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Placentophagia in Humans and Nonhuman Mammals: Causes and Consequences

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Afterbirth ingestion by nonhuman mammalian mothers has a number of benefits: (1) increasing the interaction between the mother and infant; (2) potentiating pregnancy-mediated analgesia in the delivering mother; (3) potentiating maternal brain opioid circuits that facilitate the onset of caretaking behavior; and (4) suppressing postpartum pseudopregnancy. Childbirth is fraught with additional problems for which there are no practical nonhuman animal models: postpartum depression, failure to bond, hostility toward infants. Ingested afterbirth may contain components that ameliorate these problems, but the issue has not been tested empirically. The results of such studies, if positive, will be medically relevant. If negative, speculations and recommendations will persist, as it is not possible to prove the negative. A more challenging anthropological question is "why don't humans engage in placentophagia as a biological imperative?" Is it possible that there is more adaptive advantage in not doing so?

KEYWORDS   afterbirth, amniotic fluid, placenta, placentophagia, placentophagy, POEF

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Any discussion of benefits of placentophagia in humans must first address the broader issue of the causes and consequences of placentophagia in nonhuman mammals. Our work over the past 40 years has attempted to do just that (for review, see Kristal 1980, 1991, 2009).

Placentophagia, ingestion of any or all of the components of the afterbirth (the placenta, amniotic fluid, and associated membranes) is clearly a nearly ubiquitous behavior among mammalian peripartum females (Kristal 1980; Lehrman 1961; Young and Benyshek 2010). Notable exceptions are humans (apparently) and marine mammals that deliver in water. In the latter group, particularly cetaceans, a rather explosive expulsion of the placenta into sea water immediately dilutes the chemical constituents of the afterbirth, and the behavior of the mother focuses on keeping the young breathing at the surface of the water. Other exceptions have been noted (e.g., Lehrman 1961; Young and Benyshek 2010), but among these are domestic animals (e.g., camelids—widely cited as an exception [Lehrman 1961; Young and Benyshek 2010] but for which there is little empirical evidence) whose behaviors are sometimes suspect because of selective breeding or conditions of captivity.

Indeed, ingestion of placenta at delivery has been noted in rodents (e.g., Gregg and Wynne-Edwards 2005; Lehrman 1961; Rosenblatt and Lehrman 1963; Wiesner and Sheard 1933); lagomorphs (e.g., Melo and González-Mariscal 2003); ungulates (e.g., Brummer 1972; Kristal and Noonan 1979; Lehrman 1961; Lévy, Poindron, and Le Neindre 1983; Slijper 1960; Virga and Houpt 2001); carnivores (e.g., Lehrman 1961; Slijper 1960); and among nonhuman primates, in both monkeys and apes (e.g., Brandt and Mitchell 1971; Tinklepaugh and Hartman 1930, 1932; Stewart 1984; Turner et al. 2010), to name just a few taxa. Ingestion of amniotic fluid at delivery, although rarely mentioned specifically, is at least as widely represented as placenta ingestion because of self-licking of the urogenital area observed in parturitional females immediately prior to and during delivery, and because of licking and grooming of the neonate by the mother. Therefore, with the exceptions for placentophagia noted above, there are remarkably few species that do not ingest amniotic fluid or placenta at delivery, and those that do not are likely influenced by modification or stress (domestic or captive animals; Kristal 1980; Lehrman 1961; Menges 2007; Slijper 1960). Moreover, this ingestive behavior appears limited to parturition because nonparturient female mammals, except for carnivores, and particularly scavengers, do not readily eat afterbirth material (Kristal 1980).

CAUSES AND CONSEQUENCES

Although there have been many hypotheses as to the ultimate causes (benefits) and proximate causes of placentophagia, our research goal has been

