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Morning Sickness: Adaptive Cause or Nonadaptive Consequence of Embryo Viability?

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ABSTRACT: “Morning sickness” is the common term for nausea and vomiting in early human pregnancy (NVP). Recent interest in why NVP occurs—that is, in the evolutionary costs and benefits of NVP—has spurred the development of two alternative hypotheses. The “prophylaxis,” or “maternal and embryonic protection,” hypothesis suggests that NVP serves a beneficial function by expelling foods that may contain harmful toxins and microorganisms and triggering aversions to such foods throughout pregnancy. The alternative “by-product” hypothesis suggests that NVP is a nonfunctional by-product of conflict—over resource allocation—between the pregnant woman and the embryo. The critical predictions of the prophylaxis hypothesis have been developed and tested, whereas the by-product hypothesis has not been subjected to similar scrutiny. To address this gap, we developed a graphical model and used it to derive predictions from the by-product hypothesis under two different assumptions, namely, that NVP is either (i) a by-product of current conflict between a pregnant woman and an embryo or (ii) a by-product of honest signals of viability produced by the embryo. Neither version of the by-product hypothesis is fully consistent with available data. By contrast, the timing of NVP, its variation among societies, and associated patterns of food cravings and aversions are consistent with the prophylaxis hypothesis.

Keywords: nausea and vomiting of pregnancy (NVP), morning sickness, parent-offspring conflict.

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Nausea and vomiting accompany the first trimester of two-thirds of human pregnancies. These symptoms of “morning sickness,” known in the medical literature as nausea and vomiting of pregnancy (NVP), can begin as early as 5 weeks after the last menstrual period (Sayle et al. 2002), generally peak 8–12 weeks following the last menstrual period, and decline thereafter, ceasing by the middle of the pregnancy (i.e., by 20 weeks after the last menstrual period; a small minority of women continue to experience symptoms in the second half of the pregnancy). Surprisingly, NVP apparently does not occur in other mammals (for a review of NVP-like symptoms in nonhumans, see Flaxman and Sherman 2000). Even more surprisingly, despite decades of medical research and the ubiquity of nausea and vomiting in human pregnancy, the physiology and fitness consequences of NVP remain poorly understood.

While the majority of research to date has focused on proximate mechanisms—that is, elucidating hormonal and psychological correlates of NVP—most recently a debate has surrounded the issue of whether or not NVP symptoms serve useful functions (Flaxman and Sherman 2000, 2002; Sherman and Flaxman 2001, 2002; Forbes 2002; Fessler et al. 2005).

At the heart of this debate are two opposing hypotheses. The “prophylaxis,” or “maternal and embryonic protection,” hypothesis (Hook 1974; Profet 1988; Flaxman and Sherman 2000; Fessler 2002) suggests that the physiological ability to express NVP is an adaptation that was favored by natural selection because nausea and vomiting cause pregnant women to expel and subsequently learn to avoid potentially harmful foods, such as meats and strong-tasting vegetables, that were historically likely to contain parasites, pathogens, and plant toxins. Increased protection from pathogens and plant toxins is necessary during pregnancy because of both (i) the adaptive immunosuppression of the woman (to avoid rejecting the partially unrelated embryo) and (ii) the high susceptibility of the conceptus to teratogens during early embryogenesis.

Alternatively, the “by-product” hypothesis (Forbes 2002) suggests that NVP is a nonadaptive and slightly deleterious side effect of mother-offspring conflict (Trivers

