Part I

Fetal Influences on Later Development

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War Babies

Introduction

This article reports fascinating results from an "experiment of nature." In this report we get a glimpse into one of the best-documented analyses of the impact of severe malnutrition on later development. Pregnant women facing the brunt of the Nazi siege of the Netherlands during the final seven months of World War II were reduced to near starvation. Some of these pregnant women miscarried. But if they successfully gave birth, their offspring appeared unremarkable after a period of catch-up growth. At age 18 when tested for military service, those males who were gestated by starving mothers seemed no different than their betternourished peers on a battery of mental tests. Thus, if they survived, they were unscathed.

However, the children of the Nazi siege are now over 50 years old, and many have children of their own – the grandchildren of the pregnant women of 1944. It turns out that even girls who had themselves been normal weight at birth nevertheless went on to have babies of their own (i.e., grandchildren of the starved women) who were either underweight or grew into small adults. In other words, the grandmothers of these small women gave birth to babies who were normal size, but who nevertheless passed on the effects of starvation to the next generation's offspring, a sort of "sleeper effect."

Diamond offers some evolutionary speculations for these results. But for us, the most important point is to show that nature and nurture work in tandem, and often quite mysteriously, to exert their influence. Starvation had different effects depending on two timing issues: (1) when it occurred during pregnancy, and (2) which generation was studied. Concerning the former, it often was the case that when the brunt of the famine occurred during the first trimester of pregnancy, the baby's birth weight was unaffected, whereas when starvation occurred later during pregnancy, the baby was underweight. Concerning the latter, there are effects that may not be detected in the first generation of offspring that nevertheless emerge in a later generation. In short, timing is crucial when considering the interplay between biology and ecology.

Further reading

Stein, Z. and Susser, M. (1976). Prenatal nutrition and mental competence. In J. D. Lloyd-Still (ed.), *Malnutrition and Intellectual Development*. Littleton, MA: Publishing Sciences Group.

ONE

War Babies Jared Diamond

It is easy to write now that each person got 400 calories a day. In practice it was quite another thing. . . . People sought food everywhere in the streets and the surrounding countryside. Anything edible was picked up in this way, and they were lucky who found a potato or two or a handful of greens. . . . People dropped from exhaustion in the streets and many died there. Often people were so fatigued that they were unable to return home, before curfew; so they hid in barns or elsewhere to sleep and there died. . . . Older people, who lacked the strength to go searching for food, stayed at home in bed and died.

Famine and Human Development: The Dutch Hunger Winter of 1944–1945

Among the homey images I recall from my wife's pregnancy are the bigger-than-usual milk cartons in the refrigerator and her vitamin bottles on the kitchen counter. To our generation the value of good nutrition for pregnant women seems obvious. But what makes us so sure? After all, we can't run experiments on people to prove it. Starving hundreds of pregnant women and then comparing their kids with well-nourished cousins would be absolutely unthinkable.

Yet such an inhuman experiment was indeed once conducted. By imposing a famine on part of the population of the Netherlands during the last seven months of World War II, the Nazis effectively reduced 40,000 pregnant women to starvation. These cruel circumstances resulted in a study of the effects of prenatal nutrition that was grimly well-designed, complete with a control group: while these women were starving, other mothers-to-be in the same society were eating comparatively healthy rations. Years later, when the babies who survived had grown into adults, epidemiologists could distinguish the different effects of prenatal and postnatal nutrition; they could even discern the effects of malnutrition at different stages of pregnancy, for at the time the famine took hold, some women were further along in their pregnancy than others. Even now we are still learning what toll was exacted by the events of 45 years ago. Only recently have researchers learned that the famine's effects reached far beyond its immediate victims: now that girls born to the starved Dutch women have grown up and had children of their own, it's become apparent that some of these children too are marked by the deprivations suffered years earlier by their grandmothers!

Today we accept without question that proper nutrition is important for maintaining our health as adults and even more important for the development of our children. The evidence seems most persuasive when we look at the malnourished Third World and see shorter life spans, lowered resistance to disease, and high infant mortalities. But even in the industrialized world we can readily see the positive effects of a good diet. For one thing, today's adults tend to be taller than their parents; the difference approaches six inches in Japan. On average, too, people who are poor, with comparatively limited access to food, are shorter and less healthy than their wealthier countrymen. Moreover, it is not just physical health that seems to be at risk. Many tests of mental function suggest that poor nutrition in childhood may affect learning ability throughout life.

