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Caroline Leahy

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Signatures of Honors Thesis Committee

Mentor:	Scott A. Mazzetti	
Reader 1:	Autumn Romanowski	Autumn Romanowski
Reader 2:	Karen E. Rayne	Karen E. Rayne
Director:		James J. Buss
	Signature	Print

The Effect on Obesity of Pre- and Postnatal Nutrition

By Caroline Leahy

Introduction

Many factors affect obesity and the metabolic diseases associated with high body fat. These factors can be categorized as either epigenetic or genetic. Often, people only consider lifestyle choices such as hyper-caloric eating habits, exercise, stress, medicine and how they have an effect on their body mass. People often discount or ignore the genetic and epigenetic factors, despite research showing that the early-life experiences of fetuses and infants affect the expression of obesity and metabolic diseases. The periods of conception to birth and birth through the first year are extremely important periods that are much closer to the root of the worldwide obesity epidemic than other factors people can consider. The early experiences of fetuses and infants are proven to have lifelong effects on the prevalence of obesity and metabolic diseases.

Although all periods of human development are important, a human's earliest moments are identified as being critical to the development or avoidance of lifetime obesity. The first is "the prenatal period," which includes all nine months of development. The nine months are broken into three trimesters, with the third including the first hours after birth. The when the fetus begins to develop taste and preference in the first trimester when the brain begins developing. The second is the postnatal period within the first year of life [1]. This is when the infant learns portion control and continues to develop food preferences. Both periods of life feature the closely-linked dietary relationship between the mother and child, beginning with the placenta and ending with breastfeeding if it is the chosen form of feeding. As such, people should

consider the importance of the mother's dietary habits when studying obesity and metabolic diseases.

A. Statement of the Problem

The focus of this thesis is to summarize the underlying mechanisms that are initiated during the prenatal period of life in response to maternal dietary habits that can lead to adult obesity. The time periods considered are solely pre- and post-natal, as they are described above. The circumstances discussed are solely nutrition based.

Goal The goal of this research is to summarize and discuss the various aspects of the maternal diet that can predispose adulthood obesity and the cellular and physiological mechanisms involved. These include the amount of food that the mother consumes, macronutrient content of the maternal and infant diet, folic acid supplementation, breastfeeding compared to bottle feeding, and the effect of maternal Gestational Diabetes Mellitus (GDM) and Diabetes Mellitus Type II (2DM) both in the womb and outside.

As a secondary goal, this thesis will provide a comprehensive list of maternal nutritional variables, ranking their importance in comparison to each other as they relate to the development of obesity later in life. Pros and cons for each will also be included, as well as scientific references for each. To my knowledge, such a list does not exist in the scientific literature. A maternal nutritional variable list will be a beneficial tool not only for mothers but also for nutritionists and obstetricians.

B. Mechanisms

Mechanisms in the body are the explanation of how and why processes work the way they do. All the circumstances that will be discussed express some type of alternation of either epigenetic mechanism programming or neural and hormonal

programming. Understanding these mechanisms is crucial to identifying the importance of the role each plays in developing obesity.

Epigenetics Epigenetic mechanisms are defined "as a network of biological processes that regulate the expression of genes to produce mitotically heritable changes in cellular function without changes in the underlying DNA sequences" [2]. In other words, they are modifications in the way a gene is expressed without physically altering the DNA sequence passed on by a parent. This is important because once an epigenetic change occurs this can be passed on to the next generation.

Neural Neural programming occurs because of the availability of various macro and micronutrients. The neural connections made during the beginning stages of fetal development tend to be altered easily based on available resources. They affect the way the brain tells the gastrointestinal system and other body functions to respond to food consumption, which is why they are related to obesity.

Hormonal The hormonal changes affect the concentration in the blood of the hormones related to body composition, food consumption, and various diseases. The hormonal changes can occur based on intrauterine or postnatal factors, as hormone concentrations (such as the ones released during digestion) can change throughout everyday life.

Part I: Intrauterine

The intrauterine environment begins now of conception when an embryo is formed and continues throughout development until the moment of birth. Especially within the first few weeks, epigenetic changes are of utmost concern. After that, the most

important variables of prenatal development include folic acid supplementation, GDM and 2DM, and amount of food consumed.

A. Undernutrition

Undernutrition can be defined as not consuming enough calories to sustain normal bodily functions. Undernutrition can exhibit effects on both the neural and epigenetic mechanisms of obesity. The thrifty phenotype hypothesis is a general notion regarding the effects of undernutrition on obesity.

