PICA AND NUTRITION

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INTRODUCTION

Pica is a pathological craving for normal food constituents or for substances not commonly regarded as food. It has fascinated the physician and nutrition scientist because it is frequently associated with nutrient deficiency, notably mineral malabsorption, although it can occasionally result in excessive intakes of substances such as potassium or carotene. To the psychiatrist or psychologist, it represents a behavioral challenge that is sometimes associated with mental retardation. On a world-wide scale, pica is of anthropological interest, often being a consequence of cultural patterns ingrained in the food habits of a region and possibly related to an ancestral food-shortage. To the veterinarian or zoologist, it is evidence of a nutrient-specific appetite in wild and/or domestic animals.

Against this background I discuss pica as a nutritional aberration that provides opportunities to observe deficiency diseases, to make nutritional interventions, and to reflect on the factors that determine food habits.

The word "pica" was first used to describe a syndrome by the French physician Ambrose Paré in the 16th century (82). Pica is a medieval Latin word meaning magpie, a bird which, according to Cooper (37), was known to early writers for its tendency to pick up a diversity of things to satisfy hunger or curiosity. Other terms that have been applied to this or related syndromes from antiquity to the 19th century include: mal d'estomac¹ (French); erdessen,² das Gelusten der Schwangern Frauen,³ die Schwangern Weiberlust⁴ (German); geophagy⁵ (Aristotle); allotriophagia⁶ (Sophocles); and cachexia Africana.⁵ In 1638 Boezo (16) first classified pica systematically. For Boezo the word pica denoted the craving for absurd things; the avid consumption of accustomed foods he termed malacia.

In this review, the term pica will be applied to a pathological craving both for items normally considered food by the population, such as that sometimes reported during pregnancy (e.g. for 10 heads of lettuce daily), and for substances not normally regarded as food (e.g. clay, coal). This definition does not categorize such behaviors as the chewing of gum or tobacco.

Historically the term pica has been vague and its meanings have been confounded owing to culturally based judgments. Certain early writers, for example, declared cravings for foods such as raw cabbage, yeast, and lobster to be pica (56), while in some societies earth is considered food and is used as a seasoning agent (122). In the mid 19th century it was customary for some people in northern Sweden to mix earth with flour when making bread (202). Thus the diagnosis of pica depends upon cultural attitudes as well as amounts ingested and degrees of craving. No sharp demarcation exists between pathological states and normality, nor between the ages at which some form of pica is considered normal.

Descriptions of pica as a syndrome are found in antiquity. Examples are summarized in Table 1. Records from as early as 40 B.C. indicate that Terra Sigillatta, the sacred "Sealed Earth," was used to treat a variety of diseases in Greece. Galen visited the island of Lemnos two centuries later and took back to Rome clay lozenges that for almost 2000 years had been used to treat poisoning. It is related that in Germany in 1581 a condemned prisoner

