Adaptive Significance of Nausea and Vomiting in Early Pregnancy

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Abstract
Nausea and vomiting in early pregnancy (NVP) is a common condition that affects many women worldwide. NVP is also referred to as morning sickness, but this is a misnomer as symptoms are not exclusive to the morning, and the term “sickness” implies that the condition is pathological despite the relative good health of the expectant mothers and the frequency with which it occurs in pregnant women (Flaxman and Sherman 2000). While the sensations of excessive salivation and nausea that may lead to vomiting are universal characteristics of women experiencing NVP, the cultural definitions are highly variable to the extent of defining symptoms or syndromes, and biobehavioural responses differ from one population to another (McElroy 1990). NVP has thought to have some adaptive merits throughout the course of evolution, though researchers are still not entirely certain of the benefits of this process. A further exploration of the adaptive significance of NVP is needed to understand its role in contemporary societies.

Introduction
Nausea and vomiting in early pregnancy (NVP) is a common condition that affects many women worldwide. NVP is also referred to as morning sickness, but this is a misnomer as symptoms are not exclusive to the morning, and the term “sickness” implies that the condition is pathological despite the relative good health of the expectant mothers and the frequency with which it occurs in pregnant women (Flaxman and Sherman 2000). NVP occurs in the first trimester of a pregnancy and is characterized by nausea, queasiness, food aversions, and sometimes food cravings with mild to severe vomiting (McElroy 1990). While the sensations of excessive salivation and nausea that may lead to vomiting are universal characteristics of women experiencing NVP, the cultural definitions are highly variable to the extent of defining symptoms or syndromes, and biobehavioural responses differ from one population to another (McElroy 1990).

Researchers have understood the proximate causes of NVP for quite some time but it is only in the past few decades that the ultimate evolutionary causes for this characteristic have been explored. There have been several hypotheses put forward on the evolutionary costs and benefits of NVP. The strengths and weaknesses of the prophylaxis and byproduct hypothesis will be the primary focus of this paper, with the placental development hypothesis discussed briefly. Through an examination of several studies of sample pregnant populations globally, it appears that under conditions with no physical, cultural, or
environmental stressors, women with NVP symptoms have a reproductive advantage over women who show no symptoms. An examination of available research studies on the evolutionary significance of NVP suggests that the prophylaxis and hypothesis is the most viable, as it has been thus far supported by several correlational studies.

Origins of the Prophylaxis Hypothesis

The majority of research on the adaptive significance of morning sickness focuses on the prophylaxis (or embryonic-maternal protection) hypothesis. It argues that nausea and vomiting during the first trimester are beneficial as they would allow pregnant women to expel and subsequently learn to avoid potentially harmful foods that could contain pathogens, teratogens, and abortifacents that could negatively impact embryonic development and mothers who are already immunocompromised (Flaxman and Sherman 2008). The hypothesis is based on the observation that the distinctive aromas and flavors of plants have evolved as a defense against biotic enemies; these traits, called phytochemicals, are secondary compounds that are not essential for plant functioning (Flaxman and Sherman 2000). Humans selectively use concentrations of these phytochemicals in spices and while harmless when ingested in small amounts, they can have deleterious effects if consumed in large doses, so it is thought that NVP functions to “shield the differentiating embryo from these potentially toxic chemicals” (Flaxman and Sherman 2000: 115). Often used substances like alcohol, caffeine, and tobacco that contain phytochemicals were examined for their potentially harmful effects and a list of common foods (primarily pungent vegetables) has been compiled as a guideline of foods that would contain potentially threatening chemicals to a fetus (Flaxman and Sherman 2000).

In order to properly test the prophylaxis hypothesis, there are six critical predictions to be examined: (1) NVP symptoms should peak at the time the embryo is most susceptible to toxic chemicals (between weeks 5 and 18), (2) foods that are found to be aversive by pregnant women should contain plant toxins and pathogenic microorganisms while foods that are craved should not contain these toxins, (3) food aversions should peak during the first trimester (during embryonic organogenesis) when the embryo is most sensitive, (4) NVP should be associated with positive pregnancy results, (5) NVP experiences are diet-dependent and should occur less in populations where women are not exposed to foods that would historically contain toxins, and (6) alleviating NVP symptoms should make the embryo more susceptible to exposure to harmful substances (Sherman and Flaxman 2008). Foods expected to be averted are those with bitter, pungent tastes, fried or burnt odours, and foods that smell spoiled, while foods that are more bland in smell and taste (such as cereals and grains) are predicted to be better tolerated (Flaxman and Sherman 2000).

