Summer 6-2024

Evolution of Morning Sickness and How it Relates to Maternal Nutrition and Fetal Development

Leena Macias
Portland State University

Evolution of Morning Sickness and How it Relates to Maternal Nutrition and Fetal Development

By

Leena Macias

An undergraduate honors thesis submitted in partial fulfillment of the

requirements for the degree of

Bachelor of Science

in

University Honors

and

Biology

Thesis Advisor

Radhika Reddy

Portland State University

2024

ABSTRACT:

A multitude of pregnant mothers throughout the world experience some sort of nausea and vomiting symptoms while pregnant. There is a large body of literature that has examined the evolutionary significance of nausea and vomiting of pregnancy (NVP), and why it continues to persist within our society. The purpose of this thesis is to perform a literature review and to add onto the current literature present within this multidisciplinary field. In order to do so, the field's published works were compiled and examined, being careful to only choose credible and significant sources in order to understand why pregnant mothers experience pregnancy sickness and aversions to certain foods, and how these aversions and cultural food taboos affect the nutrition and development of the mother and their fetus.

Keywords: Fetal development, morning sickness, Nausea and Vomiting of Pregnancy (NVP), teratogens, miscarriage, maternal nutrition, and birth defects.

INTRODUCTION:

Throughout history, the prevalence of nausea and vomiting has been recognized as a common symptom for most pregnant mothers. During the first trimester of pregnancy, about 70-80% of women experience nausea and vomiting of pregnancy (NVP), or roughly 4,000,000 and 350,000 mothers affected annually by NVP within the United States and Canada (Lee & Saha, 2011). Evolutionary biologists believe that pregnancy sickness may be an adaptation providing behavioral prophylaxis against diseases and infections that could arise from ingested toxins, where nausea causes aversion and repulsion from the substance and vomiting results in expulsion of the harmful substance (Fessler, 2002). The most critical time of development tends to be the first trimester when peak development occurs and the mother experiences greatest immune vulnerability. This explains why NVP could have been selected to be most prevalent

within the first trimester, so the fetus was protected from teratogens and pathogens that can deform fetal organs and limbs (Lee & Saha, 2011).

Although NVP is believed to be an adaptation selected to protect the mother and fetus from harmful teratogens early in pregnancy, a continual prevalence of NVP throughout the second and third trimester could negatively affect the nutritional status of the mother. Additionally, not all food aversions experienced by the mother could be harmful for their health or the health of the fetus. If NVP was an adaptation selected within the human's ancestral population, then discriminatory specificity should have been included within the natural selection process to avoid losing beneficial substances within the mother's diet (Fessler, 2002). If a mother experiences aversions to beneficial substances and becomes malnourished as a result, then the fetus won't get the nutrients it needs for proper growth, resulting in inadequate development that could cause negative effects throughout the child's whole life.

During mid-gestation and up to two years of age is when a child's brain development is most sensitive (Webster, 2014). Malnutrition during this stage of the child's life can cause improper development of their brain. Additionally, lower birth weights due to malnutrition and higher birth weight due to overnutrition can increase risks of certain diseases, such as diabetes, lower cognitive performance, cancer, kidney disease, etc. (Fall, 2013). During pregnancy, the nutritional requirements for the mother drastically increases. However, in addition to food aversions, some cultures place food taboos for pregnant women in order to limit resource consumption to protect mothers and fetuses from dangerous foods (Placek et al., 2017). Throughout history, these aversions and taboos were in place to aid in protection from harmful pathogens and infections during pregnancy. Nonetheless, some of these aversions and taboos are

towards foods that can be beneficial to fetal development, and restricting access to these certain food groups can cause the mother to face deficiencies in vital nutrients.

This thesis will conduct a review of the literature within this field of study in order to assess the various foods that women experience aversions to while pregnant. Additionally, an examination of various food taboos from different cultures will be conducted. The main goal of this thesis is to understand why the body experiences NVP as well as its evolutionary significance within the human population. NVP, food taboos and whether they correlate with malnutrition and deficiencies in pregnant mothers will also be assessed. In summation, this thesis will perform a meta-analysis of the current literature to deduce whether a correlation exists between NVP and birth defects due to malnutrition.

METHODS:

Due to this thesis being a literary review on the current field of study, the literature surrounding this field had to be acquired. The process of acquiring these sources was utilizing the Portland State's library database as well as google scholar to find primary and secondary sources of literature. These articles were carefully examined for credibility, whether the article had been reviewed, the information discussed within the article, and whether this article was a good match for the topic being discussed within this thesis. The sources were then selected and saved using zotero. This application helped to keep all the sources within a folder for easy access. Additionally, annotations were made for each of the articles to help keep them organized, and for quick skimming of the sources so the proper articles could be utilized for their intended section of the thesis.

The vast majority of the sources compiled were primary sources, with a select few articles being secondary sources. The secondary sources primarily consisted of articles reviewing

the current scientific literature, with two of the sources being textbooks that fit within this multidisciplinary field. The primary sources helped to give background information on the topics discussed within this paper, and aided in expanding upon the knowledge obtained from the current literature. These articles were predominantly scientific articles. Many of the sources went over the scientific and medical background of fetal development, fetal malformations, fetal and maternal nutrition, nausea and vomiting of pregnancy, and more. Through reading and compiling information from these sources, it aided in expanding upon the literature within the field and answering the thesis question posed within this paper.

RESULTS:

1. Evolution of Pregnancy Sickness & Physiology

In regards to pregnancy sickness, multiple perspectives exist across the cultural, sociological, and medical fields. Within the cultural field, researchers emphasize the importance of cultural practices and beliefs concerning pregnant individuals, because these beliefs and practices can impact and affect the attitude and experiences women have towards pregnancy sickness. In addition, the medical viewpoint has ongoing research on this topic, with a goal to grasp a better understanding of the intricate interaction betwixt the genetic, hormonal, and environmental factors that play a role in the emergence and intensity of nausea and vomiting of pregnancy (NVP). Lastly, the sociological perspective stipulates that attention needs to be drawn onto the impact NVP has on the lives of women within society. The toll pregnancy can have on the pregnant mother, both psychologically and physically, can result in decreased productivity. Thus, pregnant mother’s careers and economic independence can be affected, and therefore can affect whether a pregnant mother is stigmatized or supported due to society's response towards NVP.

During pregnancy, “morning sickness” is a common symptom a multitude of women experience. However, this symptom is a misnomer, because this gestational nausea and vomiting occur at various points throughout the day and not just in the morning. Additionally, “morning sickness” is just an accumulation of symptoms that co-occur with pregnancy and not a “sickness” per se. Women experiencing nausea and vomiting during pregnancy does not mean that they are sick or have a disease. Pregnant mothers that experience these symptoms tend to be healthy women who give birth to healthy babies. This statement is supported by Sherman and Flaxman’s article, “Nausea and vomiting of pregnancy in an evolutionary perspective,” which expresses that:

> The nausea and vomiting of pregnancy symptoms experienced by 90% to 95% of women do not fit the definition of “disease” (ie, “a departure from health” or “a condition that impairs a vital function”). Neither are they manifestations of physiological frailty in response to metabolic demands of pregnancy. Rather, nausea and vomiting of pregnancy is an intricate mechanism that probably evolved to serve a useful function: protecting the pregnant woman and embryo from food-borne infections and toxins.