to find the fewest causes that explain the behavior in the most species. Among the hypotheses that have existed in the literature over the decades were an attempt by the mother to (1) keep the nest area sanitary; (2) reduce the odors that might attract predators to the birth site; (3) replenish nutritional losses that occurred during late pregnancy or delivery; (4) acquire hormones present in the afterbirth; (5) respond to general hunger after not eating during labor and delivery; and (6) express a tendency, at parturition, toward temporary voracious carnivorousness (Kristal 1980; Lehrman 1961). These hypotheses had not been tested, but were offered by experts who saw the behavior through their own filters: nutritionists posited the "replenishment of nutrients" hypothesis, endocrinologists assumed that hormone acquisition or replacement was the key, and ethologists focused on the ultimate benefits of nest cleanliness and predator avoidance. Unfortunately, each hypothesis accounted for only a subgroup of mammals. For instance, primates that give birth in trees remain in place spending hours consuming the afterbirth, which is much more likely to attract predators than just dropping the placenta to the ground. Furthermore, afterbirth is ingested in non-nesting species, such as ungulates, that can walk away from the birth site within minutes of the birth. It might be possible that placentophagia evolved independently in various taxonomic groups to solve any of several unique survival problems, but this explanation is not parsimonious. It is far more likely that the one or two principal evolutionary or adaptive advantages to placentophages are fundamental and apply across many taxonomic groups, and that the other possibilities are secondary advantages to subgroups of mammals (Kristal 1980, 1991). This issue of proximate causality (immediate causal mechanism driving an individual's behavior) and ultimate causality (survival value) (Tinbergen 1963) also raises confusion; among the hypotheses listed above are both proximate and ultimate causes. Animals behave for a very basic set of proximate causes: the behavior directly leads to something that smells good, tastes good, or feels good, or the behavior was learned as a mechanism for obtaining something that smells good, tastes good, or feels good. Physiological processes modify this basic set of proximate causes by altering the valence of the stimuli under certain circumstances. For instance, a salt deficiency will alter taste preferences so that saltier substances become more palatable. A similar specific-hunger mechanism may indeed underlie the much greater attractiveness of afterbirth material to peripartum females than to nonpregnant females. In fact, mothers of carnivorous species and many omnivorous species that give birth to altricial young seem interested in ingesting everything expelled during delivery; the movement and sounds of the neonate usually prevent the mother from eating them too (Kristal 2009; Noirot 1972; Peters and Kristal 1983). Ultimate causes, on the other hand, drive natural selection, rely on the consequences of behavior, and may be directly or indirectly linked to the proximate causes. It is important that when invoking ultimate causality, however, we avoid the

implication that the animal is aware of the consequences of its act—that a mother will eat the placenta because she knows that not doing so might attract predators. This anthropomorphic interpretation of the behavior can be reorganized into a more appropriate assertion, which would be that the mother eats the afterbirth because it is attractive (perhaps because of a nutritional deficiency or physiological change) and that in doing so, unbeknownst to her but relevant to natural selection, she and her offspring might have a better chance of surviving because the lower level of afterbirth odor reduces the likelihood of predators in the area.

Some of the hypotheses can be rejected experimentally. Although drinking may be suppressed during the late prepartum period, rats (and giraffes) eat normally in the 24-hour period before delivery. General hunger, therefore, is not a principal proximate cause for placentophagia (Kristal and Wampler 1973; Kristal and Noonan 1979). Furthermore, although parturient females (e.g., rats and monkeys) are avid placentophages, they reject other meats at parturition. These findings provide evidence that all mammalian peripartum females are not simply temporarily voraciously carnivorous (for review, see Kristal 1980).

Consequences and Benefits to the Adult of Afterbirth Ingestion

ATTRACTION TO NEONATE

The first major benefit of placentophagia we discovered was related to pup contact. Specifically, the attractiveness of amniotic fluid and placenta would cause the adult, either the mother rat or a nonpregnant female placentophage (experimentally induced to be attracted to afterbirth material) to interact with afterbirth-covered foster pups sooner than they would with cleaned pups (Kristal, Whitney, and Peters 1981; Steuer at al. 1987). This is important because pup contact and exposure to pup-emitted stimuli facilitate the initiation of maternal caretaking behavior (Kristal 2009). The standard experimental paradigm used to examine maternal behavior in animals (usually rats or other rodents) is to co-house maternally naïve, nonpregnant females with a group of foster pups until the female shows reliable maternal behavior toward the pups—a procedure referred to as concaveation (literally, "with pups"). The pups are swapped with freshly nourished pups about every 12 hours so that the adult gets constant exposure to a group of pups with consistent characteristics (e.g., age). Therefore, changes in the behavior of the adult cannot be attributed to developmental changes in the young. Under these circumstances, maternally naïve, nonpregnant adults become enthusiastically maternal (i.e., retrieve pups to a central nest site within minutes of presentation, then immediately lick and clean the pups, and crouch over the pups allowing them to attach to her nipples, despite the fact that lactation is not occurring in nonparturient subjects). Under these conditions, maternal caretaking behavior in rats develops in several days to a week,

depending on sex and strain (Del Cerro et al. 1991; Kristal 2009; Rosenblatt 1967; Stern 1989). This slow onset represents the base rate of sensitization or turning on of the maternal neural circuitry by the stimuli emanating from the pups (i.e., smells, thermal signals, tactile signals, sounds). The base rate of sensitization is obviously too slow to be effective in nature; the young would die before the adult became maternally active. However a set of parallel and redundant mechanisms is activated during pregnancy and the periparturitional period to affect the system in a way that greatly facilitates the sensitization process, reducing the latency to begin mothering the young from days to minutes. Among these mechanisms are (1) the effects on the brain of the rise in estrogen, accompanied by the drop in progesterone, at the end of pregnancy; (2) the effect on the brain of incoming mechanical simulation from the uterus and cervix during delivery; (3) oxytocin release directly into the hypothalamus; (4) endogenous opioid release in specific parts of the brain; and (5) the attractiveness of afterbirth materials on the surface of the young (for review, see Kristal 2009, and see figure 1).

