Pica in Pregnancy: New Ideas About an Old Condition

Sera L. Young

Department of Pediatrics, University of California, Davis, California 95817; email: slyo@ucdavis.edu

Division of Nutritional Sciences, Cornell University, Ithaca, New York 14853; email: sly3@cornell.edu

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Abstract

Pica, the purposive consumption of nonfood substances, is a millennia-old nutritional enigma. Its worldwide ubiquity, prevalence among pregnant women and children, and association with both positive and negative health outcomes, especially micronutrient deficiencies, underscore the importance of understanding this behavior. Multiple proposed etiologies of pica are reviewed, including cultural expectations, psychological stress, hunger, dyspepsia, micronutrient deficiencies (Fe, Zn, and Ca), and protection against toxins and pathogens. Currently available data, although limited, best support the protection hypothesis as a cause of most types of pica, although some evidence suggests that pagophagy (ice consumption) may occur during iron deficiency. It is possible that the binding capacity of pica substances explains the association with micronutrient deficiencies; earth, starch, etc. may render micronutrients in ingesta unavailable for absorption. Increased research efforts are warranted and must be hypothesis driven, interdisciplinary, and permit the testing of multiple causal inferences.

Contents

PICA: AN ENIGMA

Pica, the craving and subsequent consumption of nonfood substances, has been the subject of scientific study for more than two millennia. Although medical literature has tended to focus on it as a pathology, other fields have considered its adaptive benefits. This review synthesizes data on pica during pregnancy from historical, biomedical, ethological, and ethnographic sources to provide an overview of the topic and to suggest some new ideas about an old condition.

Pica: the craving and purposive consumption of substances that the consumer does not define as food for more than month

PICA SINCE ANTIQUITY

Hippocrates was the first to provide a written description of pica circa 400 BCE (49), and it has since appeared in the writings of many of the most influential medical scholars of Antiquity, the Middle Ages, and the Renaissance. The literature on pica increased in the seventeenth century, with a spate of *dissertatios*, or treatises written in Latin, authored by western European scholars of medicine (e.g., 21). The pica literature expanded again in the nineteenth and twentieth centuries with descriptions of pica by explorers, missionaries, and colonialists (e.g., 79). Slave owners and the physicians who treated slaves in the Americas are the other major source of information about pica in that era (e.g., 58). In most of these early descriptions of pica, nonfood craving and consumption was considered to be a disorder with an obscure etiology.

DEFINING PICA

Pica pica is the Latin nomenclature for the common magpie, a bird thought to have an indiscriminate appetite, just as those who ate nonfood items were thought to ingest them indiscriminately. "Pica" was the descriptor first given to the condition of nonfood cravings around the fifth century CE (3), although other terms for the condition have been used, including cachexia Africana (58), citta (3), mal d'estomac (58), and malacia (18).

The definition of pica has long been problematic. Physicians have used widely varying and idiosyncratic definitions. In the *International Classification of Diseases*, *Tenth Revision*, it has been defined as "the tendency or craving to eat substances other than normal foodstuffs" (111), which is ambiguous because normalcy is distinctly culturally determined. The definition of pica in the *Diagnostic and Statistical Manual of Mental Disorders*, *Fourth Edition*, although much lengthier, is more appropriate, given that it includes time span (>1 month) and developmental appropriateness (4). Yet all of these definitions fall short because none mentions the compelling desires that are a hallmark of pica. To state that individuals "eat earth" does not convey the absolutely imperative nature of their drive. The desire for pica substances is typically so forceful that the strength of pica cravings has long been equated with those for tobacco, alcohol, and recreational drugs (114).

A fitting definition of pica is therefore "the craving and purposive consumption of substances that the consumer does not define as food for >1 month." Under this definition, the accidental consumption of a clod of earth would not be considered pica, nor would the exploratory mouthing behaviors of children. The consumption of holy earth, such as that from Esquipulas, Guatemala, by Catholics (57) would also not be considered pica, as it is motivated by religious beliefs.

PICA SUBSTANCES

The list of reported pica substances is very long; in approximately descending order of frequency, they include: earth (geophagy), raw starches (amylophagy), ice (pagophagy), charcoal, ash, paper, chalk, cloth, baby powder, coffee grounds, and eggshells. A few obviously dangerous items have occasionally been reported to be purposively ingested, e.g., lighters and needles, but these incidences have all involved people with developmental or psychiatric disturbances and are beyond the scope of this review.

Geophagy

Archeological evidence suggests that geophagy may have been practiced for more than two million years (22). There is written documentation of geophagy in hundreds of cultures on every inhabited continent (6, 75). The practice remains common during pregnancy throughout the world today; in some obstetric populations, the prevalence of geophagy exceeds 60% (90, 102) (cf. **Supplemental Table 1**; follow the **Supplemental Material link** from the Annual Reviews home page at **http://www.annualreviews.org/**). It is also found among children (**Supplemental Table 2**) and nonpregnant adults (**Supplemental Table 3**).

The amount of earth consumed varies, but quantities of 20–40 g are typically reported (37, 90, 117). Earth is consumed in many forms, e.g., broken bits of pottery, chunks from earthen-walled houses, and clumps of earth found among dry beans. Geophagists are highly selective about the earth they consume; many identify suitable earth by smelling it after it has been dampened (117). In general, ingested earth contains a high proportion of clay, i.e., it is smooth and plastic when wet and crunchy when dry (109). Clay minerals commonly found in geophagic soils include kaolin (both kaolinite and halloysite), smectite, and illite (109). Dark, moist earth with high humus content (the rich brown organic matter in soil) and earth with high sand content have only very rarely been reported to be eaten (109). Geophagic soils are frequently prepared by baking, sun-drying, and even frying them (e.g., 104, 117).

Amylophagy

In some places, as geophagy has become less socially acceptable, perceived as dangerous, or the desired soils have become more difficult to obtain, earth has been replaced by other nonfood substances (e.g., 84). Raw starch has been the most common replacement for earth (48, 84, 104), but many pregnant women have also regarded starch as the most desirable pica substance itself (61, 116). In the United States, cornstarch is the most popular amylophagy substance, but an enormous variety of raw starches are craved and consumed around the world, including uncooked rice (57, 116), wheat, cassava and rice flours (72, 107), and raw starchy tubers (57, 77). The amount of raw starch consumed daily varies from a few grams to 1 kg. A number of population-level studies of amylophagy confirm that the practice is widespread in obstetric populations (cf. **Supplemental Table 1**).

