Technical background on preconception nutrition

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Contents

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Introduction

This technical background paper is a companion piece to our **report** that reviews the latest evidence and guidelines for preconception nutrition for women and adolescent girls in undernourished contexts and offers our recommendations for what is needed next[1]. This paper provides a more detailed exploration of the complex concepts and processes underpinning preconception nutrition for those readers who would like more technical background to the topic.

In this paper, we begin with an overview of the biological processes involved in the preconception period followed by an introduction to the concept of the developmental origins of health and disease, with a focus on the evidence that explains why nutrition before conception is so critical. We then examine the role of nutrition in one-carbon metabolism – a network of interconnected metabolic pathways – and its importance in epigenetic processes. Finally, we consider the implications of these concepts, along with the existing evidence, for intergenerational health outcomes.

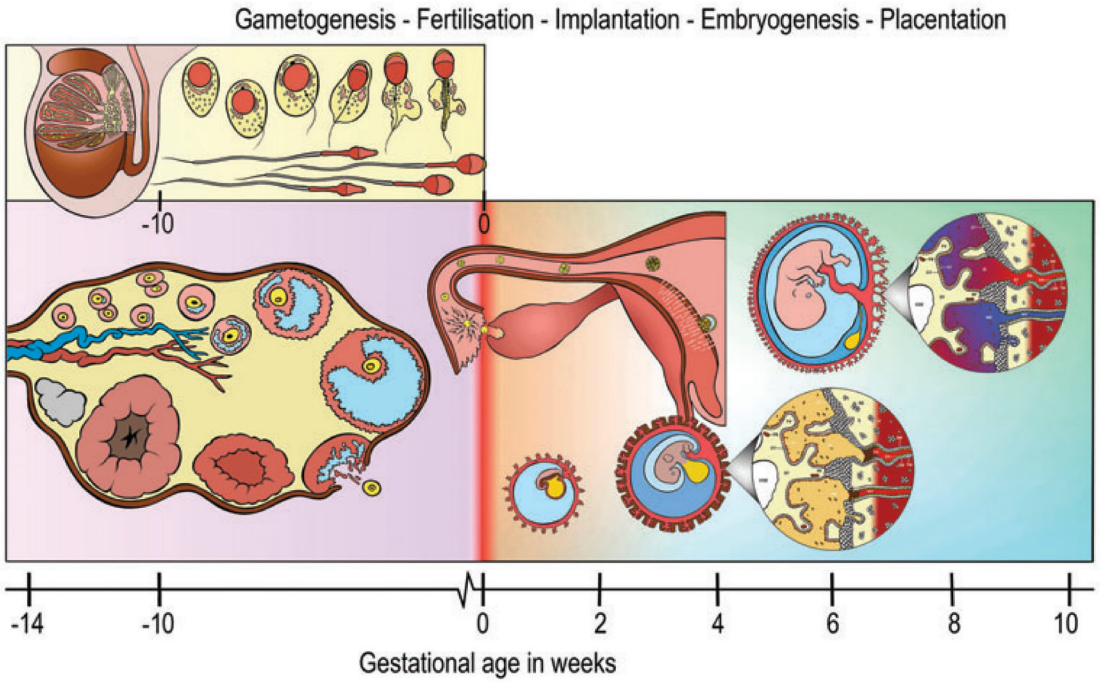
A biological definition of preconception

While in our accompanying report we focused on a pragmatic definition of preconception nutrition – the nutritional status and dietary intake of women and adolescent girls before pregnancy – there are also some widely accepted definitions of preconception that focus on the biological processes and timescales. The 'periconceptional period' spans the three months prior to conception and the first 10 weeks after conception (see **Box 1** for definitions). This period is an extremely active time when reproductive cells (gametes) develop, fertilisation occurs, genetic instructions are set, and cells become specialised into their different roles (cellular differentiation). Different factors can influence how well these biological functions work, including the nutritional status of women who go on to conceive.

Box 1: The main phases of reproductive development

Figure 1 shows the main phases of reproductive development covered by the periconceptional period. In men, the process of producing sperm cells (spermatogenesis and spermiogenesis) occurs in the testes and lasts approximately 10 weeks. In women, the immature egg cell (primordial ovarian follicle) starts growing about 26 weeks before it matures into an egg (ovum) and is released from the ovary into the fallopian tube (ovulation) where it can be fertilised by a sperm cell at conception (week 0 on Figure 1). Significant growth of the ovarian follicle happens around 14 weeks before ovulation. At about 5-6 days after fertilisation, the cells form a blastocyst, which is a bundle of cells that goes on to form the placenta and the embryo. The blastocyst attaches to the uterus wall (implantation) with implantation completing in the second week and the formation of the placenta (placentation) continuing for several weeks. In the third week, the embryo organises itself into three germ layers (gastrulation) which go on to start the development of the major organ systems between weeks 4 and 10. By week 10, the neural tube (the structure that goes on to form the brain and spinal cord) forms and all the major organs start to develop.

Figure 1. The periconceptional period



Source: Steegers-Theunissen R et al.[2]. Reproduced with permission from Steegers-Theunissen R et al. The periconceptional period, reproduction and long-term health of offspring: the importance of one-carbon metabolism. Human Reproduction Update. 2013;19(6):640–655.

Developmental origins of health and disease

The Developmental Origins of Health and Disease (DOHaD) hypothesis describes the association between certain environmental exposures experienced very early in life (particularly during the periods of pregnancy and the first two years of life – the first 1,000 days) and an increased risk of poor health outcomes later in life. You may have heard the phrases, *'what happens in the womb lasts a lifetime'* or *'you are what your mother ate'*. There is a wealth of literature that has built on the early DOHaD literature, originally drawn from the work of David Barker[3,4] and studies on the Dutch Hunger Winter[5-8] (see below). In summary, this literature showed associations between small size at birth and chronic disease risk in adulthood and old age, and that exposure to famine during different stages of pregnancy is associated with a greater risk of chronic disease many years later.

The literature base now encompasses research from a wide range of contexts, exposures, outcomes and potential mediating pathways. Decades' worth of research has described how adverse exposures, including suboptimal nutrition, during critical periods of foetal and infant development are associated with altered growth and development. It has been hypothesised that this may occur via changes to gene expression and the permanent restructuring of the body's tissues that influence metabolic function, and which have long-term consequences (e.g., increased risk of chronic disease in later life). There are several studies that have examined the influence of maternal nutrition in the preconception period and the potential impact on infant health and beyond[9-14]. Furthermore, much of the literature explores the hypothesis that effects in later life will be exacerbated if there is a 'mismatch' between the early life environment (e.g., experiencing a high degree of undernutrition in the womb and infancy) and later life environment (e.g., then experiencing nutritional excess in childhood and/or adulthood)[15].

The Barker Hypothesis

The DOHaD hypothesis was formed from the analysis of data from several cohorts, starting with David Barker's formative research which followed more than 16,000 people born in Hertfordshire in the UK between 1911 and 1930. He found that lower birthweight was associated with higher blood pressure at age 10, with an even stronger association at age 36[3]. Further observations in this cohort quickly followed, including associations between low birthweight and adult-onset chronic disease including type-II diabetes, hypertension, and hyperlipidaemia[4]. Similar patterns were observed in separate cohorts such as the Nurses' Health Study I and II in the USA[16] and another cohort in Helsinki[17].

Birthweight can provide researchers with a useful approximation of the environment in the uterus, but on its own does not tell us what the exact constraints were nor when these constraints were experienced. Subsequent studies have helped to narrow down the timing of the adverse exposure with famine studies proving particularly useful.