During the several days it takes for a naïve adult rat to become maternal, the first few days are spent avoiding the pups, the next few days are spent in apparent indifference to the pups, and the final few days are spent showing some interest in the pups (Fleming and Rosenblatt 1974; Fleming, Vaccarino, and Luebke 1980). The effect of afterbirth on the skin of pups that are presented to placentophagic adults is that it forces close contact between the adults and the pups when the adult licks and eats the afterbirth. This proximity to the pups helps eliminate the avoidance phase seen in the first few days, and the result is a significant shortening of the latency to the onset of maternal behavior (Kristal, Whitney, and Peters 1981; Lévy et al. 1983; Steuer et al. 1987). Other procedures that bring the adult and the pups into close proximity also shorten the onset to maternal behavior (cookie mash on the pups [Kristal, Whitney, and Peters 1981]; concaveation in small cages [Terkel and Rosenblatt 1971]), but not to the extent seen with afterbirth on the pups.

NEUROCHEMICAL INCREASE OF PAIN THRESHOLD

We were not satisfied that the attractiveness of the afterbirth materials on the young was the principal and ubiquitous benefit of parturitional placentophagia. Although the presence of afterbirth on the skin of the young was effective, it was probably not necessary to ensure rapid and appropriate parturitional events. The elimination of pup-licking by the mother by cesarean-section delivery does not significantly retard the onset of normal maternal behavior when the cleaned pups are returned (Moltz, Robbins, and Parks 1966).

In the mid-1980s, research on endogenous opioids seemed to capture the attention of nearly every behavioral neuroscientist. Most important for

FIGURE 1 Diagrammatic representation of processes leading up to parturitional events in most mammals. Heavier lines represent more important pathways. Note the influence of placentophagia (lower right) in the modification of maternal behavior directly (attractiveness of afterbirth on the pups), and indirectly (by modifying brain opioids) as well as effects on endogenous-opioid-mediated pain relief at delivery (hypoalgesia). This figure is modified from one that appeared in the *ILAR Journal* 50(1), Institute for Laboratory Animal Research, National Research Council, Washington, DC (www.ilarjournal.com; Kristal 2009).

our work was the finding that labor and delivery were accompanied by a rise in endogenous opioids (Facchinetti et al. 1982; Goland et al. 1981; Wardlaw and Frantz 1983) and a concomitant increase in pain threshold of the mother (Baron and Gintzler 1984, 1987; Dawson-Basoa and Gintzler 1996, 1997; Gintzler 1980; Gintzler, Peters, and Komisaruk 1983). However, it seemed to us that the level of "pregnancy-induced analgesia" was too great to be accounted for by the modest amount of endogenous opioid released. We found that rats experiencing a modest amount of opioid-mediated elevation of pain threshold, hypoalgesia (a more appropriate term than analgesia, because pain is reduced but not completely eliminated), had their pain thresholds greatly increased by the ingestion of placenta (Kristal, Thompson, and Grishkat 1985). Rats that ate beef as a meat control, did not show enhanced opioid-mediated hypoalgesia. Of critical importance was the finding that ingestion of afterbirth, alone, did not produce a change in pain threshold. This basic finding led to a long series of studies designed to elucidate the mechanism for this opioid enhancement by afterbirth ingestion. In 1988, we named the putative active substance (for effects on pain threshold) POEF, for Placental Opioid-Enhancing Factor (Kristal, Abbott, and Thompson 1988).

