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The making of you

a journey from cell to human

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Preface

WHEN I WAS SIX years old I collected hotel soaps, played with Barbie dolls and wore flashing sneakers. My taste in movies was exceptionally unoriginal and can be summed up as ‘anything with princesses’. But my favourite book? *Pregnancy and Birth: A Practical Handbook for All Future Parents*. My sister and I would take it down from the bookshelf, skim past all the dietary advice and stop when we reached page 70: *The foetus as it grows*. Fascinated, we would follow the illustrations of this tiny creature as it increased in size, thinking of our own brother-to-be curled up inside our mother’s tummy. We learned how he was transforming from a strange, primitive little animal with a tail into a chubby baby with arms and legs, confined in a space barely large enough to accommodate him. How was this possible?

Seventeen years passed before I returned to this question. I was completing a bachelor’s degree in biochemistry at the University of Oslo, and sitting up late in the library one night, reading about cell biology. In my textbook was a series of images showing how a hand is formed in the uterus. At first it resembles a duck's foot, and then the fingers gradually appear. In the caption I read that this transformation was due to mass cell-suicide. Many years ago, all the cells that linked my fingers together died, on command from their neighbours, and left me with the hands I'm writing with now.

This detail, I realised, was not included on page 70: *The foetus as it grows.* The pictures I'd seen as a six-year-old told only a small part of the story. How does this tiny creation *actually* come about? What happens in the cells, and in the DNA molecules? How does a hand know that it's going to be a hand and not a foot or an ear, for example?

In search of answers, I began digging through syllabus books and research articles. It wasn't long before I became completely immersed. Prior to the summer vacation in 2015, I borrowed three huge embryology books from the library at Oslo University Hospital and took them with me on holiday to Italy. My internet search history filled up with egg cells and foetuses. Google drew its own conclusions and began showing adverts for baby creams (I don't like to think what their algorithms made of my searches for fruit flies, fish kidneys and the gender development of sea worms).

The result of all this was the book you now hold in your hands. It is a story about distant relatives, unknown twins, dangerous placentas and strange insects. And I can say right now – without giving too much away – that it is all about *you*. Let me tell you about the beginning of your life.

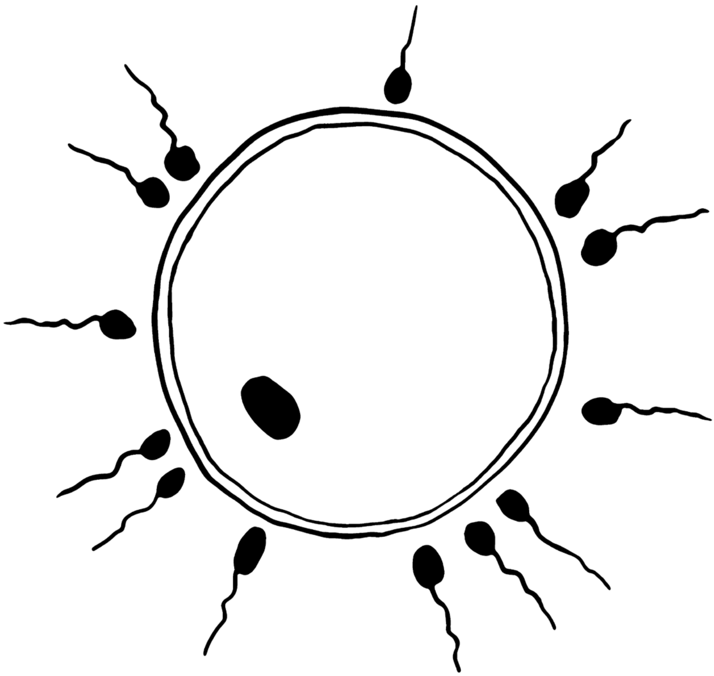
Before we begin: a few words about time and size

While working on this book, I discovered that trying to state the age of a foetus is fraught with difficulty. There are various chronological calculations involved, and it's not unusual for them to get mixed up. Doctors and midwives commonly use the *week of pregnancy*, which is calculated from the last menstruation. However, conception usually occurs about two weeks after this, so it's not until a woman begins her third 'week of pregnancy' that she's actually pregnant. In other words, the foetus is two weeks younger than the week of pregnancy: at the end of the twelfth week of pregnancy, the foetus is ten weeks old; at the end of the fourteenth week it's twelve weeks old, and so on.

I've chosen to use the conception as my starting point, so that all the time references I give reflect the real age of the foetus. Next, what is meant by a 'month'? I have counted each month as a four-week period rather than a calendar month. Thus the first month comprises weeks one to four, the second weeks five to eight and so on.

When I state the length of a foetus I mean the measurement from its crown to its rump. (You will sometimes hear this referred to as CRL, crown-rump-length.) This measurement is preferred because the legs of a foetus are often bent upwards, making it difficult to establish its length from head to toe.