1974). This hypothesis proposes that NVP was not directly favored by selection but rather is an epiphenomenon of a coevolutionary “arms race.” The logic of this hypothesis is as follows. A woman can support a finite number of pregnancies in her lifetime, and successful pregnancy, childbirth, and child rearing require considerable parental investment. The pregnant woman and embryo do not have all their alleles in common (because one-half the embryo’s genes came from its father), and therefore, the evolutionary fitnesses of the mother and embryo will probably not be simultaneously maximized at the same level of investment by the pregnant woman in the current pregnancy (Haig 1993). In most pregnancies, the embryo’s fitness would be maximized at a level of investment above the pregnant woman’s fitness-maximizing level. In other words, there may be conflicts of interest over the division of resources or sometimes even over whether the pregnancy should continue. This conflict of interest would be manifested in a physiological tug-of-war (Moore and Haig 1991) within the pregnant woman’s body, and this could potentially produce visible side effects. Thus, NVP symptoms might be an unavoidable consequence of mother-offspring physiological conflict (Forbes 2002). It should be noted that “conflict” and “tug-of-war” between pregnant women and their embryos refer to long-term evolutionary fitness effects, not to any cognitive or psychological aggression. Although Forbes (2002) included potential hormonal mechanisms (e.g., the possibility that the conflict is mediated by human chorionic gonadotropin) in developing the by-product hypothesis, these mechanisms are not crucial to our attempt to determine whether NVP has any current utility. For a discussion and review of what is and is not known about the physiological mechanisms underlying NVP, see works by Flaxman and Sherman (2000, 2002), Goodwin (2000), and Furneaux et al. (2001).

The goal of this article is to compare and contrast the prophylaxis and by-product hypotheses by providing a rigorous derivation of predictions about the nature of mother-offspring conflict in human pregnancy in general and the by-product hypothesis in particular. Previous attempts to discriminate between these hypotheses have been hampered in two main ways. First, the two hypotheses share a central critical prediction, namely, that NVP should be associated with positive pregnancy outcomes. The prophylaxis hypothesis suggests that NVP is a cause of positive outcomes, whereas the by-product hypothesis suggests that positive outcomes are a side effect of the ability of high-quality embryos to escalate conflict (thus increasing NVP). Correlations between NVP and positive pregnancy outcomes, especially reduced miscarriage rates, have been observed multiple times (Weigel and Weigel 1989*b*; Czeizel

et al. 2006) and have been interpreted as supporting both the adaptive and the nonadaptive viewpoints.

Second, it has been difficult to derive unambiguous critical predictions from the by-product hypothesis. For example, Flaxman and Sherman (2000) predicted that under this hypothesis, mother-offspring conflict and NVP symptoms should be most pronounced later in pregnancy, when fetal demands on the woman are greatest, whereas Forbes (2002) predicted that the conflict would be greatest early in pregnancy, when the placenta (i.e., the resource pipeline to the embryo) is developing (under the control of the father’s genes; Haig 1993). Flaxman and Sherman (2000) also predicted that if NVP merely signals embryo viability, then it should occur in every viable pregnancy, whereas Forbes (2002) argued that Flaxman and Sherman’s prediction was too simplistic and broad. The difficulty in developing contrasting critical predictions stems largely from the coevolutionary nature of the by-product hypothesis. Making robust predictions of what happens when one individual’s best actions (best in terms of fitness) depend on another’s actions often requires the use of formal models, which have not been developed for and applied specifically to the by-product hypothesis.

Parent-offspring conflict is the subject of a large literature, both theoretical and empirical (Cant 2006). A number of game-theoretic models of parent-offspring conflict—and conflict between relatives in general—have been developed (e.g., Godfray 1995; Godfray and Johnstone 2000; Cant and Shen 2006), including models that can be applied to conflicts in pregnancy (Haig 1996; Úbeda and Haig 2003). However, existing models are too general to be used to derive specific predictions about the characteristics of symptoms of conflict in pregnancy. For example, in Úbeda and Haig’s (2003) model, the only parameters that determine maternal and embryonic fitness are (i) a hormone that impacts resource partitioning and (ii) the coefficients of relatedness among woman, embryo, and future offspring. To make testable predictions about the circumstances in which conflict should be most (or least) pronounced, models must incorporate parameters that (i) are expected to modulate conflict and (ii) can be easily measured by investigators. In order to derive such predictions, we developed a graphical model based on robust, general fitness expressions that incorporate maternal condition and embryo viability as parameters. Although we focus on the application of these predictions to NVP, our model can be applied to test any hypothesis suggesting that a particular physiological phenomenon (e.g., pre-eclampsia, gestational diabetes; Haig 1993) is a by-product of maternal-embryo conflict.