Famine and seasonality studies

Towards the end of World War II, the western Netherlands was under German control. Between November 1944 and May 1945, there was a shortage of food caused by Nazi blockades and a severe winter, resulting in the famine termed the 'Dutch Hunger Winter', which affected 4.5 million people. Calorie intake was drastically reduced, varying by region between a daily intake of only 500-1000 kcal, and an estimated 20,000 people died[18]. Researchers discovered an association between women experiencing the famine during pregnancy and a variety of adverse outcomes in their children, ranging from lower birthweight[19] to increased adult blood pressure[5,6], obesity[7] and risk of schizophrenia[8].

It also appears that the specific timepoint at which women experienced the famine in their pregnancy made a difference. For example, men whose mothers experienced the famine in mid-gestation had twice the prevalence of obesity at age 18-19 years, whereas if their mothers experienced the famine in the third trimester the risk of obesity was decreased[7]. Similar observations have been found in China's Great Leap Forward Famine, the most severe period of which was 1959-61. For example, experiencing this famine *in utero* was associated with twice the risk of schizophrenia and increased hyperglycaemia later in life[20,21].

Studies have also considered the season of a child's birth to investigate similar hypotheses since contrasting seasons often capture differences in environmental exposures, including nutrition. See **Box 2** for details on research from The Gambia in West Africa illustrating the concept.

Box 2: Seasonality research in The Gambia

The Gambia experiences two distinct seasons. There is a rainy season from July to October, which is the main planting season with increased energy expenditure associated with agricultural work, and an increased incidence of malarial and diarrhoeal diseases. Food stores from the harvest period run low in this season, hence it is also referred to as the 'hungry' season. The cooler dry season covers the other months with harvesting occurring particularly in February to April, leading to improved food security[22,23]. Despite overall household food stores being in a better state in the dry season, it is the rainy season that is associated with women having an improved (higher) micronutrient status of folate and B vitamins[24], possibly due to the increased availability of green leaves during the rains or the scarcity of staples forcing people to increase food diversity (e.g., through seeking bush foods). The season a child is born into has an intriguing and yet still unexplained impact. Children born in the rainy season are six times more likely to die between age 15-65 years than those born in the dry season, yet mortality risks prior to puberty remain equal[23,25]. Furthermore, there is no difference in the clinical diagnosis of premature death between the seasons of birth, with most deaths being infection-related, leading researchers to believe the mortality risks are programmed early on in life[26]. The exact mechanisms remain unexplained – for example, further research investigated whether the season of birth influences immune function. Although there is a seasonal variation in the size of the thymus in infancy[27], whether this makes enough difference to affect immunity in childhood and then on into later life remains in question[28]. Further research has looked at the season of conception, rather than the season of birth. Researchers have found that women's nutrition status in metabolites related to one-carbon metabolism (e.g., folate and B vitamins, see **Box 3**) differs between the rainy and dry seasons, and that these nutritional differences at the time of conception are associated with patterns of DNA methylation (see **Box 4**) in the infants[14,24,29]. The genes implicated in these DNA methylation changes are related to the pathways relevant for immune function[30] and obesity[31].

These famine and seasonality studies provide us with fascinating evidence that the environmental exposures (or 'insults') experienced early in life may be associated with later adverse health outcomes. Although it is likely that these insults are nutrition-related, these studies alone cannot provide us with definitive evidence about whether it is nutrition status playing a causal role. Even if this is so, the studies do not specifically tell us whether the impact is from depleted energy, reduced micronutrient intake, or a combination. Indeed, there may be other exposures related to famine and seasonality that could also explain some of the associations seen, for example, maternal stress.

Potential mechanisms at work

There are several potential mechanisms involved that may connect maternal nutrition status to foetal development and later health and disease. For example, one set of ideas is sometimes referred to as 'metabolic programming'. The idea here is that certain micronutrient deficiencies in the mother could lead to hormonal adaptations and/or changes in **epigenetic regulation** that might in turn influence the number and structure of cells during the time of organ development. For example, deficiencies in iron, zinc, vitamin A or folate could lead to the suboptimal development of nephrons in the kidney leading to impaired renal function in later life. Through similar effects on cardiovascular, pancreatic and pulmonary functions, changes to tissue structure and function ('tissue modelling') could then lead to an increased risk of hypertension, insulin resistance and other cardiometabolic problems in later life[32,33].

Other mechanisms could involve oxidative stress, maternal stress, the gut microbiota, toxin exposure (especially linked to arsenic exposure, tobacco smoke, air pollutants, phthalates and bisphenol A), maternal hyperglycaemia and gestational diabetes, and infection[32,34-42]. There is also growing interest in the potential for paternal exposures to affect the infant epigenome[43-45].

The overall theme of these different mechanisms is that different physical attributes in the offspring ('phenotypes') can result from different environmental exposures, including maternal nutrition, at the time of conception, despite the sequence of DNA ('genotype') remaining unaffected. The premise is that around the time of conception there is heightened sensitivity to the environment with the embryo being able to 'sense' the environmental cues[46]. This may give the embryo the chance to optimise its development to maximise the chances of survival (e.g., a hypothesis such as famine situations at conception triggering adaptations for the developing child to better store energy). This may be particularly beneficial if the later environment matches the environment at the time of conception. However, if there is a mismatch between the environment at conception and that experienced later – for example, if the child was conceived at a time of nutritional deprivation but later grows up in an environment with more food available – the consequences could be disadvantageous[46-47].

As evidence builds, it will be necessary to explore how these multiple exposures during the periconceptional period work together to influence infant development, and to define the potential consequences more clearly for human health across the life course.

An overview of one-carbon metabolism

One-carbon metabolism is a central component as to why nutrition at preconception plays such an integral role within the DOHaD literature. One-carbon units are small molecules that have a single carbon atom bonded to various other elements. For example, a methyl group has one carbon atom bonded to three hydrogen atoms (CH_3). One-carbon metabolism refers to the complex set of interlinking metabolic pathways where these one-carbon units are formed, transferred and recycled. The metabolic pathways involved in one-carbon metabolism are at the intersection of how we metabolise folate, the amino acid methionine, the intermediary amino acid homocysteine, as well as how we convert homocysteine into the amino acid cysteine (transsulfuration) and transfer methyl groups from one molecule to another (transmethylation). Nutrients are essential for one-carbon metabolic pathways to function correctly. Direct nutrient inputs to the system ('substrates') include folate, choline, betaine and methionine, all of which we can obtain from dietary sources. To enable the metabolic reactions to occur, certain nutrients are also involved as 'cofactors', which help various enzymes to play their role in chemical reactions. These cofactors include vitamins B6, B12 and B2. Jointly, the metabolic pathways that make up one-carbon metabolism are responsible for the production of essential molecules such as DNA, RNA, phospholipids, proteins, and antioxidants, amongst many others. The transmethylation reactions supported by one-carbon metabolism are critical for chemical signalling (central to how cells communicate with each other), epigenetic mechanisms (further details below), and DNA transcription and translation where sections of DNA strands are copied into messenger RNA and then used to build proteins. One-carbon metabolism therefore plays an essential role within multiple critical components of foetal development. See **Box 3** and **Figure 2** for more details of one-carbon metabolism, and we also refer readers to an excellent review by Steegers-Theunissen et al.[2].