The thrifty phenotype hypothesis (TPH) was proposed in 1991 by C.N. Hales and D.J. Barker and is described as "the epidemiological associations between poor fetal and infant growth … and the metabolic syndrome result from the effects of poor nutrition in early life" [3]. Essentially, it is the culmination of undernutrition during fetal development. The root of these changes is that when a fetus grows with reduced resources, neurological connections are created so that anytime the infant encounters abundant resources, the body consumes and stores as much macronutrient as possible. This is so that when the infant returns to times of reduced consumption, such as during a famine, the body will be able to survive on the stored nutrients.

Famine There are many studies that show the metabolic effects of undernutrition, specifically looking into the effect of famine on the development of metabolic disease over the course of a lifetime. In places where undernutrition is consistent, such as many countries in Africa and other developing nations, fetuses who develop this phenotype will not necessarily become obese. This is an exceedingly advantageous adaptation when food supply is irregular. The issue lies when there is a famine for a handful of years and then

normal nutritional availability returns. Those fetuses will develop the connections but no longer need them when normal diet returns.

The Dutch Famine Study, performed in 1999 by Ravelli et al., investigated the medical history of 741 people exposed to famine from 1943 to 1947 in Amsterdam. At that time their resources were restricted by the Nazis, so they only received between 400 and 800 Calories per day [4]. The results showed that those exposed in the early days of gestation, more formally the first trimester, had a greater risk for metabolic and other complex diseases [5]. These results indicate that proper nutrition during the time when neural connections are being made, which is thought to be the first few months of gestation, is crucial for having a more typical appetite and body composition. Studies of other famines have indicated the same results, including in Nigeria where poverty is also a contributing factor.

Poverty Low income or poverty is a factor that greatly contributes to undernutrition, both from calorie consumption and incorrect distribution of calories. When a woman is living in poverty the nutrients she consumes tends to be much less balanced, with much more saturated and trans-fat content as well as simple sugars, and much less protein, complex carbohydrates, and unsaturated fats. Also, fewer vitamins and minerals are consumed because of a lack of fruits and vegetables or supplement availability.

Many various aspects of low-income lifestyles influence the prevalence of childhood obesity. A cross-sectional analysis of 559 low-income pregnant women showed that every mother experienced at least one of the following during pregnancy: food insecurity, difficulty paying bills, housing disrepair or displacement, or

neighborhood stress [6]. Besides neighborhood stress, all the other factors could contribute to unavailability of food or poor choices. The findings of the research showed that those with one or more of those factors had much less control over the development and metabolic diseases of their child. Food insecurity on its own was the biggest contributor [6]. Although poverty is a contributor to poor choices, macronutrient content or lack of essential vitamins could occur even without poverty. This puts it low on the list of importance for the contributors to obesity.

Conclusion When these factors are combined, the thrifty phenotype hypothesis has life-long neurological and epigenetic modifications that make it a very important factor of obesity to examine. Since it causes issues with both the amount of food consumed and the way that food is utilized by the body, and that there is no positive effect, it is one of the most crucial factors to control. All mothers should be made aware of the detrimental effects that can result from a hypocaloric diet. Also, in times of famine or poverty, finding a way to provide adequate nutrition for pregnant women should be a priority.

B. Folic Acid Supplementation

Folic Acid is a dietary supplement that acts as a methyl donor, which aids in DNA methylation. During pregnancy it is primarily used as a supplement that aids in neural tube development, but DNA methylation also has an influence on the epigenetic programming that leads to obesity. The mechanism of methylation as it is influenced by folic acid will be altered if fortified foods or supplements are not consumed.

Mechanism Methylation occurs when the molecule methionine is metabolized and donates a methyl group to DNA, protein, or another molecule in the cell. The resulting

product is then hydrolyzed and becomes homocysteine [7]. The usable form of folic acid, 5methylTHF, donates a methyl to homocysteine and converts it back to methionine. When folic acid is not present, hyperhomocysteinemia, or excess homocysteine in the blood, occurs. This causes neural tube defects and other congenital malformations, and later in life leads to atherosclerosis and other risks for cardiovascular disease (CVD) [7]. These outcomes are the reason several governments, including the U.S. and Canada, decided to fortify foods [8].