Therefore, nausea and vomiting of pregnancy is seen more as an adaptation that can prove more beneficial than harmful to the mother and embryo if these symptoms are not inordinate. During pregnancy, and specifically within the first trimester, a pregnant mother may experience immunosuppression. A lowering in the immune system is crucial for the maternal body to not reject the fetus. Within the maternal body, the fetus is seen as an invader. If the immune system’s response does not decrease, then the maternal immune system would attack and reject the growing fetus, causing the mother to experience a spontaneous abortion. A spontaneous abortion, or early miscarriage, is the “spontaneous termination of an intrauterine pregnancy during the first trimester” (Alves et al., 2023). The classification for this type of early miscarriage has had the cut-off altered from <20 weeks of gestation to <10 weeks of gestation according to some

organizations. There exists a multitude of instances that can result in early miscarriage, Alves et al. describes that;

> In more than 60% of pregnancy losses between 6 to 10 weeks of gestation, the etiology is believed to be fetal chromosomal abnormalities, including trisomies, monosomy, and polyploidy. Additionally, inflammatory and immunologic dysregulation is thought to play a role in some cases, likely due to the effect on trophoblastic invasion.

Additionally, maternal age is the most common factor for spontaneous abortions. Alves et al. augmented the fact that the risk of early miscarriage increases drastically from 9%-17% in mothers 20-30 years old, to 75-85% in mothers at 45 years of age and older. Chronic diseases are also a factor in predisposing the mother to spontaneous abortions, such as diabetes, autoimmune conditions, thyroid disease, and more.

However, in lowering the immune system to protect the fetus from immunological attack, the mother becomes more susceptible to disease or infections, which can also increase the mother's risk for early miscarriage. Within a Cornell University study (2000), the researchers stated that "the analysis of hundreds of studies covering tens of thousands of pregnancies suggests that morning sickness and the aversion to potentially harmful foods is the body's way of preserving wellness of the mother at a time when her immune system is naturally suppressed (to prevent rejection of the child that is developing in her uterus) and has reduced defenses against food-borne pathogens" (*Cornell Chronicle*, 2000). Within the article "Maternal Immunological Adaptation During Normal Pregnancy" by Abu-Raya et al. (2020), Table 1 illustrates the various illnesses and infections pregnant mothers are susceptible to due to their lowered immune system. The table indicates that pregnant mothers are susceptible to malaria, listeriosis, and tuberculosis. Additionally, mothers have an increased maternal severity to diseases such as Coccidiomyosis, Dengue fever, Ebola virus, Hepatitis E viral infection, Influenza, Invasive pneumococcal disease, and more.

In addition, Abu-Raya et al.'s (2020) article provides more information regarding the lowered immune system of pregnant mothers, stating that pregnancy has been associated with alterations in the number of T cell subsets. T cells express receptors with the potential "to recognize diverse antigens from pathogens, tumors, and the environment, and also maintain immunological memory and self-tolerance" (Kumar, 2018). In conjunction, T cells help your immune system to recognize and fight off specific antigens and bacteria. When examining the difference between the number of T helper cells and cytotoxic T cells between pre-pregnant and currently pregnant women, Abu-Raya et al. (2020) found that T cells were lower in the third and first trimester of pregnancy. Additionally, the amount of suppressor T cells was highest in the first trimester. Thus, during pregnancy, the number of T cells decreases, causing pregnant women to experience immunosuppression.

Another table from Abu-Raya et al. (2020), Table 4, illustrates an exhausted list of cellular changes experienced during pregnancy. For example, the table states there were lowered levels of T cells, B cells, $CD5^+$ B cells, IgG levels, lowered number of T helper cells and cytotoxic cells in first and third trimester, lowered plasma IL-2 levels, percent of Th2, reduced PHA-stimulated T lymphocyte proliferation, decreases in IL-2 and IFN-γ, IgA levels in the third trimester, and IgM levels in the second and third trimester in pregnant women as compared to non-pregnant women.

Additionally, the authors observed increases in IFN-γ and IL-4 secreting cells, higher B cell activating factor levels, IgG1 levels, IgG3 levels in second trimester, higher galactosylation and sialylation of Fc portion of IgG, increase in asymmetric IgG antibodies, IgA levels in first trimester, and higher IgM levels in first trimester and late-third trimester. These changes within the B cells, T cells, and other immunoglobulins during pregnancy could indicate the decrease in

immune function during pregnancy. However, Abu-Raya et al. (2020) emphasized the scarcity of data on T cell function during pregnancy, as well as the inconsistency within research. In addition, Abu-Raya et al. (2020) indicated that a clear understanding of how the immunological changes affected maternal susceptibility was still lacking. Therefore, further research still needs to be conducted. Yet, the study indicated the existence of "highly dynamic cooperative interactions between the maternal and fetal immune system, rather than a broad maternal immune suppression" (Abu-Raya et al., 2020). Thus, indicating an important immunological adaptation over time.

With this evolutionary adaptive trait, it begs the question why natural selection would favor the maternal body to become immunosuppressed if it means the maternal body will become more susceptible to pathogens and teratogens? Immunosuppression is supposed to help the mother's body not to reject the fetus, but this protective mechanism opens the door to foodborne diseases and pathogens that can result in spontaneous abortions.

During pregnancy, the maternal body is proficient in having an adaptive immunity. With the suppressed immune response, the body experiences nausea and vomiting as a way to protect the mother from harmful substances. Normally, NVP begins about five weeks after the menstrual period, if the germinal stage proves successful, and peaks around eight to twelve weeks. The first trimester is when NVP is most prevalent, but these symptoms gradually decrease during the second and third trimester. The mechanism of NVP protecting the developing fetus through causing the mother to avoid and physically expel potentially abortifacient and teratogenic foods, is known as the embryo protection hypothesis. Unfortunately, there have not been too many tests done on the embryo protection hypothesis. Currently, there are five predictions of the embryo

protections hypothesis, according to Flaxman and Sherman (2000), and these predictions are as followed:

1. NVP should be associated with positive pregnancy outcomes
2. Foods that trigger NVP should contain teratogens, mutagens, and abortifacients.
3. NVP should be more common when the embryo is most sensitive to toxic chemicals.
4. Foods containing toxins should be most aversive to women when embryonic organogenesis is most sensitive to disruption by exogenous chemicals
5. The frequency of NVP should depend on the diet of a population: symptoms should be uncommon in populations where staple foods rarely contain substances that could damage embryos.

Most literature within the field of evolutionary biology has found that NVP is positively correlated with beneficial reproductive outcomes, where mothers who experience NVP are more likely to carry to full term and less likely to experience spontaneous abortions. Data has illustrated that "NVP protects the embryo from teratogenic phytochemicals and shields both the mother and her developing embryo from foodborne pathogens and their associated toxins" (Flaxman & Sherman, 2000). Therefore, NVP has been shown to be beneficial to both the mother and her developing fetus, causing the embryo protection hypothesis to be renamed as the maternal and embryo protection hypothesis.

