus, a small organ situated behind the breastbone, and B for the bone marrow, found within the bones.

The final exam for the special soldiers takes place at the shooting range. You might have seen the training of special forces depicted on TV – they move from room to room, with cardboard figures representing everyone from terrorists and guerrilla soldiers to old grandmothers and small children popping up as they go along. They have to know in an instant whether or not it’s right to shoot. The final exam that our immune cells are put through takes a similar format – only the cardboard cut-outs of old grandmothers and small children take the form of the body’s own cells and molecules.

Only precision shooters who only ever hit the enemy – dangerous bacteria, viruses and other suspicious intruders – pass the exam. Only the cells that put every single shot right between the eyes of the streptococcus cardboard cut-outs will become the soldiers who go to war when streptococcus actually invades.

The T-cells and B-cells who fire on their own cells or molecules fail the exam – and brutally, the price of failure is their own destruction. These are, after all, the toughest of training camps, and the body gets rid of the immune cells that might attack the body itself. This is known as negative selection, and is the most important mechanism in preventing autoimmune reactions.

But despite this strict regime, incompetent soldiers still occasionally manage to sneak out of the training camps undetected. The body therefore has several safety mechanisms in place to prevent autoimmunity, including controls by the regulatory T-cells. These control functions exist to ensure that the soldiers tolerate encounters with their country’s civilians without attacking them. In medical terminology, this is known as immunological tolerance.

But these control systems can fail, wreaking havoc in the army’s lines of communication – and resulting in the soldiers receiving orders they should never have been given.

*The messengers*

The T-cells and B-cells are first-rate soldiers, but they need clear orders if they are to do their jobs properly. The immune system therefore has an arsenal of messengers, who pass communications back and forth on the battlefield, right at the centre of the fray. These messengers are known as cytokines, or signalling molecules.

Along with hormones, it was these cytokines that I measured in my research – both are couriers that carry messages from one area of the body to another. Our world would descend into chaos if we suddenly had no means of communicating with one another, and the body is also dependent on messengers to survive.

Hormones are produced by the body’s glands, and often travel long distances to get a message to the right place, such as an organ or completely different region of the body from that in which the gland is located. But the work of the cytokine messengers is more local. If I’m sitting in the office and have a message for a colleague across the street, I don’t send a letter – I can walk over and deliver the message in person. But if I need to communicate with a research colleague in New York, a walk over to them will hardly be my first choice. Simply put, the cytokines wander between the offices of their workspace, while the hormones are the emails that carry messages further afield.

When the immune system is battling the enemy, inflammation occurs. It is vital that the cells on the battlefield communicate effectively, and so they produce cytokines to send messages to other cells nearby. In an inflamed area of the body a storm of communication is raging, with various cells carrying orders back and forth and coordinating everything that happens.

An immune cell communicates via receptors on its surface. These receptors act like a keyhole – and just as a postal worker needs keys to the various postboxes on the postal route, the messengers also have keys. The messengers are only able to deliver messages to the cells to which they have the keys – which ensures that the right message gets delivered to the right addressee.

Cytokines and hormones are the driving forces behind everything that happens in the body – and they are therefore also important when we become ill. Over the past three decades, researchers of autoimmune diseases have turned their attention to cytokines – there are hundreds of different types that initiate various reactions within the body. In my research, one cytokine was particularly important – a cytokine known as tumour necrosis factor, or TNF.

TNF is the most important messenger in rheumatoid arthritis. It holds a senior position among the cytokines, and manages important parts of the inflammatory response. In rheumatoid arthritis, the TNF messengers become hooligans that whip the immune system into a frenzy, forcing it to work harder. These hooligans cause inflammation in areas where there is no need for it, and a formerly healthy person will start to experience painfully swollen joints. The TNF hooligans goad the cells of the immune system into attacking more and more of the body’s joints, and so the rheumatoid arthritis spreads.

But these hooligan messengers are acting on the orders of their superiors – so who exactly is the head of this autoimmune mafia, the Godfather pulling the strings? As yet, we don’t know. But finding him could be a critical piece of the puzzle in helping us to identify the cause of rheumatoid arthritis.