Finally, please keep in mind that all time and size references are based on average values, and that every foetus develops at a slightly different rate. So, with that said, I think we're ready to begin.



The Race

IN THE HOURS PRECEDING CONCEPTION, a race begins that is almost impossible to win. A sperm cell starts out on an intense swimming trip. It looks like a little tadpole, battling wildly upstream against the current and in unknown terrain. It has several hundred million competitors. And it must swim a distance more than one thousand times its own body length. The rules are simple: reach the finishing line first, or die.

The landscape around the sperm is confusing and inhospitable, an overgrown forest full of chaotic thickets and blind alleys. It risks being either swallowed up by immune cells or destroyed by acid on the way. It could also end up trapped in one of the deep crevices in the cervical wall. Before long, such hazards have eliminated most of the field, but our competitor is luckier: the woman's muscle contractions help to push it upwards and it manages to enter the uterus.

It is still a long way from victory. To have any chance of winning, it must first choose where to go next: right or left? The uterus is connected to two narrow channels

– the fallopian tubes – and the finish line is at the end of one of them. The walls of each tube are lined with hairs that sweep fluid down to the uterus, but the sperm cell refuses to give up. It struggles on against the flow. Somewhere up there, hidden among the deep crevasses and high peaks of the mucous membrane, a round egg is about to meet its champion.

The egg cell has waited a long time for this moment. When the woman was a tiny foetus herself she'd already made the forerunners of her egg cells. Later on she began transforming them into mature egg cells. The cell now floating down her fallopian tube was one of the lucky ones. Each month, several egg cells start maturing inside every fertile female, but only one of them gets the chance to escape. The others face certain death.

To create a mature egg cell, the forerunners divide so that the chromosome pairs containing the genes from the new foetus's grandmother and grandfather are separated. At the end, each mature egg cell has half a set of chromosomes, some from Grandma and others from Grandpa, ready to find itself a new partner. All the while, the egg cell has been packing itself with nutrients, blowing up like a giant compared with the other cells in the body. It's actually possible to see the egg cell without a microscope: it has a diameter of around a tenth of a millimetre.

The sperm cell could not be more different. Swimming frantically with its wriggling tail, there's barely any room for nutrients because its entire head is packed with the father's DNA. Among the many millions of sperm cells, only one of them carries half of your specific genes; the chances of two sperms being identical are vanishingly small. Had another of your father's sperm swum just a little faster, you would never have existed as you are now.

When your parents' sperm and egg cells were formed, the chromosomes from your grandparents sat right next to each other; and before the chromosome pairs were separated from each other for ever, they managed to exchange small pieces of DNA. So a chromosome that was originally from a grandmother can carry some genes from a grandfather when it ends up in the sperm cell. The possible combinations are endless, and so we have to be sure we cheer on the right sperm.

Returning to our race commentary, our frenetic little tadpole is made for what it's doing right now. It may be blind and deaf, but that doesn't stop it making its way through a landscape it's never even been close to before. Among other things, it can sense minute changes in temperature. Because its target is slightly warmer than its surroundings, the sperm can tell when it is getting close. In addition, the sperm is equipped with a basic sense of smell. Just as the cells in your nose do, sperm cells contain molecules called odorant receptors. Each odorant receptor is programmed to recognise a particular molecule. When air flows into your nose, the fragrance molecules become attached to different odorant receptors and create an electrical signal that is sent to the brain. In the case of sperm cells, the odorant receptors catch molecules streaming from the egg, confirming that it is on the right path.

At the finish line there are relatively few competitors left swimming, and the egg's attractor chemicals make them travel faster than ever. Soon the egg is completely surrounded by minute tadpoles. Their tails wriggle furiously as they drive forward into the jelly-like membrane protecting their goal. From their heads they spray chemical weapons, enzymes that break down the membrane and allow them to burrow even deeper.

But only one of them is fast enough. The winner discards its tail, melts into the egg and releases its valuable cargo: twenty-three of the father's chromosomes. At the same instant, the egg cell releases substances that create a hard capsule around it so that no more sperm can enter. There's no time to lose: if two sperm cells were to penetrate the egg at the same time, the result would be a cell of sixty-nine chromosomes instead of forty-six. Although the egg cell does its best to avoid this, it isn't always successful. When a group of researchers studied artificially fertilised eggs, they found that 10 per cent of them had been fertilised by more than one sperm cell. Eggs like this have no chance of developing normally, and, as we'll see later on, they are handed a death sentence.

But for now you can relax – this time there was only one winner. The chromosomes from your mother and father are now united and your very first cell has been created. The race is over. The making of you can begin.