Thus, since the mother's cell-mediated immune response is lowered during pregnancy to inhibit her body from attacking the fetus, and that the common pregnancy symptom, NVP, aids in keeping the mother and embryo away from teratogenic and abortifacient food, the maternal protection hypothesis is supported. This hypothesis is also consistent amongst the variable cravings and aversions pregnant mothers experience.

2. Food Aversions:

In accordance with nausea and vomiting of pregnancy, mothers experience food aversions and cravings during pregnancy. There can be a multiple of reasons for these cravings and aversions, for instance, Khan (2023) describes four reasons as to why this alteration happens during pregnancy. The first reason could be the maternal-fetal protection hypothesis. Since the mother's immune system is lowered during pregnancy, she experiences aversions as well as NVP to protect herself and the fetus from potential foodborne pathogens. Therefore, this innate protective mechanism within the mother could potentially be a cause for her food aversions and cravings.

The second reason could be due to hormonal changes. During pregnancy, women experience a rise in human chorionic gonadotropin hormone (hCG). hCG is primarily produced by the "syncytiotrophoblastic cells of the placenta during pregnancy. The hormone stimulates the corpus luteum to produce progesterone to maintain the pregnancy. Smaller amounts of hCG are also produced in the pituitary gland, the liver, and the colon" (Betz & Fane, 2023). This hormone helps in thickening the lining of the uterus, which is essential for fetal growth. Normally, hCG levels are high within the maternal body for the first ten weeks of gestation. High levels of hCG is correlated with nausea and vomiting, which could be the reason for the belief in the association between hormonal changes and food aversions.

Alterations in the mother's smell and taste can be another reason for food aversion and cravings. Taste buds can be altered due to NVP, changing the mother's flavor profile and influencing her food preferences. Additionally, a woman's sense of smell can become more sensitive during pregnancy. An article that reviewed studies about pregnancy and olfaction, found that "85% of pregnant women (n = 60) identified at least one odor to which they were

more sensitive and Nordin et al. (2004) reported that, relative to non-pregnant women (n = 76), more of the pregnant women (n = 144) reported "stronger-than-normal smell sensation" of particular odors, including cooking odors, cigarette smoke, spoiled food, perfumes, spices, and coffee" (Cameron, 2014). Therefore, increased sensitivity to olfaction and taste can cause women to experience certain aversions and cravings during pregnancy.

Lastly, the fourth suspected reason for food aversions and cravings could be because of cultural influences. Different cultures have various food taboos in regards to what pregnant women can and can not eat. These taboos can thus influence aversions to those specific foods. An example of a cultural food taboo comes from Fessler's article "Reproductive Immunosuppression and Diet," stating that

> In Tamil Nadu, India, meat and eggs are sometimes proscribed because they induce vomiting and also because they are "hot" foods (Ferro-Luzzi 1973); "hot" foods are often taboo during the first trimester because they are thought to be abortifacient (Pool 1986). Papaya, another "hot" food, is an even more prevalent target: mango, elsewhere a common focus of cravings, is also avoided because it is "hot" (Ferro-Luzzi 1973). While the latex present in papaya skin does indeed induce uterine contractions (Cherian 2000), there are no reports of such an effect for mango. Therefore Tamil Nadu pregnancy beliefs suggest taboo formation based on observations of causality combined with symbolic elaboration and extension.

Cultures place food taboos for pregnant mothers, because they believe that these certain foods can result in miscarriages, or that these foods could be potential allergens, and severe allergic reactions could be catastrophic to a fetus and its mother. Another article by Ferguson (2015) discussed Placek's study on Tamil Nadu, India. This study found that the women from villages in the rural countryside of Tamil Nadu largely avoided fruits. This aversion stems from the cultural belief that the consumption of fruit can harm the development of the fetus or result in miscarriage. For instance, the pregnant mothers residing in this region "believe eating mangoes, black grapes, papaya and other fruits while pregnant causes miscarriage and premature birth, as well as manthai, a disease characterized by black or blue patches on an infant's skin," (Ferguson,

2015). Thus, cultural beliefs can strongly influence the food aversions pregnant mothers may experience, because as Placek's study shows, pregnant women tend to avoid certain foods they learn can potentially be harmful for their fetus from others in their community, rather than relying on the aversions their body naturally experiences.

Additionally, Flaxman and Sherman (2000) conducted 21 studies that examined food cravings, as well as 20 studies that examined food aversions during pregnancy. Flaxman and Sherman interviewed 6,239 women about cravings, and then 5,432 women about aversions during gestation. Both authors concluded that pregnant women experienced the most aversions towards meat. Figure 2 depicts the various gestational cravings and aversions from Flaxman and Sherman's (2000) study. The triple asterisks illustrate a vast difference between cravings and aversions, whereas NS shows no difference between gestational cravings and aversions. Of the following food categories, there is meat, non-alcoholic beverages (N-A), vegetables (Veg), alcoholic beverages (Alc), ethnic strong and spicy foods (ESS), dairy (D), sweets (S), grains and starches (G&S), as well as fruits and fruit juices (F).

From the figure, it is evident that meat was the most targeted food category for aversions, and fruit was the most craved food. Since pregnant mothers experience immunosuppression, they are more likely to become ill from foods containing viruses, bacteria, and/or fungi. Meats, such as fish, poultry, eggs, beef, lamb, or pork, contain a multitude of various viruses or parasites that can result in foodborne illnesses within the mother, which then has adverse effects on fetal development and can result in miscarriages. For instance, meat contains a protozoan parasite called *Toxoplasma gondii*, which can result in schizophrenia, spontaneous abortions, neonatal diseases, as well as neurological birth defects within the developing fetus. This parasite can only be acquired through the consumption of undercooked or raw meat. Healthy individuals rarely

develop illnesses from the consumption of undercooked or raw meat, however, the same cannot be said for individuals who are immunocompromised, such as pregnant mothers.

Within Fessler's (2002) article, they examine the evolutionary perspective of NVP as well as meat consumption during pregnancy. In Fessler's section on meat, pathogens, and pregnancy, Fessler illustrates the various meat-borne pathogens and how they pose a threat to pregnant women. Fessler states that meat is one of the most dangerous food types to pregnant women, especially within their first trimester. Due to meat possessing an abundance of pathogens, it poses a great risk to maternal health and fetal development. These pathogens can greatly hinder and negatively impact organogenesis. Fessler's (2002) article contains Table 3, which illustrates the various meat-borne pathogens that pose a threat during gestation. The pathogens listed include *Toxoplasma gondii*, *Listeria monocytogenes, Escheriachia coli, Brussels abortus B. melitensis, Shigella dysenteriae, Campylobacter jejuni, Clostridium perfringens,* and *Leptospira.*

Additionally, Fessler (2002) discusses how faunal remains of human ancestors illustrate that meat was a part of our diet, and there's the potential that the consumption of meat could date back to around the beginning of our genus. Therefore, it is likely our species, overtime, has developed adaptations favoring the aversion of meat during pregnancy. Since meat contains an abundance of pathogens and the ability to harm the fitness of our population, it is logical for natural selection to select the trait in which women experienced nausea and vomiting towards meat and other potential abortifacient foods. The next section of the paper will explore fetal development, as well as when it peaks and when the fetus is most susceptible to teratogens.