Among the more relevant findings regarding the POEF effect are that amniotic fluid ingestion, as well as placenta ingestion, enhances morphine-mediated pain relief (Kristal, Thompson, and Abbott 1986). The significance of this finding is that it indicates that mothers can obtain the opioid-enhancing benefit *before* the emergence of the first fetus, or the only fetus (when amniotic fluid becomes available to the mother) rather than after the fetus, when the placenta emerges. The effect of afterbirth ingestion is not specific to exogenous opioids (i.e., morphine), but also enhances the hypoalgesic effects of endogenous opioids. We have shown that ingestion of either amniotic fluid or placenta enhances the partially opioid-mediated hypoalgesia produced by electric shock applied to the hind-paw (Kristal, Thompson, and Grishkat 1985), produced by mechanical vaginal/cervical stimulation (Hoey et al. 2011; Kristal, Thompson, Heller, et al. 1986; Thompson et al. 1991), and that which arises during late pregnancy (Kristal et al. 1990). The latter two findings are particularly relevant to the current discussion; the initiation mechanism for endogenous-opioid-mediated hypoalgesia of late pregnancy and delivery is mediated in large part by mechanical stimulation of the cervix by the delivering fetus. The demonstration that ingestion of donor amniotic fluid immediately before the onset of labor does indeed elevate pregnancy-mediated analgesia, therefore, directly supported our hypothesis that POEF potentiates the endogenous-opioid-mediated analgesia of pregnancy, which begins at the very end of pregnancy and lasts through delivery.

One series of studies investigated the doses, or volumes, or time course of afterbirth ingestion that are necessary for enhancement of the hypoalgesic effects of 3–3.5 mg/kg morphine sulfate (which produces a level of

hypoalgesia roughly equivalent to that existing at the beginning of delivery in a rat, i.e., "pregnancy mediated analgesia") . We found that the optimum amount of ingested amniotic fluid is 0.25 ml and the optimum number of placentas ingested is 1 (≈ 500 mg), both of which correspond to the amounts ingested during the delivery of one pup (Kristal et al. 1988), and that the time course of the POEF effect is observable well within 5 minutes after oro-gastric administration of the fluid and lasts 30–40 minutes (Doerr and Kristal 1989). The duration of the effect is sufficient to cover the interpup interval during rat delivery (Dollinger, Holloway, and Denenberg 1980).

We have also shown that the POEF effect is (a) not specific to a particular pain-threshold testing paradigm, which supports the construct validity of the effect; (b) specific to opioid-mediated hypoalgesia; and (c) generalizable to males and other species. The effect of afterbirth ingestion on hypoalgesia has been demonstrated, in rats, using four different algesiometric tests (DiPirro and Kristal 2004; Kristal, Tarapacki, and Barton 1990; Kristal et al. 1990; Kristal et al. 1985), so the effect is not a testing artifact. To determine the specificity of the POEF effect to opioid-mediated hypoalgesia, amniotic fluid ingestion was shown not to enhance hypoalgesia produced by the two major nonopioid analgesics aspirin (Kristal et al. 1990) and nicotine (Robinson-Vanderwerf et al. 1997) in opioid-receptor-blocked rats. The POEF effect seems to be a ubiquitous mammalian phenomenon, whether or not the individuals or species utilize it. Male rats can respond to the opiate-enhancing effects of afterbirth ingestion (elevated opioid-mediated pain threshold), even though they obviously (or probably) do not manufacture POEF. This indicates that the mechanism for responding to POEF is not sex specific (Abbott et al. 1991), even if it is not activated in males, like mammary glands and nipples. It is interesting to note that Wynne-Edwards has identified a species of hamster (*P. campbelli*) in which males seem to aid in the birth process to the extent of ingesting afterbirth material (Gregg and Wynne-Edwards 2005). Whether these males experience a POEF effect is not yet known. Furthermore, human, dolphin, and bovine afterbirth material show POEF activity when tested in rats, even though humans and dolphins do not ingest afterbirth (Abbott et al. 1991; Corpening, Doerr, and Kristal 2000), and bovine amniotic fluid enhances morphine-mediated analgesia in cows (Pinheiro-Machado, Hurnik, and Burton 1997). Therefore POEF probably is a ubiquitous mammalian substance with a molecular specificity that has been conserved evolutionarily.

It is also important to note that ingestion of the liver of pregnant rats does not enhance opioid-mediated hypoalgesia when tested in rats (Abbott et al. 1991), suggesting that POEF is not a substance that exists in all tissues. Furthermore, because ingestion of afterbirth in the absence of opioid-mediated hypoalgesia does not elevate pain threshold, the POEF effect is not due to the hypoalgesic action of the opioid content of amniotic fluid and placenta, or due to the triggering of a release of additional opioids in the eater (Kristal 1991; Kristal et al. 1985). The most likely explanation for

the effect of POEF is that amniotic fluid and placenta contain a substance(s) that acts to facilitate opioid activity, rendering more potent the opioids in the eater's system.