The Hidden Universe

BEFORE MICROSCOPES CAME ALONG, most of what happened at the very beginning of human life was hidden from us. With the naked eye it is almost impossible to see the minute details gradually emerging. Even elephants, which rise four metres above the ground, start off microscopic. It doesn't help either that we are concealed behind skin, muscles and blood vessels.

More than 2,300 years ago Aristotle wondered how new creatures might come about. In search of answers, he opened fertilised chicken eggs at different stages of gestation. In a three-day-old egg he observed a little red heart beating within the yellow yolk. When he cracked open a shell after a week, he found a tiny creature with large eyes. Of course, the later he broke the egg, the more the embryo resembled a chicken. Surely, he thought, it was the same with people too. Aristotle surmised that a man's sperm somehow instructed the woman's blood to create a human in her stomach.

That said, Aristotle also believed that living creatures could arise in very different ways. Insects could be created from the dew on leaves, moths from wool and oysters from slimy mud. Almost two thousand years later, these ideas were still popular. In the seventeenth century the Flemish chemist Jan Baptist van Helmont came up with some highly creative and entertaining recipes for the world's various life forms. For example, let's say you fancy growing some mice. The recipe for this is simple: place a dirty, slightly sweaty shirt into a container full of wheat-grain. Wait twenty-one days and – *voilà!* – your wheat has been transformed into sniffing, twitching mice.

There's no reason to doubt that van Helmont's recipe worked. Neither was he alone in providing striking examples of how animals could appear, quite spontaneously, if the conditions were right. Wet mud along the river banks could magically transform itself into frogs, rubbish into rats, and just imagine all the white larvae appearing from nowhere on rotten meat. And it was hard to imagine how oysters could possibly mate – surely they just somehow sprang into existence.

At the end of the 1600s a new idea emerged: perhaps every creature, be it a frog or a human, arose from a miniature version of itself. When God created the first humans in all their perfection, he also created all future generations. These miniature humans were nested inside each other, layer upon layer, like Russian dolls. Later they would simply germinate and grow in their mother's womb until birth. When microscopes first arrived, biologists grew even more confident that they would discover these scaled-down creatures existing somewhere. Just imagine the riches of detail that lay hidden from the eye! There seemed to be no limit to what could be found if only microscopes might improve just a little more.

One of the most talented microscope makers of the time was a Dutch merchant named Anton van Leeuwenhoek. There was little in his background to suggest that he would end up a scientist: he had no university education and no wealth. His original motivation was simply to investigate the quality of the textiles he sold. Nevertheless, one day Leeuwenhoek became curious and placed a drop of water under his lens. What he saw changed his life for ever. Each transparent droplet was teeming with mysterious creatures of every possible shape. Leeuwenhoek named them *animalcules* (tiny animals), and soon began to investigate everything he came across: the water he drank, the puddles he stepped in – even the deposits he found between his teeth.

Everywhere he looked, he found tiny animals. Forget exotic islands, forget about space, Leeuwenhoek could peer into a secret universe – barely explored – right before the tip of his nose.

Rumours of Leeuwenhoek's impressive microscopes spread fast. One day he was visited by a medical student who brought with him a sperm sample taken from a sick patient. Leeuwenhoek had for some time declined to study sperm; as a religious man, he feared that it would be considered profane. On the other hand, this *was* clearly a medical case . . . He resolved to take a look. The sample he examined wasn't much larger than a grain of sand. And yet, under the lens he could see more than a thousand minuscule creatures. They had round heads and long, transparent tails – like tiny tadpoles. Had they come about because of the man's disease? Had the sample been stored for too long, perhaps?

Like any good scientist, Leeuwenhoek realised that he had to compare his observations with a sample taken from a healthy subject. In 1677 he reported his findings in a letter to the president of the Royal Society of London – one of the world's leading research institutes – in which he gave a detailed description of the animals he'd observed in the healthy sample, and wrote that it was examined 'immediately after ejaculation, before six pulse strokes had passed'. Afterwards, he was keen to emphasise that the sample was, of course, not obtained in any sinful way, but 'made available' to him 'quite naturally, through marital activity'. (It couldn't have been easy to be his wife.) At the end of the letter, Leeuwenhoek requested strongly that the president keep their correspondence to himself, should he feel that the observations risked causing disgust among the scholars. A scandal was the last thing he wanted.

Leeuwenhoek was convinced that semen played a decisive role in the beginning of life. This was no clear, empty fluid – it was packed with swarms of microscopic creatures! Could this be the place that miniature humans existed? Surely he needed only a good enough microscope to reveal it. For years Leeuwenhoek worked persistently, but despite continually improving his lenses, he found nothing. He even attempted to remove the membrane around the sperm cell's head with a tiny brush in the hope of finding something hidden inside. Despite the absence of proof, Leeuwenhoek was certain that the sperm cell contained a great secret – albeit one so small that humankind would never be able to see it.