The by-product hypothesis is open to two alternative interpretations, depending on the assumption that is made about the precise nature of the conflict between pregnant

women and embryos. Following the arguments presented above, it could be assumed that the severity of NVP reflects the degree of maternal-embryo conflict at that time in the current pregnancy. Under this view, NVP is a by-product of short-term (immediate) mother-offspring conflict.

Alternatively, it could be assumed that NVP is not caused by conflicts in the current pregnancy but rather is an unavoidable by-product of honest signals that embryos have—over evolutionary time—been favored to produce to indicate their quality. In this scenario, embryos have been selected to produce strong signals in order to indicate their viability to the pregnant woman, who requires such indications as assurance that the pregnancy is a good investment (in terms of her fitness). We do not speculate about the precise physiological mechanism(s) that might provide such indications because, to date, physiological investigations have failed to uncover definitive triggers for NVP (Flaxman and Sherman 2000, 2002; Furneaux et al. 2001). However, for the hypothesis to be valid, we must assume that—whatever the mechanism—the signaling provided by the embryo brings NVP with it as an unavoidable consequence (a pleiotropic effect) that selection could not eliminate without eliminating the signal itself. We develop this version of the by-product hypothesis in greater detail below by drawing on the theory of honest signaling (Zahavi 1975; Grafen 1990). In contrast to the “immediate” nature of conflict assumed by the interpretation discussed above, this latter view of the by-product hypothesis assumes that historical (i.e., over evolutionary time) conflict has caused the coevolution of maternal demands for information and embryonic signals.

A Model of Current Conflict

The measure of direct fitness we use is reproductive value: the expected number of live offspring an individual will produce in the future. This provides a common fitness currency for both the pregnant woman and the embryo. For any individual, reproductive value increases monotonically from conception to birth (having an expected value of 2 at birth for individuals in a stable, sexually reproducing population) and continues to increase thereafter until it reaches a peak (for women, the peak is near 20 years of age), after which it declines monotonically, reaching a value of 0 when reproduction is no longer possible (for an example, see Fisher 1930, p. 28). A pregnant woman's reproductive value does not include the current embryo but does include all expected future births. Similarly, the embryo's reproductive value is the expected total number of live offspring it will produce in its lifetime.

We assume that the pregnant woman's reproductive value, V_p , is a function of her body condition, c_p , and the amount of resources, R , drawn from her body and invested

in the current embryo, which we write as $V_p(c_p, R)$. Smaller R can be thought of as a larger investment in self-maintenance and future pregnancies. The embryo's reproductive value is similarly defined as a function, $V_e(c_e, R)$, where c_e is a measure of embryonic viability. For notational simplicity, we frequently refer to these reproductive value functions simply as V_p or V_e , respectively. If we assume random mating in an outbred population, coefficients of relatedness between individuals are as follows. A pregnant woman is one-half related to her own future offspring and one-quarter related to the future offspring of the embryo. The embryo is one-half related to its own future offspring and related by an amount r ($0.25 \leq r \leq 0.5$) to its future siblings, where r can vary due to extrapair mating or mate switching by its mother. As such, the inclusive fitnesses of the pregnant woman, W_p , and the embryo, W_e , are, respectively,

$$W_p = 0.5V_p(c_p, R) + 0.25V_e(c_e, R), \quad (1a)$$

$$W_e = rV_p(c_p, R) + 0.5V_e(c_e, R). \quad (1b)$$

It should be noted that the coefficients of relatedness we use here differ from those in Úbeda and Haig's (2003) model because that model considered fitness differently, from the perspective of paternally and maternally inherited sets of alleles rather than from the perspective of individuals and the alleles that they will pass on to future offspring. Our relatedness coefficients in equations (1) reflect the fact that alleles (not individuals) are the units of heredity. For example, a woman's own reproductive value is devalued by one-half in her fitness expression because any particular allele has a probability of only 0.5 of actually being passed on to any particular offspring.