Box 3: One carbon metabolism in more detail

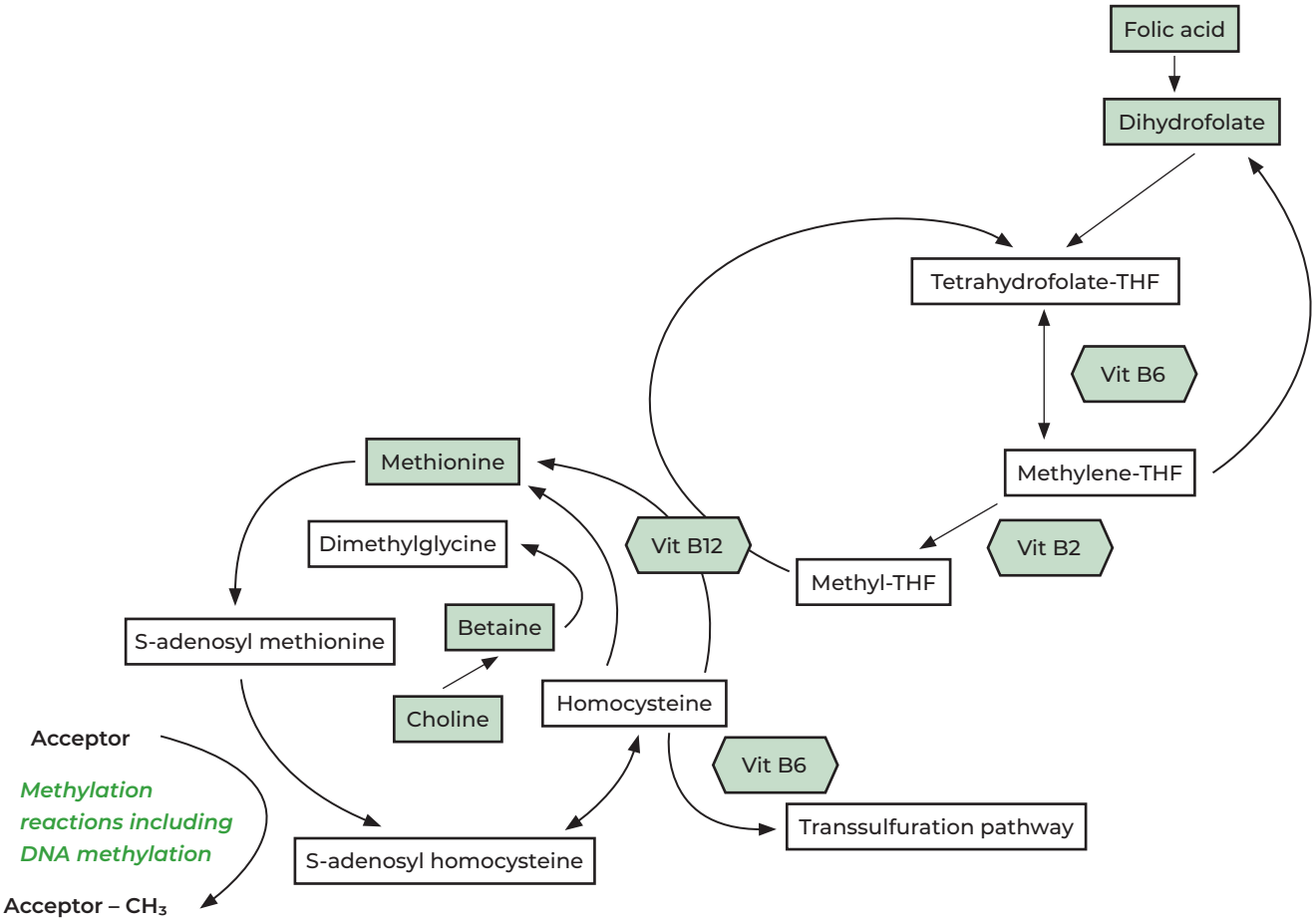
One-carbon units are used as substrates for a whole range of intricate biochemical processes, including cellular biosynthesis (processes that result in the creation of essential molecules such as DNA and protein), redox status regulation (helping to keep cells healthy by balancing the action of antioxidants and free radicals), genome maintenance (keeping our DNA healthy by supplying and maintaining the pool of nucleotides that are the building blocks of DNA), and methylation reactions (transferring a methyl group, CH_3, from one molecule to another)[48]. The folate, methionine, homocysteine, transsulfuration and transmethylation metabolic pathways all interplay in fine balance to ensure these essential biological reactions can function.

There are two main carriers that activate, transport and transfer one-carbon units: tetrahydrofolate (produced by folate metabolism) and S-adenosyl methionine (SAM). SAM methylates (donates a CH_3 group) to a wide variety of acceptors in reactions that are catalysed by enzymes called methyl transferases. Over 200 methylation reactions are required for a wide range of biological purposes, including DNA transcription and translation, protein localisation (directing proteins to the right places in cells so they can carry out their function properly) and signalling purposes[49]. SAM also donates methyl groups to methylate cytosine bases and amino acids on histone tails within the structure of DNA. These reactions play a key role in epigenetic mechanisms (see **Box 4**).

If too much homocysteine builds up in our bodies, this can impede methylation reactions[50]. To maintain favourable methylation conditions, we therefore need to be able to remove homocysteine from the system. One way to do this is through permanently degrading homocysteine, eventually forming the amino acid cysteine, in the transsulfuration pathway requiring vitamin B6. The other way is to methylate homocysteine to form the amino acid methionine. There are two distinct pathways that can be used. The major pathway involves homocysteine accepting a methyl group originating from folate metabolism. This pathway requires vitamins B12 and B2 as cofactors. The alternative pathway, predominantly used in the liver and kidneys, uses the methyl group from betaine, a product formed through the oxidation of choline.

Genetic variants coding for enzymes that catalyse reactions in one-carbon metabolism can affect how easily and effectively metabolites flow through these pathways[51,52]. For example, one of the better-known genetic variants affects the gene which codes for methylenetetrahydrofolate reductase (MTHFR), an enzyme critical for the functioning of the folate metabolic pathways. People with a mutation in the MTHFR gene can experience a build-up of homocysteine, which in turn is associated with an increased risk of cardiovascular disease and pregnancy complications, amongst many other diseases[53].

Figure 2: A simplified diagram of one-carbon metabolism with nutritional inputs shaded in green. Vitamins in hexagonal boxes represent essential co-factors that enable certain enzymes to function



Given the centrality of one-carbon metabolism to so many key biological processes it becomes easier to understand how the periconceptional nutritional status of nutrients that feed into these metabolic pathways can influence the development of the foetus, with implications for the child's later health and development across the life cycle.

Epigenetics

As mentioned above, epigenetic mechanisms are just one of the processes that rely on one-carbon metabolism. Epigenetic processes describe changes to the genome that can impact the ways that genes are expressed (switched on or off) without changing the underlying DNA sequence[54]. These changes involve processes such as DNA methylation, histone modifications, RNA-based mechanisms, and the interactions between them all (described further in **Box 4**). DNA methylation is important for a host of biological processes, including transcriptional silencing (turning genes off), X-chromosome inactivation (helping to switch off one of the X chromosomes in females to ensure genes are only expressed once), genomic imprinting (controlling a certain type of gene that we inherit specifically from our mother or specifically from our father) and for maintaining cellular identity (keeping cells focused on a specific role by switching certain genes off and on, i.e., keeping a skin cell from behaving like a liver cell)[55]. In summary, DNA methylation helps to control which genes are used, when they are used, and where they are used (in which cells). This process is vital for the proper development and functioning of our bodies. Given one-carbon metabolism is required for DNA methylation, and in the section above we covered the nutritional components of one-carbon metabolism (folate, betaine, methionine, vitamins B2, B6, B12), we can start to build our understanding of how nutrition may affect epigenetic mechanisms.