In summary, we have an immune system that we are born with – our home guard – which responds with lightning speed when our body comes under attack. When the home guard is unable to defeat invaders alone, the body also has an arsenal of special forces with more sophisticated weaponry – the T-cells and B-cells. These are trained throughout our childhood and youth, making the immune system stronger and stronger over the first years of life.[[1]](#footnote-1)

Because the T-cells and B-cells are so highly specialised, there is always the risk that mistakes might be made. The body may start to attack itself. The immune system has a number of control mechanisms to prevent an autoimmune breakdown, like the checklist a pilot uses prior to takeoff. Mum developed rheumatoid arthritis because of an error in this system. Because just as a plane might crash despite checklists and control measures, so can errors in the immune system trigger a catastrophe.

**The billion dollar companies arrive**

‘Many in the field believe we are at the dawn of a golden age which will see major benefits for patients in the form of both treatments and cures.’

From *60 Years of Immunology: Past, Present and Future*,

The British Society for Immunology, 2016.

Was there something we were missing? We’d seen test patients throw out their crutches after just a few weeks. Others travelled long distances by bicycle after previously having struggled to get out of bed. We saw blood tests indicating that patients’ inflammation had almost completely vanished. The potential market for a new medicine to treat inflammation is huge – millions of patients use cortisone, TNF inhibitors and other anti-inflammatory medications daily. For a pharmaceutical company, it had to be worth investing a few kroner to find out whether GnRH inhibitors work. So why weren’t any of them interested?

Inven2 had been in touch with their business contacts in the relevant companies, and we discussed whether a brief summary of our findings would be enough to convince them.

‘We can’t claim to treat a spectrum of autoimmune diseases with just a couple of pages of explanation’, I said to Jørund and Anders. I understood the need to be brief and catchy in dealings with the business world, but it seemed unprofessional to send out a short note stating that we might be able to treat rheumatoid arthritis, MS, psoriasis, and a number of other things. Who would believe us?

Once again, I sought Andrew Schally’s advice, sending an email to him and his right hand man at the lab in Miami, Norman Block. I attached a brief explanation, together with the video of the test patients.

‘I hope you’ll agree that there’s potential here. I think we could help many patients’, I wrote, and asked whether they had any suggestions as to who I might contact within the pharmaceutical industry. It was a Friday, and the weekend was fast approaching, so I sent off the email and thought little more about it.

But Monday morning took an unexpected turn. Block forwarded the email to an acquaintance, one of the senior managers in Ferring Pharmaceuticals. Ferring owned the rights to one of the medications we had used.

‘Take a look at this video – it’s very impressive’, Block wrote to his contact.

Just a few hours later, the manager responded. ‘I’m fascinated by Dr. Kåss’s research’, he started, explaining that this was an opportunity he had never considered before. ‘I clearly need to broaden my horizons!’ he said, and politely asked whether he could share the email with his colleagues within the company.

In just a couple of days, things were suddenly underway. Ferring were definitely interested, and invited us to a meeting at their headquarters in Copenhagen.

Along the way, I’d learned something very important – to be sure to contact the actual decision-makers within the organisations. And the video was crucial – it enabled people to see the patients’ improvements with their own eyes.

I scoured the web for the email addresses of senior managers within the major pharmaceutical companies – some of them were extremely well-hidden. Sometimes I could spend an entire day hunting down just a single email address. I wrote a sixteen-page summary and formulated a new email message. The people to whom I was directing my enquiry were specialists – they needed a thorough explanation of my findings, not just a summary in one or two pages. I inserted links to videos of the test patients, both before and after treatment. And then I started to send out my queries.

Pharmaceutical giant Pfizer was the first company I contacted – it was like sending an unsolicited email to the CEO of Coca-Cola and hoping for a response. I took a deep breath and clicked ‘Send’. That was that, I told myself, and returned to my daily tasks thinking that it would be at least a couple of weeks before I received an answer – if I received any response at all.

It took twenty-five minutes. Pfizer requested more information.

Over the next few weeks I worked my way down the list, sending emails to the managing and medical directors of AbbVie, AstraZeneca and MSD, among others – all companies with a relevant medication in their portfolio. ‘I hope you’ll agree that there is significant untapped potential for GnRH inhibitors’, I concluded my email. Every company I contacted responded – and not only with polite but empty phrases. Several of them were genuinely interested. I now knew that this might actually work – that we could do it.

‘Woohoo!’ I wrote to Jørund and Anders when one of the larger companies requested a meeting. Our energy had returned – things were finally happening. We started to believe again.

The sun was shining. I went out into the park behind the hospital and lay on my back beside the statue of a local polar explorer. My lab coat became a snow angel in the grass. I lay there like that for several minutes, just to enjoy the feeling.