Geophagy (or geophagia): the purposive consumption of earth (Gr. geo—earth)

Amylophagy (or amylophagia): the purposive consumption of raw starch (Gr. amylon—starch)

Pagophagy (or pagophagia): the purposive consumption of large quantities of ice (Gr. pagos—ice or frost)

Clay: the finest inorganic component of soils, <0.002 mm

Clay minerals: term used to refer to groups of clays with similar layer structures. Clay mineral families include kaolin (to which kaolinite and halloysite belong), smectite [to which montmorillonite and palygorskite (formerly known as attapulgite) belong], and illite

Supplemental Material

IDA: iron deficiency anemia

Pagophagy

Pagophagists consume from several glasses (94) to several kg (24) of ice per day. Like geophagists, pagophagists are also highly selective about ice (24). Pagophagy is prevalent in a number of obstetric populations (cf. **Supplemental Table 1**).

THE PUBLIC HEALTH IMPORTANCE OF PICA

Pica merits elucidation for reasons beyond its worldwide ubiquity; it has been regularly associated with both negative and positive health conditions. Investigators from diverse fields have explored its causal role in negative conditions such as iron deficiency anemia (IDA) and other micronutrient imbalances. The role of pica in other detrimental health conditions including heavy metal poisonings (especially Pb) (2, 97), alimentary canal damage (5), and gestational weight gain (107) has also been studied, but the infrequency or dwindling frequency obviate the need to address them at length in this review. Potential positive health effects of pica include providing micronutrients, soothing gastrointestinal distress, and preventing harmful chemicals or pathogens from entering the bloodstream.

In addition to its potentially harmful or healthful consequences, pica is important to understand because it is predominantly found among the most biologically vulnerable populations: pregnant women and children. Furthermore, the association between pica and pregnancy is both thousands of years old (49) and very strong. Dozens of observational studies among antenatal populations worldwide indicate that pregnant women regularly engage in pica (cf. **Supplemental Table 1**). Children are the demographic group second most likely to purposively consume nonfood substances (cf. **Supplemental Table 2**), although currently available evidence suggests that the prevalence among pregnant women is far greater. Other subpopulations known to engage in pica include people undergoing renal dialysis (107) and individuals with celiac disease (66) or hemoglobinopathies (60). For these and other reasons, the need to understand pica has been repeatedly acknowledged (e.g., 30, 37).

Supplemental Material

PROPOSED ETIOLOGIES OF PICA

It would seem that the etiology of pica could easily be determined by asking consumers why they crave nonfood substances. Yet this ostensibly straightforward question is frequently difficult, and often impossible, to answer (e.g., 24, 34, 37, 114). In the absence of satisfactory explanations by consumers themselves, a number of etiologies of pica have been proposed. These are outlined in turn below.

Cultural Expectations

"Culture," broadly put, has been suggested as an impetus for pica. In past centuries, pica was attributed to an absence of "civilized culture" (e.g., 1). Modern behavioral scientists have elucidated more nuanced and less judgmental meanings of pica, especially geophagy. They have suggested that it "makes sense" that women eat earth in some societies because of, e.g., their traditional roles as potters and gardeners (51) or "the cultural associations of soil-eating with blood, fertility and femininity" (38).

Culture indubitably informs much of human behavior; it is therefore reasonable to expect that sociocultural notions reinforce or inhibit pica behavior. However, culture, broadly put, is not a satisfactory explanation of pica because it does not explain the worldwide variation in attitudes about its acceptability. Furthermore, the widespread occurrence of pica in the animal kingdom (73, 74) is a strong indication that there are impetuses for pica beyond symbolic relationships.

Psychological Stress

A handful of scientists have suggested that pica is a "protective" response to psychological stress (30). Under this hypothesis, it is a nervous habit, analogous to nail biting, that soothes the individual. Proposed mechanisms are ambiguous at best; e.g., pica is "a mediator of stress, acting through the immune system" (30). Unfortunately, the few studies of the relationship between pica and psychological stress were individual case studies or population-level studies in which stress was measured in nonstandard ways (e.g., 12, 30). Thus, more exploratory research is needed before this hypothesis can be deemed to be of high research priority.

Hunger

Pica has also been attributed to hunger (75). Indeed, earth has been eaten during periods of food shortages and famine in China (11), South America (106), and several European countries (53). Hunger continues to motivate some geophagy in the twenty-first century (67).

Yet these instances of earth consumption during periods of hunger cannot explain the bulk of pica worldwide. For one, the geophagy in these episodes is not actually pica; earth was not craved, it was eaten as a last resort. Second, a number of pica items could provide more nutritional value if cooked; cooking rice and cornstarch greatly increases their digestibility. Furthermore, most pica in ethnographic reports does not occur among populations experiencing food shortage (S.L. Young, P.W. Sherman, J.B. Lucks, & G.H. Pelto, unpublished observations).

Dyspepsia

It has also been proposed that upper gastrointestinal distress, namely nausea and heartburn, is the impetus for pica. Indeed, the few pica practitioners who can give an explanation for their pica usually attribute it to the reduction of heartburn or nausea (e.g., 35). Most pica items are more alkaline than gastric pH (109) and would thus function to reduce the gut acidity responsible for dyspepsia. Furthermore, the increase in pica during pregnancy is consistent with the increase in dyspepsia concomitant with many pregnancies. However, most people cannot explain why they engage in pica, and some explicitly state that it is not a response to any particular gastrointestinal condition (24, 114).

Micronutrient Deficiencies

The most frequently proposed hypotheses are those that suggest that pica is a response to micronutrient deficiencies. As such, this hypothesis is subdivided into three sections: iron (Fe), zinc (Zn), and calcium (Ca) deficiencies.

Iron deficiency. The association between pica and anemia was first written about in 30 AD (18); it has been remarked upon repeatedly since. Some scholars have suggested that anemia causes pica, whereas others have hypothesized that pica causes anemia.

There are hundreds of case studies in which pica has been found in conjunction with IDA and/or anemia and 28 population-level studies of this association (cf. **Supplemental Table 3**). In many, but not all, of these cross-sectional observational studies, there has been a positive association between iron deficiency or anemia and the many forms of pica.

Supplemental Material

Can pica contribute bioavailable Fe? It has been posited that Fe deficiency or anemia causes individuals to engage in pica to ameliorate their low Fe status (e.g., 55, 75). This hypothesis is supported by evidence of rectification of dietary deficiencies with nonfood substances in livestock (69). Furthermore, those who are most likely to engage in pica, pregnant women and young children, have greater per-kg Fe requirements (59).

However, no nutrient-specific cravings have been identified in humans besides that for Na (88). Furthermore, data on bioavailability of Fe from pica substances provide little support for this hypothesis. Some pica substances clearly contain very little Fe, e.g., raw unfortified rice, cornstarch, and chalk. The Fe content of other items is less obvious, particularly that of earth.

Typically, the mineral content of geophagic samples has been analyzed using total acid digests, i.e., substances are completely dissolved in a strongly acidic solution, and their elemental composition is then calculated. Researchers have used total acid digests to conclude that a number of nutritionally relevant elements are present in pica substances, including Fe, Zn, Cu, and Ca (e.g., 50, 55, 81, 105).

