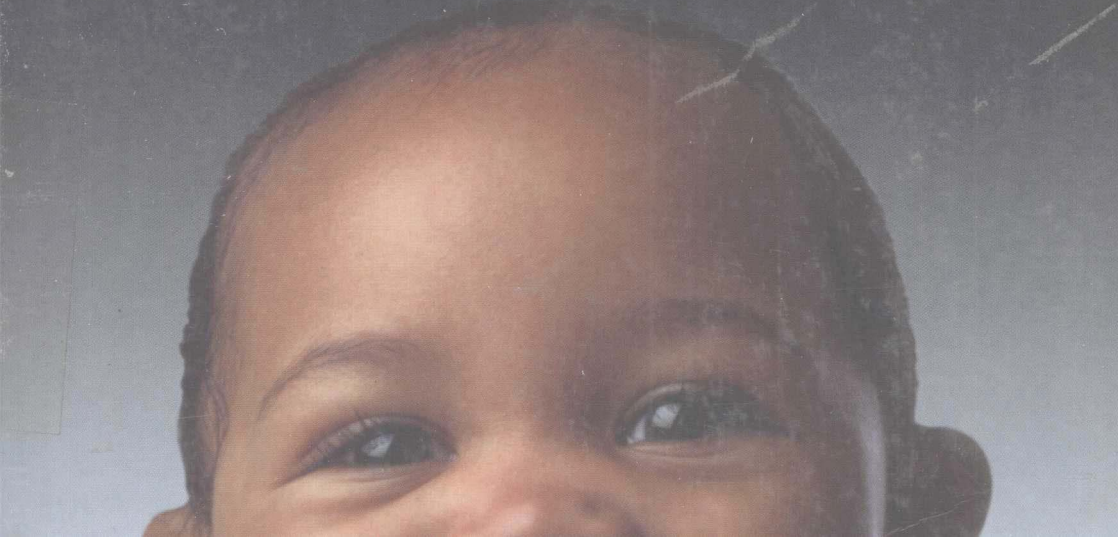
MAKING BABIES

THE SCIENCE OF PREGNANCY

DAVID BAINBRIDGE



Making Babies:

The Science of Pregnancy

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And I will put enmity between thee and the woman and between thy seed and her seed; it shall bruise thy head, and thou shalt bruise his heel.

Unto the woman he said, I will greatly multiply thy sorrow and thy conception; in sorrow thou shalt bring forth children.

Genesis iii, 15–16

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Prologue

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I got the call at 2.30 in the afternoon. I was setting up a machine to characterise a particular human gene that I was studying, but that would now have to wait. I knew that Michelle was seeing her midwife that afternoon, but all her previous visits had been uneventful, so I had put the visit to the back of my mind. Ever since we had nearly lost the baby when Michelle went into premature labour at twenty weeks, we had both felt a mounting sense of relief as the kicking bump had stayed resolutely put for the next ten weeks. At thirty weeks, I think we both thought that we were home free.

But Michelle was sobbing. All she said was 'I've got pre-eclampsia', and I picked up my car keys and left. I drove home along the Ridgeway wondering what would happen now. A little knowledge is a dangerous thing, and I had a little knowledge about pre-eclampsia. That was the irony of the situation – for the last year I had been working in a lab where almost everyone else was working on pre-eclampsia. So I knew that it is the main cause of maternal death in Britain, killing about ten women a year. I also knew that it leads to the death of five or six hundred babies a year. It attacks mothers' blood vessels, forcing their blood pressure to rise, damaging their kidneys and causing sudden fits – *eclampsia* is Greek for 'flash of lightning'. Pre-eclampsia can also slowly strangle the blood vessels that connect the baby to its mother, gradually starving and asphyxiating it. Yes, I knew all the things that could happen, but I just didn't know how likely they were.

I was home in half an hour and then we were on our way to the Radcliffe Hospital in Oxford. I knew the way, as my main lab was on level 3 of the Women's Centre there. I had not yet realised that Michelle was going to spend much of the coming months on level 5. Although I tried to reassure her, we were quiet for much of the journey. We had fallen into the usual trap of complacency. It was as if we had thought that the mere act of having all those scans, all those visits to the doctor, would somehow ward off any problems. I can't help feeling that we had treated the twenty-week ultrasound scan more as a way to get to know our baby than as a way to find out if anything was wrong. Now we were shaken, and everything was uncertain once more.