*Relief*

Many lengthy email exchanges with the pharmaceutical giants now awaited me, and the process was a rollercoaster ride. But one organisation – Ferring – stood out. The company was started in Sweden by a German researcher fleeing the Nazis between the wars, and is still owned by the same family today. The company’s founder died some years ago, but on their website I read his advice to young researchers: ‘It’s best to undertake research without thinking about money. Research with a pre-determined goal is astoundingly unproductive.’ This was a company that shared my values. Jørund, Anders and I set out for their headquarters in Copenhagen.

Ferring’s high-rise office premises are situated just a short taxi ride from Kastrup airport, where they tower tall and lonely above Ørestad train station. At the top of the building, the blue letters of the company’s name asserted their authority. We waited in reception, all of us silent. Jørund switched off completely, as if suddenly struck by the gravity of the situation. He fished out his mobile phone and started to play a game of chess, perhaps psyching himself up for possible objections and critical questions. I tried to appear unfazed at suddenly finding myself and my research in such a position.

The meeting room was on the top floor, and Ferring had put one of their most senior members of staff on the case. He was snobby in a charming sort of way, a bit like James Bond. Later, Jørund warned me not to fall for his charm.

‘He knows that all you’re interested in is a bigger study; that you don’t care about the money’, he said.

We sat around the conference table. It was time to convince the company that we had something worth listening to. As the meeting progressed, I noticed that the tone in the representative’s voice changed from one of scepticism to one of curiosity. This is actually going well, I thought to myself.

‘We’re open to doing a study on this’, the representative from Ferring said finally. I did my best to keep a straight face. We were close. Very close.

As we left the building, Jørund and Anders were enthusiastic – I had no idea what was normal at such meetings, but I knew that something good had happened and let myself be carried along by their excitement. I glanced back over my shoulder, towards the dark façade.

‘We probably shouldn’t look completely ecstatic, right under their noses’, I said.

‘Right’, said Jørund, and we all bundled into a taxi.

At the airport, we raised a glass and toasted our successful meeting, all of us relieved and happy. ‘Smile!’ said Jørund – he was sure we had it in the bag. ‘Anita – you’re going to be rich!’ he joked, the world’s biggest grin plastered across his face. I couldn’t help but laugh.

Negotiations take time, and I’m an impatient person. In the spring of 2015 I took yet another look down the list of relevant pharmaceutical companies and stopped at Astellas. The company had developed a GnRH inhibitor in tablet form. They were worth a try.

I formulated a new email of the type I was by now extremely well-practised at writing. ‘I hope you’ll agree that there is significant untapped potential for GnRH inhibitors’, I concluded the message, before sending it off to the land of the rising sun – Japan.

Astellas’ headquarters are situated in Tokyo. Despite not being as widely known as Pfizer, Merck and Bayer, the company is estimated as being worth over 200 billion kroner. Astellas developed ASP1701 for the treatment of prostate cancer. I suggested that they should test the drug for the treatment of rheumatoid arthritis.

Just a few days after sending the email I received a polite response requesting more information, and over the following days the Japanese indicated that they were ready for action. One of the company’s managers sent a personal reply to my email, and hoped that we could have ‘productive discussions and a possible collaboration’. Jørund was excited at the prospect of another proposal. ‘We have to go to Japan!’ he said. ‘And make sure we take a nicely wrapped gift with us’, he added with a smile. We were suddenly in negotiations with two different companies.

The Japanese were serious and left nothing to chance – they wanted to know every last detail about the studies I’d carried out. There was definitely something in the air. Now it was just a question of which company would make the deal.

*Money problems*

The discussions with the pharmaceutical companies took the form of a long, drawn out process, and the months went by. I would soon be out of funding, and the chances of undertaking more research were starting to look slim. Unless things changed soon, I’d have to return to work as a normal doctor. The director of Betanien Hospital was aware that money had become a problem.

‘What will you do if you can’t get hold of more research funding?’ he asked me one day.

It was a difficult question to answer.

‘I’m going to keep banging on doors. Again and again and again’, I said.

But I was worried. I was running the risk of leaving the entire project high and dry. Might it be possible to find funding outside the traditional channels? We contacted the Telemark Development Fund – a fund established from the profits of the hydropower industry and which supported local projects.

‘I understand the problem – I’ll see what we can do’, said the fund manager. He was efficient and arranged a meeting with possible sources of support from the surrounding area.

On the day of the meeting I was late and so hurried towards the blue-grey concrete block of a building on Klosterøya in Skien city centre. It was pouring with rain, and I splashed through the puddles in my high-heeled shoes as I passed the factory chimney from the industry that had once dominated the little island.