Opioids work both within and outside of the central nervous system, and on a variety of opioid receptors. Therefore it was necessary to determine whether POEF was having its effect on opioids in the central nervous system or in the periphery and whether there was opioid receptor specificity involved in the phenomenon. We found that the effect of afterbirth ingestion on morphine hypoalgesia depends on enhancement of the central nervous system actions rather than the peripheral nervous system actions of morphine (DiPirro, Thompson, and Kristal 1991). Furthermore, in the central nervous system, POEF enhances the effect of δ- and κ-opioid-receptor-mediated hypoalgesia and attenuates the action of μ-opioid-receptor-mediated hypoalgesia (μ-receptor activity is also responsible for many of the negative side effects of opiates; DiPirro and Kristal 2004).

An additional series of studies aimed at determining where and how POEF works showed that enhancement by POEF seems to require ingestion of afterbirth materials; subcutaneous or intraperitoneal injection does not work (Abbott et al. 1991). Follow-up studies have shown that an intact gastric vagus nerve is necessary for the effect (Tarapacki, Thompson, and Kristal 1992), and that suppression of digestion with famotidine, which blocks gastric acid and pepsin secretion, is insufficient to block the enhancing effect of ingested afterbirth material (Robinson, Abbott, and Kristal 1995). These findings indicate that the action of POEF is via gastric vagal receptors; that POEF, itself, does not need to reach the central nervous system to be effective on opioid systems within the central nervous system; and that POEF is apparently not manufactured by the digestive process.

Afterbirth ingestion also facilitates postpartum estrus, during which most pregnancies occur in mammals, by reducing the likelihood that intense vaginal/cervical stimulation, such as that occurring at delivery, will produce pseudopregnancy (Thompson et al. 1991). Pseudopregnancy prevents both the postpartum ovulation and behavioral estrus, and thereby reduces the possibilities for fertilization.

The amount of morphine necessary to produce a significant elevation of pain threshold, greater than that seen in pregnancy-mediated analgesia, in a parturient rat disrupts the execution of maternal behavior (Bridges and Grimm 1982; Grimm and Bridges 1983; Rubin and Bridges 1984). However, a lower level of morphine, in conjunction with ingestion of afterbirth material produces the same level of pain relief as the larger dose of morphine, but without a deleterious effect on the execution of maternal behavior (Tarapacki, Piech, and Kristal 1995). It would seem then that afterbirth ingestion produces a greater opioid effect from less opioid and that this enhancement is selective for some effects of opioids, but not others. The effect of POEF on parturitional pain threshold seems to be based on an

elegantly orchestrated system of behavioral and biochemical events, exquisitely timed, that serves to counter the pain of delivery, partially, without increasing μ-opioid activity to a level that might compromise the mother's health (i.e., producing negative side effects) or her ability to care for the young (i.e., reducing maternal caretaking behavior). This finding in 1995 suggested to us that the adaptive significance of placentophagia may extend beyond pain suppression

NEUROCHEMICAL ENHANCEMENT OF MATERNAL BEHAVIOR

In 1996, we showed that opioid activity in the ventral tegmental area, a structure involved in reward and motivation and that is part of the "maternal neural substrate" (Numan 1994), affected the rate of onset of maternal behavior during concaveation. By microinjecting morphine (a relatively non-specific opiate) into this area we significantly speeded up the rate at which naïve, nonpregnant rats show maternal behavior toward foster pups (Thompson and Kristal 1996). Furthermore, if we blocked endogenous opioid activity in that area pharmacologically, in mothers that had just given birth but that had not yet started engaging in maternal behavior, we significantly delayed the onset of maternal behavior (Thompson and Kristal 1996).

Based on these results, we reasoned that this opioid mechanism for modifying maternal behavior might be affected by afterbirth ingestion, just as is the opioid mechanism for modifying parturitional pain threshold. To test this, we repeated the basic study that showed that a microinjection of morphine into the ventral tegmental area speeded up the rate at which naïve, nonpregnant rats would show maternal behavior toward foster pups, and we added amniotic fluid (or a saline control) ingestion as a variable (Neumann et al. 2009). The results were clear: ingestion of amniotic fluid potentiated the facilitative effect of morphine injection on the latency to show maternal behavior toward foster pups. More precisely, a 0.03 μg morphine microinjection into the ventral tegmental area, alone or in conjunction with an orogastric saline infusion significantly reduced the latency for the adult to mother the foster young. A 0.01 μg morphine microinjection, alone or in conjunction with an orogastric saline infusion did not. However, a 0.01 μg morphine microinjection, in conjunction with a 0.25 ml orogastric infusion of amniotic fluid reduced the onset latency as much as the 0.03 μg microinjection. Therefore, as we observed numerous times in the studies on pain threshold, afterbirth ingestion potentiates the effects of opioids in a way that renders an ineffectively low dose effective (more opioid effect with less opioid).

