HEALTH IN TRANSITION

Translating developmental origins of health and disease science to improve future health in Africa

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RELATION BETWEEN FAMINE AND HEALTH IN FUTURE GENERATIONS: POTENTIAL KNOWLEDGE TRANSLATION TO AFRICA

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Nutrition provides the essential building blocks for human health. Although there is enough food on the planet to feed all its inhabitants, inequality in access to food poses serious threats to humanity. Poor nutrition, especially during critical periods of human development, permanently affects the structure and function of organs with lasting adverse consequences for an individual's susceptibility to disease, not only affecting the individual but society as a whole with considerable loss of human capital.

This chapter summarises the evidence from studies investigating the effects of prenatal exposure to the Dutch famine on later mental and physical health.

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The Dutch famine of 1944-1945 was remarkable in several ways, and its unique features have contributed to the fact that the Dutch famine has most often been used in studies examining the long-term consequences of prenatal undernutrition. The Dutch famine was an acute period of undernutrition that was circumscribed in time and place; it had an abrupt beginning and end and struck a population that was previously and subsequently well nourished. Also, the administration was well organised, and records were kept allowing researchers to investigate the consequences of starvation in the decades that followed.

While the acute effects of famine are devastatingly apparent in most cases, the effects of famine for those as yet unborn may not become apparent until decades later. Prenatal famine exposure increases the risk of chronic degenerative diseases and mental health problems. It not only increases health care costs but also puts an extra burden on the economy by decreasing human capital. In this way, famine leaves lasting marks on populations – even for generations to come, highlighting the importance of securing access to food for all, with particular relevance for Africa – with a rapidly growing population and intense urbanisation. Food security for all should remain a priority, as food is essential for the health and wealth of the population today and generations of the future.

Famine and its occurrence in time and place

Food is of fundamental importance to human health. The availability of food has varied in time and place. Throughout history, famines have plagued society. Every inhabited continent in the world has experienced a period of famine in the past. Famines were commonplace across the world, but in the last decades, Africa has been struck by famine more than other continents. Since 2010, Africa has been the most affected continent in the world. Despite tremendous efforts in combatting hunger as part of the Millennium Development Goals, in 2017, the UN officially declared famine had returned to Africa, with about 20 million people at risk of death from starvation in Nigeria, in South Sudan, in Yemen, and Somalia.²

There are several complex and interrelated factors contributing to Africa's vulnerability to food insecurity. The majority of Africans are directly dependent on subsistence farming on a continent that is prone to extreme natural disasters, including severe drought and floods. These natural disasters lead to failed crops, as well as insufficient pasture feed and water for livestock. In addition, the majority of African countries facing food insecurity are experiencing internal conflict, impeding both access to food and food production. Moreover, the African region also has the lowest per capita income in the world and the highest poverty levels,

2 Wikipedia. 2020. Famine. [<https://en.wikipedia.org/wiki/Famine>].

meaning that a high dependence on food imports increases their vulnerability to fluctuations in food prices. The vicious cycle of poverty and undernutrition has proven to be difficult to break.

Hunger in an age of plenty

Poor diets, due to insufficient, imbalanced or excessive intakes of nutrients, can impair growth and development and induce disease. Today the world faces a double burden of malnutrition that includes both under-nutrition and over-nutrition.³ Counterintuitive as it may seem, both undernutrition and overnutrition are reducing the health of millions of individuals around the globe. Hunger and inadequate nutrition contribute to early deaths for mothers, infants and young children, and account for more losses of life than Aids, malaria and tuberculosis combined.⁴ Deficiencies in the diets of children can impair growth and development and lead to stunting and wasting in childhood while deficiencies in adulthood can lead to blindness, scurvy or anaemia. Such cases are most often seen in developing countries, while in developed countries, the consequences of imbalanced or excessive diets lead to obesity, diabetes and cardiovascular diseases.