Inside, those who had been invited to the meeting were already seated around a large conference table. ‘Hi Anita’, said Jørund, getting up from his chair. He had the face of a businessman used to keeping calm under pressure. ‘Relax. Here, have a coffee’, he said, pouring me a cup. It was embarrassing to be late – especially as I was usually always half an hour early. There was a lot on the line. This might be our last chance to secure project financing.

I opened my laptop, glancing at my fingers as I did so. Red nail varnish had seemed like a bad idea, and so I’d stopped off at the supermarket on the way to buy some nail polish remover. In the car I’d scrubbed away the colour – I now stank of the strong chemical. Could it get any worse? I looked up at the group and smiled. A posh British accent wasn’t going to do much good here.

‘Thank you all for coming’, I said, and received a few nods in return. I introduced myself and the project, and explained why further research was important. ‘We’re looking to land a global deal with a pharmaceutical company’, I said in conclusion – a big claim coming from an unknown researcher at a little hospital in Skien. But we sold ourselves as best we could.

Jørund and I left the meeting together. We’d long discussed what was required to take the research a step further. The problem with GnRH inhibitors is that they also act as a form of chemical castration – which for young patients is particularly unfavourable. There is always uncertainty surrounding the long-term use of medications, and so far studies had only followed the use of GnRH inhibitors for up to five years. We therefore had no idea whether treatment over a longer period of time would lead to as yet unknown side effects. With greater knowledge comes new ideas, and I started to mull over a thought I had come to have greater and greater belief in over time. Was it possible to create a medication that worked just as effectively, but without chemically castrating the patients?

GnRH doesn’t just act locally in the brain – it is also able to bind to several of the body’s immune cells directly. Some immune cells are even able to produce and extract GnRH themselves. The hormone is therefore also found outside the closed system of the brain, and in my mind this could mean only one thing: the hormone was of wider significance than its role in the chain reaction that produces the sex hormones. It worked directly on the immune cells. Was that why it seemed to have an effect on the inflammatory response? Perhaps treatment wasn’t about blocking the sex hormones. Instead, maybe it was about preventing GnRH from binding with the immune cells. The idea was to create a medication that could block the hormone outside the brain – so the sex hormones could roam free.

Before we each went our separate ways in the rain, Jørund took hold of my shoulder.

‘Do the lab tests that need to be done to move another step forward’, he said.

‘And who’s going to do that?’ I asked, staring uncomprehendingly at him.

‘You’, Jørund said.

‘How am *I* going to do it? I hardly know where the “on” button on half the lab equipment is!’ I said, laughing.

‘You’ll figure it out’, he said.

Just a few weeks later we received our decision from the meeting participants – they would provide us with two million kroner. A short while later, we also received funding from the Research Council of Norway. I could breathe a sigh of relief.

Now all I needed was a laboratory.

*The lab in the storeroom*

I needed a laboratory where I’d be able to work alone, day and night. I would have to learn how to use advanced lab equipment, and so went on YouTube and worked my way through instructional videos and ABCs for lab machines. Of course, I was doomed to make a fool of myself on the first few attempts – and would prefer to be able to do so without looking like the world’s biggest buffoon in front of other researchers.

I checked out whether it would be possible to set up a provisional lab at Betanien Hospital. The equipment I needed would cost millions of kroner and so it wasn’t an option to buy everything outright, but I found a loophole – the companies hired out their equipment for a trial period, allowing people to test it before possibly making a purchase. Just a few telephone conversations were enough – I suddenly had all the equipment I needed. All I had to do was remember to send it back when the trial period came to an end.

Great, I thought – now all I needed was a room in which I could set everything up. On the second floor of the hospital was an old storage room with no windows. It would have to do. I made sure that conditions were sterile and set everything up as best as I could. Now the practical side of things was up and running there was only one thing missing – sufficient knowledge of chemistry.

A GnRH inhibitor is an artificial form of GnRH. The medication binds to the receptors on the cells, much like a key that fits inside a lock. But despite the key fitting the keyhole, it has no function and can’t be turned – the door therefore remains closed, and the GnRH doesn’t work. In order to create a GnRH inhibitor, I would have to replace small parts of the hormone with something else, and to do this I would need to know the chemical structure of the hormone. I was no chemist, but I could read. And so I purchased five medical chemistry textbooks and started to learn how I should approach my task.