Yet acid digests alone ignore much of the body's biochemistry, most critically, the pH of the intestine, the site of Fe absorption. Because intestinal pH is much higher than that of the stomach, and Fe is most soluble at low pH, equating the total elemental composition with the amount of elements bioavailable vastly overestimates the available nutrient content (109). Therefore, methods that involve only an acid digest can merely indicate if there is any element of interest present; the establishment of bioavailability requires more sophisticated methodologies (114).

Only five studies of soil nutrients have considered intestinal biochemistry in their analyses. Two studies have used the physiologically based extraction test, which includes a phase that mimics the pH and digestive enzymes in the gut, to study Ugandan (98) and Indian geophagic soils (2). In these studies, less than 5% of the total Fe present was bioavailable. The authors concluded that the Indian, but not the Ugandan, soils could provide biologically significant quantities of Fe (approximately 7 mg of Fe from one sample and 15.4 mg from the other), although their calculations made some problematic assumptions about absorption, and they had not inquired about the quantity typically consumed. Negligible amounts of other biologically relevant minerals, including Zn, were available.

Kikouama et al. (71) investigated trace elements released by six West African geophagic clays under oral, gastric, or intestinal conditions (samples were not passed through each stage consecutively). They found the availability of both ferric and ferrous Fe to be lowest under intestinal pH, but they did not calculate potential Fe contribution to the diet, likely because of the absence of information on amount of earth consumed.

A fourth study that attempted replication of intestinal conditions was conducted by Dreyer et al. (28) on two samples of South African geophagic soils. They added soils to Fe-enriched Ringer's lactate solution and measured the precipitation of elements at gastric and intestinal pH. Black geophagic earth absorbed Na, K, and Fe and liberated Ca and Mg at pH 6.2. Fe from the Ringer solution was absorbed by the red geophagic earth at pH 6.2; no change in other elements was seen. In short, neither substance provided Fe or Zn, and one could possibly provide Ca and Mg.

Hooda et al. (52) conducted the most sophisticated study of bioavailability. They examined the nutrients that geophagic materials could contribute in vitro as well as their capacity to bind nutrients in suspension, thus rendering them unavailable. Results indicated that the five geophagic samples from around the world provided bioavailable Ca, Mg, and Mn but significantly reduced the availability of Fe and Zn in suspension, suggesting that these soils do not contribute micronutrients and are likely to bind the Fe and Zn available in ingested foods (**Figure 1**).

In brief, the idea that humans are consuming earth as a response to Fe deficiency is an attractive theory, but no data exist that suggest that pica substances ameliorate poor Fe status.

Does the treatment of Fe deficiency cause the cessation of pica? An alternative explanation of the association between pica and Fe deficiency is that pica is a response to Fe deficiency, but that it is a nonadaptive one, i.e., it does not increase Fe status. Under this hypothesis, pica is considered an aberrant epiphenomenon. Only vague mechanisms have been suggested, mostly related to tissue enzyme deficiency, including Fe and Zn deficiencies in "key appetite-regulating brain enzymes" (112).

If Fe deficiency does cause pica, a corollary is that pica should disappear when Fe levels return to normal. There is a multitude of case studies in which the treatment of Fe deficiency or anemia coincides with the cessation of pica. However, the role of medical attention, medical advice, other treatments administered, the placebo effect of such treatments, and the absence of controls makes causal inferences based on these studies untenable, and they are not discussed further.

Several intervention studies of the effect of Fe supplementation on pica have been conducted. The three single-blinded studies of the effects of iron supplementation on pica behavior were inconclusive. Although the administration of intramuscular Fe injections (IM Fe) (82, 95) and ferrous fumarate syrup (86) initially seemed to cause cessation of pica when compared to control injections (82), syrups (86), or subjects' own behavior prior to supplementation (95), study irregularities make it impossible to attribute changes in pica behavior to supplementation alone.

In the first of the only two controlled double-blind studies of Fe supplementation and non-pagophagy pica, IM Fe or saline injections were administered to 32 children with pica in the Washington, D.C., area (46). Their pica behavior and hemoglobin (Hb) were reevaluated at 2–3 months and again at 9–10 months. No correlation was found between changes in pica and changes in Hb. The authors concluded that Fe was not significantly more effective than a placebo in "curing" pica, i.e., improving Fe status did not cause pica to cease. This conclusion would have been strengthened by measurement of Fe stores in addition to Hb.

In the second controlled double-blind trial of micronutrient supplementation and geophagy, neither randomization to 10 months of Fe supplementation nor 10 months of multivitamins significantly reduced geophageous behavior among 402 Zambian schoolchildren (89). In multivariate logistic models of geophagy at the conclusion of the study, neither Fe supplementation nor multimicronutrient supplementation was significant in predicting geophagy ($p = 0.44$, $p = 0.88$, respectively). The study had a number of problems, including 54% loss to follow-up and low compliance, but the loss to follow-up was equally distributed across treatment groups, and compliance was similarly low across all groups. A further weakness was that there was not much potential for the children to benefit from Fe supplements; mean Hb concentration at baseline was 12.9 g/dl (95% CI 12.7–13.1) for geophageous children versus 13.0 g/dl (95% CI 12.6–13.4) for nongeophageous children.

The two studies of the effects of Fe supplementation on pagophagy offer better support of the hypothesis that Fe deficiency causes pica. In 1969, Coltman (23) conducted a single-blind study of seven Fe-deficient female adult patients. Prior to any intervention, participants' ice consumption was quantified for one week. Participants were then given a single intramuscular injection of saline; a week later, they were given a single injection of 5 cc of iron dextran. Ice consumption was quantified daily. Pagophagy diminished rapidly after the administration of Fe but did not disappear completely (**Figure 2**). The authors attributed this to an inadequate dose of Fe. Coltman had access to patients with other types of pica; it would have been informative if he had studied the effect of Fe supplementation on the pica behavior of non-pagophagists.

The strongest evidence in support of Fe deficiency causing pica comes from a study in which anemic rats consumed a significantly greater proportion of their daily water in the form of ice than did nonanemic controls (96% in anemic versus 45% in controls) (110). Recovery from anemia eliminated their pagophagy.

In summary, the intervention studies that have examined whether the correction of Fe deficiency caused the cessation of pica have had a number of problems, including small sample sizes and thus limited power, problematic designs, and ambiguous results. Specific conclusions about the effects of Fe supplementation on pica during pregnancy are impossible to make; only one pregnant woman was involved in all aforementioned studies. Results from the two randomized, double-blind studies (46, 89) suggest that Fe supplementation does not cause the cessation of geophagy or amylophagy, although the pagophagy investigations conducted by Coltman and Woods & Weisinger suggest that the correction of

IM Fe: intramuscular Fe injections

Hb: hemoglobin

Fe status may sometimes cause pagophagy to disappear.