Original models of the prophylaxis hypothesis suggest that NVP began to evolve during the Pleistocene, a time when women would be experimenting with toxic foods, and periods of scarcity would be adequate for selection pressures for pregnancy sickness (Holland and O’Brien 2003). However, it would seem that times of food scarcity would select against NVP symptoms, as maternal intakes of nutrients would already be restricted and the dietary stress of food scarcity would make women with
NVP “lose their reproductive edge over women not experiencing nausea if for no other reason than that they are less able to use (scarce) food resources” (Holland and O’Brien: 708). The evolution of cultural practices that would ease the stressors of a pregnant woman during the Neolithic Revolution beginning around 10,000 years ago would seem to be a better evolutionary context in which NVP symptoms would have been selected for: the increasing sedentism during this period resulted in population growth. The larger nuclear family units would have allowed pregnant women to reduce their daily activity levels while their children took on some of their workload; this allowed mothers to compensate for the symptoms of pronounced fatigue (Holland and O’Brien 2003). The subsistence shift to cereals and grains would have also been beneficial to pregnant women, as these foods would have been easily digested when experiencing nausea. In their cross-cultural analysis of NVP symptoms, Flaxman and Sherman (2000) found that women in populations that subsisted entirely on carbohydrate-rich plants (especially maize) were not observed to experience NVP.

It appears that the cultural and environmental changes experienced during the advent of agriculture “blunted selection’s heavy toll on women and the children they carried” (Holland and O’Brien 2003). However, Holland and O’Brien do not clearly explain what sort of “heavy toll” pre-agricultural women would have encountered during their pregnancies, and while the changes in diet and lifestyle during the Neolithic would allow for women to experience NVP symptoms in a more conducive environment, this anthropological argument does not mention ethnographic accounts of contemporary hunter-gatherer populations (as a way of comparing agricultural food stresses to foraging food stress). Rates of NVP in these populations would be important to examine when arguing for a specific time period in which NVP symptoms would have become adaptively significant. The Holland and O’Brien article does not recognize that periods of food scarcity would be much more severe in agricultural societies due to the high population densities and the increasing demands (2003). It is also assumed that the dietary conditions of NVP would have been a significant cost to hunter-gatherer women despite lower caloric demands being characteristic of the first trimester (Holland and O’Brien 2003).

**Testing the Prophylaxis Hypothesis**

Several studies have followed the initial examinations of embryonic and maternal protection carried out in the 1980s. A close look at the correlations between nausea and food aversions seems to be the strongest evidence supporting the hypothesis, but researchers have also looked at the relationships between NVP and olfactory responses as well as infant outcome (Swallow et al. 2005, Lee et al. 2004).

Brown et al. (1997) examined some of the predictions put forward earlier in the 1980s and tested whether women with nausea or NVP were more likely to avoid pungent and bitter vegetables than women without these symptoms, and how likely it was that women who did consume these foods experienced negative pregnancy outcomes (such as miscarriage, fetal death, or congenital defects at birth). The hypotheses were tested by using data previously recorded for the Diana Project (a sample of females working in a health maintenance organization in the Minneapolis region who were attempting to become
Factors that were assessed included health status, dietary intake, and other variables during the temporal span of preconception to 6-8 weeks postpartum (Brown et al. 1997). Food items identified as harmful included broccoli, brussels sprouts, cabbage, cauliflower, eggplant, kale, spinach, and some other bitter and pungent vegetables. Coffee, tea, and cola were also included in the harmful substances list. The study found that, of the 546 pregnancies, 452 were live-born infants with no congenital defects by 6-8 weeks postpartum, and 94 of the pregnancies resulted in miscarriages, fetal deaths, and congenital abnormalities (Brown et al. 1997). The article reports 79.4% (n=436) percent of the women in the study reported NVP symptoms in the first two months, but no significant differences in mean intake of all or each individual food substances were identified between women with and without NVP symptoms (Brown et al. 1997). Thus, the intake of proscribed foods failed to predict any increased risk of adverse pregnancies and it was suggested that, based on the results, intakes of the foods proscribed by initial studies were not hazardous for pregnant women to consume. The sample population used was restricted and consisted of healthy, middle-class white women, which would be ideal in examining the potential benefits of NVP symptoms and its relationship with successful pregnancies in an environment with few stressors, but this relationship was not at all examined. Instead, focus was on how harmful bitter and pungent vegetables were. Given the sample used, it is difficult to ascertain much because of regional specificity: many of the bitter vegetables in this study would not be commonly consumed by this population, especially since Western society depends on cereals and grains for a large proportion of their diet.