One might speculate that if we are so susceptible to the effects of poor nutrition as children, we must be especially sensitive to those effects while we're still in the womb, when our brain and body are forming. And, indeed, many studies have shown an association between poor nutrition, low weight at birth, and poor physical and mental performance later on. Yet it's not easy to prove that inadequate prenatal nutrition itself is the culprit. Sadly, babies poorly nourished in the womb are likely to be poorly nourished after birth as well. Furthermore, diet may not be the only thing influencing their health. Access to medical care, schooling, and stimulation outside school may play a part.

Figuring out just how big a role prenatal malnutrition plays in this miserable chain of events, then, is difficult at best. But the starvation in the Nazi-occupied Netherlands nearly half a century ago offers some thought-provoking answers.

The Dutch tragedy was the result of one of the most controversial decisions of World War II. After the Allied forces invaded Normandy and liberated France in the summer of 1944, our generals debated two strategies for completing Germany's defeat: to advance northeastward from France into Germany's Ruhr industrial region or to push eastward into the Saar. Had all our resources been concentrated on a single strategy, either might have succeeded. In fact both advances were attempted at once, and both ground to a standstill.

The northern advance hinged on the famous Battle of Arnhem, which inspired the film *A Bridge Too Far*. On September 17, 1944, British paratroops were dropped on the Dutch city of Arnhem to take command of a crucial bridge over the Rhine; other Allied forces, meanwhile, tried to join them from the south. Dutch railroad workers courageously called a general strike to impede the Nazis' efforts to bring up reinforcements. But stiff Nazi resistance forced the Allies to retreat, on September 25, after heavy losses. The Allies then shifted their military effort away from the Netherlands, most of which remained under German occupation until May 1945.

In retaliation for the Dutch strike an embargo on transport in the Netherlands, including transport of food, was ordered by the notorious Nazi Reichskommissar Seyss-Inquart, later tried and hanged at Nuremberg. The predictable result of the embargo, which began in October 1944, was a famine that became progressively worse as stored food supplies were exhausted and that was not lifted until the Netherlands was liberated the following spring. Because an unusually severe winter hampered relief efforts, the famine became known as the Dutch Hunger Winter.

Intake dropped as low as 400 calories a day, down from an alreadyreduced daily ration of 1,500 calories. Still, some people were better off than others. The hunger was milder in the farming regions of the north and south; it was most severe in the large industrial cities of the west, such as Amsterdam, Rotterdam, and The Hague. Those people with enough strength went to the countryside to seek food, including tulip bulbs, in the fields. The hunger was also somewhat selective by social class: people of higher socioeconomic status were able to use money, property, and influence to obtain additional food.

Altogether 10,000 people starved to death, and malnutrition contributed to the deaths of countless others. Adults in the famine cities who survived lost, on average, 15 to 20 percent of their body weight. Some women weighed less at the end of their pregnancy than at its inception.

When the Allies finally liberated the Netherlands in early May 1945, they rushed in food, and conditions quickly improved. But by then 40,000 fetuses had been subjected to the hardships of famine. Depending on their date of conception, these babies were exposed at various stages of gestation, for periods as long as seven months. For example, babies conceived in April 1944 and born in early January 1945 were exposed to the starvation just in the last trimester of pregnancy; those conceived in February 1945 and born in November 1945 were exposed only in the first trimester. Babies unlucky enough to be conceived in August 1944 and born in May 1945 spent their entire second and third trimesters inside increasingly malnourished mothers.

In the late 1960s four researchers at Columbia University School of Public Health – Zena Stein, Mervyn Susser, Gerhart Saenger, and Francis Marolla, all of whom had studied malnutrition in urban ghettos – realized that much might be learned from the now-grown babies of the Dutch Hunger Winter. The outcomes of pregnancies in the stricken cities of the west could be compared with those in towns to the north or south, outside the worst-hit area. In addition, the results of pregnancies during the famine could be compared with those that occurred before and after it.

Hospital records and birth registries yielded statistics on the health of the wartime mothers and their newborns. And at least for the boys, follow-up information on those same children as young adults could be extracted from the records of the Dutch military draft system. Virtually all boys at age 19 were called up for an exam that recorded their height and weight, medical history, results of mental-performance tests, level of schooling completed, and father's occupation; the latter served as a rough indicator of socioeconomic status.