This line of research is ongoing. We are attempting to determine whether the specific opioid receptor types influenced in the ventral tegmental area by amniotic fluid ingestion to affect maternal behavior are the same

as those influenced by amniotic fluid ingestion in the modification of pain threshold (e.g., an enhancement of δ-opioid activity and an attenuation of μ-opioid activity). We are also examining the possibility that the output of these ventral tegmental opioid changes is the modification of dopamine in mesolimbic area, a connection that would show the link between opioid events in the ventral tegmental area and the dopamine influence on reward and motivation.

PLACENTOPHAGIA IN HUMANS

The Questionable Phenomenon of Human Placentophagia

We should begin with the premise that someone in the past, present, or future, has done, is doing, or will do, anything conceivable to the human mind. Given that premise, it is necessary to separate the rules from the exceptions. As a species, modern *Homo sapiens* does not routinely practice placentophagia (Kristal 1980; Young and Benyshek 2010). Whether it is done in some remote cultures, or was done in the past by various cultures, has yet to be determined. In 1980, an extensive anthropological literature search did not turn up any instances of routine placentophagia in documented cultures (Kristal 1980). This finding was confirmed in a much more elaborate and systematic study published in 2010 (Young and Benyshek 2010). However, we must bear in mind, that, as William Cowper is said to have observed in the 18th century: "absence of proof is not proof of absence." The 1980 search revealed that there were many cultures with taboos against placentophagia that seemed to express the attitude that "animals do that, we are not animals, therefore we should not do that," and that placentophagia was essentially a form of cannibalism. Taboos are generally formed against likely behaviors or those that are recognized as possible; not against behaviors that are exceedingly unlikely (e.g., a taboo against eating rocks is unnecessary). There were also many cultures in which there was symbolic ingestion: the afterbirth would be buried at the roots of a tree or bush, and in the next season, a ceremony would occur in which the fruit of the tree or bush was eaten or tea was brewed from the leaves. In several cases, a piece of umbilicus or placenta was saved as a talisman or for medicinal purposes (e.g., *Zi He Che* in Chinese herbal medicine). Clearly, placentophagia can occur, as does cannibalism, in dire circumstances where death by starvation is imminent. This may be the basis for the biblical passage in Deuteronomy 28 (verses 53–57), cited by Ober (1979), that predicts cannibalism and placentophagia in besieged Israelite cities.

Among the problems that confronted early anthropologists, and that may have influenced the data gathered on birth practices, were modesty (on the part of either the culture members or the anthropologists); secretiveness (on the part of the culture members); culture members telling

the anthropologists what they thought the anthropologists wanted to hear (Freeman 1983); and the casting of aspersions (e.g., one tribe saying that they do not engage in the taboo behavior, but they know a nearby enemy tribe that does—often used with cannibalism). It is interesting to note that the fate of amniotic fluid, a colorless, innocuous liquid, is never mentioned. Our research has shown that amniotic fluid ingestion is probably as important for the effects we study (Kristal 1991) as is placenta ingestion, because amniotic fluid is available before the infant is expelled, and placenta only afterward.

Modern Western media and literature are rife with exceptions to the general human "no placentophagia" rule (for a review, see Menges 2007; Young and Benyshek 2010). These exceptions are all anecdotal, and many are not first- or even second-hand observations (possible urban legends). The reasons given by placentophagic individuals and groups are usually based on beliefs in (1) putative general health benefits, (2) putative specific medical benefits, and (3) the philosophical advantages of "naturalness" ("animals do that, we are animals, therefore we should do that"). Reports from the 1970s of members of communes cooking up a human placenta stew for all to share were not uncommon (check the key words "placenta recipe" on a Web search engine), despite the fact that cooking almost certainly destroys any unique and specific, potentially beneficial, peptide components; for instance, POEF is inactivated by temperatures above 40 °C. One of the few systematic studies on human medical benefits of ingested placenta was conducted in Czechoslovakia in the 1950s. In an attempt to improve lactation in postpartum women, freeze-dried placenta or beef was fed to women experiencing lactational difficulty and the response was noted (although not stringently quantified). The authors reported that more than a third of the placenta-fed women showed a "strong reaction" whereas none of the beef-fed women did (Kristal 1980; Soyková-Pachnerová et al. 1954). By today's scientific standards, we cannot draw meaningful conclusions from that study, even if there is a real effect.