¹stomach illness

²earth eating

³the hunger of pregnant women

⁴the pregnant wives' craving

⁵consumption of soil or clay

⁶indiscriminate craving

⁷wasting away in Africans

Table 1 Historical record of information concerning pica

Year	Event	References
10 B.C.	Clay lozenges ingested to treat illness and poisoning	211
1000 A.D.	Avicenna treated pica with iron	16
1542	Aëtius associated pica with pregnancy	2
1630	Earth eaten in bread dough. 30 Years War: pica associated with superstition	121
1638	Distinction made between pica for food items and pica for nonfood items	16
1668	Stress suggested as cause of pica	124
1698	Hereditary basis for pica proposed	47
1742	Food allergy and idiosyncrasy associated with pica	212
1799-1804	First explorer report of endemic pica in South America	222
1831	Pica associated with lack of nutritious diet	89
1835	Geophagia in Africa—Cachexia Africana described	38
1843	Cachexia Africana disappeared in Dominica secondary to life-style changes	100
1845	Cachexia Africana spreads from West Indies to Southern US with slave trade	24, 38, 169
1846	Animal studies indicate relationship between geophagia and nutrient deficiency	123
1849	Pica reported among insane	215
1851	Infusorial earth mixed with bread flour by choice in Northern Sweden	202
1868	Case report of pica cured by iron	68
1870	Pica associated with anemia	129
1880	Pica associated with worm infestation	37
1900	Pica thought to be a racial phenomenon	150
1900	Pica in India reported among all classes and both sexes	97
1910	Geophagia reported in Egyptian Sudan, pica in pregnant women assumed normal	29
1912	Analysis of soil from 16th century, cation exchange properties noted	211
1924	Lead poisoning associated with pica	182
1960s	Further studies of pica responding to iron therapy	119
1960	Dwarfism, hypogonadism, hepatosplenomegaly and iron deficiency syndrome identified in the Middle East	86
1961	Zinc deficiency described in the syndrome of dwarfism in Middle East	170, 171
1968	Analysis of clay shown to have property of cation exchange	147
1970	Geophagia and amylophagia associated with pregnancy	109
1970s	Pagophagia identified and responds to iron therapy	33, 175
1981	Geophagia and other types of pica in the mentally retarded associated with low plasma iron and zinc	43

asked to be given 6 grams of mercuric chloride (2 grams were considered fatal) if he could eat terra sigillata at the same time. By taking his poison along with "a dram of Terra Sigillata in olde wine" he survived and was freed (211).

In the early 16th century, Aëtius of Amida (2) attributed the pica of pregnancy to pressure on the viscera associated with the growth of the fetus, while in Germany Hubrigkt (98) interpreted the same phenomenon as due to fantasies associated with pregnancy. Avicenna (85), who lived around 1000 A.D., first mentioned beneficial effects of iron therapy in pica. Others recommended the consumption of pigeons along with their bones, thus foreshadowing treatment for the malabsorption of minerals associated with certain types of pica (16). During the remainder of the 17th century, physicians continued to speculate on the origins and nature of pica, prescribing varied and exotic measures, including both dietary treatment (including iron supplementation) and the need for psychological intervention against the mental aberrations supposed to underlie pica.

During the course of expeditions and colonization in various parts of the world in the 18th and 19th centuries, pica was identified under a variety of new circumstances. The Otomac Indians of South America were observed to eat clay colored with iron oxide without ill effects (222). In Java, a reddish baked clay was sold in the public market; its ingestion was supposed to make the individual slender (5, 77). Clay items to be eaten were sold in sections of India, Ghana, Afghanistan, Africa, and other tropical areas (5, 75, 85, 97, 101, 122, 199, 222). In Peru dietary powdered lime was sold in the market place (222). The Chinese, wrote the traveler Medhurst, mixed gypsum into a jelly for consumption (137, 141).

Pica was practiced by the native inhabitants of North America before the arrival of Columbus (131, 219). On plantations of the United States and the Caribbean, slaves sometimes exhibited a craving for clay, a practice probably passed down from their African forebears. When pica is superimposed on the classical pellagragenic diet of salt pork, corn bread, and molasses a variety of deficiency states may appear (169). On the American plantations, symptoms of these deficiencies were known as cachexia Africana, which consisted of weakness, pallor and edema, enlargement of the liver, spleen, and lymph nodes, anorexia, and rapid pulse, with later pre-terminal ulceration of the skin and eventual death (5, 24, 38, 55, 84, 100). It was commonly accepted that nutritional treatment, including administration of iron sulfate was effective in reversing the syndrome (89, 135). In this context, Hancock (89) noted that slaves on Tiger Island, who also practiced clay-eating, did not develop the cachexia, presumably because they used water from an iron cistern. Volpata (221) reported that in 111 males and 115 females with geophagia, 85% developed subsequent gastroenteritis, 91% chlorosis, and 46% pellagra. The role of various B-vitamin deficiencies concurrent with pica remains confusing (156).