Zinc deficiency. There are only six studies of the association between Zn deficiency and pica (**Supplemental Table 4**), although some of the cross-sectional studies of the relationship between anemia and pica (**Supplemental Table 3**) may also be a measure of association with Zn deficiency, as Zn is a necessary component of Hb. Mechanisms by which humans seek Zn when deficient have not been elucidated, although some research has suggested that taste sensitivity may be altered by Zn deficiency (20); this in turn could cause nonfood substances to have an appealing taste.

Supplemental Material

Can pica contribute bioavailable Zn? Data on the bioavailability of Zn are ambiguous and incomplete. Smith & Halsted's study in rats (99) indicated that modified Iranian geophagic soil could contribute dietary Zn to rats. These results contrast starkly with bioavailability data from in vitro analyses of unadulterated geophagic soils, which indicated that little Zn was available and that some geophagic soils bound dietary Zn, rendering it unavailable (2, 28, 52). The bioavailability of Zn in other pica substances, e.g., freezer frost from older freezers with Zn lining and raw starches, has not been studied.

Does the treatment of Zn deficiency cause the cessation of pica? There have been only three studies of the effects of Zn supplementation alone on human pica behavior. After physicians gave oral Zn sulfate to 10 geophagic children in India, all ceased pica within eight weeks (10). There was no indication, however, of other messages given to the children, no controls, and no evidence of increase in Zn levels. In 1985, of 47 Chinese children with pica who received daily Zn supplementation, 46 ceased pica within three months (19). Again, there was no use of placebos or controls and no measurement of other micronutrient indices. In the third study, Zn tablets were given to 128 mentally retarded individuals with pica with a serum level less than 0.85 μg/dl (80). The average number of pica incidents per person fell from 23 to 4.3 incidents over a two-week period, and mean serum Zn increased from 0.7 μg/dl to 1.3 μg/dl. The authors concluded that Zn deficiency had caused pica. In sum, sufficient data are not available to permit conclusions about the efficacy of Zn treatment in causing the cessation of pica. Clearly, research with controls is necessary.

Ca deficiency. The discussion of Fe and Zn deficiency as the cause of pica dwarfs that of Ca deficiency, although of all elements, Ca is the one most likely to be supplied by pica substances. The high Ca content of some clays, chalk, and plaster together with the relatively greater bioavailability of Ca compared to Fe and Zn make it possible that dietary Ca is provided by geophagic soils (28, 52). Further support for this hypothesis comes from the fact that geophagy was more common in nondairying African cultures, where there was less Ca in the diet, than in dairying ones (108). However, if increased Ca requirements motivated pica, we would expect to see pica occur more frequently among lactating women than among pregnant women, as they have the highest Ca requirements (59); this, however, is not the case.

Experimental data in support of the Ca hypothesis are scant. The sole experimental data to test the Ca hypothesis come from a study in which 12 children with pica were given vitamin and mineral supplements that included Ca, but no Fe, daily for 6–7 weeks; 12 other children with pica were given placebos (45). After seven weeks of treatment, five had pica in each group; 3–13 months after treatment ended, three in each group had pica. Calcium supplementation seemed to have no effect on pica behavior.

An Increased Need for Protection from Toxins and Pathogens

A final hypothesis about the etiology of pica proposes that pica substances offer protection from harmful chemicals and pathogens. Hladik & Gueguen (50) first proposed that clays were protective against toxins consumed by primates, and Profet (93) first suggested that clays could be protective against human teratogens. The potential for nonearth pica substances to provide detoxification and protection has received attention only very recently (114; S.L. Young, P.W. Sherman, J.B. Lucks, & G.H. Pelto, unpublished data).

Many plants produce toxic chemicals, such as tannins and glycoalkaloids, to protect themselves against pathogens and herbivores that would otherwise harm them; these are called plant secondary compounds. In humans, ingestion of these secondary compounds can cause gastrointestinal distress, dizziness, and muscle pains; in sufficient quantities, they are teratogenic, mutagenic, or carcinogenic (54). Other sources of harmful chemicals are enterotoxins secreted by food and waterborne bacteria such as *Escherichia coli*, *Staphylococcus aureus*, *Salmonella enterica*, and *Listeria monocytogenes*. Pathogens to be protected from include these and other harmful bacteria as well as viruses and parasitic nematodes, all of which can do great damage to humans. In short, this hypothesis proposes that pica reduces the long-term harmful effects of the ingestion of harmful plant secondary compounds and food- or waterborne parasites or pathogens.

Mechanisms of protection. One mechanism by which pica substances may offer protection is through the reduction of the permeability of the gut wall (**Figure 3*a***). The intestinal mucosal layer acts as a physical barrier between ingesta and the bloodstream by filtering out large molecules, as well as a chemical barrier by maintaining a pH gradient. Erosion of the mucosal layer is dangerous because it increases the permeability of the gut and can lead to increased entry by toxins and pathogens into the bloodstream (41).

Several clays found in geophagic samples can strengthen the mucosal layer. Smectite (41) and palygorskite (attapulgite) (87) are known for their ability to bind to mucus, thereby increasing the effectiveness of the mucosal barrier. Smectite can also repair mucosal integrity and stimulate mucin production (41). It is possible that other clays could work similarly to reinforce the mucin layer, although no others have been studied.

A second mechanism by which pica substances may offer protection is by binding toxins and pathogens, thereby rendering them unabsorbable by the gut (**Figure 3*b***). A number of clays found in geophagic earths have proven adept at binding pathogens, including viruses, fungi, and bacteria. Suspensions of montmorillonite and kaolin, both of which are clay minerals commonly found in geophagic soils, have been demonstrated to bind reoviruses (a family of viruses to which rotavirus, the leading single cause of severe diarrhea among infants and young children, belongs) in vitro (78). Montmorillonite has been shown to interfere with Fe nutrition of the fungus *Histoplasma capsulatum*, which in turn reduced fungal respiration (76). Palygorskite, halloysite, and kaolinite have been demonstrated to adsorb the *Staphylococcus aureus* bacteria (8). More recently, the broad-spectrum antibacterial properties of two smectite-illite clays have been demonstrated (47).

Because of these mechanisms, clays are effective in the treatment of diarrhea. Kaopectate^{TM} took its name from the clay mineral kaolin, the original active ingredient, although kaolin is no longer used in formulations of Kaopectate in the United States. A number of other clays have been used in antidiarrheal preparations (e.g., 43).