The evidence presented in this chapter shows that the consequences of undernutrition may not be limited to the individuals suffering from undernutrition. Undernutrition before birth profoundly affects fetal growth, development and health. Those most affected by undernutrition may indeed be those as yet unborn during a famine. The consequences are apparent throughout the life-course and might even extend into the following generation. Similarly, imbalances in prenatal nutrition caused by maternal obesity and gestational diabetes can also negatively affect offspring's health.

The Dutch famine as a model to test the DOHaD hypothesis

Every living creature is plastic and able to adapt to its environment. Adaptations to the environment during the earliest stages of development have profound implications for further development, growth and health of the individual. The notion that maternal diet, metabolism and stress during pregnancy have lasting effects on the health of the offspring has been supported by a strong solid scientific evidence base from various scientific disciplines.⁵ The hypothesis that

3 World Health Organization (WHO). 2020. Nutrition: Challenges. *WHO Health Topics*. [<https://www.who.int/nutrition/challenges/en/>].

4 Ibid.

5 Barker, D., Barker, M., Fleming, T. & Lampl, M. 2013. Developmental biology: Support

undernutrition in utero permanently changes the body's structure, function and metabolism in ways that lead to chronic degenerative disease in later life was formulated based on epidemiological studies consistently showing small size at birth was linked to higher disease risk in later life.⁶ Small size at birth was taken as an indication of reduced fetal growth due to limited supply of nutrients to the fetus.⁷ Animal studies have experimentally shown that restricted fetal nutrition indeed induces adaptations that lead to altered structure and function of organs, increased rates of disease and shortened lifespan.⁸ However, the experimental evidence for the hypothesis in humans is impossible to obtain.

While famine is sadly not uncommon in many parts of the world, studying effects of undernutrition during pregnancy is hampered by the fact that undernutrition is usually not restricted to pregnancy alone, and effects of chronic undernutrition and accompanying problems of infection complicate the situation. The tragic circumstances of the Dutch famine of 1944-1945 created a unique opportunity to assess the effects of prenatal famine exposure on health in later life. The Dutch famine has been used by various investigators as an equivalent to an experimental set-up to investigate the effects of prenatal undernutrition in humans. What is unusual about the Dutch famine is:

- ☐ that the famine was imposed on a previously well-nourished population;
- ☐ there were sudden onset and relief from the famine; and
- ☐ despite the adversities of the war, midwives and doctors continued to offer professional obstetric care and kept detailed records of the course of pregnancy, the delivery and the size and health of the baby at birth.⁹

Furthermore, detailed information is available on the weekly rations provided during the famine, and in several afflicted cities birth records were kept which

mothers to secure future public health. *Nature*, 504(7479), December:209-211. [<https://doi.org/10.1038/504209a>].

6 Barker, D.J. 2007. The origins of the developmental origins theory. *Journal of Internal Medicine*, 261(5), June:412-417. [<https://doi.org/10.1111/j.1365-2796.2007.01809.x>].

7 Ibid.

8 Ozanne, S.E. & Constância, M. 2007. Mechanisms of disease: the developmental origins of disease and the role of the epigenotype. *Nature Clinical Practice Endocrinology & Metabolism*, 3(7), August:539-546. [<https://doi.org/10.1038/ncpendmet0531>].

9 Roseboom, T.J. 2019. Epidemiological evidence for the developmental origins of health and disease: effects of prenatal undernutrition in humans. *Journal of Endocrinology*, 242(1), July: T135-T144. [<https://doi.org/10.1530/JOE-18-0683>].

allowed researchers to trace those born around the time of the famine and thus to study the long-term effects of prenatal famine exposure.¹⁰