In 1998 the United States decided to mandate fortification of foods such as bread, cereal and flour, which are commonly eaten in most diets [8]. This is so that even those without the money or knowledge for supplements can receive at least some folic acid in their daily diet. This helped pregnant women reach the daily recommended amount of 600 micrograms which decreased the prevalence of neural tube defects in infants born in the US because of consumption both before and during pregnancy.

The prenatal environment is affected by choices made even before conception occurs. Early supplementation with folic acid is recommended, especially when a couple is actively trying to get pregnant. Supplementation before conception in a study of women who planned to get pregnant showed that supplementing daily with 4mg of folic acid greatly decreased risk for neural tube defects (NTDs) as well as small-for-gestational-age births (SFGA), which influences obesity that will be discussed in the postnatal section [9].

IGF2 If there is a lack of folic acid supplementation there is an effect on the DNA methylation of IGF2. IGF2 is a regulator of fetal growth that is influenced by consumption of folic acid [2]. Altered methylation of this gene has a positive correlation

with increased adiposity at many sites used in a skinfold test [2], a body composition test used by many labs in obesity research. This positive correlation shows that with decreased methylation, there is an increase in the amount of adiposity in several parts of the body. Increased folic acid supplementation would regulate the methylation and therefore decrease the adipose deposits throughout body.

Conclusion The most crucial time to reach the recommended daily intake of folic acid is during the main neural development period (first trimester). If that is not met (i.e. unexpected pregnancy) the risk of obesity will still be decreased through the IGF2 mechanism when supplementation begins [2]. All things considered, folic acid is an extremely important dietary factor for fetal development. Even though asthma and other issues can develop later in pregnancy from supplementation, the avoidance of hyperhomocysteinemia causing congenital malformations is much more crucial. Fortified foods should be consumed instead of or in conjunction with supplements to ensure adequate levels are achieved.

C. Overnutrition

Overnutrition is characterized by consuming an excess of calories, or more than the amount expended during daily activity. If a precise number of calories is consumed, it should ensure that the body has enough to sustain the resting metabolic rate (RMR), which is necessary in daily bodily functions, as well as daily activity. If not, the excess macronutrients will be stored as fat or other substrates in the body.

Macronutrients The macronutrients that have caloric value are protein, lipids (fat) and carbohydrates (sugars). A balanced diet consists of 55% carbs, 15% protein, and 30% fat. Carbs and proteins are four calories per gram, and fat is nine. If the distribution is

distorted by eating too much of one macronutrient, the result is another form of overnutrition and additional risk of adiposity. During pregnancy the excess macronutrients can travel through the placental barrier and affect the fetus.

1. High Fat

A high fat diet consists of consuming more than 30% of daily calories from fat. Due to the high caloric content of one gram of fat, when excess fat is consumed typically the number of calories multiplies (over nutrition). The excess fats moving through the blood can cross into the baby's blood and make changes in the way fat is stored.

High fat diets during fetal development have a strong influence on the way fat is stored, usually leading to increased adiposity. A study on the effect of high fat and fructose diets (HFFD) consumed by pregnant rats found that the average body weight of the HFFD baby rat was 1.5-fold that of the normal rat diet. Even more critical, the body fat percentage was 35%, almost 3 times the control group [11]. Although the research cannot directly pinpoint the effect of the high fat compared to high fructose, there is a clear influence on the way body stores fat. The abnormal storage also affects other processes in the body.

High fat diets may be a risk factor for developing diabetes. Maternal obesity as well as increased blood concentration of fatty acids is thought to be a contributor to insulin resistance through a mechanism that affects beta islet cells (the pancreatic cells responsible for producing insulin) [11]. Autophagosomes, which are a key part of breaking down cells that are no longer functioning properly, have decreased activity during high fat diets. When those cells are not functioning correctly, malfunctioning beta islet cells cannot be recycled, and the pancreas no longer functions correctly [11]. The

result is reduced insulin production, which is Type I diabetes. This lack of insulin causes starved cells, increased food consumption, and then obesity.

Although high fat diets during fetal development do influence the development of obesity, there are other risk factors that play a much more crucial role. The more important bigger picture of this risk factor is to be sure the correct number of calories is consumed and that only about 30% of those calories come from fat. If that is achieved, these risks will not be as great as others.

1. High Protein

Nutritionists consider a diet to be high protein if more than 15% of food consumed comes from protein. Since protein only has a caloric value of four, it does not have as much of an effect on caloric intake as fat does. However, protein has a greater influence on the way in which energy is utilized.