What Have We Learned about the Scientific Study of the Benefits of Afterbirth Ingestion?

There are many impediments to determining whether placentophagia, or administered afterbirth components, have a beneficial effect on maternal health or behavior, especially in humans. From an experimentalist's point of view, the question of health benefits can be best answered by using an animal model. An animal model provides a degree of control by the experimenter that eliminates confounding variables, including the placebo effect (which, if only believers are used as participants, may elevate the results of the control group thereby masking differences between control and experimental groups), and allows for more, often more valid, operational

definitions because they are unencumbered by regulations that apply to human participants. However, there is no adequate animal model for human postpartum pathology. If the critical test is one of the beneficial effects of ingested afterbirth, none of the animal models currently being developed fit the pattern (e.g., Craft et al. 2010; Stoffel and Craft 2004). An appropriate model requires a group of animals (e.g., rats) that do not ingest afterbirth and preventing this ingestion is, for all practical purposes, impossible. Attraction to placenta is so strong in parturitional rats that it is easier to remove the pups at delivery than the placentas. Blocking ingestion of amniotic fluid is even more difficult, involving techniques that would compromise parturition, itself, or produce an inordinate amount of acute stress in the mother (Kristal 1991). (Washing pups or lambs before presentation, a technique that has been used in numerous studies, does not eliminate the possibility of a biochemical effect due to ingestion of amniotic fluid during labor and delivery, and does not necessarily remove an attractant to render the neonate a neutral stimulus; a washed pup or lamb may actually be aversive, thereby reducing the likelihood of immediate maternal behavior. There is no real control for this possibility.) Add to these complications the need for modifying the physiology or neurophysiology of the mother in order to produce the desired postpartum problem or disorder, which often has no naturally occurring counterpart in laboratory animals, and the model strays even farther from normal. The usefulness of animal models is therefore limited to those investigations in which the dependent variable does not require a preceding parturition during which placentophagia is totally absent.

The animal-research based evidence, gathered to date, about the beneficial effects of placentophagia show that any beneficial effects will be greatly influenced by preparation of the afterbirth, time of administration relative to parturition and the measurement of the effect, and amount of exposure (e.g., volume, weight or dose of afterbirth). For example, in regard to POEF, we have shown that the beneficial effects of afterbirth ingestion wane if the afterbirth material is left for 24 hours at room temperature, but can be preserved for months by immediate freezing at -20 °C. Frozen afterbirth must then be heated to 35 °C to 40 °C, but no higher, to be effective (unpublished observations). The acute effects of afterbirth ingestion on opioid enhancement, in rats, are apparent well within 5 minutes of ingestion and last approximately 40 minutes (Doerr and Kristal 1989) thereby covering the interval between pup deliveries. In addition, as it relates to opioid-enhancing effects on pain sensitivity, more afterbirth is not necessarily better: in rats, a small amount—that consistent with the birth of a single pup—enhances analgesia; larger amounts ingested at one time are not effective or are possibly inhibitory (Kristal, Abbott, and Thompson 1988; Kristal, Thompson, and Grishkat 1985). It is important to note that we can estimate the appropriate parameters for these variables by analysis (observation) of the natural behavior (placentophagia at parturition), but there is no comparable source

(natural behavior) to use to identify the appropriate parameters in humans and an extrapolation from nonhuman animals to humans will be challenging at best.

Isolation of beneficial substances from placenta and amniotic fluid is likely a daunting task. For instance, the beneficial substances in afterbirth are likely to be peptides or steroids, working either alone or in combination. Amniotic fluid is known to contain, as of 2006, at least 240 known, probably placenta derived, molecules, with molecular weights that range from 88 to 940,000 Daltons (Wood 2006). The overwhelming majority of these molecules are peptides, with some steroids, indoleamines, and catecholamines thrown into the mix. Tolerating the gastric environment is critical and we have shown that gastric vagal receptors are involved, so, if POEF is a peptide, it appears that it can work before being denatured.

Without an appropriate animal model, the likely outcome for placentophagia research conducted in humans will be a spate of negative findings until, by trial and error, appropriate parameters are found. Because there is no natural behavior (placentophagia) to compare in humans there is no strategy with which to differentiate negative findings from null results. Therefore, the process becomes one of finding a needle in haystack. This strategy is even more challenging in those instances in which the human construct in need of investigation (e.g., postpartum depression or a lack of generalized feelings of well-being) is not operationally well defined, adding another layer of ambiguity to the variations in the dependent measures. The benefits may still outweigh the cost of the search, but then there is a possibility that the absence of placentophagia in humans is in fact, an avoidance of placentophagia. Placentophagia, particularly if the afterbirth materials are raw, may have negative biological effects for some humans. Therefore subjecting participants to placentophagia may incur harm and yield few meaningful data.