When we arrived at the hospital, the omens were good. Although Michelle's blood pressure was up, there was no protein in her urine and the baby's heartbeat seemed to be rattling along purposefully. It didn't seem to realise that anything was wrong. Yet the staff at the Radcliffe are careful – some would say obsessive – about dealing with pre-eclampsia, so Michelle was admitted for the night. I did all the usual lone-husband things: I drove home, overfed the cats, packed an entirely inadequate overnight bag for Michelle and drove back to the hospital. Michelle was perched on her bed, fat and forlorn, not knowing whether to be scared or bored. Nothing had changed – her blood pressure remained high, but she still had no symptoms. It was early December, but the overenthusiastic hospital heating system had made her room stifling. Would we get to Christmas?

Pre-eclampsia is not rare – it affects between 5 and 10 per cent of all pregnancies, and perhaps 2 per cent are affected severely. While 'eclampsia' is a vague term for anything that makes pregnant women have fits, 'pre-eclampsia' is a well-defined syndrome. It happens when an unknown substance in the blood of a pregnant woman starts to damage her blood vessels. The vessels react to this damage by constricting, and this makes the woman's blood pressure go up. The mystery substance can also affect the fine blood vessels in the kidneys, so that they start to leak protein into the urine. Blood vessels around the body may also lose protein into the tissues, and this causes swelling of the arms, legs and face. If it

happens in the brain, however, the mother can start to have fits and may even fall into a coma and die. This is what is known for certain about this strange disease – somehow pregnancy is attacking the mother's blood vessels.

Pre-eclampsia can be treated, but not cured, by drugs; they simply reduce the symptoms. Drugs like nifedipine and methyldopa can help to reduce blood pressure, and valium can also reduce the chances of fits. Unfortunately, we do not know the root cause of the disease, so these treatments are the best we have. Sometimes these drugs are not enough and the mother's condition worsens. When this happens, all that is left is the ultimate cure – to deliver the baby. The baby's presence is the cause of pre-eclampsia, so removing it is the solution to the disease. In most cases, pre-eclampsia starts after thirty weeks of pregnancy, so the baby usually survives if it has to be delivered. Yet some cases can start as early as twenty weeks, when the baby has far less chance of survival.

Michelle came home the next day, stable but not better, and with strict instructions to rest. As Christmas approached, we returned to the hospital again and again. Sometimes her blood pressure was normal. Sometimes it was dangerously high. Always she felt fine, and always the baby's heart pounded away enthusiastically. It hated the straps of the fetal heart monitor and always tried to kick them off. We were to thank that baby again and again for its bloody-minded resilience. There seemed to be no pattern to Michelle's blood pressure – we would ensure that we reached the hospital in good time so that she was relaxed for her visit, but it never seemed to make any difference. Her blood pressure rose and fell as it liked.

As the weeks went on, things got worse. Her blood pressure gradually rose until she was given nifedipine, and then it rose some more until she was given methyldopa. This made her a depressed insomniac plagued by nightmares, but at least it kept her blood pressure down. But the baby plodded on completely oblivious as Christmas and New Year passed. With January came the first swollen fingers, the sign that Michelle's system was finally giving in and allowing itself to show some symptoms. Next she began to see flickering lights, a sign that the blood vessels in her brain were

being damaged. Her stays in hospital became longer and longer as the weeks went on; thirty-four, thirty-five, thirty-six.

Despite decades of study, no one knows what causes pre-eclampsia – how a baby actually damages its mother's blood vessels. Pre-eclampsia affects an intriguing selection of women, however, and this has led to most of our theories about what causes it. It is commoner in women's first pregnancies, especially if they are older when they first become pregnant. In successive pregnancies, the risk of pre-eclampsia gets smaller and smaller, although it never disappears. Because of this, it has been claimed that the disease happens in women whose wombs are somehow 'underdeveloped' when they first become pregnant. Yet a few women get pre-eclampsia in their second pregnancy, but not in their first, so this cannot be the whole answer.