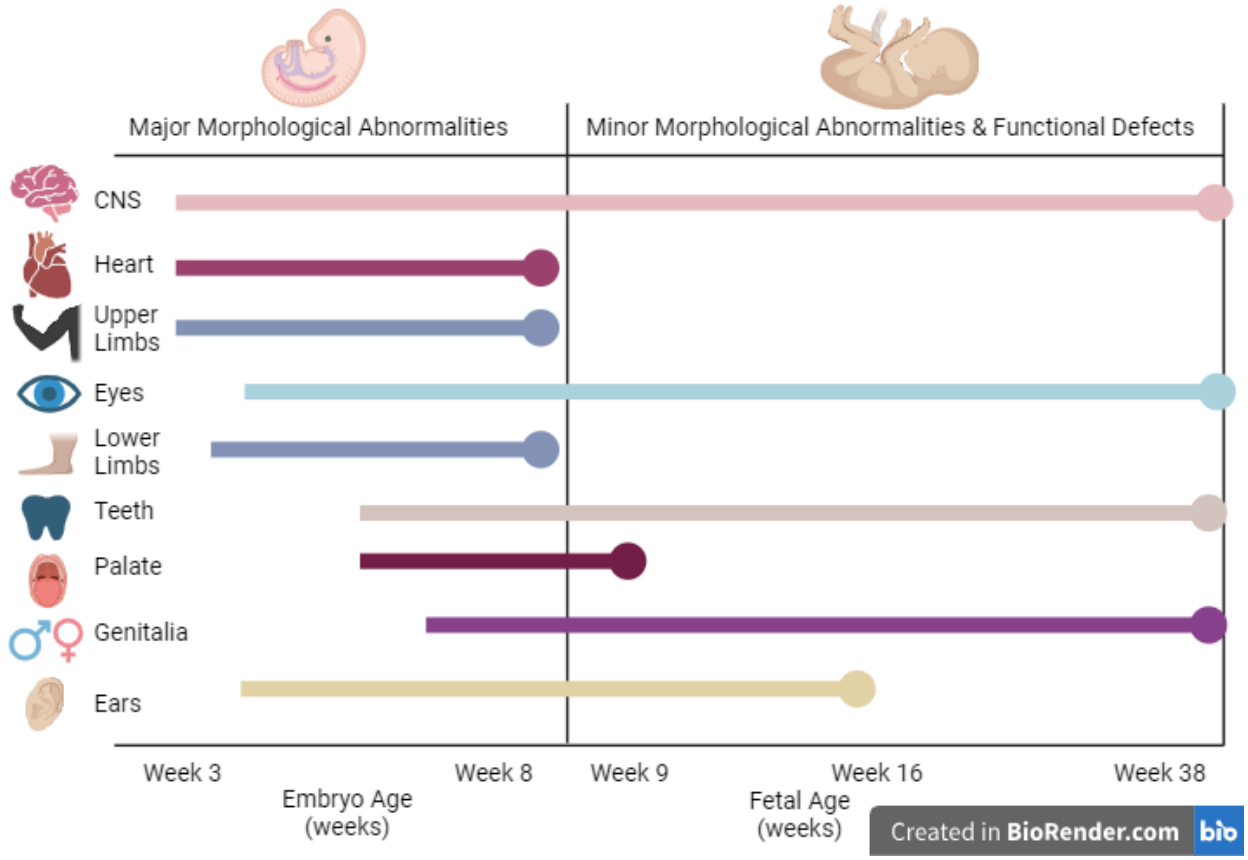
3. Fetal Development

In accordance with prenatal development, there exists three distinct stages of development. The first stage is the germinal period, which occurs between weeks 0-2. This period begins immediately after conception and focuses on cell division and implantation of the zygote into the mother's uterus. This period is the shortest out of the three. After the sperm implants itself into the egg, the zygote is created and travels down the fallopian tube towards the uterus. During its journey, the zygote divides into two distinct structures, the embryo and the placenta. The zygote continues to divide its cells until it becomes a blastocyst. Once it becomes a blastocyst, it has arrived to the uterus and implants itself into the uterine lining. If successful, the blastocyst will continue to undergo development and traverse onto the second stage.

The second stage of development is the embryonic stage, which occurs between weeks 3-8 of gestation. Within this stage, the embryo undergoes organogenesis. This process gives the blastocyst more human characteristics, transforming the blastocyst into an embryo. Organogenesis helps to form structures such as the "neural tube (which later becomes the brain and spinal cord), head, eyes, mouth and limbs form" (Fetal Development, 2024). Around the sixth week, the arms, legs, and heart begin to form. Additionally, the heart will begin to pulse around this time. At the eighth week, which marks the end of this stage, most of the embryonic systems and organs have developed and taken shape. A lot of mothers experience nausea and vomiting around this time, and the main reason for this could be due to the fact that the fetus is most susceptible during this period of organogenesis. There are many environmental factors that can harm fetal development such as malnutrition, disease, stress, age, poverty, and teratogens. Below is a figure created with BioRender.com, to summarize the timeframe and severity of fetal

abnormalities as depicted within the human development textbook Human Development Teaching & Learning Group (2020). *Human Development*. Pg 76).

Figure 1. Timeline illustrating the magnitude of adverse effects to fetal development.



Thus, by looking at the figure, it is evident that organogenesis is a period in which harm done onto the embryo has the greatest range of consequences on development. Additionally, the danger of these factors in this phase are "greatly exacerbated by the fact that, *during precisely this period,* the mother's ability to resist infection is severely compromised" (Fessler, 2002). Since the mother is immunocompromised, she is more susceptible to illnesses and environmental factors such as teratogens and abortifacients. Table 4 depicts a summation from the Human Development Teaching & Learning Group (2020) on teratogens and their effects on fetal development.

Table 1. Teratogens and how they affect the developing fetus.

Teratogen	**Effects**
Alcohol	Fetal alcohol syndrome. Physical abnormalities (flattened noses, small heads, small eye holes) Poor cognitive function (higher rate of ADHD, poor judgment, poor impulse control, lower IQ, and leaning issues)
Caffeine	Increases the risks of miscarriage. Recommended that mothers should not consume more than 200 mg of caffeine a day.
Nicotine/Tobacco	Fetus exposed to nicotine, carbon monoxide, and tar → lessens oxygen availability to fetus. Low birthweight, ectopic pregnancy, placental abruption, placenta previa, fetal growth restriction, stillbirths, birth defects, early puberty for girls, learning disabilities, and sudden infant death (SIDS).
Cocaine	Stillbirths, low birth weight, and spontaneous abortions.
Marijuana	Cause issues with brain development if used heavily.
Methamphetamines	Lower birth weight, developmental issues, high infant mortality, as well as behavioral issues.
Heroin	Attentional deficit problems, motor control impairments, difficulty in behaviors, as well as withdrawal. **Neonatal abstinence syndrome = when the mother uses addictive drugs during pregnancy, the infant, while in the womb, can become addicted to that drug and go through withdrawal after birth.
Mercury	Negatively impacts hearing and vision, as well as causes brain damage. Mercury is present in bigger fish such as tuna, and consumption should be limited.
Pesticides	Low birth weight, miscarriage, birth defects, premature birth, and learning issues.
Lead Poisoning	Delays in neurological development, prematurity, miscarriage, and lower birth weight. Ex. Flint, Michigan has high levels of lead in their water.