Luckily, GnRH is a relatively simple hormone, and it was therefore possible to find out what kinds of structures might have potential as a new medicine. I worked extremely hard in yet another field within which I had little prior knowledge. It was often simply a case of trial and error. Eventually, I received assistance from a doctor from India and a bioengineer from Sri Lanka. Both of them were receiving social benefits and needed on-the-job training – and I needed help.

We stood in the poky storeroom for days and nights on end. A huge hole in the wall had been patched up with grey breeze blocks, and cardboard boxes full of equipment were stacked on the blue shelves. On the walls, we hung notes detailing how things should be done. After months of trying we finally discovered how we could test the various substances that might prove suitable medicines. We purchased immune cells from patients with rheumatoid arthritis and studied how the various substances affected them.

It was manual work and extremely labour intensive – but also absolutely possible once we understood how.

Other researchers might be lucky enough to be offered lab space, the latest equipment and assistants on a silver platter – and I must admit that I often envied them as I stood in the stuffy, windowless storage room in the middle of the night. But at the same time, it was a special feeling, doing everything from scratch. I was on a voyage of discovery.

On Christmas Eve of 2015 I received a message on my mobile. It was from Jørund.

‘Merry Christmas, Anita! Be sure to check your email once more before new year :)’.

The email said that one of the companies had made a decision. They wanted to make a deal.

*‘It’s a deal’*

In April, I received another text message. Jørund and Anders wanted to give me and the director of the hospital an update on the negotiations. I could tell that it was good news. We sat down in front of the computer screen in the director’s office and soon made contact with Jørund and Anders via Skype.

‘It’s a deal with Astellas’, said Jørund.

I looked at the director – he was struggling to maintain his professional expression. I leaned over and kissed him on the cheek, making both of us relax and burst out laughing. We signed the contract that summer – the deal was finally done.

The money involved in such agreements is often overhyped, and this was certainly true for us. But the fact is that everything depends on the medicine actually being proved effective through further research. No payment is received upon signing the contract – the money will only start to trickle in as the company takes new steps towards approval of the drug. In order to sell the medication for the treatment of rheumatoid arthritis, Astellas would have to carry out several studies to see whether it actually works.

But if all this proves successful, the potential earnings comprise several hundred million kroner. Overall, our deal was the largest licence agreement between a hospital and a pharmaceutical company ever to be signed in Norwegian history.

I was relieved to finally have a deal wrapped up, but also felt uneasy. It was important that the next stages of the research be undertaken properly and with care – and not least, I wanted to stay involved. I was, after all, the only person in the world with experience in using GnRH inhibitors in the treatment of autoimmune diseases. But the Japanese wanted to take the next steps on their own. My opportunity for further involvement was sacrificed at the negotiating table.

Research and business are two different planets. During these hectic years, I sometimes felt as if my research was nothing but a commodity – that concern for the patients was shoved to the background. The main point should be to ensure that further research can succeed, but I was excluded from important discussions on exactly this point. I had brought the research all this way almost single-handedly, but that no longer seemed to count for anything.

I’m sure that many researchers have experienced the discomfort of losing control of their work when their findings suddenly become business ventures. I was left with the fear that people would fail to take good care of the research baby I had given birth to and raised over the past several years.

But by now, the grapevine was also in full swing. Emails from desperate patients wanting to try a GnRH inhibitor rapidly accumulated in my inbox. They had tried everything, but now they had new hope.

‘Please consider me as a volunteer’, one wrote. ‘This is a cry in the dark’, wrote another, begging for any advice that might help his wife. A woman in her fifties told me she had been living with rheumatoid arthritis since she was six years old. ‘Since I was small I’ve hoped and believed that one fine day, a medicine that can give me a better life will be discovered. I’m still hoping’, she wrote.

These patients deserved a larger study that would clarify whether GnRH inhibitors actually work. *That’s* what was really on the line – people’s lives. Everything to do with money and patents mustn’t result in patients losing opportunities and hope. I understood that the companies needed to earn money; that they wanted exclusive deals to protect themselves from the competition. That’s how the system works. But would it help the hundreds of patients who had sent me desperate emails?

In early 2017, the media broke the news of the deal with Astellas. And once again, my life changed overnight.

1. The immune system is one of the body’s most complicated networks, and this chapter is therefore by necessity a gross oversimplification. The system contains a range of other cells and molecules with far more functions than I am able to describe here, and the communication between them is extremely complex. Researchers are still striving to understand the intricate interactions that take place within the immune system. [↑](#footnote-ref-1)