The historical course of events that led to the Dutch famine 1944-1945

After the invasion of the Allied forces on June 6, 1944, a few weeks of heavy fights followed. Then, the Allied forces finally broke through German lines. Quickly, the Allied troops took possession of France, Luxembourg and Belgium. By September 4, 1944, the Allies had the strategic city of Antwerp in their hands, and on the 14th they entered the Netherlands.¹¹ The Dutch expected that the German occupation would soon be over, and so did the commanders of the Allied forces. Hoping to capture strategic bridges across the river Rhine to open a pathway for rapid invasion into Germany, the Allied forces launched a parachute attack behind the Nazi forces near the city of Arnhem.¹² However, the operation failed with significant losses. Operation Market Garden had failed. Subsequently, the Dutch government called for a strike of the Dutch railways to support the Allied offensive. As a reprisal, the Germans banned all food transports. The food situation in the western part of the Netherlands worsened dramatically. Food stocks ran out rapidly, and soon rations for adults dropped to below 1 000 calories a day.¹³ The embargo on food transports was lifted in early November 1944, when food transport across the water was permitted again. Because most canals and waterways were frozen due to the early and extremely severe winter, it had become impossible to bring in food from the rural east to the urban west of the Netherlands.¹⁴ Food rations declined to extremely low levels between February and May 1945, with daily rations varying between 400 and 800 calories a day. During the famine, infants were relatively protected, because their official daily rations never fell below 1 000 calories. Pregnant and lactating women were entitled to an extra amount of food, but at the peak of the famine, these extra supplies could not be provided anymore. Also, extra food came from the black market, central kitchens, church organisations and foraging trips to the countryside. The period of famine ceased in early May 1945 immediately after the

10 Ibid.

11 Roseboom, T.J., De Rooij, S. & Painter, R. 2006. The Dutch famine and its long-term consequences for adult health. *Science Direct: Early Human Development*, 82(8), August:485-491. [<https://doi.org/10.1016/j.earlhumdev.2006.07.001>].

12 Roseboom, 2019.

13 Ibid.

14 Ibid.

final surrender of the Germans. The food situation quickly improved, and within a month, rations were above 2 000 calories.¹⁵

In addition to the immediate provision of food after the war, medical aid was a top priority for the Netherlands. The famine had a profound effect on the general health of the population. In Amsterdam, the mortality rate in 1945 had more than doubled compared to 1939, and most of this increase in mortality was likely attributable to undernutrition.¹⁶ Doctors from the UK and the US were sent to survey medical needs. Clement Smith from Harvard Medical School was among the first to witness the effects of the famine on the health of the Dutch population. He immediately saw the opportunity to obtain information that would help resolve important questions on how poor maternal nutrition affects pregnancy and the development of the fetus before birth.¹⁷ Using obstetric records from Rotterdam and The Hague, he studied effects of prenatal exposure to famine on pregnancy and the fetus which he described in his paper, *The effect of famine on pregnancy and its product*.¹⁸ This paper describes that babies born during the famine were lighter at birth.

Since the Dutch famine lasted five-six months, investigators have been able to not only assess effects of prenatal undernutrition per se but also to differentiate between effects of undernutrition according to its timing during gestation and the organs and tissues developing at that time. Although the exact definitions differ between studies, all studies assessing the effects of prenatal famine exposure have differentiated between the effects of famine in early, mid or late gestation.¹⁹

Consequences of prenatal famine exposure

Overall, studies of individuals born around the time of the Dutch famine studies have shown that prenatal undernutrition increased disease susceptibility. The effects of famine exposure appeared to depend on its timing during gestation and the organs and tissues developing at that time.

15 Ibid.

16 Roseboom et al., 2006.

17 Ibid.

18 Smith, C. 1947. The effects of wartime starvation in Holland on pregnancy and its product. *American Journal of Obstetrics & Gynecology*, 53(4):599-608.
[[https://doi.org/10.1016/0002-9378\(47\)90277-9](https://doi.org/10.1016/0002-9378(47)90277-9)].