To put our model into more intuitive cost-benefit terms, we note that with increasing investment (R) in the current pregnancy, V_p will decrease, and V_e will increase. Let C represent the costs of investment in the current pregnancy. This cost can be measured as a loss of (or negative change in) reproductive value that results from investing limited resources in the current pregnancy. We thus let C be defined as a function, $C(V_p(c_p, R)) \equiv -V_p(c_p, R) + \varepsilon$, where ε takes the value necessary to make this cost function equal to 0 when $R = 0$ (i.e., $\varepsilon = V_p(c_p, 0)$). Thus, the embryo seeks to maximize

$$0.5V_e - rC, \quad (2a)$$

and its mother seeks to maximize

$$0.25V_e - 0.5C. \quad (2b)$$

Mother-offspring conflict arises because the embryo

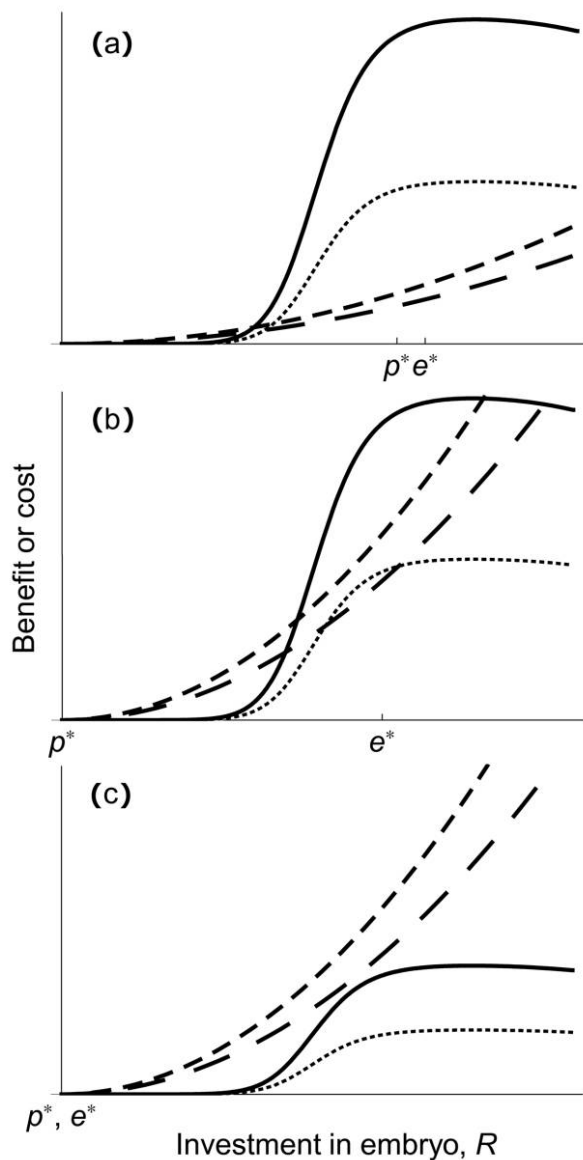


Figure 1: Graphical model of conflict between pregnant women and embryos. *Solid line* = benefits of investment to embryo ($=0.5V_e$); *dotted line* = benefits of investment to the pregnant woman ($=0.25V_e$). These benefit curves start tapering downward at very high levels of investment due to a decreased probability of survival of the pregnant woman (the embryo's vehicle), but this tapering has no effect on the predictions of the model. *Short-dashed line* = costs from pregnant woman's perspective ($=0.5C$); *long-dashed line* = costs from embryo's perspective ($=rC$). In each case, the pregnant woman favors the level of investment, p^* , which maximizes equation (2b) ($=$ dotted line minus short-dashed line), and the embryo favors the level of investment, e^* , which maximizes equation (2a) ($=$ solid line minus long-dashed line). *a*, The pregnant woman is healthy, and the embryo is of at least average quality. There is no conflict over survival and a small zone of conflict over the exact level of investment. *b*, The pregnant woman is in poor condition, or the embryo is of marginal quality. The pregnant woman favors zero investment in this embryo,