Bisphenol A (BPA)	Causes birth defects due to a disruption of certain genes. Found in plastics, and beverage containers.
Radiation	Impaired neurological development, miscarriage, cancer, birth defects, and low birthweight.
Prescription Drugs	Issues with overall health, birth defects, issues with fetal development. Ex. Ibuprofen can cause issues in blood flow to the fetus during the last three months of gestation. **Only medications prescribed by providers that know the mother is pregnant is okay.
Tosoplasmosis (toxoplasma gondii parasite)	Stillbirths, birth defects in the eyes and brain, as well as premature births. Most babies don't show symptoms, but 10% experience pneumonia, eye infections, jaundice, as well as enlarged spleen and liver. **These parasites can be contracted from coming in contact with dirty fruits and vegetables; eating raw or undercooked meat as well as coming in contact with utensils that touch raw meats; soil; sand; and cat feces (litter box).
Sexually Transmitted Infections (STIs)	Chlamydia, gonorrhea, and syphilis can be passed on from the infected mother to the child. Results in ectopic pregnancy, premature rupture of amniotic sac, birth defects, stillbirths, premature birth, and miscarriage.
Human Immunodeficiency Virus (HIV)	Mothers with HIV can transmit it to the fetus during labor, breastfeeding, or prenatally. Mothers can take antiviral medications to reduce the risk of transmission from 25% ro 2%. Mothers should deliver babies via C-section and avoid breastfeeding to also lower transmission risks.
Rubella (German Measles)	Contraction of Rubella in the first three months of pregnancy can result in birth defects, such as damage to the heart, eyes, brain, and ears. Vaccination as a child significantly helps reduce the possibility of contracting this virus.

Aside from teratogens and abortifacients, there are a multitude of maternal factors that affect the developing fetus. Maternal age poses risks for the developing fetus. Mothers over the

age of 35 are at a greater risk for miscarriages, diabetes, fertility problems, high blood pressure, premature birth, placenta previa, cesarean section, stillbirths and “a baby with a genetic disorder or other birth defects,” (Human Development Teaching & Learning Group, 2020). Women are born with all the eggs they are ever going to have, so as women progress in age, the quality of these eggs go down due to environmental teratogens affecting the quality of these eggs. However, prenatal screening tests can be beneficial for older mothers to determine potential health risks the fetus may face.

Conversely, becoming a mother too young carries risks as well. Teenagers are at risk for high blood pressure and anemia Additionally, teenagers tend to give birth to infants that are low in birth weight or premature, which can cause a multitude of health risks for these infants. According to Human Development Teaching & Learning Group (2020),, the authors state that;

> Premature and low birthweight babies may have organs that are not fully developed which can result in breathing problems, bleeding in the brain, vision loss, and serious intestinal problems. Very low birthweight babies (less than 3 1/3 pounds) are more than 100 times as likely to die, and moderately low birthweight babies (between 3 1/3 and 5 ½ pounds) are more than 5 times as likely to die in their first year, than normal weight babies (March of Dimes, 2012c). Again, the risk is highest for babies of mothers under age 15. A primary reason for these health issues is that teenagers are the least likely of all age groups to get early and regular prenatal care. Additionally, they may engage in risky behaviors during pregnancy, including eating unhealthy food, smoking, drinking alcohol, and taking drugs. Additional concerns for teenagers are repeat births. About 25% of teen mothers under age 18 have a second baby within 2 years after the first baby’s birth.

In addition, gestational diabetes is another factor that can impact fetal development. Untreated gestational diabetes can result in premature birth; low blood glucose levels; problems during birth/labor, because babies can become heavier than nine pounds; breathing problems for the infant; jaundice; and stillbirth. High blood pressure/hypertension is another factor impacting development. Mothers experiencing hypertension can have either gestational or chronic hypertension. If mothers have this condition, it can result in preeclampsia, placental abruptions, premature birth, and low birth weight.

Rh disease can also negatively impact fetal development. Rh is a protein within the blood, where if this Rh factor is present, it signifies that an individual has a positive blood type (A+, B+, AB+, O+). Conversely, if the Rh factor is absent, then that signifies the individual has a negative blood type (A-, B-, AB-, O-). If a mother who is Rh negative has a child whose blood type is Rh positive, then they are at risk of the fetus developing a form of anemia referred to as Rh disease (March of Dimes, 2009). During pregnancy, the baby's blood cells will mix into the mother's bloodstream through her placenta, resulting in her immune system to produce antibodies to fight off the 'foreign invaders.' Thus, the fetus is at risk for Rh disease, which can result in jaundice, brain damage, heart failure, anemia, stillbirth, and death after birth (March of Dimes, 2009). However, there are treatments for Rh disease, and most of the time the infant recovers fully.

Another maternal factor that can affect fetal development is weight gain during pregnancy. Mothers need to gain a healthy amount of weight during pregnancy to aid in their child's development. If too little weight is gained, that can result in an infant who is lower in weight. On the other hand, if too much weight is gained during pregnancy, the infant is more likely to be larger in size and/or premature. Higher weight also puts the mother more at risk for preeclampsia and diabetes. Table 3.1 from the Human Development Teaching & Learning Group (2020) demonstrates what is considered healthy and unhealthy weight gain during pregnancy. The table states that mothers who were at a good weight before pregnancy need to gain 25 to 35 pounds. For mothers that are underweight, they need to gain a total of 28-40 pounds for a healthy pregnancy. Mothers who were overweight before pregnancy need to gain only 12 to 25 pounds, and those who were obese need to gain no more than 11 to 20 pounds. Within the first trimester, it is suggested that mothers of all weights should gain one to four and a half pounds. Within the

second and third trimester, mothers of a good weight should gain one pound per week, underweight mothers should gain a bit more than one pound a week, overweight mothers should gain a little bit more than half a pound per week, and obese mothers should gain less than half a pound per week. Additionally, this section within the textbook stated putting on weight slowly during pregnancy was best for fostering a healthy fetus.

Lastly, stress and depression are other maternal factors that can negatively impact fetal health and development. High levels of stress can result in the mother giving birth prematurely, and having a child lower in birth weight. Additionally, stress can result in negative side effects to the function of the infant's immune system and brain development. Depression can occur during pregnancy, as well as pre and post-pregnancy. Maternal depression can result in giving birth to babies lower in birth weight, giving birth prematurely, having fewer facial expressions, higher irritability, less attentiveness, and less active (Titchenal et al., 2020). Thus, maternal health is crucial during pregnancy and fetal development.