19 Roseboom, 2019.

Early gestation

The landmark studies of Stein and Susser performed in the early seventies initially found no effect of undernutrition during gestation on the adult mental performance.²⁰ However, they subsequently showed that those exposed in early gestation had a two-fold increase in the risk of schizophrenia and anti-social personality disorder.²¹ Later studies also found increased rates of addiction.²² Some studies have found indications of effects of exposure to famine in early gestation on cognition though other studies did not detect such effects.²³ Imaging studies of the brain have shown lasting effects of famine exposure on brain size and structure.²⁴ Men who had been exposed to famine in early gestation had smaller intracortical volumes and total brain volumes than unexposed men. They also had smaller volumes of total cortical grey matter, white matter cerebellar grey matter, thalamus, caudate nuclear and accumbens area and a large number of more specific cortical

- 20 Stein, Z., Susser, M., Saenger, G. & Morolla, F. 1975. Famine and Human Development. *The Dutch Hunger Winter of 1944-45*. New York: Oxford University Press.
- 21 Hoek, H.W., Susser, E.Z., Buck, K., Lumey, L.H., Lin, S.P. & Gorman, J.M. 1996. Schizoid personality disorder after prenatal exposure to famine. *American Journal of Psychiatry*, 153(12), December:1637-1639. [https://doi.org/10.1176/ajp.153.12.1637]; Neugebauer, R., Hoek, H.W. & Susser, E. 1999. Prenatal exposure to wartime famine and development of antisocial personality disorder in early adulthood. *The Journal of the American Medical Association*, 282(5), Augustus:455-462. [https://doi.org/10.1001/jama.282.5.455].
- 22 Franzek, E.J., Spranger, N., Janssens, A.C., Van Duijn, C.M. & Van de Wetering, B.J.M. 2008. Prenatal exposure to the 1944-45 Dutch 'hunger winter' and addiction later in life. *Addiction*, 103(3), March:433-438. [https://doi.org/10.1111/j.1360-0443.2007.02084.xx].
- 23 De Rooij, S.R., Wouters, H., Yonker, J.E., Painter, R.C. & Roseboom, T.J. 2010. Prenatal undernutrition and cognitive function in late adulthood. *Proceedings of the National Academy of Sciences of the United States of America*, 107(39), September:16881-16886. [https://doi.org/10.1073/pnas.1009459107]; De Groot, R.H., Stein, A.D., Jolles, J., Van Boxtel, M.P., Blauw, G.J., Van de Bor, M. & Lumey, L.H. 2011. Prenatal famine exposure and cognition at 59 years. *International Journal of Epidemiology*, 40(2), March:327-337. [https://doi.org/10.1093/ije/dyq261]; Stein, M., Susser, G., Saenger, F. & Marolla F. 1972. Nutrition and mental performance. *Science*, 178(4062):708-713. [https://doi.org/10.1126/science.178.4062.708].
- 24 Hulshoff Pol, H.E., Hoek, H.W., Susser, E., Brown, A.S., Dingemans, A. & Schnack, H.G. 2000. Prenatal exposure to famine and brain mortality in schizophrenia. *American Journal of Psychiatry*, 157(7), July:1170-1172. [https://doi.org/10.1176/appi.ajp.157.7.1170]. De Rooij, S.R., Caan, M.W., Swaab, D.F., Nederveen, A.J., Majoie, C.B., Schwab, M., Painter, R.C. & Roseboom, T.J. 2016. Prenatal famine exposure has sex-specific effects on brain size. *Brain*, 139(8), July:2136-2142. [https://doi.org/10.1093/brain/aww132].

white and grey matter areas. The overall reduction in brain size after prenatal famine exposure was ~five per cent.²⁵

Stein and Susser's landmark study found that 19-year old conscripts exposed to famine in early gestation were more likely to be obese.²⁶ These effects on obesity were also found in two other studies which examined effects on anthropometry in adulthood with the effects being more pronounced among women than men.²⁷ Women who had been exposed to famine in early gestation had higher BMI and appeared to be more centrally obese than those who had not been exposed to famine prenatally. These differences in adiposity could at least in part be mediated by differences in food preferences and food intake as there are indications that those exposed to famine in early gestation had higher energy intakes, higher protein intakes and higher intakes of fat.²⁸ They also had more atherogenic lipid profiles, with higher LDL and lower HDL cholesterol levels, again the effects being more pronounced in women than in men.²⁹ There were indications that those exposed to famine in early gestation more often had disturbed blood coagulation, and were

25 Roseboom, 2019.

26 Ravelli, G.P., Stein, Z.A. & Susser, M.W. 1976. Obesity in young men after famine exposure in utero and early infancy. *The New England Journal of Medicine*, 295(7), August:349-353. [<https://doi.org/10.1056/NEJM197608122950701>].