Studies of the binding capacities of items that are common pica substances indicate that many are powerful absorbents. For example, clays are valued in the agricultural industry for their ability to control aflatoxicosis in livestock, an infection caused by mycotoxins produced by *Aspergillus* spp. fungi (92). The detoxification capacity of clays is further underscored by animal behavior. Rats, who are not able to rid themselves of toxins through emesis, will eat kaolin when exposed to poisons and successfully reduce poison-related morbidity and mortality (100). Activated charcoal is used to treat many types of acute poisoning in humans and animals (25). The concomitant administration of clays, starch, charcoal, and/or magnesium trisilicate (a common antacid) together with pharmaceuticals such as antibiotics (70), heart medicines (14), and antimalarials (83) is known to bind these pharmaceuticals, rendering them less effective. A study comparing the capacity of activated charcoal, kaolin, magnesium trisilicate, and raw starch to manage ciprofloxacin (an antibiotic) poisoning indicated that all bound significant quantities of the antibiotic under in vitro conditions (91) (**Figure 4**).

The above studies have investigated items that are common pica substances, but they did not use specimens actively sought by humans. The toxin-binding capacity of only a few geophagic clays has specifically been studied. Johns & Duquette (64, 65) have demonstrated the capacity of geophagic clays to bind plant secondary compounds, including glycoalkaloids and tannins, under in vitro conditions, thereby rendering them both safer and more palatable. Dominy et al. (27) examined the capacity of geophagic soils to bind plant toxins using the TNO Intestinal Model. In this experiment, a 300 mL test meal to which either alkaloids or tannins had been added was processed with and without 10 g of kaolin; the kaolin absorbed ~30% of toxins. Because the model included no mucosal layer, there was no possibility of clay adhering to the mucin layer as would likely happen in vivo, so this is likely an underestimate of in vivo binding. Finally, Gilardi et al. (39) studied the detoxifying capacity of geophagic clays in Amazonian parrots that engage in geophagy. They administered a plant secondary compound, quinidine, and geophagic clay solution using a feeding tube to four parrots, and a quinidine and water solution to another four, and sampled their blood at one, two, and three hours post dose. Circulating quinidine levels in parrots dosed with clay were ~60% lower than in the control group.

In sum, at least some pica substances reduce harmful effects of pathogens and toxins by enhancing mucosal secretion, thereby reducing permeability of the intestinal walls. Some pica substances also help reduce bacterial and parasitic populations and the deleterious effects of toxins by binding them and facilitating their removal from the gut before entry into the bloodstream. However, more studies on the binding capacity of substances specifically sought by pica consumers are necessary to fully determine the explanatory capacity of this hypothesis.

Do those who engage in pica require gastrointestinal protection? Under the protection hypothesis, those who engage in pica would be those most susceptible to the harmful effects of toxins and pathogens. The most vulnerable life stages are those during which rapid growth and cell division occur: embryogenesis and preadolescence (9). Furthermore, because pregnant women are adaptively immunosuppressed (to avoid rejecting the embryo), avoidance of parasites and pathogens is important for gravidae's own health during gestation (32, 33). Therefore, this hypothesis predicts the occurrence of pica among pregnant women and children more commonly than among any other age or sex group.

There have been only four studies of the prevalence of pica across an entire community, i.e., in which the prevalence of pica among adult men and women (pregnant and nonpregnant), adolescents, and children is documented (15, 96, 104, 116). In each of these studies, the prevalence of pica was at least twice as high among pregnant women as among children, and the prevalence in these two groups was far higher than among other sectors of the population, which is consistent with this hypothesis.

The protection hypothesis further predicts that pica would be more likely to occur early in pregnancy, during embryogenesis (32, 33), when embryonic tissues are most susceptible to damage from teratogens. Finally, this hypothesis predicts that pica would be more prevalent in tropical regions because foodborne pathogens multiply rapidly in hot, humid, tropical climates, and species of pathogens and infectious diseases are most diverse nearest to the equator (44). There are few data to test either of these predictions.

In short, although the quantity and quality of the data to test the protection hypothesis are limited, the data that are available are consistent with this hypothesis.

COULD PICA CAUSE MICRONUTRIENT DEFICIENCIES?

Mechanisms of Deficiency Causation

Because available data do not support a micronutrient deficiency as the impetus for pica, the strong positive association between pica and micronutrient deficiencies remains unexplained. One possibility is that pica, rather than remedying micronutrient deficiencies, exacerbates them. Pica could cause a micronutrient deficiency in three ways: by replacing micronutrient-rich foods with nonnutritive items, by causing geohelminth infection that results in blood loss or poor micronutrient absorption, or by binding with dietary micronutrients and rendering them unusable.

The replacement mechanism is unlikely; pica substances tend to be eaten in addition to the foods that would normally be consumed, not in place of them (24, 31). Soil has been used instead of food only when food is unavailable (11, 53, 67, 106). However, a careful dietary record would be useful to confirm that women who consume pica substances do not therefore eat less food.

Pica, especially geophagy, may indirectly cause micronutrient deficiency through the spread of geohelminths that cause blood loss and gut irritation and therefore inhibit absorption of micronutrients. Although there is strong epidemiological and biological evidence that geophagy is not a significant mechanism for hookworm infection, there are mixed findings about it as a vector for ascariasis and trichuriasis (36, 104, 115). However, a number of facts suggest that geohelminth infection cannot explain the strong, frequent association between pica and micronutrient deficiencies: Most earths are collected from areas unlikely to be contaminated with geohelminths; earths are heated prior to consumption; other pica substances, e.g., cornstarch, are unlikely to be vectors for geohelminth infection; and anemia is associated with pica even in areas where geohelminth infections are rare (104, 115).

The third mechanism by which pica may cause a micronutrient deficiency is through the inhibition of micronutrient absorption. This could occur if substances bind dietary micronutrients or decrease the permeability of the mucin layer. As discussed above, some pica substances have been established to be capable of both actions.

Much of the binding capacity of soils depends on their cation exchange capacity (CEC), a measure of how readily a substance can exchange adsorbed cations with cations in a surrounding solution (114). If the CEC is low, pica substances are less likely to form an insoluble complex through adsorption by cation or ligand exchange reactions, with cations such as Fe^{3+}, Fe^{2+}, Mg^{2+}, K^{+}, etc.; these are then more likely to be able to pass through the brush border. If the CEC is high, cations are likely to become bound tightly to the pica substance and thus be unavailable for absorption. Because the CEC of clay minerals varies enormously, from ~5 meq/100 g in kaolinite to ~150 meq/100 g in some smectites and vermiculites, cation binding will behave differently according to the clay minerals in geophagic samples. In pica studies, CEC has only been irregularly measured, and then only in geophagic earths.

Cation exchange capacity (CEC): a measure of how readily a substance can exchange adsorbed cations with cations in a surrounding solution

Studies of Micronutrient Deficiency Causation by Geophagy

Most of the studies of the effects of geophagy on micronutrient absorption are rather outdated. In 1968, Minnich et al. (85) published a series of small studies of Fe absorption in the presence and absence of geophagic clay. Subjects ingested either radio-labeled $FeSO_4$ or radio-labeled heme alone or after ingesting 5 g of Turkish soil. The mean proportion of Fe absorbed in the presence of clay was reduced by 9% to 40% for each type of Fe. They also conducted similar experiments using three

Laundry starch: a blend of rice, corn, and/or potato starches, once available in chunk form to be dissolved in water, now primarily sold in aerosol cans

American clays. American clays had a smaller impact on Fe absorption, causing a 0% to 5% absolute reduction in Fe absorption. It should be noted that none of the clays in this fascinating series of experiments was procured by geophagists, which is an unfortunate shortcoming. These results were subsequently replicated using other Turkish soils in 1972 by members of the same research group (16).