Proper nutrition and health during pregnancy is vital in regards to epigenetics. For instance, "Maternal diets or nutritional compositions contribute to the establishment of the epigenetic profiles in the fetus that have a profound impact on individual susceptibility to certain diseases or disorders in the offspring later in life" (Li, 2018). Epigenetics functions to alter phenotypes without altering the DNA sequence, as well as to regulate gene expression. The health of the mother can influence the child's epigenetic status. For instance, during pregnancy, the infant experiences a stage of plasticity where the development of the fetus can be subjected to changes due to the environment or genetic profile. This is known as fetal programming, where factors influencing fetal development can cause life-long implications.

DNA methylation more specifically, plays a vital role in this critical moment of fetal plasticity. Research in the UK discovered that gestational diabetes caused alterations within methylation patterns at the CpG sites within the genome. Additionally, excessive weight gain during pregnancy was seen to increase the levels of DNA methylation which affected developmental programming in the child (Geraghty, 2016). Early embryogenesis is the period that is critical for re-establishment of epigenetic profiles. The way in which the epigenetic profile is re-written can either result in positive or negative outcomes for the fetus. If mismatches occur during embryogenesis, then poor alterations can occur such as increased risk for specific diseases, embryonic lethality, or developmental malformations.

However, there exists beneficial re-writing, where this can lead to disease prevention and other advantageous outcomes for the infant (Li, 2018). Epigenetic mechanisms are greatly influenced by environmental factors, such as maternal nutrition and teratogens. Figure 1 within Li's (2018), illustrates how environmental factors influence the infant's epigenetic reprogramming. According to the figure, maternal diet and exposure to certain teratogens and abortifacients has a direct correlation with fetal development. After conception, the fetus uses the maternal nutrient stores to help it grow and develop. Without adequate nutrients, the development of the fetus will be negatively impacted, because their high metabolic demands won't be met. In addition, maternal diet plays an important role in early-life epigenetic programming and fetal gut microbiomes. Thus, improper diets and exposure to teratogens can result in alterations in gene expression and phenotypes within the fetus.

4. Effects of Deficiencies on health and development

Nutrition is crucial during pregnancy, for both the mother and the fetus. Many pregnant mothers experience deficiencies for certain vitamins and minerals, which can prove harmful for the developing fetus. There exists a multitude of women, especially those of a lower socioeconomic class, that enter pregnancy already deficient in key nutrients. Thus, the gestational needs will exacerbate these deficiencies and cause harm to the mother and her fetus's development. A new study written by Kelley, 2023, who researches in the Lifecourse Epidemiology of Adiposity (LEAD) Center at the University of Colorado Anschutz Medical Campus, found that during pregnancy, about 90% of women do not receive proper nutrients. Pregnant mothers have to take supplements, since the food they are consuming does not give them the adequate amount of nutrients needed to satisfy gestational demands. However, the study also found that 99% of affordable supplements lack the proper dose of nutrients needed to regulate the nutritional imbalance.

Micronutrients are essential nutrients that are required by the body in small amounts, but play a crucial role in maintaining overall health and well-being. During pregnancy, the importance of micronutrients becomes even more pronounced, as they are essential for the normal growth and development of the fetus, as well as the health of the mother. These nutrients support many metabolic activities, such as motility, differentiation, cell signaling, proliferation, and apoptosis. Thus, these nutrients aid in homeostasis, tissue function, regulation, and growth. For the fetus to develop into a healthy neonate, these vitamins and minerals are crucial since they promote healthy gestation through their support of the maternal, placental, and fetal stages. Another study conducted by the University of Southampton, 2023, stated that;

> Scientists from the University of Southampton, working with experts worldwide, surveyed more than 1,700 women and found most were missing essential nutrients found

in abundance in meat and dairy products. These included vitamins B12, B6 and D, folic acid and riboflavin which are essential for the development of fetuses in the womb.

Due to NVP symptoms and food aversions, this can also explain the abundance of malnutrition in pregnant mothers. Since pregnant women largely experience food aversions towards meat, this can inadvertently result in deficiencies within the vitamins listed above. For instance, an article written by OB-GYN Pierre-Lambert, 2023, discussed how pregnancy sickness is a common pregnancy complication which can result in nutritional deficiencies. Deficiencies in certain vitamins can result in different effects on the developing fetus. Deficiencies in certain vitamins can cause varying consequences on the developing fetus. Below is a table that has been constructed to summarize the different nutrients and harm the deficiencies can cause to the fetus based on what was discussed in Daston and Uriu-Adams' (2024) article.

Table 2. Effects of vitamin deficiencies on fetal development.

Nutrient Type	**Deficiency Effects**
Iodine	Cretinism and goiter = neurological disorder. Can also cause fetal death, abnormal bone development, mental impairment, and severe growth restrictions.
Vitamin A	Visual impairment and blindness.
Riboflavin, niacin, folic acid, and pantothenic acid	Structural malformations
Pyridoxine and thiamine	Increase embryonic mortality and decrease fetal growth
Folate	Neural tube defects
Vitamin B12	Megaloblastic anemia, neurological development delay, and is an independent risk factor for neural tube defects

Choline	Negatively alter brain structure and function
Vitamin D	Neonatal hypocalcemia, lowered infant growth, and poor bone mineralization.
Vitamin K	High percentage of miscarriages and prematurity. Bone abnormalities, cognitive impairment, and optic atrophy.
Zinc	Affects development of almost every organ. Fetal malformations and CNS malformations.
Copper	Menkes' disease = X-linked disorder of copper metabolism. Cognitive impairment and severe connective tissue and cardiovascular defects that typically result in fetal death by the age of three.

However, not only can deficiencies in vitamins cause harm to the mother and the fetus, megadoses of vitamins can also be harmful. For example, taking too much vitamin A can be teratogenic, negatively impacting organogenesis. The nutrient retinoic acid is an active form of vitamin A that aids in controlling genes responsible for establishing the embryonic body pattern (Daston & Uriu-Adams, 2024). For proper regulation of gene expression, the embryo ensures proper regulation of vitamin A levels. If improperly regulated and there is an abundance of vitamin A present within the fetal body, these control mechanisms would cease to function properly, resulting in abnormal development.

Therefore, maintaining the proper amount of vitamins and minerals needed is necessary for the health and development of the mother and fetus. An article published by Christian et. al., 2016, discusses micronutrient deficiencies in pregnancy, as well as its health effects and preventions against such deficiencies. Their tables are informative on the Recommended Dietary

Allowances (RDA) requirements for pregnant mothers and the importance of specific vitamins and minerals. Table 1 within Christian et. al., 2016 article, illustrates Canada and the USA's RDA recommendations for micronutrient intake for pregnant and nonpregnant women. For vitamin A, pregnant mothers need 770 μg RAE (retinol activity equivalents) while nonpregnant mothers need 700 μg RAE. For folate, pregnant mothers need 600 μg DFE (dietary folate equivalents) whereas nonpregnant women need 400 μg DFE. The table includes a large variety of essential micronutrients and the RDA recommendations for how much pregnant and nonpregnant women need.

In general, the RDA requirements for pregnant mothers tends to be higher than regular women. Within the first trimester, the pregnant mother's energy requirements are the same as a nonpregnant, nonlactating woman. However, within the second trimester, her energy requirements increase. The IOM states that in her second trimester, the mother should consume an extra 340 calories per day, and then an additional 450 calories a day within her third trimester. Mothers need more energy and nutrients when pregnant. Therefore, it is vital for pregnant mothers to receive adequate amounts of carbohydrates, calories, vitamins, and minerals within their diet.