places both greater weight on the benefits ($0.5 > 0.25$) and smaller weight on the costs ($r \leq 0.5$) compared to the pregnant woman. The embryo will thus always favor a level of investment greater than or equal to that favored by its mother. If we draw benefit and cost curves for each entity as a function of investment, the embryo's benefit curve will always be twice the magnitude of the pregnant woman's benefit curve (because $0.5 = 2 \times 0.25$). The embryo's cost curve would be equal to its mother's cost curve if $r = 0.5$, and it would have one-half the magnitude of the pregnant woman's cost curve if $r = 0.25$. The real weighting by embryos would likely be an evolutionary average between these two values because embryos cannot assess their relatedness to future offspring that have not been conceived. We use $r = 0.375$ as a conservative value in our representation of the model, but our predictions are qualitatively unchanged by changes in r . Note that if $r = 0.5$ (i.e., a woman has the offspring of only one man), from equations (2) we see that the cost functions will be exactly the same for the pregnant woman and the embryo. However, the benefit functions will still differ for the pregnant woman and the embryo, leaving the stage set for conflict and for the three qualitatively different scenarios we consider below.

To make predictions about when conflict will occur in pregnancy, we assume that the benefits function, V_e , has a logistic shape, reflecting the fact that some minimum amount of investment is necessary to sustain a pregnancy but that increases in investment eventually lead to diminishing returns. We assume that the cost function, C , increases slowly but in an accelerating manner, because although moderate investment is probably not very costly, very high investment could divert resources away from the pregnant woman's critical physiological (maintenance) functions. We use these assumptions to construct a graphical model of costs and benefits (fig. 1), but our predictions from this model are robust to changes in the shapes of the curves. For example, with simple decelerating benefit curves or linear cost curves, we arrive at the same qualitative conclusions.

Predictions of the Current Conflict Model about Conflict in General

Our model (fig. 1) can be used to derive predictions about the degree of conflict in pregnancy based on the difference

whereas the embryo favors continuation of the pregnancy at a positive level of investment. *c*, If the embryo is of very poor quality, there is no conflict because both the pregnant woman and the embryo are in agreement that investment will be better spent on future offspring. (Note that the scale of the Y-axis is not assumed to be constant between the different panels.) See text for definitions of variables.

between the pregnant woman's and the embryo's optimal levels of investment. We denote these optimal levels as p^* and e^* , respectively. Three qualitatively different cases are possible.

Case 1: High c_e and high c_p . If the pregnant woman is healthy and her embryo is highly viable (fig. 1a), there is no conflict over the continuation of the pregnancy, but there is a narrow zone of conflict over the precise level of investment, reflected by the small distance between p^* and e^* .

Case 2: Mediocre c_e and/or low c_p . If the embryo is of marginal quality and/or the pregnant woman is in poor condition (few resources available), continuing the pregnancy would be costly. Either condition would lower the benefit curves relative to the cost curves. This could cause values of V_e and C such that equation (2a) would be positive for some value of R , whereas equation (2b) would never be positive (fig. 1b). In such a situation, there would be conflict over the continuation of the pregnancy itself, and the distance between the optimal levels of investment from each party's perspective would be maximized compared to other scenarios (fig. 1a, 1c). In other words, the degree of conflict, as measured by $e^* - p^*$ (fig. 1), is greatest in this scenario.

Case 3: Very low c_e . If the embryo is of very low viability, the favored value of R is 0 for both the pregnant woman and the embryo. There is no conflict because both parties favor termination of the pregnancy (fig. 1c) so that investment can be diverted into future pregnancies.