In 1970, Talkington et al. (101) tested the impact of two popular Texan geophagic clays on Fe absorption using radio-labeled Fe. The consumption of 10 g of red Kilgore clay by four adults was associated with an increase in Fe absorption, from 15% to 18%; 10 g of white Marshall clay was associated with an increase from 18% to 19% in four adults (no tests of statistical significance performed). They also examined Hb levels in one patient who ate 12 g of red Texan clay (containing 480 mg of Fe) for 11 days. On the eleventh day, her Hb was unchanged (7.1 g/dl), but her serum Fe had declined from 21 μg/100 mL to 13 μg/100 mL. The authors concluded that neither clay inhibited Fe absorption, despite this marked change in serum Fe.

Sayers et al. (96) studied Fe absorption among five habitual geophagists in South Africa. ^{55}Fe ascorbate absorption was greatly decreased when 250 g of geophagic earth from participants' own supplies was eaten (mean 17.4% without earth versus 5% with). It would have been useful to establish the amount of material consumers ingested daily prior to deciding on a protocol in which such a large quantity was consumed.

The effects of clay on Zn absorption specifically have been examined in only two studies. The first involved 17 Turkish children 8–21 years of age with IDA (7); 12 were geophagists, 5 were not. Twenty-seven mg of elemental Zn was orally administered, and serum Zn was measured at baseline as well as at 2, 4, and 6 h after the test dose. All patients with geophagy demonstrated impaired Fe and Zn absorption, although the timing of the Zn administration versus earth consumption was not stated. The second study of Zn absorption in the presence and absence of 5 g geophagic clay indicated that clay impeded Zn absorption (17) (**Figure 5**). The authors suggested that earth might bind not just with dietary Zn but also with endogenous Zn released from the pancreas.

In the most recent in vivo study of the binding capacity of clays, pregnant rats were fed varying amounts of clay in a nutritionally complete diet. The rats as well as their pups suffered skeletal and fur changes and slowed development but exhibited no differences in Hb or red blood cell count after 60 days; other micronutrient indices were not evaluated (29). This suggests that some micronutrients may have been chelated, but data are inconclusive.

Based on these few, small experimental studies, we can conclude that some geophagic clays are able to interfere with absorption of cations, which, in turn, can lead to micronutrient deficiency. Future absorption studies should always determine the CEC of pica substances.

Studies of Micronutrient Deficiency Causation by Ash and Starch

There is far less research on the impact of nonearth pica substances on micronutrient nutrition. In the sole study of the consequences of ash consumption on Fe absorption, Fe absorption in the presence of 100 g of ash was reduced (14.5% versus 9.6%) (96).

Four studies have been conducted to determine the consequences of amylophagy on Fe absorption; potential effects of starch on other micronutrients have not been explored. In 1968, Blum et al. (13) orally administered radio-labeled ferrous citrate to four adults in the presence and absence of at least 8 g of laundry starch. The authors determined that starch consumption caused Fe absorption to be reduced from 93% to 40%. In contrast, in a 1970 study among 18 subjects who ingested 60 g of starch, Fe absorption increased from 15% to 16% (no P values presented) (101). In a 1971 study of mice fed diets composed of lab chow and 0% cornstarch (controls), 50% cornstarch, and 100% cornstarch, the Hb values of the controls did not significantly differ from those of the intervention group after 10 weeks, although greater mortality and lower fertility were observed in groups with greater starch in the diet (68). This experiment, however, does not succeed in its stated purpose of pinpointing the micronutrient binding capacity of starch; the increased morbidity and mortality could be attributable to inadequate nutrient intake.

In the fourth study, Thomas et al. (103) studied the absorptive capacities of laundry starch in incubating flasks as well as in rats. In vitro, laundry starch bound 19% to 80% of the available $^{59}FeSO_4$ and 34% to 68% of the available ^{59}Fe-Hb. In anemic and nonanemic rats, administration of a suspension of laundry starch (100 mg) 1 h before the administration of $^{59}FeSO_4$ or ^{59}Fe-Hb caused a decrease in Fe absorption compared to those given a saline control solution ranging from 8.0% to 21.2%. However, when laundry starch was administered simultaneously with or after ingestion of Fe, Fe absorption was not changed. These data indicate that laundry starch can bind appreciable quantities of inorganic Fe and Hb in vitro and in vivo.

It is clear that some ash and starches can decrease Fe absorption. The demonstration of the importance of timing on inhibitory consequences of starch by Thomas et al. (103) is an important one, and it may explain the variation of findings of absorption of inhibition in these studies. Unfortunately, the time elapsed between starch ingestion and Fe ingestion was not specified in three of the five studies (13, 85, 101). Differences in observed effects of pica on micronutrient absorption in these studies may also be attributable to dissimilar chemical properties of the substances, variation in time elapsed between measurements, or unmeasured changes in the subjects' own Fe metabolism across time.

Thus to date, with these limited data on pica substances causing micronutrient deficiencies, there is evidence to support the statement that some, but not all, earths, raw starches, and ash interfere with absorption of Fe, Zn, and K and thus can contribute to deficiencies.

SHORTCOMINGS OF PREVIOUS RESEARCH

It is clear that notwithstanding the interest in pica by a variety of disciplines, the information available to date is incomplete and irregular. There are many reasons for this. The first is underreporting: Pica consumers sometimes conceal their behavior because of their fear of judgment or chastisement by family members, friends, or medical professionals (34, 42, 56). It is also concealed because it is may be thought to be an indication of pregnancy (which some women may want to keep private) (56), poverty (116), or mental illness (24). Furthermore, researchers sometimes do not know to inquire specifically about pica and discover it only by accident (e.g., 24, 105). An additional difficulty of studying pica is that it does not easily fit into a conceptual category. People may think of pica substances as medicine, a food additive, or "just a craving," such that food recall questions do not probe with appropriate prompts (113).

The study designs of previous research, most of which have been cross-sectional and descriptive, are another reason for our limited understanding of pica. Although these studies have been important in establishing the prevalence of pica and associations with a number of conditions of public health concern (cf. **Supplemental Tables 1, 2, 3,** and **4**), they have done little to further causal arguments. Furthermore, many of these descriptive studies have often extrapolated about the quantities of soil consumed (e.g., 2, 57), overestimated the bioavailability of elements (e.g., 50, 55, 81, 105), and relied on very small sample sizes of study participants or soils analyzed (e.g., 13, 57, 65). Many of the intervention studies have been conducted without randomization or even any controls. Furthermore, research methods have frequently been incomplete or inadequate for determining the physico-chemical properties of the substances, e.g., CEC, or the nutrient-, toxin-, and pathogen-binding capacities.