DISCUSSION:

In regards to maternal nutrition, an article *Maternal Nutrition* published under UNICEF, stresses the importance of proper nutrition before, during, and after pregnancy. Having a nutritious diet before pregnancy is vital for building energy and nutrient reserves, because during pregnancy and breastfeeding the need for energy and nutrients increase. The journal article goes in depth on nutrient needs, innovations for maternal nutrition, as well as ten key actions to better the nutrition of adult and adolescent women. However, there are numerous women who's

nutritional status is poor simply because they cannot afford or don't have access to nutritional foods. Thus, pregnant and breastfeeding mothers are not able to ensure their babies have the best chance to develop and survive. As discussed within this thesis, poor nutrition and deficiencies can have harmful effects on the mother and her developing baby. "Worldwide, women's diets are influenced by various factors, especially food access and affordability, gender inequality and social and cultural norms that may constrain women's ability to make decisions about their nutrition and care" (*Maternal Nutrition | UNICEF*, n.d.). Therefore, it is vital women around the world have access to healthy foods to not only support their development, but the development of their kids.

Additionally, teaching healthy cooking skills and healthy meal interventions can prove beneficial for the nutritional status of the mother and her offspring. With the presence of NVP, it is hard for some women to maintain a healthy diet. The presence of nausea and vomiting can inhibit some women from being able to eat full meals or get the proper nutrients into their diet. A study conducted by Garcia et al., 2021, illustrates that their findings "support the development of cooking skills interventions for pregnant women as a strategy for improving maternal and child nutrition and provide rich data to inform program development." For instance, practice in meal preparation, budgeting on food, and/or batch cooking can aid in maintaining a healthy diet, as it diminishes the stresses of managing and cooking meals, especially when coupled with the stresses of prepping for a newborn..

CONCLUSION:

The purpose of this thesis was to answer how nausea and vomiting of pregnancy (NVP) affects maternal and fetal health. NVP is hypothesized to be an evolutionary adaptation to help deter pregnant mothers from teratogens that can be harmful to her and her developing fetus.

These teratogens can negatively impact development and result in miscarriages, so NVP is important in mitigating these harmful outcomes. However, the presence of nausea and vomiting can negatively impact the nutritional status of the mother, making it harder for her to maintain a healthy diet. This can thus result in nutrient deficiencies, which can also harm the development of the fetus and result in birth defects. Spina bifida is an example of a birth defect caused by a folate deficiency.

Therefore, NVP has its costs and benefits, where nausea and vomiting protects the mother and fetus from teratogens, but can negatively impact her diet depending on the severity of NVP symptoms. Additionally, inaccessibility to healthy foods due to unaffordability, inequality, racial disparity, and food venues without healthy products was seen to negatively affect maternal nutrition. In conjunction, future research on education about NVP and maternal nutrition; increasing accessibility to healthy food for all minorities and socioeconomic classes; and interventions for healthy cooking skills is important for the betterment of maternal health and fetal development.

Bibliography

Abu-Ouf, N. M., & Jan, M. M. (2015). The impact of maternal iron deficiency and iron deficiency anemia on child's health. *Saudi Medical Journal*, *36*(2), 146–149. https://doi.org/10.15537/smj.2015.2.10289https://www.unicef.org/nutrition/maternal

Abu-Raya, B., Michalski, C., Sadarangani, M., & Lavoie, P. M. (2020). Maternal Immunological Adaptation During Normal Pregnancy. *Frontiers in Immunology*, *11*. https://www.frontiersin.org/articles/10.3389/fimmu.2020.575197

Alves, C., Jenkins, S. M., & Rapp, A. (2024). Early Pregnancy Loss (Spontaneous Abortion). In *StatPearls*. StatPearls Publishing. http://www.ncbi.nlm.nih.gov/books/NBK560521/

Bayley, T. M., Dye, L., Jones, S., DeBono, M., & Hill, A. J. (2002). Food cravings and aversions during pregnancy: Relationships with nausea and vomiting. *Appetite*, *38*(1), 45–51. https://doi.org/10.1006/appe.2002.0470

Betz, D., & Fane, K. (2024). Human Chorionic Gonadotropin. In *StatPearls*. StatPearls Publishing. http://www.ncbi.nlm.nih.gov/books/NBK532950/

Cameron, E. L. (2014). Pregnancy and olfaction: A review. *Frontiers in Psychology*, *5*, 67. https://doi.org/10.3389/fpsyg.2014.00067

CDC. (2023). *Data & Statistics on Birth Defects | CDC*. Centers for Disease Control and Prevention. https://www.cdc.gov/ncbddd/birthdefects/data.html

Communications staff, Washington State University. (2015). Culture affects food aversions of pregnant women. *WSU Insider*. Retrieved November 3, 2023, from https://news.wsu.edu/press-release/2015/12/10/culture-affects-food-aversions-of-pregnant-women/

Fall, C. H. (2013). Fetal malnutrition and long-term outcomes. *Nestle Nutrition Institute*

Workshop Series, *74*, 11–25. https://doi.org/10.1159/000348384

Fessler, D. M. T. (2002). Reproductive Immunosuppression and Diet: An Evolutionary Perspective on Pregnancy Sickness and Meat Consumption. *Current Anthropology*, *43*(1), 19–61. https://doi.org/10.1086/324128

Fetal Development: Week-by-Week Stages of Pregnancy. (2024). Cleveland Clinic. Retrieved May 6, 2024, from https://my.clevelandclinic.org/health/articles/7247-fetal-development-stages-of-growth

Flaxman, S. M., & Sherman, P. W. (2000). Morning Sickness: A Mechanism for Protecting Mother and Embryo. *The Quarterly Review of Biology*, *75*(2), 113–148.

Forbes, S. (2017). Embryo quality: The missing link between pregnancy sickness and pregnancy outcome. *Evolution and Human Behavior*, *38*(2), 265–278. https://doi.org/10.1016/j.evolhumbehav.2016.10.003

Garcia, T., Duncanson, K., Shrewsbury, V. A., & Wolfson, J. A. (2021). A Qualitative Study of Motivators, Strategies, Barriers, and Learning Needs Related to Healthy Cooking during Pregnancy. *Nutrients*, *13*(7), 2395. https://doi.org/10.3390/nu13072395

Georgieff, M. K. (2020). Iron Deficiency in Pregnancy. *American Journal of Obstetrics and Gynecology*, *223*(4), 516–524. https://doi.org/10.1016/j.ajog.2020.03.006

Georgieff, M. K. (2023). The importance of iron deficiency in pregnancy on fetal, neonatal, and infant neurodevelopmental outcomes. *International Journal of Gynecology & Obstetrics*, *162*(S2), 83–88. https://doi.org/10.1002/ijgo.14951

Geraghty, A. A., Lindsay, K. L., Alberdi, G., McAuliffe, F. M., & Gibney, E. R. (2016). Nutrition During Pregnancy Impacts Offspring's Epigenetic Status—Evidence from Human and Animal Studies. *Nutrition and Metabolic Insights*, *8*(Suppl 1), 41–47.