Box 4: Epigenetic modifications

DNA is tightly woven around histone proteins, forming compact structures of DNA and protein called nucleosomes. Nucleosomes in turn are packed together to form chromatin (**Figure 3**). Epigenetic mechanisms include:

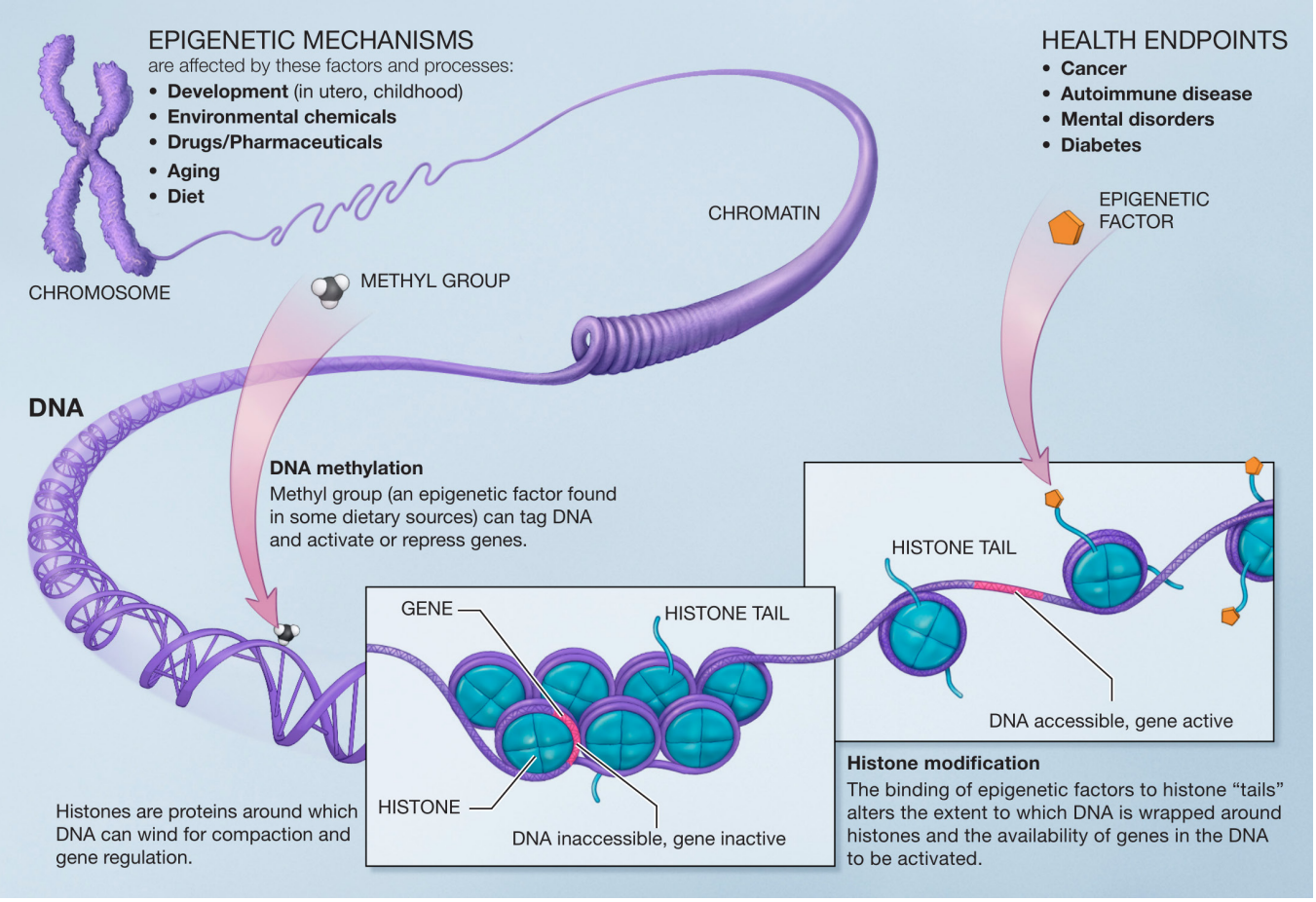
a) DNA methylation: this most commonly occurs at places in the genome where a cytosine base is found next to a guanine base on a DNA strand along its linear sequence, hence termed 'cytosine-phosphate-guanine' or CpG sites. It involves the covalent bonding of a methyl (CH3) group to the cytosine to form 5-methylcytosine. CpGs are generally unmethylated at promoter regions of regions (regions responsible for switching a gene on) and methylated in other (non-promoter) regions. Methylation at CpG sites in promoters is usually associated with silencing the gene (i.e., switching it off), although not consistently[56].

b) Histone modifications: The attachment of certain chemicals to the amino acid chains that make up histone structures ("tails")[57].

There are several mechanisms by which chemical modifications of CpG sites and histones are thought to influence gene expression by affecting how open or closed the chromatin structure is.

c) Non-coding RNAs. These are strands of RNA that are not used to build proteins but can have many other functions and may affect gene expression[58]. Of those that influence gene expression, microRNAs have been the most studied to date. These are short pieces (~22 nucleotides) of RNA, which affect the epigenome through binding to target messenger RNAs controlling the expression of key regulators of gene expression.

Figure 3: Epigenetic mechanisms



Source: https://commons.wikimedia.org/wiki/File:Epigenetic_mechanisms.png

The periconceptional window and epigenetics

The first 1000 days window is a period of exceptionally rapid cellular growth and development, where epigenetic mechanisms are critical to ensure healthy development. Periods of foetal development and infancy therefore represent windows of time that may be particularly susceptible both to epigenetic errors and to environmental influences[59]. For example, the first 48 hours after conception sees highly complex epigenetic processes at work. Immediately after fertilisation, there is a period where the majority of the genes experience a stripping of methyl groups from the DNA (demethylation), which happens very quickly amongst the genes inherited from our father (the paternal genome) and a little more slowly amongst the genes inherited from our mother (the maternal genome)[60]. Erasing these epigenetic marks in the very first cell that goes on to make a human being (the zygote) is critical so that all developing cells can be made into any type of cell that is needed (i.e., the cells need to become a blank slate so that they can be programmed for specific tasks or, in biological terms, become 'pluripotent')[55]. This then enables the developing cells to be methylated afresh, where the methyl groups label the cells according to the specific role the cells will go on to play. A second wave of demethylation occurs in the cells that develop in the foetus to become the eggs or the sperm cells of the developing baby (the primordial germ cells)[61]. These cells are wiped clean so that they can be re-methylated in patterns specific to the sex of the developing baby. Re-methylation of sperm cells occurs before the birth of the child, but re-methylation of the developing egg cells (the oocytes) happens over the whole period of their maturation, up until ovulation[61]. The periconceptional period is therefore one of intensive and complex epigenetic activity representing a window in which epigenetic errors could have significant consequences for the health of the child.