The analytical decisions made present a further shortcoming. For example, disparate pica substances have frequently been lumped together in the analyses of health consequences (e.g., 26, 30). Because the causes or effects of ice cravings could be quite different from those of earth cravings, they should always initially be analyzed separately.

Finally, pica is a complex behavior that requires familiarity with nutrition, anthropology, biochemistry, and soil science, among other fields. Pica research thus requires multidisciplinary methods. However, the research approaches frequently used by those who have studied it have been limited to their own particular specialty, e.g., nutritionists have discussed dietary issues, cultural anthropologists have been concerned with symbolic interpretation, and soil scientists have focused upon mineralogical characteristics. The most informative studies are those that have drawn on techniques from a number of fields and considered the possibilities of multiple etiologies of pica; the work of P. Wenzel Geissler, James Gilardi, and Timothy Johns, together with their colleagues, is exemplary in this respect.

NEXT RESEARCH STEPS

Clearly, there is much work to be done to elucidate the relationship between pica and pregnancy. First, more community-based research is necessary. Studies in which the entire community, from young children (beyond the phase of mouthing) to the elderly, are surveyed about current and past pica behavior would be useful for ascertaining if pica is indeed most common among pregnant women and young children. Pregnant women should be surveyed prospectively about the precise onset and cessation of pica during pregnancy.

Elucidating the criteria on which pica substances are selected is likely to offer insight clues to the function of pica. For example, geophagists' fondness of the smell of freshly dampened earth suggests that geosmin (63) may be a proximate trigger for geophagic earth selection.

Research methods for determining nutrient bioavailability and detoxification capacity can be ameliorated and more widely implemented. For example, in vitro bioavailability studies can be improved upon through the use of the CACO-2 model, which offers a very good in vitro approximation of Fe bioavailability (40). A greater variety of pica substances should be evaluated for bioavailable nutrients and toxin-binding capacities. All studies of bioavailability should include analyses with and without test meals, so that the capacity of pica substances to bind dietary nutrients is examined as well.

Ice is an anomalous pica substance, as almost every other craved nonfood item is dry and absorptive. Some have pointed to the continuum in crunchy texture across ice and other pica substances; Jenkins has suggested that ice might be a "behavioral analogy to a skeuomorph, an object which possesses the same function in a different physical form as a result of culture change" (62). Inquiries about the organoleptic properties that appeal to the consumer might help to explain why ice is desired along with the other absorptive substances.

Finally, future research should be hypothesis driven, rather than merely descriptive. Research designs used to study pica need to be more powerful and consider the possibility of multiple etiologies. Intervention studies in animal models in which appropriate controls are used and longitudinal studies in humans that determine the order of onset of pregnancy, pica, and micronutrient deficiencies would be extremely useful for elucidating this enigmatic ingestive behavior.

SUMMARY POINTS

1. Pica is the craving and purposive consumption of items that the consumer does not define as food for >1 month.
2. Earth (geophagy), raw starch (amylophagy), and ice (pagophagy) are the most common picas.

3. Pica merits greater scientific attention because of its ubiquity among pregnant women and children and its association with both positive and negative health conditions.
4. Many etiologies of pica have been suggested, including culture, stress, hunger, dyspepsia, micronutrient deficiencies, and protection from toxins and pathogens.
5. Available data suggest that protection from toxins and pathogens is the most promising explanation of geophagy and amylophagy.
6. Pagophagy may be caused by iron deficiency.
7. Some pica substances, e.g., clays and raw starches, may bind dietary micronutrients, thus causing micronutrient deficiencies, especially anemia.

FUTURE ISSUES

1. Current data on pica are incomplete and irregular due to underreporting, weak study designs, inadequate research methods, poor analytical decisions, and single-discipline investigations.
2. The prevalence of pica across entire communities should be studied to determine if pica is indeed most prevalent among pregnant women and young children.
3. The elucidation of the timing of pica within pregnancy would be helpful for hypothesis testing.
4. The bioavailability of micronutrients in pica substances should be evaluated under conditions mimicking the gut, rather than by total elemental composition using solely acid digests, which has been standard practice.
5. The capacity of nongeophagic pica substances to bind dietary micronutrients, toxins, and pathogens needs to be more thoroughly assessed.
6. Future study designs should have the capacity to test multiple hypotheses.
7. Intervention studies in animal models and longitudinal studies in humans that determine the order of onset of pregnancy, pica, and micronutrient deficiencies would be extremely useful for ascertaining causality.

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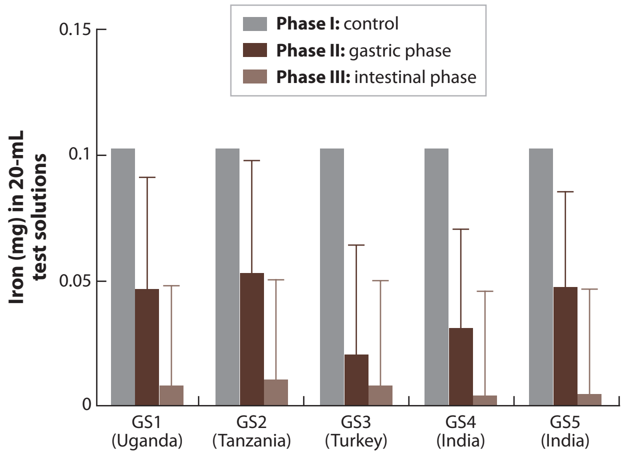

Figure 1

The effect of gastrointestinal simulation on potentially bioavailable Fe in five geophagic samples in a test solution of Fe. A change in Fe content of the solution following the gastric (Phase II) and intestinal (Phase III) simulations signifies a loss in bioavailability. Error bars on Phase II and Phase III represent least significant difference when compared to control. Redrawn from Reference 52.