27 Stein, A.D., Kahn, H.S., Rundle, A., Zybert, P.A., Van der Pal-de Bruin & K., Lumey, L.H. 2007. Anthropometric measures in middle age after exposure to famine during gestation: evidence from the Dutch famine. *American Journal of Clinical Nutrition*, 85(3), March:869-876. [<https://doi.org/10.1093/ajcn/85.3.869>]; Ravelli, A.C., Van Der Meulen, J.H., Osmond, C., Barker, D.J. & Bleker, O.P. 1999. Obesity at the age of 50 y in men and women exposed to famine prenatally. *American Journal of Clinical Nutrition*, 70(5):811-816. [<https://doi.org/10.1093/ajcn/70.5.811>].

28 Stein, A.D., Rundle, A., Wada, N., Goldbohm, R.A. & Lumey, L.H. 2009. Associations of gestational exposure to famine with energy balance and macronutrient density of the diet at age 58 years differ according to the reference population used. *Journal of Nutrition*, 139(8), June:1555-1561. [<https://doi.org/10.3945/jn.109.105536>]; Lussana, F., Painter, R.C., Ocke, M.C., Buller, H.R., Bossuyt, P.M. & Roseboom, T.J. 2008. Prenatal exposure to the Dutch famine is associated with a preference for fatty foods and a more atherogenic lipid profile. *American Journal of Clinical Nutrition*, 88(6), January:1648-1652. [<https://doi.org/10.3945/ajcn.2008.26140>].

29 Roseboom, T.J., Van der Meulen, J.H., Osmond, C., Barker, D.J., Ravelli, A.C. & Bleker, O.P. 2000a. Plasma lipid profile in adults after prenatal exposure to the Dutch famine. *American Journal of Clinical Nutrition*, 72(5), November:1101-1106. [<https://doi.org/10.1093/ajcn/72.5.1101>]; Lumey, L.H., Stein, A.D., Kahn, H.S. & Romijn, J.A. 2009. Lipid profiles in middle-aged men and women after famine exposure during gestation: the Dutch Hunger Winter Families Study. *American Journal of Clinical Nutrition*, 89(6), May:1737-1743. [<https://doi.org/10.3945/ajcn.2008.27038>].

more responsive to stress.³⁰ Exposure to famine in early gestation was furthermore associated with increased rates of cardiovascular disease at a younger age.³¹

Although based on small numbers, there is evidence to suggest that women exposed to famine in early gestation have increased rates of breast cancer.³² Analyses of mortality data suggest that those exposed to famine in early gestation have increased mortality, which is mainly found in women and mostly due to cardiovascular causes and cancer.³³ Uniquely, Ekamper used a large national birth cohort to assess effects on mortality up to age 63 years and found a 12 per cent increase in mortality among those who had been exposed to famine in early gestation.

The effects of famine exposure in early gestation are not limited to health but appear to have economic consequences too. The most striking finding was the significantly lower probability of being employed among those who had been exposed to famine in early gestation.³⁴ This result fits with findings of poorer