Prenatal diets rich in protein have been found to decrease energy expenditure and increase adiposity in lab rats. A study performed on rats who were fed either adequate or high protein diets while their fetus developed showed that the pups of the high protein diet were born with a low body weight and had an abnormally rapid catch-up period (which will be discussed in the postnatal section). Both of those led to a five-fold increase in body fat in the first year compared to their adequate protein counterparts, who experienced a threefold increase [12]. This epigenetic change seems to last much longer than the first year, and in turn has some effect on lifetime obesity.

Although much more research to determine how this type of diet affects human development is necessary, the studies available have shown a link between increased

protein intake and obesity. The research does not point to this being a key factor for obesity development, but it is important to achieving a balanced diet.

1. High Simple Sugars

Carbohydrates, or sugars, should make up 55% of the daily diet. Simple sugars, such as mono- and disaccharides, have a very simple structure which makes them easily and quickly digestible [13]. Although glucose is important for cell fuel and the only source of energy for the central nervous system, excess simple sugars cause neural and epigenetic adaptations that lead to health issues and obesity.

Taste begins to develop while in utero. Although the nutrients are not physically entering through the fetus's mouth, but rather through the placenta, the amniotic fluid contains simple molecules derived from the mother's diet [14]. While the fetus forms neural connections that fire in response to sweet, salty, and the other tastes, the presence of extra glucose begins forming the connections for an addiction. Unfortunately, the fetus begins wanting and expecting to receive the sweet taste in its normal diet and those preferences tend to remain throughout a lifespan, only changed by strict modification [13]. This change can lead to the epigenetic programming for diabetes.

High carbohydrate exposure in utero is the beginning of developing diabetes, independent of the mother's diabetic state (although it is typically linked to her body mass). Many studies have found that the maternal overnutrition with high carbohydrate diets increases glucose-induced insulinogenesis (GIIG) [15]. Insulin is produced in the pancreas and released in response to high blood glucose (BG) to aid in transportation across the cell membrane. This increase in GIIG in utero has a tremendous negative effect later in life due to some unknown mechanism. Researchers believe it may be beta

islet cell death or exhaustion, or decreased glucose sensitivity. Either way, there is a decline in insulin production and an increase in body mass [15]. Due to the prevalence of obesity, many researchers have focused on that mechanism and found it to be correct.

Although carbohydrate consumption is crucial for healthy development in utero, it is essential to follow the guidelines stated previously. Roughly 55% of calories should be consumed from carbohydrates. More specifically, most of that should be from starch, lactose and sucrose [15]. Starches and other complex carbohydrates are important for preventing CVD and regulating digestion because they are difficult to break down. Simple sugars have detrimental effects on the development of neural and epigenetic programming, which will have lifelong effects on obesity. Again, a healthy distribution of macronutrients can decrease the risk of developing lifelong health issues.

D. Mothers with GDM and 2DM

Diabetic mothers pose a potential threat to their fetus, one which can be avoided with proper and careful care. As previously discussed with high carbohydrate diets, having excess sugars in the amniotic fluid can train the fetus to desire sugary foods throughout its life. This is undoubtedly a concern with diabetic mothers, as they have high BG from decreased insulin sensitivity, so more can cross the blood-blood barrier in the placenta. To understand the pathophysiology of either type of diabetes, normal physiology must be understood.

Normal Physiology In a non-diabetic state, insulin is produced and regulated by the pancreas. It helps transport glucose into the cell by stimulating the signaling cascade that moves GLUT4 (the glucose transporter) to the cell membrane and allows glucose to cross. This process is what is altered in the pathophysiology of 2DM and GDM.

2DM Pathophysiology 2DM is the form of diabetes when the pancreas is producing enough insulin, but the cells become desensitized to it. Desensitization can be caused by many factors but the primary one is that visceral adiposity produces too many inflammatory compounds, which shut down the signaling pathway. This reduces GLUT4 translocation and reduces glucose uptake into the cell. From there BG increases and the cell begins to starve and to tell the brain to eat more food [5]. BG is then further increased and, when a fetus is in utero, causes some of the excess glucose to spill over the placental barrier. This can begin at any time during life.