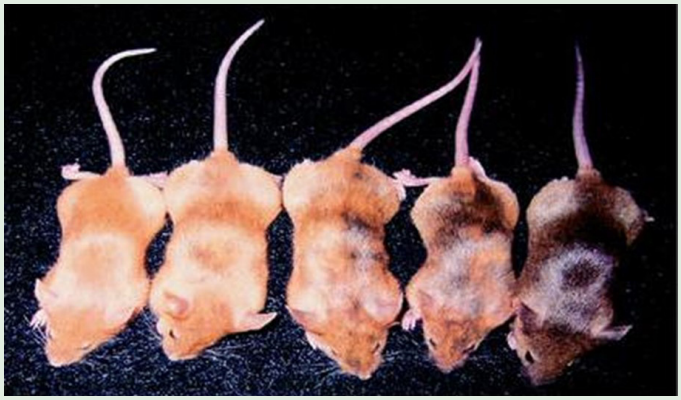
The evidence base linking periconceptional nutrition with epigenetic mechanisms

The above sections have explained why epigenetic modifications to the genome may, at least partially, explain some of the observations described in the DOHaD literature. For example, studies from the Dutch Hunger Winter, as described above, suggest that exposure to famine in pregnancy, particularly around conception, is associated with different levels of DNA methylation in genes linked to growth and development[62], and that famine exposure is also related to a wide range of offspring cognitive health and cardiometabolic risk factors six decades later[6,8,63]. The role of epigenetic dysregulation within health and disease has already generated a great deal of interest, including investigating potential causes within conditions such as Russell –Silver Syndrome (an under-growth disorder), Beckwith-Wiedemann Syndrome (an over-growth disorder)[64,65], intrauterine growth restriction[66], small-for-gestational age[67], birth weight[68,69] and later adiposity[70]. It has been suggested that exposures experienced in the womb could mould an 'epigenetic signature' that may programme the physical characteristics that are adapted to the external environment being sensed, which may be problematic if the environment into which the child is born then changes[71]. Under this hypothesis, malnutrition in pregnancy could programme so-called 'thrifty' epigenotypes to reduce the metabolic rate and store energy in response to a nutritionally poor environment. This may subsequently trigger symptoms of metabolic disease if the environment changes to one of relative nutritional abundance.

The clearest evidence to date of the link between maternal nutrition, epigenetics and offspring health comes from animal studies. See **Box 5** for details of a famous animal experiment that demonstrates some of these principles. Such animal studies have been pivotal in demonstrating the proof of concept and have motivated the continued interest in exploring the potential links between preconception diet, epigenetics and infant health in humans.

Box 5: The Agouti mouse experiment

Several animal experiments have shown that the maternal diet can influence offspring health and development. For example, in a famous experiment by Waterland and Jirtle[72], pregnant mice (dams) were fed a diet that differed by concentration of vitamin B12, folic acid, betaine and choline. The dams that were fed diets higher in these micronutrients produced pups that had higher levels of DNA methylation near the agouti gene. This in turn affected the colour of the pup's fur, leading to browner rather than yellow fur colour. This also affected body composition later in the life of the pups – the browner pups were also leaner and less likely to develop insulin resistance than the yellow pups[73]. All the pups were isogenic (having the same genotype) but had different phenotypes (i.e., fur colour, adiposity) according to the diet their mothers had in pregnancy. This is an example of epigenetic mechanisms at work, where gene expression is affected by environmental factors, in this case, maternal nutrition, without changing the underlying sequence of DNA (see image).



Reproduced with permission from: Waterland RA & Jirtle R L. Transposable Elements: Targets for Early Nutritional Effects on Epigenetic Gene Regulation. Molecular and Cellular Biology. 2003;23(15): 5293–5300.

In humans, there are many studies looking at nutrition in preconception and pregnancy stages and associations with epigenetic patterns (DNA methylation is the most studied) in the infant (36). Studying nutritional status at or around the time of conception is extremely challenging, and hence there are many more studies that look at nutrition across later timepoints in pregnancy compared to preconception nutrition status. However, studies specifically investigating the periconceptional window have found associations between DNA methylation of various genes in infants and the periconceptional nutrition status of their mothers, including folate intake[74,75], folic acid intake[75-77], betaine intake[78], methionine intake[78], multivitamin supplementation[79,80], exposure to famine[81-83], and differing one-carbon metabolite plasma concentrations associated with the season of conception[14,30,31,84]. This is also evidence that the associations between periconceptional nutritional exposures and offspring DNA methylation are still measurable later in childhood, in children aged 7-9 years[85].

DNA methylation of various genes in infants (measured at birth either in placenta tissue, cord blood, buccal cells or peripheral blood) has been associated with birthweight[68,69,86-88], small-for-gestational age[67,89-91], BMI at age one year[92], obesity at age 11 years[93], adiposity at age nine years[70], bone mineral content at age four years[94], and a variety of cognitive outcomes[95-98].

However, there are far fewer studies that have been able to look at the whole picture, namely preconception nutrition exposure to later disease risk, mediated by epigenetic mechanisms in the infant. One study found that pre-pregnancy vitamin B2 status was associated with infant DNA methylation at the ZAC1 gene, which in turn was associated with foetal weight at 32 weeks of gestation and BMI at age one year. Another study found associations between one-carbon metabolite status at the time of conception with infant DNA methylation at the POMC gene, which in turn was associated with increased obesity in children and adults[31]. A third study found an association between periconceptional folic acid supplementation, DNA methylation in the infants at the IGF2 gene and an associated reduction of birthweight[77].

In many of these studies, it is difficult to establish the direction of causality since disease states can also influence epigenetic patterns[99,100], especially for those studies that have used a retrospective cohort design. Stronger evidence comes from prospective cohorts investigating, for example, maternal folate, homocysteine, vitamin B12 and B6 levels in early pregnancy, the impact on DNA methylation in infant cord blood, and the potential impacts on birthweight and later infant growth[68,70,101].

Reviewing the existing data overall, the findings are not consistent across studies[36,102] so there is not yet any clear consensus on the extent to which epigenetics are involved in the causality of suboptimal growth and development[103]. We are therefore a long way from being able to identify the best nutrition interventions to 'correct' epigenetic errors during preconception, and to demonstrate that these interventions have meaningful impacts on infant growth and development.

Conclusion

The science of preconception nutrition reveals how specific nutritional factors influence key biological processes that shape health outcomes across the life course and generations. Understanding these mechanisms reinforces the importance of investing in nutrition well before pregnancy begins. The evidence presented in this paper highlights the potential for targeted interventions during the preconception period to improve maternal, foetal, and long-term population health. As policy and programming increasingly prioritise prevention, these insights provide a growing scientific basis to shape effective responses, particularly in low- and middle-income countries where the burden of maternal and child undernutrition remains high. As our understanding of preconception nutrition continues to evolve, sustained research and cross-sector collaboration will be essential to translate evidence into meaningful impact in these settings.

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References

1 Ohly H, Fuller S, Mates E and James P. Preconception nutrition for women and adolescent girls in undernourished contexts: A review of evidence and guidelines. Kidlington, Oxford, UK: Emergency Nutrition Network (ENN); 2025.

2 Steegers-Theunissen RP, Twigt J, Pestinger V, Sinclair KD. The periconceptional period, reproduction and long-term health of offspring: the importance of one-carbon metabolism. Hum Reprod Update. 2013;19(6):640-55.

3 Barker DJ, Osmond C, Golding J, Kuh D, Wadsworth ME. Growth in utero, blood pressure in childhood and adult life, and mortality from cardiovascular disease. BMJ. 1989;298(6673):564-7.

4 Barker DJ, Gluckman PD, Godfrey KM, Harding JE, Owens JA, Robinson JS. Fetal nutrition and cardiovascular disease in adult life. Lancet. 1993;341(8850):938-41.

5 Roseboom TJ, van der Meulen JH, van Montfrans GA, Ravelli AC, Osmond C, Barker DJ, et al. Maternal nutrition during gestation and blood pressure in later life. J Hypertens. 2001;19(1):29-34.

6 Stein AD, Zybert PA, van der Pal-de Bruin K, Lumey LH. Exposure to famine during gestation, size at birth, and blood pressure at age 59 y: evidence from the Dutch Famine. Eur J Epidemiol. 2006;21(10):759-65.

7 Ravelli GP, Stein ZA, Susser MW. Obesity in young men after famine exposure in utero and early infancy. N Engl J Med. 1976;295(7):349-53.