An analysis of cross-cultural variation in quantity of diet regarding NVP rates is crucial in understanding the significance (if any) in different populations. Pepper and Roberts (2006) analyzed associations between NVP prevalence in 21 countries and the quantitative estimates of intake of the major dietary categories using factor analysis based on data previously collected from the Food and Agricultural Organization (FAO). The study found a positive correlation between NVP rates and intake of all macronutrients (Pepper and Roberts 2006). Populations with a low cereal intake and a higher intake of sugars, stimulants, vegetables, meats, milk, and eggs were found to have significantly higher NVP rates (Pepper and Roberts 2006). Additionally, the significantly high meat intake in global and regional examinations correlates with high NVP rates which supports earlier predictions that food-borne pathogens are somehow avoided through pregnancy aversions (Pepper and Roberts 2006). The results from factor analysis are consistent with previous studies, but the researchers suggest that the correlations may be confounded by an unknown, non-dietary third compounding factor that correlates with both NVP and dietary patterns. The study is important in identifying quantifiable dietary trends globally and their associations with nausea and vomiting in early pregnancy, but it does not address anything beyond correlations (though this is helpful in building further support for the prophylaxis theory).

A study by Bayley et al. (2002) examined the temporal associations between first occurrence of NVP symptoms and the first occurrences of food aversions and food cravings. Ninety-nine women completed questionnaires about the occurrence, timing of first
onset, duration, strength, and targets of their symptoms based on 7-point scales and yes/no answers, and eighty percent of women experienced nausea, with 56% of those with nausea also experiencing vomiting (Bayley et al. 2002). While aversion rates did not differ with age, there was a positive correlation found between the week of onset of nausea and aversions. This research is broadly consistent with past studies and is strengthened in that it found no correlations between NVP and craving occurrences (though the study fails to account for the mechanism of acquisition of food aversions) (Bayley et al. 2002). Fifty-five percent of the aversions reported were found to be due to the exposure of coffee, tea, spicy/flavoured foods, and meat dishes (likely due to their strong odours); the prevalence of such aversions is suggested to be due to past evolutionary encounters with these food substances (Bayley et al. 2002). It is likely that current exposures to these foods differ substantially from when NVP adaptability was developing in human populations. Refrigeration has only become a widespread phenomenon in recent human history, and prior to this “meat [and] high protein dishes were likely to be heavily laden with microorganisms and their toxins” (Bayley et al. 2002: 50). The clear relationship identified between onset of nausea and onset of aversions in the study by Bayley et al. (2002) study is indicative of a correlation between the development of learned aversions to present NVP symptoms and food preferences, but does not indicate the mechanism.

Increased olfaction as a mechanism for adapting NVP symptoms is a possible explanation for such a development to aversions, as olfaction response would be invoked to provide protection to the mother and embryo (Swallow et al. 2005). The study by Swallow et al. (2005) looked at a sample British population consisting of pregnant women, non-pregnant women, and men whose sensitivity to stimuli was tested. The stimuli consisted of three “safe” odours (melon, vanilla, and strawberry) and three potentially hazardous odours (cabbage, coffee, and fish), which were rated on likeness, pleasantness, and strength (Swallow et al. 2005). Pregnant women were found not to differ in ratings between safe and harmful odours, so no evidence was found to suggest that pregnancy would change olfaction in any way.

However, in a subsequent study, olfaction was found to be an important stimulus relating to NVP symptoms in pregnant women (Swallow et al. 2005). Using questionnaires to determine aversions, it was determined that 57% of the sample reported aversive foods or smells, and of those, 65% stated that their olfactory systems were the mechanism responsible for making their NVP symptoms worse (Swallow et al. 2005). Only one percent of the sample distinctly reported aversive tastes. This study was important in noting the difference between olfactory-induced aversions with consumption-based aversions: “with earlier research, women may have indicated ‘meat’ for example, when they really meant ‘the odour of meat frying,’” which suggests the need for research to be more specific in how aversions are to be reported in questionnaires (Swallow et al. 2005: 548). The study also supports the consistent relationship between high levels of NVP when exposed to aversive stimuli and reduced intake of food (Swallow et al. 2005).