GDM Pathophysiology GDM is described as "the balance between increased insulin resistance and maternal insulin production . . . disturbed mostly due to insulin secretion defects of pancreatic beta islets [during pregnancy] . . . and results in maternal hyperglycemia, fetal hyperinsulinism, and fetal overnutrition" [5]. This mechanism is very similar to 2DM and can be caused by both obesity before pregnancy and advanced maternal age, as well as other factors [5]. The fetus receives higher concentrations of glucose, but still not enough to satisfy the high insulin concentration passed from the mother. That puts the brain in starvation mode, which is comparable to TPH. If this goes on long enough without intervention the fetus will develop the neural connections of TPH which will cause obesity as well as the epigenetic programming for diabetes. Many researchers have investigated both cases and reached the same conclusion.

Due to the urgency of reversing the effects of these diseases, many researchers have spent countless hours researching it. One study performed on rats found that the mothers who consumed high fructose diets bore pups with hyperinsulinemia, which suggests insulin resistance. Also, those effects carried on weeks into their life, with a

140% increase in blood insulin levels 12 weeks after birth [16]. This indicates that the effects of a high simple sugar diet on diabetes can be long term. There have been other studies done on rats that have had comparable results.

In some studies, mother rats are given diabetes, so the researcher can see the difference in diabetic and nondiabetic mothers' pups. The rats who have induced diabetes are prone to having pups with diabetes and other endocrine abnormalities [5]. In a study when embryos with the genetic predisposition from their parents were transferred into a normal glycemic mother, they were found to still develop 2DM. The same study found that the embryos of the normal glycemic mothers who were transferred into the diabetic mothers had a dramatic increase in diabetic risk [17]. This study shows that both genetic predisposition and epigenetic programming for diabetes can have tremendous effects on fetal development, both of which relate to the development of obesity.

Unfortunately, obesity and diabetes often occur simultaneously. As previously stated, when 2DM is present and there is a decreased insulin sensitivity, cells feel starved. This causes them to tell the brain that more food is needed, so more is consumed. This is a continuous cycle that increases caloric intake and eventually leads to adiposity. This same mechanism of cell "starvation" is what also causes the TPH. These two pathways along with many others are the reasons that obesity and diabetes work together in a detrimental cycle.

GDM and 2DM are two of the biggest risk factors for prenatal development. Unlike the other components previously discussed, this cycle continues endlessly throughout development and into adulthood. This is not to say that women with 2DM or GDM will pass on the disease, but attentive management and help from a dietitian and

obstetrician will ensure the best outcome possible. If a mother displays signs of GDM or is already diagnosed with 2DM, very careful planning and management are needed to ensure the healthiest development possible.

D. Conclusion

All the factors considered are important parts of the intrauterine environment. Although there are many more factors, these dietary considerations are the ones that have the most influential effect on adiposity, obesity, and metabolic diseases. It is very important to consume a diet with adequate calories and avoid high fat and carbohydrate as well as low folic acid. It is recommended that women speak to an obstetrician (OB) and/or dietitian before making decisions regarding pregnancy diet, as every woman and fetus have unique needs and recommendations.

Part II: Postnatal

Roughly an hour after a baby is born, postnatal life begins. This means that anything that was provided through the placenta now needs to be provided in another way. The first choice tends to be breast milk, but another option is formula. This typically lasts between six months and a year, depending on the culture and personal choices of the mother, as well as the physician's input. There are positive and negative aspects to both breast milk and formula.

Although both achieve baseline necessities for infants, several factors are involved in deciding which the best form is for that mother and baby. This has to do with the composition of the breast milk compared to the formula the mother would choose (or could afford). It also depends on the needs of the baby, including allergies and other

health conditions. This section will discuss the benefits and risks of breastfeeding compared to bottle feeding.

A. Breastfeeding

Breast milk is the most natural food for an infant to consume. It is produced in the mammary glands in the breast and, during lactation, travels through ducts and exits through the nipple. Lactation is the last step of the human reproductive cycle. Colostrum, the first product secreted, begins about a day before labor. After birth, milk is secreted during lactation [18]. Breast milk should contain the correct balance of macro and micronutrients needed for infant development, including all the necessary vitamins and minerals, unless issues like diabetes are present [19]. Due to the composition, healthy breast milk should have a positive effect on metabolic processes.

Breastfeeding has been found to greatly reduce the risk of obesity. A meta-analysis of 28 studies reported that breastfeeding reduced the risk of obesity by 13% when compared to bottle feeding [20]. Although the direct mechanism relating breast feeding to obesity is not known [21], there are several elements in breastmilk that would have a direct or indirect effect on body composition. These include insulin and glucose in diabetic mothers, and Insulin like Growth Factor 1 (IGF-1).