These studies provided some important insights, the first of which concerned the famine's effect on fertility. During the winter of 1944 conceptions quickly declined to one-third the normal level. This suggests that the women's fertility became impaired as their fat reserves, already depleted due to reduced wartime rations, were rapidly used up. The decline was more pronounced for wives of manual workers than of nonmanual workers, presumably because the former had less means to buy their way out of starvation.

The Dutch results agree with other evidence that body weight affects our reproductive physiology. Women in German concentration camps often ceased to menstruate (while low sperm counts and impotence were common among male inmates). Moreover, studies have shown that girls begin menstruating earlier in well-fed industrialized nations than in underfed Third World countries. The same trend applies to the present generation of American women compared with their less well nourished grandmothers. All these pieces of evidence suggest that a woman's fertility is dependent on having sufficient body weight to support conception.

Among the famine babies themselves, the most obvious effects were seen in those who were exposed during the last trimester, which is normally the period when a fetus undergoes its most rapid weight gain: these babies had markedly lower average birth weights (6 pounds 10 ounces) than those born before the famine began (7 pounds 6 ounces). Starvation during the third trimester also resulted in babies who were born slightly shorter and with smaller head circumferences, indicating slightly slower than normal growth of the bones and brain. But the main impact was to retard the growth of muscle and fat.

The prefamine pregnancies had taken place while wartime rations still hovered around 1,500 daily calories – meager for a pregnant woman, who normally requires 2,500 calories a day. Medical records showed that these expectant mothers lost weight themselves but were able to maintain a normal birth weight for their babies. Once rations dropped below 1,500 calories, however, babies began to share the impact. And eventually, as the famine wore on and severe starvation struck, all further weight loss was suffered by the baby rather than the mother. Birth weight recovered quickly when food supplies improved, though: babies born three months after the famine's end had normal weights.

Both during and right after the Hunger Winter there was a sharp rise in infant deaths in the Netherlands' hard-hit cities. For babies exposed to famine only in the first trimester, the rate of stillbirth nearly doubled. Those babies had been conceived just three months before the famine's end, and so they in fact completed most of their gestation inside mothers who were relatively well nourished. Yet malnutrition during those first three months had evidently planted a slow-fuse time bomb that went off at birth.

Still greater, however, was the effect on babies exposed during the second, and especially the third, trimesters. Those babies had a higher-than-normal death rate in their first week of life, and the rate continued to climb until they were at least three months old. Some of these babies died of malnutrition itself, others succumbed to normal childhood infections to which they had lowered resistance. Fortunately, once the famine babies reached the age of one year, their increased risk of death disappeared.

Let's now see how the babies who survived the perils of birth and early infancy were faring 19 years later, when the boys were called up for the draft. In many respects these young men were similar to any others their age. Their height, for example, showed all the usual effects of socioeconomic factors, including family size and diet: sons of manual workers averaged nearly an inch shorter than sons of wealthier fathers, children from families with many mouths to feed were shorter than only children, and later-born sons were shorter than first-born sons. The common thread is that children who have access to less food end up shorter. But postnatal, rather than prenatal, nutrition was the culprit here. If you picked any given group – say, sons of manual workers – the young men whose mothers were starved during pregnancy were no shorter than their peers.

Records from the Dutch draft exams also allowed the Columbia researchers to see if poor nutrition in pregnancy might cause lasting mental deficits as well as physical ones. Experiments with rats had shown that offspring of mothers that are starved in pregnancy end up with fewer-than-normal brain cells and learning disabilities. So when the researchers compared the grown-up famine babies' performance on tests of mental proficiency with the performance of those who had received better prenatal nourishment, they expected to find poorer scores for those who had been starved during gestation.

No such result was forthcoming. The draft exam, which included tests of verbal, arithmetic, clerical, and mechanical skills, clearly showed the effects of social environment, which were parallel to the physical effects already mentioned – thus, sons of manual laborers, sons from large families, and sons born late into a family of several children tended to score below other young men. But no effect whatsoever could be attributed to prenatal starvation. One possible explanation is that our brain has enough extra cells to preserve mental function even if some of our cells are lost. At any rate, whatever effects can be attributed to nutrition must be due to nutrition after birth, not before it.

This, then, was the good news, such as it was. Those starved children who made it to adulthood were no worse off than their better-nourished

counterparts. However, the medical records of the male famine babies who never made it to a draft physical did reveal one consequence of prenatal starvation – and it was sobering. Fetuses exposed to famine during their first three months in the womb were twice as likely as others to have defects of the central nervous system, such as spina bifida (in which the spine fails to close properly) and hydrocephalus (a related condition, characterized by fluid accumulating in the brain). The birth defects, it now appears, almost certainly arose from starvation during the first trimester, when the nervous system was being laid down.