8 Susser E, Neugebauer R, Hoek HW, Brown AS, Lin S, Labovitz D, et al. Schizophrenia after prenatal famine. Further evidence. Arch Gen Psychiatry. 1996;53(1):25-31.

9 Rao S, Yajnik CS, Kanade A, Fall CH, Margetts BM, Jackson AA, et al. Intake of micronutrient-rich foods in rural Indian mothers is associated with the size of their babies at birth: Pune Maternal Nutrition Study. The Journal of Nutrition. 2001;131(4):1217-24.

10 Yajnik CS, Deshpande SS, Jackson AA, Refsum H, Rao S, Fisher DJ, et al. Vitamin B12 and folate concentrations during pregnancy and insulin resistance in the offspring: the Pune Maternal Nutrition Study. Diabetologia. 2008;51(1):29-38.

11 Hambidge KM, Westcott JE, Garcés A, Figueroa L, Goudar SS, Dhaded SM, et al. A multicountry randomized controlled trial of comprehensive maternal nutrition supplementation initiated before conception: The Women First trial. American Journal of Clinical Nutrition. 2019;109(2):457-69.

12 Nguyen PH, Young MF, Khuong LQ, Tran LM, Duong TH, Nguyen HC, et al. Maternal Preconception Body Size and Early Childhood Growth during Prenatal and Postnatal Periods Are Positively Associated with Child-Attained Body Size at Age 6–7 Years: Results from a Follow-up of the PRECONCEPT Trial. The Journal of Nutrition. 2021;151(5):1302-10.

13 Moore SE. Early life nutritional programming of health and disease in The Gambia. J Dev Orig Health Dis. 2016;7(2):123-31.

14 Dominguez-Salas P, Moore SE, Baker MS, Bergen AW, Cox SE, Dyer RA, et al. Maternal nutrition at conception modulates DNA methylation of human metastable epialleles. Nat Commun. 2014;5:3746.

15 Hanson MA, Gluckman PD. Early developmental conditioning of later health and disease: physiology or pathophysiology? Physiol Rev. 2014;94(4):1027-76.

16 Curhan GC, Chertow GM, Willett WC, Spiegelman D, Colditz GA, Manson JE, et al. Birth Weight and Adult Hypertension and Obesity in Women. Circulation. 1996;94(6):1310-5.

17 Eriksson JG, Forsen T, Tuomilehto J, Winter PD, Osmond C, Barker DJP. Catch-up growth in childhood and death from coronary heart disease: longitudinal study. BMJ. 1999;318(7181):427-31.

18 Lumey LH, Stein AD, Kahn HS, Van der Pal-de Bruin KM, Blauw GJ, Zybert PA, et al. Cohort profile: The Dutch Hunger Winter families study. International Journal of Epidemiology. 2007;36(6):1196-204.

19 Smith CA. The effect of wartime starvation in Holland upon pregnancy and its product. American journal of obstetrics and gynecology. 1947;53(4):599-608.

20 St Clair D, Xu M, Wang P, Yu Y, Fang Y, Zhang F, et al. Rates of adult schizophrenia following prenatal exposure to the Chinese famine of 1959-1961. JAMA. 2005;294(5):557-62.

21 Li Y, He Y, Qi L, Jaddoe VW, Feskens EJM, Yang X, et al. Exposure to the Chinese famine in early life and the risk of hyperglycemia and type 2 diabetes in adulthood. Diabetes. 2010;59(10):2400-6.

22 Prentice AM, Whitehead RG, Roberts SB, Paul AA. Long-term energy balance in child-bearing Gambian women. Am J Clin Nutr. 1981;34(12):2790-9.

23 Moore SE, Cole TJ, Collinson AC, Poskitt EM, McGregor IA, Prentice AM. Prenatal or early postnatal events predict infectious deaths in young adulthood in rural Africa. International Journal of Epidemiology. 1999;28(6):1088-95.

24 Dominguez-Salas P, Moore SE, Cole D, da Costa K-A, Cox SE, Dyer RA, et al. DNA methylation potential: dietary intake and blood concentrations of one-carbon metabolites and cofactors in rural African women. The American Journal of Clinical Nutrition. 2013;97(6):1217-27.

25 Moore SE, Cole TJ, Poskitt EME, Sonko BJ, Whitehead RG, McGregor IA, et al. Season of birth predicts mortality in rural Gambia. Nature. 1997;388(6641):434.

26 Moore SE. Early-Life Nutritional Programming of Health and Disease in The Gambia. Ann Nutr Metab. 2017;70(3):179-83.

27 Collinson AC, Moore SE, Cole TJ, Prentice AM. Birth season and environmental influences on patterns of thymic growth in rural Gambian infants. Acta Paediatr. 2003;92(9):1014-20.

28 Moore SE, Collinson AC, Prentice AM. Immune function in rural Gambian children is not related to season of birth, birth size, or maternal supplementation status. Am J Clin Nutr. 2001;74(6):840-7.

29 James PT, Dominguez-Salas P, Hennig BJ, Moore SE, Prentice AM, Silver MJ. Maternal One-Carbon Metabolism and Infant DNA Methylation between Contrasting Seasonal Environments: A Case Study from The Gambia. Current Developments in Nutrition. 2019;3(1):nzy082-nzy.

30 Silver MJ, Kessler NJ, Hennig BJ, Dominguez-Salas P, Laritsky E, Baker MS, et al. Independent genomewide screens identify the tumor suppressor VTRNA2-1 as a human epiallele responsive to periconceptional environment. Genome Biology. 2015;16(1):118.

31 Kühnen P, Handke D, Waterland RA, Hennig BJ, Silver M, Fulford AJ, et al. Interindividual Variation in DNA Methylation at a Putative POMC Metastable Epiallele Is Associated with Obesity. Cell Metabolism. 2016;24(3):502-9.

32 Christian P, Stewart CP, Sachdev HS, Margetts BM, Osmond C, Wells JCK, et al. Maternal Micronutrient Deficiency, Fetal Development, and the Risk of Chronic Disease. Journal of Nutrition. 2010;140(3):437-45.

33 Gluckman PD, Hanson MA, Buklijas T. A conceptual framework for the developmental origins of health and disease. J Dev Orig Health Dis. 2010;1(1):6-18.

34 Claycombe KJ, Brissette CA, Ghribi O. Epigenetics of inflammation, maternal infection, and nutrition. The Journal of Nutrition. 2015;145(5):1109S-15S.

35 Ma RCW, Tutino GE, Lillycrop KA, Hanson MA, Tam WH. Maternal diabetes, gestational diabetes and the role of epigenetics in their long term effects on offspring. Progress in Biophysics and Molecular Biology. 2015;118(1-2):55-68.

36 James P, Sajjadi S, Tomar AS, Saffari A, Fall CHD, Prentice AM, et al. Candidate genes linking maternal nutrient exposure to offspring health via DNA methylation: a review of existing evidence in humans with specific focus on one-carbon metabolism. Int J Epidemiol. 2018;47(6):1910-37.

37 Fall CHD, Kumaran K. Metabolic programming in early life in humans. Philosophical Transactions of the Royal Society B: Biological Sciences. 2019;374(1770):20180123.

38 Babenko O, Kovalchuk I, Metz GAS. Stress-induced perinatal and transgenerational epigenetic programming of brain development and mental health. Neuroscience & Biobehavioral Reviews. 2014;48:70-91.

39 Anway MD, Skinner MK. Epigenetic transgenerational actions of endocrine disruptors. Endocrinology. 2006;147(6 Suppl):S43-9.

40 Perera F, Herbstman J. Prenatal environmental exposures, epigenetics, and disease. Reproductive Toxicology. 2011;31(3):363-73.