- 30 Roseboom, T.J., Van der Meulen, J.H., Ravelli, A.C., Osmond, C., Barker, D.J. & Bleker, O.P. 2000b. Plasma fibrinogen and factor VII concentrations in adults after prenatal exposure to famine. *British Journal of Haematology*, 111(1), November:112-117. [https://doi.org/10.1111/j.1365-2141.2000.02268.x]; Painter, R.C., De Rooij SR, Bossuyt PM, Phillips DI, Osmond C, Barker DJ, Bleker OP, Roseboom TJ. 2006. Blood pressure response to psychological stressors in adults after prenatal exposure to the Dutch famine. *Journal of Hypertension*, 24(9), September:1771-1778. [https://doi.org/10.1097/01.hjh.0000242401.45591.e7].
- 31 Roseboom, T.J., Van der Meulen, J.H., Osmond, C., Barker, D.J., Ravelli, A.C., Schroeder-Tanka, J.M., Van Montfrans, G.A., Michels, P.P. & Bleker, O.P. 2000c. Coronary heart disease after prenatal exposure to the Dutch famine 1944-45. *Obstetrical and Gynecological Survey*, 84(6), December:595-598. [https://doi.org/10.1136/heart.84.6.595]; Painter, R.C., De Rooij, S.R., Bossuyt, P.M., Simmers, T.A., Osmond, C., Barker, D.J., Bleker, O.P. & Roseboom, T.J. 2006. Early onset of coronary heart disease after prenatal exposure to the Dutch famine. *American Journal of Clinical Nutrition*, 84(2), September:322-327. [https://doi.org/10.1093/ajcn/84.1.322].
- 32 Painter, R.C., De Rooij, S.R., Bossuyt, P.M., Osmond, C., Barker, D.J., Bleker, O.P. & Roseboom, T.J. 2006. A possible link between prenatal exposure to famine and breast cancer: a preliminary study. *American Journal of Human Biology*, 18(6), November:853-856. [https://doi.org/10.1002/ajhb.20564].
- 33 Ekamper, P., Van Poppel, F., Stein, A.D. & Lumey, L.H. 2014. Independent and additive association of prenatal famine exposure and intermediary life conditions with adult mortality between age 18-63 years. *Social Science and Medicine*, 119, October:232-239. [https://doi.org/10.1016/j.socscimed.2013.10.027]; Van Abeelen, A.F., Veenendaal, M.V., Painter, R.C., De Rooij, S.R., Dijkgraaf, M.G., Bossuyt, P.M., Elias, S.G., Grobbee, D.E., Uiterwaal, C.S. & Roseboom, T.J. 2012. Survival effects of prenatal famine exposure. *American Journal of Clinical Nutrition*, 95(1), December:179-83. [https://doi.org/10.3945/ajcn.111.022038].
- 34 Scholte, R.S., Van den Berg, G.J. & Lindeboom, M. 2015. Long-run effects of

performance on cognitive tasks in men who had been exposed to famine in early gestation.³⁵ It seems that the effects of famine on employment are at least partly explained by effects on cognition. Mental disorders such as schizophrenia and anti-social personality disorders, more common after exposure to famine in early gestation, may contribute to this, as well as physical health.³⁶ It could be argued that the effects of famine exposure on health reduced individual productivity and hence employability.

Mid-gestation

Mid-gestation exposure to famine was linked to an increase in the occurrence of microalbuminuria in adulthood and a decrease in creatinine clearance.³⁷ It may be that mid-gestational exposure to famine – the period of the rapid increase in nephron number – may prevent the formation of sufficient glomeruli and thus increase the risk for microalbuminuria and deteriorating renal function in adulthood. This finding supports the concept that intrauterine conditions during distinct, organ-specific periods of sensitivity may permanently determine health outcome in later life.³⁸ Another example of this phenomenon is the finding in the same study that people who had been exposed to famine in mid-gestation had an increased prevalence of obstructive airways disease.³⁹ These observations were not paralleled by reduced lung function or increased serum concentrations of Immunoglobulin E, suggesting that the increased prevalence of symptoms and disease may be attributable to increased bronchial reactivity rather than to irreversible airflow obstruction or atopic disease. Because the bronchial tree grows most rapidly in mid-gestation, these findings support the hypothesis that fetal undernutrition

gestation during the Dutch Hunger Winter Famine on labor market and hospitalization outcomes. *Journal of Health Economics*, 39, January:17-30. [<https://doi.org/10.1016/j.jhealeco.2014.10.002>].