It also seems that women who already have children become more susceptible to the disease again if they start a new family with a new father. It is almost as if their pregnancy slate is wiped clean by the new partner. Whatever causes pre-eclampsia, it almost seems to 'remember' who has fathered the woman's children in the past. Not many parts of the human body are able to 'remember' things like this, but the immune system can, and many people are currently studying the possible role of the mother's immune system in pre-eclampsia. Does the female body remember who has fathered its children in the same way that it remembers whether it has been vaccinated for measles?

Pre-eclampsia remains an enigma, and it remains a killer. Frustratingly, it is also a uniquely human killer, as the disease has not been shown to afflict any other species. This is probably one reason why we have made such slow progress in our attempts to understand it. All we can say for sure is that pre-eclampsia is caused by some failure in the normally smooth process of pregnancy. A baby is entirely dependent on its mother before birth and it continually has to struggle to maintain her cooperation. Pre-eclampsia is a sign that the baby is losing its battle to keep its privileged status as a visitor. If the baby fails it will die, and its mother could die too. Although we often do not realise it until things go wrong, pregnancy can be a very fragile thing.

At thirty-eight weeks, Michelle's obstetricians decided to quit while they were ahead. She was induced, and Eleanor screamed her way into the world at 2 o'clock in the morning of 3 February 1998, wondering what all the fuss was about.

Introduction

Pregnancy is a uniquely intimate relationship between two people. All of us luxuriate in this relationship once, and half of us are lucky enough to be able to do it all over again a second time, from the other side, as it were. Never again outside pregnancy can we be so truly intertwined with someone else, no matter how hard we try. In our impersonal, high-technology world, pregnancy remains the one visceral process in which we all take part.

This tiny, red-faced baby that has just landed in our laps and looks as if it is trying to scream itself inside out – what sort of journey has brought it here? How can we make one of these amazing little people, seemingly out of nothing? These are questions that people have asked throughout history: not just the great thinkers among us, but ordinary people like you and me. The miracle of pregnancy – for that is what it is – is one of the few mysteries that almost all of us have pondered. Pregnancy is a very democratic scientific challenge and it can inspire anyone.

This is why I decided to write this book. Ever since I first started to study pregnancy, I have been surprised by the interest that non-scientists have shown in my work. So, I have written this book for people with little or no scientific training who would simply like to know how pregnancy actually works. In my experience, a few major questions crop up in most people's minds when they wonder how we make our children. I like to call these the five 'big questions' of pregnancy, and I have made them the scheme for my book. Each chapter describes our attempts to answer one of these

questions – to tell us a little more about the process that makes every one of us.

First of all, people have long wondered why we reproduce in the way we do. Obviously, humans breed by having sex, by making sperm and eggs, and by a woman becoming pregnant, but why? Until the twentieth century, we simply had to accept that this is how people make children, and we often dignified this acceptance by making sex, fertility, male and female into primal forces in our myths of how the universe conducts its affairs. In the last century, however, science has told us the answers to all these questions, and this is the subject of my first chapter. We now know the reasons why there are men and women, why they have to unite to make a baby, which parent contributes more to the baby, and why it is women who get pregnant.

The first time that most couples know they are to become parents is when the little line on the pregnancy test turns blue. After the initial shock has subsided, many then wonder at the changes that are going on inside the mother's body. She is no longer alone – she has a visitor. Although this visitor is tiny, it can completely take over its mother's body almost straight away. In Chapter 2, I will recount how a Renaissance doctor first wondered how the baby manages to secure its own future by stopping its mother menstruating. We will see how biologists had to crack the hormonal code that controls women's menstrual cycles before they could find out how the embryo stops these cycles. The insidious take-over of a woman's body by her baby is the cause of many of the hardships of pregnancy, including breathlessness, anaemia and morning sickness.

Many parents are amazed at how something as intricate as their baby can be put together in the space of nine months, and in Chapter 3 we will see how this is done. Since the ancient Greeks first speculated about how a baby is made from a formless mass of tissue, there have been many theories about what drives embryonic development. In fact, much of the history of biology has been driven by the quest to find out how a child is constructed. Over the centuries, it has gradually become clear how, within the first seven hectic weeks of pregnancy, the embryo changes from a single cell

into a recognisable baby with eyes, ears, fingers and toes. During this scientific quest we have found out not only how we are made, but also why we are made this way.