Predictions of the Current Conflict Model about NVP as a By-Product of Conflict

If NVP is a by-product of conflict between pregnant women and embryos and the degree of NVP correlates with the degree of conflict, then we can make three predictions: (1) NVP should not occur in pregnancies in which embryos are of very low viability (fig. 1c), (2) NVP should be most pronounced when embryos are of marginal quality and/or pregnant women are in poor condition (fig. 1b), and (3) mild NVP should occur in pregnancies in which the embryo is of high quality and the pregnant woman is healthy, due to conflict over resources (fig. 1a). Consistent with the first prediction, NVP usually is absent in pregnancies that terminate very early, and there is an inverse correlation between the degree of NVP experienced (within the normal range) and the probability of miscarriage among healthy, well-nourished women (Tierson et al. 1986; Weigel and Weigel 1989a). However, this inverse correlation contradicts predictions 2 and 3 because women with high levels of NVP should, on average, have higher miscarriage rates than women with mild NVP for the fol-

lowing reason. Conflict—and NVP—should be most intense when the embryo favors continuing the pregnancy (high investment) whereas the pregnant woman favors ending it (zero investment). This will occur when the embryo's quality is marginal, that is, below the pregnant woman's threshold for continuation of the pregnancy but above the embryo's threshold (fig. 1b). Graphically, this can be seen by noting that $e^* - p^*$ is maximized in figure 1b compared to figure 1a and 1c. This prediction is robust to a variety of biologically realistic assumptions about the shapes of the cost-benefit functions that generate it. Thus, if NVP indicated the degree of current conflict, (1) women with intense NVP should be those carrying embryos of borderline viability and should therefore be more likely to miscarry than women with mild NVP, and (2) women in borderline condition should experience NVP to a greater extent than women in good condition. However, available data (Tierson et al. 1986; Weigel and Weigel 1989b; Czeizel et al. 2006) indicate that, contrary to these predicted patterns, pregnancies that are accompanied by the highest (but still normal) levels of NVP are the most likely to involve viable embryos. Furthermore, studies looking for correlates of NVP have found no consistent relationships between various measures of maternal condition—such as weight, socioeconomic status, or body mass index—and the severity of NVP (Midwinter 1971; Palmer 1973; Järnfeldt-Samsioe et al. 1985; Klebanoff et al. 1985; Tierson et al. 1986; Weigel and Weigel 1989a; Rofé et al. 1993; Gadsby et al. 1997).

An Alternative Conflict Model: Historical Conflict and Embryo Signaling

The model represented in figure 1 was developed to address current conflicts over resource partitioning between an embryo and its mother. Suppose, however, that NVP is not a direct consequence of the current conflict but rather is an evolutionary by-product that has resulted from the repeated occurrence of such conflicts throughout human history. Consider the following argument. Over evolutionary time, the quantity and duration of investment per offspring by human parents has reached a level unparalleled in any other species. Therefore, natural selection would presumably have favored mechanisms that allowed women to assess the viability and quality of their embryos as early in pregnancy as possible. One way that a woman could avoid wasting a lifetime of effort and resources on a subviable embryo would be to require certain physiological signals during embryogenesis, for example, signals indicative of proper embryonic growth and organ system development. Receipt of such signals would indicate to the mother's body the likelihood that her embryo was of high

quality and therefore worth continued investment, whereas absence of such signals would indicate that further investment was unlikely to be beneficial. In turn, this would have triggered the coevolution of signals and detection mechanisms as follows. First, embryos would have been selected to strongly deliver signals of their quality. Next, pregnant women's bodies would have been selected to pay attention only to embryonic signals that were either (1) indicators—impossible to fake—of proper development or (2) indicators only high-quality embryos could afford to produce. In turn, this would have intensified selection pressure on embryos to produce such signals even more strongly, thus generating a coevolutionary cycle of increasing requirements by pregnant women and stronger signaling by embryos.