Diabetic Mother As previously discussed, people with diabetes have more glucose and insulin in their blood. Like the way the amniotic fluid was affected by these concentrations, they also affect the composition of breast milk. GDM and 2DM can both contribute, as colostrum is produced during pregnancy so GDM is still present [21]. There have been many studies that investigate the effect of diabetic breast milk on the development of obesity on both rats and humans.

Due to the effect of diabetes on breast milk, a lot of money is put into funding research about it. Several studies on rats have shown that even pups who were born to healthy mothers but cross-fed by mothers with diabetes had a dramatic increase in the risk of developing obesity and diabetes later in life [21]. Also, in a study on humans born to mothers with GDM or 2DM, it was found that during the first week postnatal, there is a dose dependent relationship between consuming diabetic breast milk and future obesity [22, 23]. Although these do show the direct effect, they did not look closer into the mechanism behind the influence.

Although the mechanism is not very well understood, researchers do know that mothers with GDM and 2DM produce milk differently from other mothers. They produce a larger volume of milk with a much higher energy content. This energy content comes/ from a high concentration of glucose [23, 24]. This hyperglycemic milk has a similar effect to that of the sugary amniotic fluid, as it trains infants to desire a sweet diet. It also puts infants at a higher risk for insulin resistance, as they will be producing insulin for themselves as well as receiving it in excess through breast milk [24]. These factors culminate and form an environment ideal for obesity to develop.

The same mechanism that allows for hyperglycemic breast milk can also have a positive effect. The taste is variable based on what the mother eats, which makes the infant more likely to be adventurous with food when they grow up [21]. If the mother eats various vegetables, the baby will become accustomed to the taste. This is good because it means that in general children will be more likely to make healthier food choices throughout their lives.

Although breast milk is the most ideal option for feeding an infant for at least the first few months of life, the effect of a diabetic state on the potential development of obesity must be considered. If a mother has 2DM it may be beneficial to find a formula that is most closely comparable to breast milk. If GDM is present, using a formula or even breast milk from a bank for the first week of life or until normal glucose and insulin concentrations are reached may greatly improve the risk of obesity. Other factors such as IGF-1 should also be considered before making that decision.

IGF-1 Concentration IGF-1 concentration in infants has been found to be a significant variable in the development of adiposity. In the first six months of life it has been found that breast fed infants have a considerably lower concentration of IGF-1. The reason for this low concentration compared to formula fed infants is one of the benefits of breast milk.

IGF-1 is a growth hormone stimulant used by the body during growth and development [25]. It has a structure similar to insulin with many polypeptides. It is secreted by the liver and due to the structure being so similar to insulin, it can bind with the insulin receptors on cells and perform its action [26]. Its job is to promote the effect of Human Growth Hormone in the body and assist with linear and anabolic growth [26]. This function is the reason its concentration in the body influences obesity.

The protein content of breast milk is the determining factor for the concentration of IGF-1 in the baby's body. Human breast milk has two major proteins present, casein and whey. They are 40% and 60% of the protein content, respectively. This is a bit different from cow's milk (which is used for formula) which is 20% and 80% respectively [19]. The concentration does not appear to be affected by the mother's diet

[19] but is thought to be the reasons for an improved IGF-1 concentration in breast fed infants.

Although the direct mechanism for this difference in IGF-1 concentration is unknown, there seems to be a direct connection. A study called the DARLING study which compared breast-fed infants to formula-fed found that breast fed infants are found to be leaner in weight-to-length ratios at 4 and 18 months [27]. Another study found that infants in the highest category of protein intake from 9-12 months had a significantly higher BMI at six years old [20]. This is likely because when there are fewer growth hormones there will be less growth, both length and width. Some find this growth alarming, but they should not.

The IGF mechanism is programmed within the first few months, determining growth rate for the rest of a person's life. Many studies have shown that there is supposed to be a steady increase in the concentration of IGF from the beginning of life until puberty [20]. If an infant has a slow growth rate early in life it is not a cause for concern because it means that they will not have excessive amounts of IGF when they reach puberty. Dozens of research teams have confirmed that growth patterns in the first year can absolutely differentiate between children who will and will not become obese later in life.

In conclusion, the protein content of breast milk is directly correlated to the IGF-1 concentration in a baby. With the correct distribution of whey to casein, a baby will have ideal levels of IGF-1, which stimulates growth. This growth lasts throughout life and helps to avoid unhealthy levels of adiposity.