41 Harary D, Akinyemi A, Charron MJ, Fuloria M. Fetal Growth and Intrauterine Epigenetic Programming of Obesity and Cardiometabolic Disease. Neoreviews. 2022;23(6):e363-e72.

42 Xu R, Hong X, Ladd-Acosta C, Buckley JP, Choi G, Wang G, et al. Contrasting Association of Maternal Plasma Biomarkers of Smoking and 1-Carbon Micronutrients with Offspring DNA Methylation: Evidence of Aryl Hydrocarbon Receptor Repressor Gene-Smoking-Folate Interaction. J Nutr. 2023;153(8):2339-51.

43 Soubry A. Epigenetic inheritance and evolution: A paternal perspective on dietary influences. Progress in Biophysics and Molecular Biology. 2015;118(1):79-85.

44 Illum LRH, Bak ST, Lund S, Nielsen AL. DNA methylation in epigenetic inheritance of metabolic diseases through the male germ line. Journal of Molecular Endocrinology. 2018;60(2):R39-R56.

45 Carter T, Schoenaker D, Adams J, Steel A. Paternal preconception modifiable risk factors for adverse pregnancy and offspring outcomes: a review of contemporary evidence from observational studies. BMC Public Health. 2023;23(1):509.

46 Fleming TP, Watkins AJ, Velazquez MA, Mathers JC, Prentice AM, Stephenson J, et al. Origins of lifetime health around the time of conception: causes and consequences. The Lancet. 2018;391(10132):1842-52.

47 Negrato CA, Gomes MB. Low birth weight: causes and consequences. Diabetology & Metabolic Syndrome. 2013;5(1):49.

48 Fox JT, Stover PJ. Folate-mediated one-carbon metabolism. Vitamins and Hormones. 2008;79:1-44.

49 Lu SC, Mato JM. S-adenosylmethionine in liver health, injury, and cancer. Physiological Reviews. 2012;92(4):1515-42.

50 Scotti M, Stella L, Shearer EJ, Stover PJ. Modeling cellular compartmentation in one-carbon metabolism. Wiley Interdisciplinary Reviews: Systems Biology and Medicine. 2013;5(3):343-65.

51 Fredriksen A, Meyer K, Ueland PM, Vollset SE, Grotmol T, Schneede J. Large-scale population-based metabolic phenotyping of thirteen genetic polymorphisms related to one-carbon metabolism. Human Mutation. 2007;28(9):856-65.

52 Rooney M, Bottiglieri T, Wasek-Patterson B, McMahon A, Hughes CF, McCann A, et al. Impact of the MTHFR C677T polymorphism on one-carbon metabolites: Evidence from a randomised trial of riboflavin supplementation. Biochimie. 2020;173:91-9.

53 Moll S, Varga EA. Homocysteine and MTHFR Mutations. Circulation. 2015;132(1):e6-9.

54 Jaenisch R, Bird A. Epigenetic regulation of gene expression: how the genome integrates intrinsic and environmental signals. Nature Genetics. 2003;33 Suppl:245-54.

55 Messerschmidt DM, Knowles BB, Solter D. DNA methylation dynamics during epigenetic reprogramming in the germline and preimplantation embryos. Genes & Development. 2014;28(8):812-28.

56 Illingworth RS, Bird AP. CpG islands--'a rough guide'. FEBS Letters. 2009;583(11):1713-20.

57 Kouzarides T. Chromatin modifications and their function. Cell. 2007;128(4):693-705.

58 Mattick JS, Makunin IV. Non-coding RNA. Human Molecular Genetics. 2006;15 Spec No:R17-29.

59 Langley-Evans SC. Nutrition in early life and the programming of adult disease: a review. Journal of Human Nutrition and Dietetics. 2015;28:1-14.

60 Seisenberger S, Peat JR, Hore TA, Santos F, Dean W, Reik W. Reprogramming DNA methylation in the mammalian life cycle: building and breaking epigenetic barriers. Philosophical Transactions of the Royal Society of London Series B, Biological Sciences. 2013;368(1609):20110330.

61 Smallwood SA, Kelsey G. De novo DNA methylation: a germ cell perspective. Trends in Genetics : TIG. 2012;28(1):33-42.

62 Heijmans BT, Tobi EW, Stein AD, Putter H, Blauw GJ, Susser ES, et al. Persistent epigenetic differences associated with prenatal exposure to famine in humans. Proceedings of the National Academy of Sciences of the United States of America. 2008;105(44):17046-9.

63 de Rooij SR, Painter RC, Roseboom TJ, Phillips DIW, Osmond C, Barker DJP, et al. 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. 2006;49(4):637-43.

64 Piedrahita JA. The role of imprinted genes in fetal growth abnormalities. Birth Defects Research Part A, Clinical and Molecular Teratology. 2011;91(8):682-92.

65 Bliek J, Terhal P, van den Bogaard M-J, Maas S, Hamel B, Salieb-Beugelaar G, et al. Hypomethylation of the H19 gene causes not only Silver-Russell syndrome (SRS) but also isolated asymmetry or an SRS-like phenotype. American Journal of Human Genetics. 2006;78(4):604-14.

66 Einstein F, Thompson RF, Bhagat TD, Fazzari MJ, Verma A, Barzilai N, et al. Cytosine methylation dysregulation in neonates following intrauterine growth restriction. PloS One. 2010;5(1):e8887-e.

67 Bouwland-Both MI, van Mil NH, Stolk L, Eilers PHC, Verbiest MMPJ, Heijmans BT, et al. DNA methylation of IGF2DMR and H19 is associated with fetal and infant growth: the generation R study. PloS One. 2013;8(12):e81731-e.

68 Hoyo C, Daltveit AK, Iversen E, Benjamin-Neelon SE, Fuemmeler B, Schildkraut J, et al. Erythrocyte folate concentrations, CpG methylation at genomically imprinted domains, and birth weight in a multiethnic newborn cohort. Epigenetics. 2014;9(8):1120-30.

69 St-Pierre J, Hivert M-F, Perron P, Poirier P, Guay S-P, Brisson D, et al. IGF2 DNA methylation is a modulator of newborn's fetal growth and development. Epigenetics. 2012;7(10):1125-32.

70 Godfrey KM, Sheppard A, Gluckman PD, Lillycrop KA, Burdge GC, McLean C, et al. Epigenetic gene promoter methylation at birth is associated with child's later adiposity. Diabetes. 2011;60(5):1528-34.

71 Stöger R. The thrifty epigenotype: An acquired and heritable predisposition for obesity and diabetes? BioEssays. 2008;30(2):156-66.

72 Waterland RA, Jirtle RL. Transposable elements: targets for early nutritional effects on epigenetic gene regulation. Mol Cell Biol. 2003;23(15):5293-300.

73 Waterland RA, Dolinoy DC, Lin JR, Smith CA, Shi X, Tahiliani KG. Maternal methyl supplements increase offspring DNA methylation at Axin Fused. Genesis. 2006;44(9):401-6.

74 Gonseth S, Roy R, Houseman EA, de Smith AJ, Zhou M, Lee S-T, et al. Periconceptional folate consumption is associated with neonatal DNA methylation modifications in neural crest regulatory and cancer development genes. Epigenetics. 2015;10(12):1166-76.

75 Pauwels S, Ghosh M, Duca RC, Bekaert B, Freson K, Huybrechts I, et al. Maternal intake of methyl-group donors affects DNA methylation of metabolic genes in infants. Clinical Epigenetics. 2017;9(1):16-.

76 Hoyo C, Murtha AP, Schildkraut JM, Jirtle RL, Demark-Wahnefried W, Forman MR, et al. Methylation variation at IGF2 differentially methylated regions and maternal folic acid use before and during pregnancy. Epigenetics. 2011;6(7):928-36.