A systematic strategy for proceeding, which would take placentophagia out of the realm of unsubstantiated remedies like megavitamin therapy and laetrile might be to (1) define and analyze the underlying mechanisms that mediate the target postpartum phenomenon (e.g., postpartum depression, lactational insufficiency); (2) characterize the components of placenta and amniotic fluid that could affect these mechanisms in a simplified model that does not required induction by parturition; and (3) in humans, determine if these components affect the underlying mechanisms identified in (1).

CONCLUSIONS: WHY ISN'T PLACENTOPHAGIA COMMON AMONG HUMANS?

The complementary question to "Why do mammals eat placenta at parturition?" is "Why *don't* humans eat placenta at parturition?" Strictly speaking,

if placentophagia is not a biologically determined behavior in humans, we should assume that there must be a good adaptive reason for its elimination.

Evolutionarily, *Homo sapiens,* as a species, has very few advantages other than an extraordinary brain and a complex, tightly knit social structure that enables humans to participate in group activities and facilitates the transmission or collection of shared information. Morris has emphasized the importance of solidifying social bonds, in *The Naked Ape*, as an explanation of the prevalence of (and necessity for) nonprocreative sex in humans (Morris 1967). The same may be true for placentophagia. If a principal benefit of placentophagia, to humans, were the enhancement of opioid-mediated pain relief at delivery, then perhaps the absence of such an enhancement, and consequently a higher level of pain, is adaptive. A level of pain that is tempered by endogenous opioids, but that is not further reduced by opioid enhancers in ingested afterbirth, might necessitate greater help by others during delivery. Participation by others, particularly women, would have a significant effect on the strengthening of social bonds in the group; would facilitate the transmission of birth information from older, experienced women to younger, inexperienced women; and would facilitate care and survival of the neonate and the mother. In this way, we might view the suppression of placentophagia in humans as being more adaptive than the practice. An additional source of evolutionary pressure for the socialization of delivery is increased difficulty of birth resulting from the change in birthing position of the young necessitated by the emergence of bipedalism, and the relatively large head size of the fetus: Assistance increases infant survival rate (Rosenberg and Trevathan 2002). This need for greater sociality during delivery then, in combination with the consequent pressure to conform to cultural norms, led to a strengthening of socials bonds and a reduction in the likelihood of placentophagia.

An alternative to that scenario, just to cover all the bases, is the possibility that amniotic fluid ingestion is at least as important as placenta ingestion, but goes unnoticed because our attention is focused on placenta, which is so obvious and obtrusive, and the expulsion of which is a medical necessity. It is certainly possible that until recently (200–300 years in Western cultures), delivering mothers routinely, but inadvertently, ingested small amounts of amniotic fluid that got on their hands or on the infant, through the process of licking or kissing.

A second alternative is the possibility that for humans, raw placenta and amniotic fluid are, or at some point became, harmful to ingest. Because the placenta contains enzymes that perform all of the major processes of metabolism (oxidation, reduction, hydrolysis and conjugation; Sastry 1995) and operates as a filtering mechanism as well, environmental toxins directly (filtered) or indirectly (induction of the formation of molecules by the placenta) may render ingested raw afterbirth tissue a toxicological, endocrinological, or immunological threat to some women

(Clark et al. 1995; Kristal 1980; Morgan 1979; Young, Benyshek, and Lienard 2012). It is conceivable that differences in placental histology and cytology between humans and other mammals make this a more serious problem in humans. Cultural transmission of the knowledge of problems arising from placentophagia would be expected to spread more quickly than suppression of the behavior by natural selection.

Nevertheless, the quest for medicinal or behavioral benefits of components of afterbirth is important, for the same reasons that the quest for plant-based medicinal substances is important. The outcome of such a quest need not be an exhortation for women to eat afterbirth, but for scientists to isolate and identify the molecule or molecules that produce the beneficial effect and use it to design pharmacological tools. In the case of POEF and enhanced opioid-mediated analgesia, we have determined that not only is the effect nonspecific in regard to species, but it is also nonspecific in regard to sex (Abbott et al. 1991). That means that although males, which in all probability do not make the molecule, have the ability to respond to it. However, we do not raise this to suggest that both men and women eat placenta, but instead to point out that scientific efforts should focus on the characterization and either extraction or synthesis of the POEF molecule so that it can be used for pharmacological pain management in both sexes. The same logic would apply to whatever other afterbirth constituent affected health or behavior.

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