Conclusion Breastfeeding is the ideal mode of infant feeding because it is the most natural. It not only contains antibodies, vitamins, minerals and the correct distribution of macronutrients, it also has other advantages. The likelihood of making healthier food choices throughout life if the mother does is a great benefit.

However, when the mother either has GDM or 2DM; because consuming diabetic breast milk makes the child more likely to develop obesity and diabetes, it should be avoided as much as possible. If insulin and glucose levels are closely watched

B. Bottle Feeding

There are three different forms of bottle feeding. It can be all breast milk, all formula, or a combination of both. For the reasons discussed previously, breast milk is typically the most preferable option; however, some women or babies cannot handle actual breastfeeding. Using a bottle makes it easier. For some women with GDM or 2DM their pediatrician may advise them to use formula for a balanced amount of glucose. However, there is a clear difference between formula-fed and breastfed infants.

Energy Formula fed infants have a higher total energy intake. During breastfeeding there is an adjustment period for both mother and baby where the baby is consuming less. When bottle feeding is the method, only the baby must adjust, and the mother is more adamant about being sure the entire bottle is empty. This creates an issue with self-regulation, meaning infants create neural connections that tell them to eat until nothing is left. The DARLING study found that even when complementary foods were introduced in the diet, the breast-fed infants left about 25% of the food behind and the bottle-fed infants left nothing [27]. This excess energy is then stored as adipose tissue in the body.

Typically, within the first few weeks after birth a baby's weight decreases. On average infants lose about 7% of their birth weight and then recover it within the first month once feeding is regulated [28]. This goes back to finishing the bottle, and the result is the baby never experiencing an adiposity rebound. That means that even if infants gain a healthy amount of weight, they still gain it faster. A study found that the earlier an infant's BMI increases by 3 kg/m2, the more likely they will be obese later in life. They also found that first year and 12-year BMI are directly related [28]. Without the dip in birth weight that is much more likely to occur. This shows that even if mothers choose to bottle feed they need to be very conscious of not forcing the baby to finish every bottle.

As previously stated, a dip in weight and slow weight gain is healthier for infants. Many women will go to their pediatrician and express concern about that growth pattern. In response, to make the mother feel more proactive, doctors tend to counsel the woman to supplement the baby with formula. A study proved this to be unnecessary and even unhealthy [27]. This creates even more of an excess of energy in the baby and has an inverse effect on the self-regulation the baby was attempting to learn. Women need to be reassured that the growth patterns they witness from breastfeeding are not only normal but healthy and likely preventing obesity.

Another way formula may lead to a higher energy intake is due to a lack of a hormone called leptin. This hormone is something passed from mother to baby in breast milk and is called the "satiety hormone". This has a key role in long-term weight stability. Many studies found that there is a direct correlation between obesity and lack of leptin in infancy [29]. When formula is used, this hormone is either not present or in a synthetic form which is not as effective. This means that infants would struggle with

satiation and be more likely to want more food throughout the day. These factors will lead to a struggle with weight management and obesity later in life.

Protein The prevalence of late obesity is strongly correlated to protein intake in pregnancy. There is a 66-70% higher protein content in formula than there is in breast milk which is proposed to stimulate higher IGF-1 secretion [30]. This tends to lead to a shorter, more round stature. This relationship has been studied by many research teams due to its importance in obesity risk.

The protein difference has a significant impact on an infant. A study found that when a baby was switched from solely breast to solely formula milk there was a dramatic increase in protein in the body. The energy from protein increased from 9 to 15% during the 3-month difference in feeding types [31]. This was directly linked to an increase of risk of obesity through an IGF-1 related mechanism.

There is a definitive difference in body composition due to protein concentration in formula. A systematic review of 15 studies comparing body composition of breast and formula-fed infants showed that there was a significant pattern of more fat accumulation in formula fed babies [20]. This higher protein content leads to IGF-1 increasing growth velocity [31]. The concentration directly influences obesity at school age. A study found that those with high IGF-1 concentrations had a 2.43 times higher risk of obesity at age 6 [32]. These and other studies show the importance of the IGF-1 concentration in infancy and how it can affect lifelong obesity.

Conclusion There are a few reasons why a mother and pediatrician may choose formula as the right option for a particular baby. This may be due to unsafe breast milk or an issue with adjustment. However, if possible, the research indicates that breast milk

should always be used. The difference in protein and hormone concentration between breast and formula milks have a tremendous impact on obesity later in life. If a more balanced formula option is created it may be more useful, but right now it does not appear that the benefits outweigh the risk. Also, bottle feeding breast milk is better but will still have an impact on self-regulation if excess feeding occurs.