Just how did a lack of food have such a dire result? Animal experiments have raised the suspicion that such defects can arise from a deficiency of the B vitamin folic acid early in pregnancy. A year ago this finding was confirmed for humans in a study of 22,776 pregnant women in Boston. Babies born to mothers who took multivitamins including folic acid during the first six weeks of pregnancy had a nearly fourfold lower frequency of central nervous system defects than did babies born to women who did not take such supplements. Brands of multivitamins that lacked folic acid, or multivitamins taken only after the seventh week of pregnancy, offered no protection.

All the results from the Dutch famine studies that I've discussed so far describe the effects of starvation on mothers and their children. But recent findings have raised disturbing questions about the famine's effect on a third generation. By now the famine babies are 45 or 46, and most of the girls have long since had children of their own; the "girls" themselves are women at the end of their reproductive careers. More than 100 of these women happened to have had their babies in the same Amsterdam hospital in which they themselves were born, which makes for an easy comparison of birth records. An examination of those records has revealed something very odd: it turns out that those women who were themselves fetuses in their first and second trimester during the Dutch Hunger Winter gave birth to underweight babies. That is, the babies were somehow affected by the starvation of their grandmothers many decades earlier.

This result might have been easier to understand if the mothers themselves had been underweight at birth or were small as adults. Neither was true. Recall that starvation in the first or second trimester produced babies with normal birth weights. Only third-trimester starvation led to small babies. Yet, paradoxically, when these small babies later became mothers, they gave birth to normal-size babies. It was the women who were themselves normal size at birth who became mothers of underweight infants.

Somehow the grandmothers' suffering programmed their children in utero so that the grandchildren would be affected. This astonishing result will undoubtedly inspire experiments aimed at identifying the still-unknown cellular mechanism. But what is indisputable is that the Dutch famine left its harsh imprint on at least three generations.

From the perspective of evolutionary biology, the famine posed to the bodies of pregnant mothers an agonizing dilemma. What would you do in a situation threatening both your life and your child's life if anything you did to help one would hurt the other? Think quickly: If you see a car about to crash head-on into your car, do you throw yourself in front of your child sitting strapped in the seat beside you or do you try to protect yourself instead? Now let's make the choice more agonizing: What if your child's subsequent survival hinges on your own? You've all heard the airlines' standard safety announcement that in the event of a loss of cabin pressure, place the oxygen mask on yourself first, *then* place the mask on your child. In that situation, you have to help yourself first, because you'll be in no state to help your child if you are unconscious.

Similarly a mother starving in the Netherlands in 1944 was forced to unconsciously "choose" whether to devote the few available calories to her own body or to her fetus. This is a classic example of a conflict between two genetically related individuals. Natural selection favors the individual who passes on his or her genes to the most descendants. The genetic interests of the fetus are served by saving itself, and hence we evolve as fetuses to be parasites on our mother, commandeering her nutrients as efficiently as possible. But the mother's genetic interests are served by passing her genes to offspring. She gains nothing if her nutritional sacrifices kill not only herself but her child. Perhaps she would be best off, from an evolutionary point of view, if she sacrificed that fetus and tried again later. Yet there is no certainty that she will have another chance later.

The outcome of the Dutch famine indicates that natural selection struck a compromise. When the famine began, a mother's body at first accepted the full brunt, losing weight while preserving the weight of the fetus. In the next stage of famine both the fetus and the mother shared the hardship. In the last stage all weight loss came at the expense of the fetus, because any more weight loss by the mother would have threatened the mother's survival and thereby the survival of her child.

These pregnant women had no say in how their body allocated its precious resources, of course. Natural selection proceeded along its inexorable journey oblivious to any human agony or ethical dilemma. To ask whether the decisions it made were wise, whether they were somehow the "right" decisions, is irrelevant. The choices were arrived at in accordance with the cold logic of evolution and nothing more.

But what about the decisions that created such cruel conditions in the first place? What about the reasoning that even today, in the guise of wartime expediency, can compel one group of people to consciously impose starvation on another and thus scar the lives of unborn generations? For that matter, what about the reduction of social programs in our own society that might subject untold numbers of children, both before and after birth, to the dangers of malnutrition simply by failing to ensure proper nourishment for them and their mothers? The lessons of the Dutch Hunger Winter are there for the learning. We can ignore them only at our children's, and our grandchildren's, expense.