Based on this scenario, an alternative version of the by-product hypothesis can be put forth: physiological signals produced by embryos to honestly signal their quality bring NVP with them as an unfortunate but physiologically unavoidable consequence. In other words, NVP is an unselected pleiotropic by-product of an evolved honest communication system between two parties that (sometimes) have fitness conflicts of interest (for general theory about honest signaling in biological systems, see Zahavi 1975; Grafen 1990). This “signaling” hypothesis yields two critical predictions. First, the highest-quality embryos should trigger the strongest NVP symptoms because only the highest-quality embryos will deliver consistently strong physiological signals. The well-known relationship between NVP severity and positive pregnancy outcomes cited previously accords with this prediction. Second, the hypothesis predicts that NVP should accompany all viable pregnancies because the signals that cause NVP are required for continuation of the pregnancy. This second prediction is strongly contradicted by a variety of data sets from both industrialized and traditional societies (Flaxman and Sherman 2000). In brief, although NVP does accompany the majority of healthy pregnancies, pregnancies with no NVP are likely to continue to term (Flaxman and Sherman 2002). Moreover, there are a number of traditional societies in which NVP has never been recorded, although healthy children are routinely born (Flaxman and Sherman 2000).

It might be argued that our second prediction is too strict. However, consider the following. There are two possible ways to relax the second prediction: by supposing either that strong embryonic signals are not necessary or that pleiotropic effects of the signals are not necessary. If we were to relax the prediction by supposing that strong embryonic signals are not and were not essential for continuation of pregnancies, then selection would probably never have favored the evolution of a costly signaling system that also brought about costly side effects (for infor-

mation on the physiological, social, and economic costs of NVP, see Pike 2000; Coad et al. 2002; Quinlan and Hili 2003; Piwko et al. 2007). Simply put, if signals are required for a normal pregnancy, then necessary by-products of those signals must accompany normal pregnancies; however, if signals are not required, then there is no selection pressure for embryos to provide signals and hence no reason that nausea-inducing signals would ever have evolved and been maintained. The signaling hypothesis cannot be construed in both ways simultaneously. Alternatively, suppose we relax the prediction by eliminating the assumption that NVP is a necessary pleiotropic effect of strong embryonic signals; that is, suppose that NVP is not an unavoidable by-product of strong embryonic signals. If the latter is true, then the signaling hypothesis cannot predict or explain patterns of the occurrence of NVP because selection would be expected to eliminate any costly phenomenon that is not tightly linked with a positively selected trait.

Discussion

The model we developed provides testable predictions about the nature of parent-offspring conflict in human pregnancy. We focused on predictions made by considering two variables—maternal condition and embryo quality—that can be quantified in observational studies (often the only option for studying human pregnancy). When the intricate mechanisms of NVP and maternal-embryo signaling become better understood, it may be possible to examine resource investment and conflict as well, but for now, we must restrict our analyses to factors that are well understood.

Given assumptions that are consistent with what is presently known about the biology of pregnancy, our model makes straightforward predictions that are largely intuitive. Under the current conflict version of the by-product hypothesis, the greatest mother-offspring conflict is expected when embryonic quality is below the mother's threshold of quality necessary for continuation of the pregnancy but above the embryo's threshold for continuation. Mild conflict may occur in pregnancies in which embryos are of average or greater than average quality. Certainly no conflict is expected when an embryo is not viable. Accordingly, NVP—and any other physiological phenomenon that is a direct by-product of current conflict—should occur most frequently and severely in pregnancies that turn out to have an elevated probability of miscarriage relative to pregnancies in which NVP and other physiological by-products are expressed mildly. Additionally, women who experience mild NVP should be carrying the healthiest embryos.

A central aim of our modeling effort was to develop the latter predictions and apply them to the hypothesis that NVP is a by-product of current mother-offspring conflict. Contrary to these predictions, (i) women who experience the most severe symptoms (both nausea and vomiting) have lower rates of spontaneous abortion than women who have only mild nausea (Tiersen et al. 1986; Weigel and Weigel 1989a), and (ii) the majority of women that do not express NVP carry their pregnancies to term (Flaxman and Sherman 2002). The hypothesis that NVP is a by-product of current conflict between an embryo and the pregnant woman carrying it is not supported by these findings.

However, the alternative hypothesis that we outlined—the signaling hypothesis—is perhaps more consistent with the original intents of proponents of the idea that NVP is a by-product of conflict (Haig 1993; Forbes 2002). Under the signaling hypothesis, NVP is a by-product of (i) the need for pregnant women to obtain reliable information about the quality of their embryos in order to physiologically “decide” about the advisability of continuing to invest and (ii) physiological attempts by embryos to signal their “high quality” as strongly as possible so as to secure continued high levels of maternal investment. If strong signals from embryos were indeed required for pregnancies to be maintained, then NVP would accompany nearly every viable pregnancy. However, this does not occur.