An interesting study by Korean researchers examined 143 pregnant Korean women in their first trimester to explore the effects of NVP on dietary diversity, nutritional intakes, maternal weight gain, and infant outcome (Lee et al. 2004). The women were
divided into four experimental groups based on the severity of their symptoms (none, mild, moderate, and severe) and demographics were ascertained with questionnaires while data was analyzed with SAS software (Lee et al. 2004). Foods from all five major food groups were consumed by 46.1% of the None group, who were also found to have higher dietary diversity scores, which led to the conclusion that diets of mothers without symptoms were more diverse than their NVP-experiencing counterparts (Lee et al. 2004). The women with severe NVP symptoms had only 6.7% of their group consuming all major food groups which would mean that the high rates of nausea and vomiting would force these women to eliminate most food from their diets, with less energy, micronutrients, and protein examined (Lee et al. 2004). Increasing severity of NVP was found to be correlated with decreasing maternal weight gain in the first trimester, and infants born to mothers with even mild NVP had significantly lower weights, heights, and chest circumferences (Lee et al. 2004). The authors recognize that their data was not consistent with two previous studies on birthweight and NVP correlations, and concluded that pregnant women experiencing NVP had poor dietary diversity and reduced energy intakes, which adversely affected infant outcome and maternal weight gain during the first trimester (Lee et al. 2004). This study argued that interventions are needed for pregnant women suffering from NVP to alleviate symptoms, which is one of few arguing that NVP is a more deleterious condition than beneficial for pregnancy outcome. This study is important due to its lack of consistency with previous studies: the adverse infant outcomes are interesting, and while it could be a reflection of overall socioeconomic status of the sample population, it could also indicate that studies within different regions of the world will reveal that the universal NVP symptoms are associated with differential pregnancy and infant outcomes.

**Byproduct Hypothesis**

The byproduct hypothesis takes a look at the genetic conflicts between mother and the developing embryo, and suggests that NVP symptoms are just a non-adaptive and slightly deleterious side effect of these conflicts (Flaxman and Sherman 2008). Direct results of these maternal-embryonic conflicts are conditions such as pre-eclampsia and gestational diabetes. The argument suggests that the mother and embryo do not have all their alleles in common (as half of the embryonic genes would be paternal) and so the evolutionary fitness of the mother and embryo will not likely be simultaneously maximized at the same level of investment for the pregnant mother; in most pregnancies, the embryo's fitness would be maximized at a level of fitness similar to the mother's (Haig 1993). The conflict of interest arises in the sharing of resources and possibly whether or not the pregnancy should continue (Flaxman and Sherman 2008).

The issue of who decides whether the pregnancy continues or not is examined by Forbes (2002). The important hormone involved in this process is human chorionic gonadotrophin (hCG), an allocrine hormone that is produced by one individual in order to manipulate the endocrine system of another individual (Forbes 2002). The hCG hormone stimulates the corpus luteum to produce progesterone and estradiol, crucial hormones for the continuation of a pregnancy (Forbes 2002). Human chorionic gonadotrophin levels have been suggested to be the proximate causes of NVP, but establishing a direct link between hCG and
NVP is difficult due to the variability of hCG hormone forms (Forbes 2002).

The endocrine control of gestation by the mother can be disrupted by the embryo. Forbes suggests a “mutation that causes an embryonic gene encoding luteinizing hormone (LH) production to be turned on, thus adding to the maternal supply” (2002: 115). If this mutation were to occur, embryos exposed to low maternal LH production would be able to survive, and since this is a substantial selective advantage for reproductive success, it is argued that the mutation would become quickly fixed and spread in a population (Forbes 2002). This mutation has been seen in some studies as a series of gene duplications and in response to the increased embryonic LH production, the mother retaliates until the conflict escalates to the point of being too much of an evolutionary cost for both parties and physiological manifestation of this evolutionary tug-of-war is seen when the mother experiences nausea and vomiting during this early stage in gestation (Forbes 2002). Positive pregnancy outcomes under this hypothesis are considered to be associated with NVP due to the ability of high-quality embryos to escape conflict (while simultaneously increasing NVP symptoms in the mother) (Flaxman and Sherman 2008). An examination of first trimester spontaneous abortions using karyotyping technology and ultrasounds revealed that 50-70% of these recognized spontaneous abortions are due to internal genetic defects and are unrelated to diet: “an absence of NVP during the first trimester does not cause low-quality embryos to be destined to be aborted... rather, low-quality embryos cause spontaneous abortion. Advocates of the embryo protection hypothesis have reversed the direction of causality” (Forbes 2002: 118). While the studies on proximate causes of spontaneous abortion are suggestive of some potential underlying genetic causation, Forbes’s argument is weak in that he himself manipulates his wording to change the potential causality. It is difficult to adhere to his argument when it is poorly structured, but it does provide an interesting alternative to the widely accepted prophylaxis hypothesis.