One of the most remarkable things about pregnancy is that it ever succeeds at all. Animals have spent most of their evolution trying to stop themselves being exploited by parasites, and to do this they have developed a formidable array of weapons to destroy would-be invaders. Yet female mammals, including women, have had to turn this defence policy on its head so they can become pregnant. The fetus is a foreign being – half of it comes from its father – but even so, it is not attacked by its mother. The story of how a baby avoids being treated like a parasite or an organ transplant is told in Chapter 4. The coexistence of mother and baby is a triumph of the natural world, but it can have strange unforeseen effects – it can make the mother vulnerable to fatal diseases, and it may be the cause of homosexuality in men.

Finally, birth is the climax of pregnancy – the moment at which the baby must make its bid to survive in the outside world. For much of human history, childbirth was the most dangerous time in a woman's life, and all too often it ended in disaster for the baby as well. Humans drew the short straw as far as birth is concerned – women have been left the evolutionary legacy of babies with enormous heads, and a pelvis only recently adapted for walking upright. Although birth is now much safer in many countries, it remains a fundamental turning point in the life of both mother and baby. The baby must quickly adapt to survive in a completely alien environment – gasping, suckling and clinging its way into life. The mother must turn into a nurturing machine, hell-bent on giving her child the best possible start. A woman's entire life story is designed with the express aim of making a success of pregnancy and birth. Menstruation, menopause, the pain of human childbirth – all these burdens are now thought to exist for the sake of that tiny baby.

Throughout history, human pregnancy has been notoriously difficult to study for many different practical and ethical reasons. Yet the realisation that humans are animals just like any other has made our progress much easier. The world is crammed with

millions of different species of animals, each reproducing in its own distinctive way – a veritable treasure-trove of reproductive possibilities. All through this book, I will compare human pregnancy with other animals, especially animals that do things differently. Although studying human pregnancy in isolation can sometimes tell us how things work, a more 'zoological' approach can often help to explain why we make our children in the way we do. Only by discovering what sort of animals we are can we start to explain the idiosyncrasies of how we breed.

Since I started to work on the biology of pregnancy, I have found that it has a unique 'feel' to it – it is where our deepest emotions and driest analytical inquiries collide. Working all day in the lab on some placental gene or other, and then coming home to see my wife's pregnant belly swelling ever larger, made me realise that pregnancy can be one of the hardest things to be objective about. It is never just a science – it is an integral part of our lives that has been woven into our bodies, our history and our mythology. Most of all, pregnancy is a story, and this is why I have written this book as the chronology of a single pregnancy from conception to breastfeeding.

Within the last twenty years, we have finally learnt enough about pregnancy for almost all of its story to be told. Now, for the first time, a coherent story of pregnancy can be told in a form that anyone can understand. This is why I believe this book is important: it is a guide to the 'hows' and 'whys' of pregnancy, at a time when pregnancy is about to become a controversial and emotive issue. Modern technology will soon change pregnancy for ever, possibly even making it redundant. This change will affect all of us, and we need to know how pregnancy makes people if we are to make the right choices about whether to let people change pregnancy.

Yet despite the impending furor about how we can change pregnancy, this is a book about pregnancy 'pure and simple'. Although a great deal has been written in the last few years about surrogacy, designer babies, human cloning and so on, I hope this book will convince you that natural pregnancy is far more interesting than any crude tinkerings that scientists have so far

attempted. Nor does this book deal with the politics of childbirth, although many of the scientific findings that I discuss inform our attitudes and treatment of pregnant women and their babies. As far as drama is concerned, natural pregnancy has it all: sibling rivalry, a battle of the sexes, questions of gender identity. We will see that studying pregnancy can help to tell us why people behave the way they do, and why so many of us want to have children. It can even help us to understand who we are. After all, each of us is a little miracle, the product of a million-to-one coincidental meeting of one sperm and one egg that burgeons into a living, breathing person. Although everyday life may make us forget it, this chance encounter is at the root of each one of us.

Why do we reproduce
in the way we do?