Forbes (2002) argued that the latter prediction was too strict and overly simplistic because NVP has a multifactorial etiology. However, if we accept Forbes’s argument, then we must necessarily accept a weakened (in terms of explanatory power) form of the signaling hypothesis. This is because Forbes’s argument—that NVP is multifactorial—implicitly is an acknowledgement of the failure of the signaling hypothesis to explain large variations in frequency of NVP that exist among countries and cultures. Indeed, this weakened form of the signaling hypothesis supposes that embryonic signals merely set the physiological stage for manifestations of conflict such as NVP, but other triggers are required to make symptoms appear. We must then ask what the actual triggers are and whether NVP is triggered in useful, neutral, or deleterious ways for the pregnant woman, embryo, or both.

Neither the current conflict nor the evolutionary signaling version of the by-product hypothesis directly addresses questions about known sources of variation in NVP. First, why is NVP so variable among countries and cultures (Flaxman and Sherman 2000) when conflict between pregnant women and embryos should be prevalent everywhere? Second, why do some types of foods and food smells (especially meats, strong-tasting vegetables, alcoholic beverages, and cigarette smoke) reliably trigger NVP symptoms (Fessler et al. 2005)? Third, why are these types

of foods and food smells so consistent across different societies? Fourth, given that there is so much variation in NVP, why is it maintained in human populations? Finally, why is NVP apparently limited to humans when mother-offspring conflict should occur in all placental mammals? These questions do not suppose adaptive answers; they merely suppose that answers exist, and it is clear that a view of NVP exclusively as a symptom of conflict (current or historical) cannot provide the answers.

However, the maternal and embryonic protection hypothesis not only explains NVP’s association with reduced probability of miscarriage but also provides answers to the latter questions. The logic of the maternal and embryonic protection hypothesis, its critical predictions, and evidence for and against these predictions were explored in great depth by Flaxman and Sherman (2000). In that study, they synthesized data from the primary obstetrics literature and anthropological reports on traditional societies related to NVP. In response to the first four questions, the maternal and embryonic protection hypothesis predicts that NVP will be consistently associated with certain foods and their smells, and variation in NVP from one society to another is predicted if those societies differ in their diets. Specifically, the hypothesis predicts that foods that were historically most likely to contain harmful pathogens or toxins—meats and strong-tasting vegetables—should be most likely to trigger NVP. Societies consuming relatively high amounts of meats and strong-tasting vegetables should have the highest incidence of NVP; those in which bland plant products form the staples should have the lowest. Flaxman and Sherman (2000) documented such associations, and a recent independent meta-analysis of 56 studies confirmed that NVP is reliably predicted by low cereal consumption and high intake of meats, sugars, oil crops, and alcohol across 21 countries (Pepper and Roberts 2006).

With regard to the fifth question, why humans alone express NVP, we offer the following hypothesis. Humans have an extraordinarily broad diet compared to that of other mammals, including other primates. The breadth of the human diet is so great that evolving a comprehensive suite of enzymes to detoxify plant secondary compounds and to annihilate all species of food-borne bacteria and other parasites and deal with their toxins is probably prohibitively costly or physiologically impossible. Other mechanisms of protecting ourselves from food-borne dangers—such as nausea and vomiting and the learned avoidance behavior they produce—might be easier for natural and cultural selection to mold (Sherman and Flaxman 2001). In an earlier study, we concluded that available data were most consistent with the hypothesis that NVP protects women and embryos from harmful substances in food (Flaxman and Sherman 2000). This conclusion re-

mains valid today. Whereas no new evidence in support of either version of the by-product hypotheses has been published, additional information that supports the maternal and embryonic protection hypothesis has recently been presented (e.g., Czeizel et al. 2006; Pepper and Roberts 2006).

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