https://doi.org/10.4137/NMI.S29527

Gernand, A. D., Schulze, K. J., Stewart, C. P., West, K. P., & Christian, P. (2016). Micronutrient deficiencies in pregnancy worldwide: Health effects and prevention. *Nature Reviews. Endocrinology*, *12*(5), 274–289. https://doi.org/10.1038/nrendo.2016.37

Godfrey, K. M., Titcombe, P., El-Heis, S., Albert, B. B., Tham, E. H., Barton, S. J., Kenealy, T., Chong, M. F.-F., Nield, H., Chong, Y. S., Chan, S.-Y., Cutfield, W. S., & NiPPeR Study Group. (2023). Maternal B-vitamin and vitamin D status before, during, and after pregnancy and the influence of supplementation preconception and during pregnancy: Prespecified secondary analysis of the NiPPeR double-blind randomized controlled trial. *PLOS Medicine*, *20*(12), e1004260. https://doi.org/10.1371/journal.pmed.1004260

Herring, C. M., Bazer, F. W., Johnson, G. A., & Wu, G. (2018). Impacts of maternal dietary protein intake on fetal survival, growth, and development. *Experimental Biology and Medicine*, *243*(6), 525–533. https://doi.org/10.1177/1535370218758275

Human Development Teaching & Learning Group (2020). *Human Development*.

Kelley, L. (2023). *Study Reveals Prenatal Supplements Don't Offer Adequate Nutrition for Women and Babies*. Retrieved May 6, 2024, from https://news.cuanschutz.edu/news-stories/new-study-reveals-thousands-of-prenatal-supplements-fail-to-provide-adequate-nutrition-for-pregnant-women-and-babies

Khan, S. (2023). Reasons for Food Aversions During Pregnancy & How to Manage Them. *eMediHealth*. https://www.emedihealth.com/nutrition/reasons-food-aversions-pregnancy

Kumar, B. V., Connors, T., & Farber, D. L. (2018). Human T cell development, localization, and function throughout life. *Immunity*, *48*(2), 202–213. https://doi.org/10.1016/j.immuni.2018.01.007

Lee, N. M., & Saha, S. (2011). Nausea and Vomiting of Pregnancy. *Gastroenterology Clinics of North America*, *40*(2), 309–vii. https://doi.org/10.1016/j.gtc.2011.03.009

Li, Y. (2018). Epigenetic Mechanisms Link Maternal Diets and Gut Microbiome to Obesity in the Offspring. *Frontiers in Genetics*, *9*, 342. https://doi.org/10.3389/fgene.2018.00342

Maternal nutrition | UNICEF. (n.d.). Retrieved November 3, 2023, from https://www.unicef.org/nutrition/maternal

Medical Genetics: Teratogens. (2023). Retrieved May 6, 2024, from https://www.nationwidechildrens.org/conditions/health-library/medical-genetics-teratogens

Morning sickness is Mother Nature's way of protecting mothers and their unborn, Cornell biologists find | Cornell Chronicle. (2000). Retrieved November 3, 2023, from https://news.cornell.edu/stories/2000/05/morning-sickness-protects-mothers-and-their-unborn

Nijsten, K., Jansen, L. A. W., Limpens, J., Finken, M. J. J., Koot, M. H., Grooten, I. J., Roseboom, T. J., & Painter, R. C. (2022). Long-term health outcomes of children born to mothers with hyperemesis gravidarum: A systematic review and meta-analysis. *American Journal of Obstetrics & Gynecology*, *227*(3), 414-429.e17. https://doi.org/10.1016/j.ajog.2022.03.052

Parker, S. E., Starr, J. R., Collett, B. R., Speltz, M. L., & Werler, M. M. (2014). Nausea and Vomiting during Pregnancy and Neurodevelopmental Outcomes in Offspring. *Paediatric and Perinatal Epidemiology*, *28*(6), 527–535. https://doi.org/10.1111/ppe.12151

Placek, C. D., Madhivanan, P., & Hagen, E. H. (2017). Innate food aversions and culturally transmitted food taboos in pregnant women in rural southwest India: Separate systems to

protect the fetus? *Evolution and Human Behavior : Official Journal of the Human Behavior and Evolution Society*, *38*(6), 714–728. https://doi.org/10.1016/j.evolhumbehav.2017.08.001

Rh disease. (n.d.). [Health Topic]. Retrieved May 6, 2024, from https://www.marchofdimes.org/find-support/topics/planning-baby/rh-disease

Şanlı, E., & Kabaran, S. (2019). Maternal Obesity, Maternal Overnutrition and Fetal Programming: Effects of Epigenetic Mechanisms on the Development of Metabolic Disorders. *Current Genomics*, *20*(6), 419–427. https://doi.org/10.2174/1389202920666191030092225

Sherman, P. W., & Flaxman, S. M. (2002). Nausea and vomiting of pregnancy in an evolutionary perspective. *American Journal of Obstetrics and Gynecology*, *186*(5), S190–S197. https://doi.org/10.1067/mob.2002.122593

Uriu-Adams, J., & Daston, G. P. (2024). *Society for Birth Defects Research and Prevention*. Retrieved October 28, 2023, from https://www.birthdefectsresearch.org/primer/nutrition.asp

Szucs, L. E., Demissie, Z., Steiner, R. J., Brener, N. D., Lindberg, L., Young, E., & Rasberry, C. N. (2023). Trends in the teaching of sexual and reproductive health topics and skills in required courses in secondary schools, in 38 US states between 2008 and 2018. *Health Education Research*, *38*(1), 84–94. https://doi.org/10.1093/her/cyac032

Titchenal, A. et al. (2020). *Human Nutrition.* University of Hawaii Manoa. ISBN 13: 9781948027014. https://open.umn.edu/opentextbooks/textbooks/622.

Webster, R. (2014). *How does nutrition affect the developing brain?* ZERO TO THREE. Retrieved November 3, 2023, from

https://www.zerotothree.org/resource/distillation/how-does-nutrition-affect-the-developing-brain/

Pierre-Lambert, C. (n.d.). *What You Need to Know about Pregnancy and Food Aversions*. Retrieved May 6, 2024, from https://www.orlandohealth.com/content-hub/what-you-need-to-know-about-pregnancy-and-food-aversions

Singh, P. K. (2023). *World Birth Defects Day: Many birth defects, one voice*. Retrieved October 9, 2023, from https://www.who.int/southeastasia/news/detail/02-03-2023-world-birth-defects-day-many-birth-defects-one-voice

Wu, G., Bazer, F. W., Cudd, T. A., Meininger, C. J., & Spencer, T. E. (2004). Maternal nutrition and fetal development. *The Journal of Nutrition*, *134*(9), 2169–2172. https://doi.org/10.1093/jn/134.9.2169

Yalew, A., Tekle Silasie, W., Anato, A., & Fikrie, A. (2021). Food aversion during pregnancy and its association with nutritional status of pregnant women in Boricha Woreda, Sidama Regional State, Southern Ethiopia, 2019. A community based mixed crossectional study design. *Reproductive Health*, *18*, 208. https://doi.org/10.1186/s12978-021-01258-w