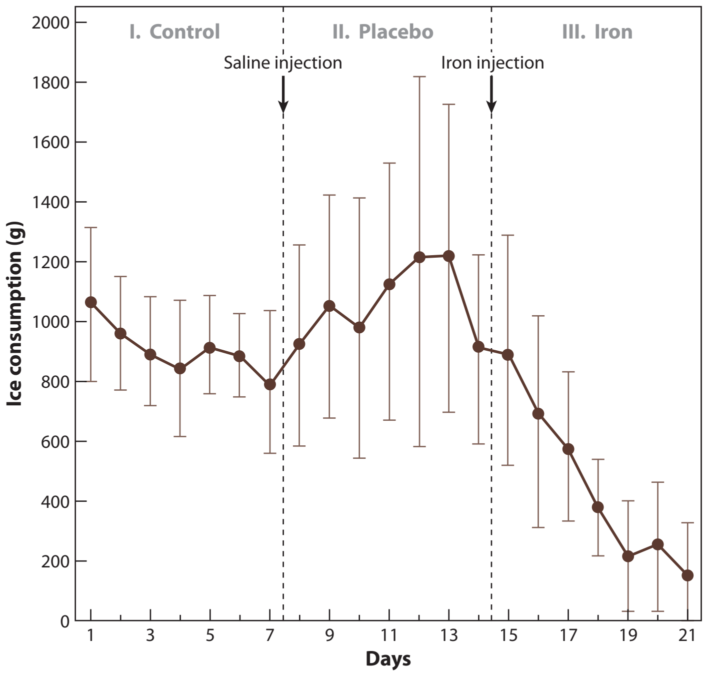

Figure 2

Mean ± 1 standard deviation of the daily ice consumption (g) by seven pagophagists during the three phases of Coltman's single-blind study. Ice consumption was elevated in the control phase (I) and the placebo phase (II) compared to after the injection of 5 cc of iron dextran (III). Redrawn from Reference 23.

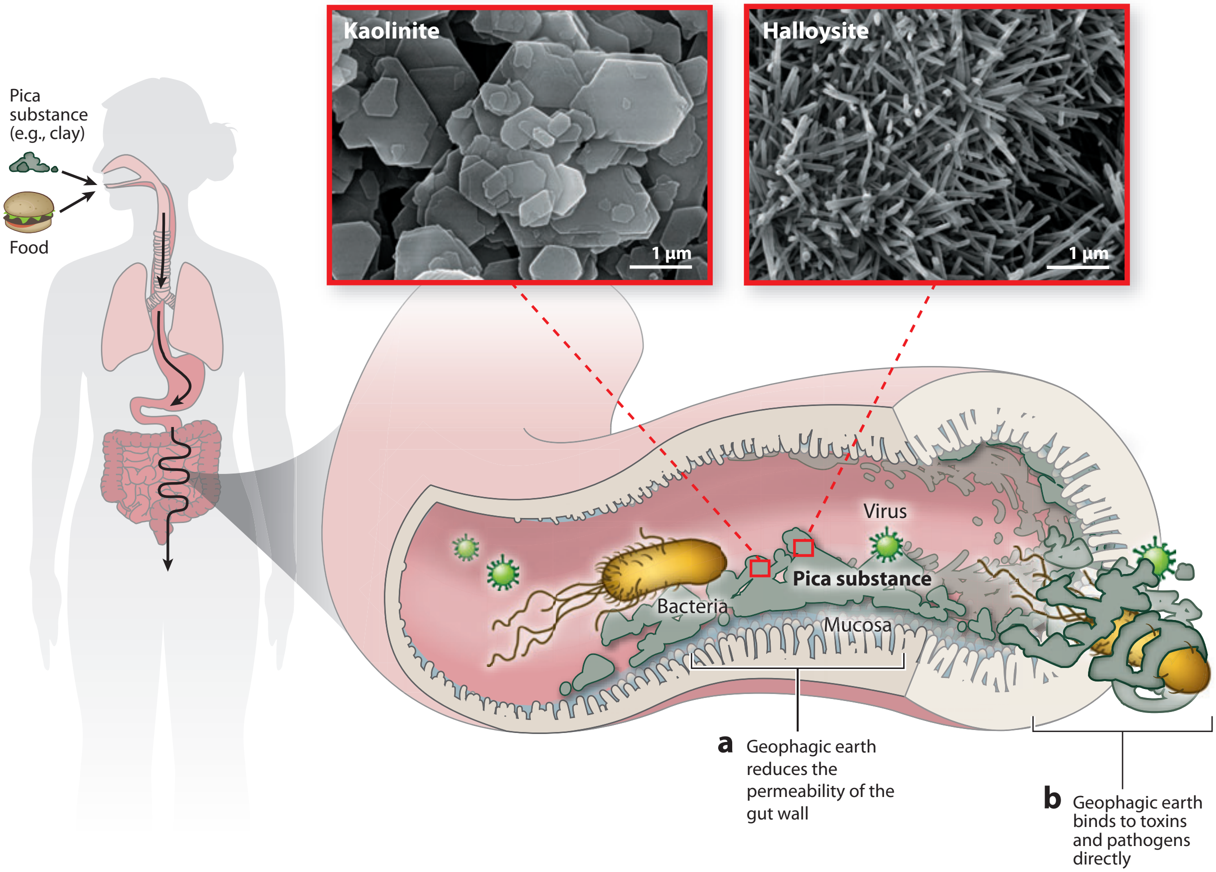

Figure 3

Geophagic earth may protect against toxins and pathogens by (*a*) strengthening the mucosal layer by binding with mucin and/or stimulating mucin production, thereby reducing the permeability of the gut wall, and (*b*) binding to toxins and pathogens directly, thereby rendering them unabsorbable by the gut. (Scanning electron microscope photo insets kindly provided by Evelyne Delbos of the Macaulay Institute.)

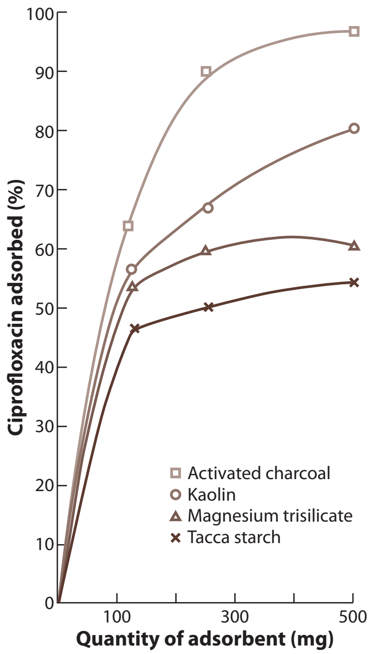

Figure 4

Four substances commonly consumed by those engaging in pica all demonstrate a dose-dependent capacity to adsorb the antibiotic ciprofloxacin (10 ug/ml) in vitro. Redrawn from Reference 91.

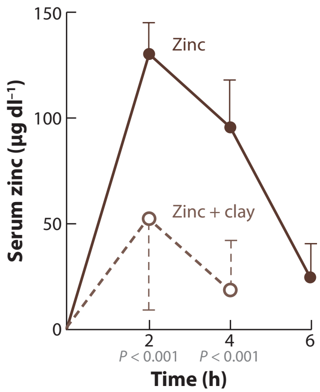

Figure 5

Oral Zn absorption (mean ± 1 standard deviation) differs significantly in the presence (- - -) and absence (—) of 5 g of ingested Turkish geophagic clay (n = 17)* P < 0.001. Redrawn from Reference 17.

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Errata

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