C. Conclusion

The postnatal diet is much more influenced by protein than the prenatal diet is. The difference in protein distribution between human breast milk and cow milk (what is used in formula) plays a dominant role in the mechanism of obesity. The stimulation of IGF-1 secretion by the proteins present in formula cause a lifelong increase in adiposity. Also, the concentration of IGF-1 in breast milk cause a slow, steady increase in BMI which is positively correlated to a healthy growth rate throughout development.

Breastfeeding is consistently shown to be the most beneficial option for postnatal feeding. This is because the baby learns self-regulation, consumes adequate energy and protein amounts, and receives antibodies and hormones that help with immunity and regulation. The next best option should be bottle feeding breast milk. This is because the baby will still get all the content-based benefits but may struggle with self-regulation if the mother feeds until the bottle is empty. If this does not happen, bottle feeding breastmilk may provide the same benefits as breastfeeding, but not enough research has gone into controlling that specific variable. The least positive option based on the research is formula feeding. This is because there is little self-regulation (again, more research needs to go into controlling this variable), the protein distribution causes high

IGF-1, and it does not have the important hormones and antibodies passed from the mother.

III. Conclusion

Ultimately, there are many situations that occur between conception and the end of the first year of life that may cause obesity. Besides the ones focused on in this research, alcohol, smoking, antibiotics, and stress are just a few of the environmental factors that can have detrimental effects on body mass throughout a lifetime. However, if the dietary concerns discussed are controlled, the child will begin life with much better prospects.

Below are tables listing the diseases and considerations discussed in order of importance. Each table also includes guidelines based on what the research has indicated is "healthy" for pregnant women. As always, women should always consult a doctor before making any dietary changes during such a crucial time. Each woman and baby have her own specific needs and an obstetrician or pediatrician will be able to give a more specific dietary plan.

Table 1: Prenatal risk factors in order of importance. Type 2 Diabetes Mellitus (2DM), Gestational Diabetes Mellitus (GDM), Neural Tube Defects (NTDs), Small for Gestational Age (SFGA). Speak with a professional (obstetrician or dietitian) before making any decisions about pregnancy diets.

Rank	Risk Factors	Recommendation	Importance	Citations
1	Diabetes (2DM and GDM)	Manage hyperglycemia and hyperinsulinemia during pregnancy	To decrease or avoid risk of thrifty phenotype, diabetes development	[5, 17]

2	Folic Acid Supplementation	Begin supplementation before consumption (4 micrograms) and continue throughout first trimester	Avoid NTDs, SFGA. Proper DNA and protein methylation. Only first trimester to avoid asthma, eczema, etc.	[2, 7, 8, 9, 10]
	Other Concerns			
3	Carbohydrate Consumption	Only 55% of daily caloric intake recommended.	Avoid hyperglycemic environment, decrease diabetes risk	[5, 13, 14, 15, 16, 17]
4	Fatty Acid Consumption	Only 30% of daily caloric intake recommended.	Avoid beta islet cell damage, increased adiposity.	[11]
5	Protein Consumption	Only 15% of daily caloric intake recommended		[12]

Table 2: Postnatal risk factors in order of importance. Type 2 Diabetes Mellitus (2DM), Gestational Diabetes Mellitus (GDM). Speak with a professional (obstetrician or dietitian) before making any decisions about pregnancy diets.

Rank	Risk Factor	Recommendation	Importance	Citations
2	2DM	Manage hyperglycemia and hyperinsulinemia. If necessary, use formula	Avoid excess glucose and insulin in breast milk to protect baby from diabetes and obesity	[21, 22, 23, 24]
2	GDM	Use formula or banked breast milk until breast milk is normal	Waiting until healthy blood glucose will avoid excess glucose when feeding the baby	[21, 22, 23, 24]
	Other Concerns			
1	High Protein	If necessary, bottle feed with breast milk to avoid excess protein	Avoid increased secretion of IGF-1 which increases adiposity	[19, 20, 25, 26, 27, 28, 30, 31, 32]

3	Feeding until bottle is empty	When bottle feeding, do not force the baby to finish the bottle	Allows baby to learn self-regulation and not increase appetite	[28]
4	Hormones and antibodies	Breast feed so that babies receive regulatory hormones and antibody protection	Help with self-regulation and protection from sickness.	[29]

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