35 De Rooij et al., 2010.

36 Roseboom, 2019.

37 Painter, R.C., Roseboom, T.J., Van Montfrans, G.A., Bossuyt, P.M., Krediet, R.T., Osmond, C., Barker, D.J. & Bleker, O.P. 2005. Microalbuminuria in adults after prenatal exposure to the Dutch famine. *Journal of the American Society of Nephrology*, 16(1), February:189-194. [<https://doi.org/10.1681/ASN.2004060474>].

38 Roseboom, 2019.

39 Lopuhaä, C.E., Roseboom, T.J., Osmond, C., Barker, D.J., Ravelli, A.C., Bleker, O.P., Van der Zee, J.S. & Van der Meulen, J.H. 2000. Atopy, lung function and obstructive airways disease after prenatal exposure to famine. *Thorax*, 55(7), July:555-561. [<https://doi.org/10.1136/thorax.55.7.555>].

permanently affects the structure and physiology of the airways during 'critical periods' of development that coincide with periods of rapid growth.⁴⁰

Late gestation

Different studies have shown exposure to the Dutch famine during any stage of gestation were found to have raised glucose and insulin levels as adults.⁴¹ The effects being most pronounced among those exposed to famine in late gestation, seemingly reflecting an insulin secretion defect.⁴² It may suggest the effects of prenatal exposure to famine on beta-cell development with lasting adverse consequences for its function.

What do these historic studies teach us about population health today?

Findings from studies of people born around periods of famine suggest that maternal nutrition before and during pregnancy play an important role in later disease susceptibility. They have shown that maternal undernutrition during gestation has lasting adverse consequences for the offspring's health.⁴³ Many chronic diseases that plague our society may originate in the womb. The effects seem to be large and depend on the timing during gestation and the organs and tissues developing at that time.⁴⁴ Also, the effects are independent of the size of the baby at birth. Most notably, those exposed to famine in early gestation did not have lower birth weights than those who were not exposed to famine prenatally but did

40 Roseboom, 2019.

41 Ravelli, A.C., Van der Meulen, J.H., Michels, R.P., Osmond, C., Barker, D.J., Hales, C.N. & Bleker, O.P. 1998. Glucose tolerance in adults after in utero exposure to the Dutch famine. *The Lancet*, 351(9097), January:173-177. [[https://doi.org/10.1016/s0140-6736\(97\)07244-9](https://doi.org/10.1016/s0140-6736(97)07244-9)]; Lumey, L.H., Stein, A.D. & Kahn, H.S. 2009. Food restriction during gestation and impaired fasting glucose or glucose tolerance and type 2 diabetes mellitus in adulthood: evidence from the Dutch Hunger Winter Families Study. *Journal of Developmental Origins of Health and Disease*, 1, January:S164; De Rooij, S.R., Painter, R.C., Roseboom, T.J., Phillips, D.I., Osmond, C., Barker, D.J., Tanck, M.W., Michels, R.P., Bossuyt, P.M. & Bleker, O.P. 2006. Glucose tolerance at age 58 and the decline of glucose tolerance in comparison with age 50 in people prenatally exposed to the Dutch famine. *Diabetologia*, 49(4), April:637-643. [<https://doi.org/10.1007/s00125-005-0136-9>]; De Rooij, S.R., Painter, R.C., Phillips, D.I., Osmond, C., Michels, R.P., Godsland, I.F., Bossuyt, P.M., Bleker, O.P. & Roseboom, T.J. 2006. Impaired insulin secretion after prenatal exposure to the Dutch famine. *Diabetes Care*, 29(8), September:1897-1901. [<https://doi.org/10.2337/dc06-0460>].

42 De Rooij et al., 2006.

43 Roseboom, 2019.

44 Ibid.

have the worst health outcomes as adults, possibly implying that adaptations that enable the fetus to continue to grow may nevertheless have adverse consequences for health in later life.⁴⁵ The chronic degenerative disease may be viewed as the price paid for adaptations made to an adverse intrauterine environment.