77 Steegers-Theunissen RP, Obermann-Borst SA, Kremer D, Lindemans J, Siebel C, Steegers EA, et al. Periconceptional maternal folic acid use of 400 microg per day is related to increased methylation of the IGF2 gene in the very young child. PloS One. 2009;4(11):e7845-e.

78 Pauwels S, Ghosh M, Duca RC, Bekaert B, Freson K, Huybrechts I, et al. Dietary and supplemental maternal methyl-group donor intake and cord blood DNA methylation. Epigenetics. 2017;12(1):1-10.

79 Bakulski KM, Dou JF, Feinberg JI, Brieger KK, Croen LA, Hertz-Picciotto I, et al. Prenatal Multivitamin Use and MTHFR Genotype Are Associated with Newborn Cord Blood DNA Methylation. Int J Environ Res Public Health. 2020;17(24):9190.

80 Antoun E, Issarapu P, di Gravio C et al. DNA methylation signatures associated with cardiometabolic risk factors in children from India and The Gambia: results from the EMPHASIS study. Clinical Epigenetics. 2022;14.

81 Tobi EW, Lumey LH, Talens RP, Kremer D, Putter H, Stein AD, et al. DNA methylation differences after exposure to prenatal famine are common and timing- and sex-specific. Human Molecular Genetics. 2009;18(21):4046-53.

82 Tobi EW, Slagboom PE, van Dongen J, Kremer D, Stein AD, Putter H, et al. Prenatal famine and genetic variation are independently and additively associated with DNA methylation at regulatory loci within IGF2/H19. PloS One. 2012;7(5):e37933-e.

83 He Y, de Witte LD, Houtepen LC, Nispeling DM, Xu Z, Yu Q, et al. DNA methylation changes related to nutritional deprivation: a genome-wide analysis of population and in vitro data. Clin Epigenetics. 2019;11(1):80.

84 Silver MJ, Saffari A, Kessler NJ, Chandak GR, Fall CHD, Issarapu P, et al. Environmentally sensitive hotspots in the methylome of the early human embryo. eLife. 2022;11.

85 Saffari A, Shrestha S, Issarapu P, Sajjadi S, Betts M, Sahariah SA, et al. Effect of maternal preconceptional and pregnancy micronutrient interventions on children's DNA methylation: Findings from the EMPHASIS study. The American Journal of Clinical Nutrition. 2020.

86 Lin X, Lim IY, Wu Y, Teh AL, Chen L, Aris IM, et al. Developmental pathways to adiposity begin before birth and are influenced by genotype, prenatal environment and epigenome. BMC Medicine. 2017;15(1):50-.

87 Hoyo C, Fortner K, Murtha AP, Schildkraut JM, Soubry A, Demark-Wahnefried W, et al. Association of cord blood methylation fractions at imprinted insulin-like growth factor 2 (IGF2), plasma IGF2, and birth weight. Cancer Causes and Control. 2012;23(4):635-45.

88 Nakanishi M, Funahashi N, Fukuoka H, Nammo T, Sato Y, Yoshihara H, et al. Effects of maternal and fetal choline concentrations on the fetal growth and placental DNA methylation of 12 target genes related to fetal growth, adipogenesis, and energy metabolism. J Obstet Gynaecol Res. 2021;47(2):734-44.

89 Qian YY, Huang XL, Liang H, Zhang ZF, Xu JH, Chen JP, et al. Effects of maternal folic acid supplementation on gene methylation and being small for gestational age. Journal of Human Nutrition and Dietetics. 2016;29(5):643-51.

90 Kappil MA, Green BB, Armstrong DA, Sharp AJ, Lambertini L, Marsit CJ, et al. Placental expression profile of imprinted genes impacts birth weight. Epigenetics. 2015;10(9):842-9.

91 Lesseur C, Armstrong DA, Paquette AG, Koestler DC, Padbury JF, Marsit CJ. Tissue-specific Leptin promoter DNA methylation is associated with maternal and infant perinatal factors. Molecular and Cellular Endocrinology. 2013;381(1-2):160-7.

92 Azzi S, Sas TCJ, Koudou Y, Le Bouc Y, Souberbielle J-C, Dargent-Molina P, et al. Degree of methylation of ZAC1 (PLAGL1) is associated with prenatal and post-natal growth in healthy infants of the EDEN mother child cohort. Epigenetics. 2014;9(3):338-45.

93 Huang R-C, Galati JC, Burrows S, Beilin LJ, Li X, Pennell CE, et al. DNA methylation of the IGF2/H19 imprinting control region and adiposity distribution in young adults. Clinical Epigenetics. 2012;4(1):21.

94 Harvey NC, Sheppard A, Godfrey KM, McLean C, Garratt E, Ntani G, et al. Childhood bone mineral content is associated with methylation status of the RXRA promoter at birth. Journal of Bone and Mineral Research. 2014;29(3):600-7.

95 Rijlaarsdam J, Cecil CAM, Walton E, Mesirow MSC, Relton CL, Gaunt TR, et al. Prenatal unhealthy diet, insulin-like growth factor 2 gene (IGF2) methylation, and attention deficit hyperactivity disorder symptoms in youth with early-onset conduct problems. Journal of Child Psychology and Psychiatry. 2017;58(1):19-27.

96 Paquette AG, Lester BM, Lesseur C, Armstrong DA, Guerin DJ, Appleton AA, et al. Placental epigenetic patterning of glucocorticoid response genes is associated with infant neurodevelopment. Epigenomics. 2015;7(5):767-79.

97 Lester BM, Marsit CJ, Giarraputo J, Hawes K, LaGasse LL, Padbury JF. Neurobehavior related to epigenetic differences in preterm infants. Epigenomics. 2015;7(7):1123-36.

98 Lesseur C, Armstrong DA, Murphy MA, Appleton AA, Koestler DC, Paquette AG, et al. Sex-specific associations between placental leptin promoter DNA methylation and infant neurobehavior. Psychoneuroendocrinology. 2014;40(1):1-9.

99 Relton CL, Davey Smith G. Two-step epigenetic Mendelian randomization: a strategy for establishing the causal role of epigenetic processes in pathways to disease. International Journal of Epidemiology. 2012;41(1):161-76.

100 Ulahannan N, Greally JM. Genome-wide assays that identify and quantify modified cytosines in human disease studies. Epigenetics & chromatin. 2015;8(1):5.

101 McCullough LE, Miller EE, Mendez MA, Murtha AP, Murphy SK, Hoyo C. Maternal B vitamins: effects on offspring weight and DNA methylation at genomically imprinted domains. Clinical Epigenetics. 2016;8(1):8.

102 van Vliet MM, Schoenmakers S, Gribnau J, Steegers-Theunissen RPM. The one-carbon metabolism as an underlying pathway for placental DNA methylation – a systematic review. Epigenetics. 2024;19(1):2318516.

103 Toure DM, Baccaglini L, Opoku ST, Barnes-Josiah D, Cox R, Hartman T, et al. Epigenetic dysregulation of Insulin-like growth factor (IGF)-related genes and adverse pregnancy outcomes: a systematic review. The Journal of Maternal-Fetal & Neonatal Medicine. 2016;18:1-11.

104 James P SM, Prentice A. Epigenetics, Nutrition, and Infant Health. In: Karakochuk C WK, Green T and Kraemer K, editor. The Biology of the First 1,000 Days. CRC Press; 2017. p.335–54.

105 James P SM, Prentice A. Epigenetics, Nutrition, and Infant Health. Sight and Life. 2015;35-8.

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