Predictions from the byproduct hypothesis state that the greatest embryonic-maternal conflict should be seen when the embryo is of lower quality than the threshold of quality needed by the mother to sustain a pregnancy while also above the embryo’s threshold of continuation. Thus, NVP should occur more frequently in pregnancies that are at a greater risk for miscarriage and women with mild NVP symptoms should be carrying the healthiest embryos (Flaxman and Sherman 2008). To measure direct fitness in the genetic conflict, reproductive value was used (the expected number of live offspring an individual will produce in the future) and statistical coefficients of relations were calculated (Flaxman and Sherman 2008). The model created by Flaxman and Sherman (2008) to test the predictions of the byproduct hypothesis found results contrary to what was expected: women with the most severe symptoms had the lower rates of spontaneous abortion and women with no expression of NVP carried pregnancies to term. The inability of the model to adhere to the predictions assumed by the byproduct hypothesis certainly makes it less credible, especially when compared to the amount of recent research testing different aspects of the prophylaxis hypothesis.
Placental Development

A final argument for the adaptive significance of NVP examines the association between NVP and placental development. Many studies have suggested a favourable association between nausea and vomiting in early pregnancy and birth outcome; it is suggested that in the placental development hypothesis that this association is mediated through reduced energy intake (Huxley 2000). The reduction of energy intake in early pregnancy has an impact on placental growth (and subsequently fetal growth).

Data from the Dutch Hunger Winter studies has shown that when maternal undernutrition was experienced during only the first trimester, infants were born within normal birth weight range and had an increased placental weight, suggesting compensatory placental growth during nutritional stress on the embryo (Huxley 2000). Some human epidemiological studies also support this as they suggest that increases in food intake during early gestation result in infants with lower placental and birth weights — specifically, women with higher carbohydrate intakes during early pregnancy had infants with lower birth and placental weights, independent of mother’s height and body mass.

As insulin growth factor-1 (IGF-1) and insulin are potent factors in fetal growth, IGF-2 regulates embryonic and placental growth during early gestational periods as IGF-2 appears to be less affected by deviations in nutritional and hormonal changes (Huxley 2000). The placental development hypothesis proposes that the forced reduction of nutrient intake through NVP lowers maternal levels of anabolic hormones (IGF-1 and insulin) to ensure the adequate placental growth.

The placental development theory seems interesting, but the lack of studies examining or supporting it make it difficult to credit at this stage. However, it is possible that ensuring adequate placental growth during the first trimester of pregnancy is part of why NVP is prevalent in many populations and could be found to be associated with cultural dietary responses. Further studies examining the relationship between placental development and nutritional intake/food aversions during early gestation could reveal significant associations to better explain this condition.

Conclusions

While dietary changes are culturally adaptive forms for treating NVP symptoms, the association between NVP and adaptation still remains unclear. However, the scientific literature strongly accepts the prophylaxis hypothesis in its ability to supports its six predictions during many tests, and the hypothesis is able to explain NVP’s association with reduced probability of miscarriage. The prophylaxis hypothesis also consistently shows an association between NVP symptoms and aversion to stimuli that would have been historically more likely to contain harmful toxins. Ultimately, it is difficult to ascertain any solid argument for why NVP is adaptive until the variability of NVP symptoms across regions is better understood; currently there is little data available to explain the marked differences in severity among populations when NVP seems like a condition that should be prevalent in all populations. A broader analysis of causal mechanisms concerning biological expression of nausea and vomiting in early pregnancy, beyond the correlations of diet and symptoms, would be important.
to explore all possible reasons for this evolutionary development.

References Cited