These findings confirm experimental evidence from studies in animals that show undernutrition during gestation permanently affecting the structure and function of organs, thereby affecting behaviour as well as disease risk, and ultimately shortening lifespan.⁴⁶ Findings from studies of the Dutch famine's long-term consequences were replicated or examined in other settings to study the effects of famines. Studies in other settings, of famines with different durations and severity affecting different populations, support these findings and suggest that the results of studies on the Dutch famine are not uniquely linked to the characteristics and setting of the Dutch famine, but rather reflect biologically fundamental processes that describe human plasticity.⁴⁷

A study in Nigeria showed that prenatal undernutrition also affects later health in African populations.⁴⁸ People exposed to the Biafran famine during the Nigerian civil war (1967-1970) in utero were found that have increased rates of hypertension and type 2 diabetes at the age of 40 compared to those who had not been exposed to the Biafran famine in utero.

Similarly, studies of people exposed to the Great Leap Forward famine in China have shown similar effects of prenatal famine exposure in later life risk of diabetes, hypertension and schizophrenia.⁴⁹ Undernutrition in early life contributes significantly to the increasing prevalence of hypertension and glucose intolerance. Therefore, prevention of fetal and infant undernutrition should be given high priority in national health, education, and economic agendas to limit the increase of non-communicable diseases in many developing countries.

Evidence for the importance of early nutrition for later health has come from many cohort studies across the globe. Pooled analyses of several cohorts from

45 Ibid.

46 Ozanne & Constância, 2007.

47 Gluckman, P.D. & Hanson, M.A. 2004. Living with the past: evolution, development, and patterns of disease. *Science*, 305(5691), September:1733-1736. [<https://doi.org/10.1126/science.1095292>].

48 Hult, M., Tornhammar, P., Ueda, P., Chima, C., Bonamy, A.K., Ozumba, B. & Norman, M. 2010. Hypertension, diabetes and overweight: looming legacies of the Biafran Famine. *PLoS One*, 5(10), November:e13582. [<https://doi.org/10.1371/journal.pone.0013582>].

49 Chen, Y. & Zhou, L.A. 2007. The long-term health and economic consequences of the 1959-1961 famine in China. *Journal of Health Economics*, 26(4):659-681. [<https://doi.org/10.1016/j.jhealeco.2006.12.006>].

low and middle-income countries has shown that not only are babies who were larger at birth more likely to be healthy. They are also more likely to complete secondary school.⁵⁰ These findings have implications for public health policy and nutrition interventions. An analysis of evidence-based interventions and focus on improvement in nutrition in pregnancy and linear growth in the first two years after birth could lead to substantial reductions in stunting and improved survival.⁵¹ These improvements form the basis for the emphasis on the first 1 000 days of life.⁵² The 1 000 days between a woman's pregnancy and her child's second birthday offer a unique window of opportunity to shape healthier and more prosperous future. The right nutrition and care during this 1 000-day window can have a profound impact on a child's ability to grow, learn, and rise out of poverty. It can also shape a society's long-term health, stability and prosperity.⁵³

Conclusion

Hunger is caused by poverty and inequality, not scarcity. For the past two decades, the rate of global food production has increased faster than the rate of global population growth. The world already produces more than enough food to feed everyone on the planet. We should prioritise an equal distribution of food across the world so that both the consequences of poor diets due to undernutrition and overnutrition will be prevented. Priority should be given to women of reproductive age. Adequately feeding women before and during pregnancy will allow future generations to reach their potential and lead to healthier and more productive lives, ultimately leading to healthier and more equitable future. Breaking the vicious cycle of poverty and undernutrition will most likely succeed if we provide women with sufficient food to provide their children with a good start in life.⁵⁴

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Figure 5.1 The effects of prenatal exposure to famine depend on its timing during gestation and the organs and tissues developing at that time.