INCIDENCE OF PICA

The incidence of pica is difficult to establish, although several surveys of selected groups have been made. Interpretation of survey findings is complicated by inconsistent definitions of pica, reluctance of subjects to admit to the practice, limitations of statistical methods applied, and the impossibility of generalization from a few observed cases. Table 2 provides examples of selected estimates.

The craving for particular food substances during pregnancy is a widely recognized phenomenon (39, 51). In one series of women studied in Bir-

Table 2 Incidence of pica selected reports

Study (Ref.)	Number of subjects	Description and/or age of group	Percentage population with pica
1937, Baltimore (107)	30	retarded children	50
1950, Mississippi (57)	331	pregnant ♀, black	44
1957, Baltimore (37)	386	black, > 6 mo.	27
	398	white, > 6 mo.	17
1962, Washington DC (145)	486	black, 1-6 years	32
	294	white, 1-6 years	10
1963, Washington DC (131)	859	children, low income	55
		children, high income	30
1966, Boston interview (9)	439	children, 1-6 years	15
Mail survey	277	children, 1-6 years	20
1966, England (163)	40	institutionalized, psychotic, 3-13 years	66
1967, Georgia (165)	200	pregnant ♀	55
1968, Chicago (110)	987	pregnant ♀	35
1969, Chicago (112)	500	pregnant ♀	24
1971, California (19)	25	Spanish American, pregnant ♀	38
	10	Spanish American, nonpregnant 9	15
	21	Spanish American children	32
1979, Mississippi (219)	56	nonpregnant ♀	57
	115	children	16
	33	males	0
	27	adolescents	0
	112	pregnant 9	28
1981, Boston (41)	991	institutionalized, retarded, 11–89 years	26

mingham, England (91), 51% reported food cravings, with or without aversions and alterations in their sense of taste. The most common cravings were for fruit and other sweet-sour, sour, or sharp-tasting foods. Several positive correlations emerged, including one between pica during pregnancy and a history of pica and food fads in childhood. Similar food preferences were observed in a series of pregnant women studied in New York (96); but in Aberdeen, Taggart (206) did not find pica among 800 pregnant women studied. Pregnant women sometimes also eat nonfood substances. Fifty percent of the pregnant Southern black women in two studies (57, 165) ate clay and starch. In a one-year study, Keith et al (111) noted that 35% of 987 pregnant black and white women exhibited amylophagia (starch eating). Bruhn & Pangborn (19) reported a similar proportion (38%) of pica in pregnant Mexican women. McGanity et al (140) found 28% of 800 pregnant adolescents had a history of pica for clay, soil, starch, and refrigerator frost. Some authors have reported a decline over time in the incidence of pica among similar populations of pregnant women—e.g. of geophagia in rural populations from 55% in 1967 (165) to 18% in 1974 (18), and of amylophagia in urban populations from 35% in 1968 (110) to 20% in 1969 (112). The reasons for these changes are not evident.

Pica in adult men appears to be underreported. Some studies note that the incidence of pica may be decreasing in some male populations as its victims convert to smoking or chewing tobacco (131). In a study of 302 adults in Columbus, Ohio, 25% of the pica cases were male (85). Sayers et al (188) found that 11% of their male outpatient population reported consumption of ash or earth.

Pica is also prevalent among children, being reported especially in black children. Three authors (9, 37, 145) agree that about 30% of black children aged 1-6 years and 10-18% of white children of the same age attending their clinics have pica, mostly for nonfood substances. Among psychotic mentally retarded children, the incidence of pica exceeds 50% (107, 163). In a group of 991 mentally retarded adults the incidence of pica was found to be 26% (41), greater than that of such other eating dysfunctions as anorexia, rumination, or hyperphagia.

In 1974, Klein (115) estimated that 5-10% of all children 1-5 years of age had lead poisoning. More than 30% of children with pica have been found to have lead poisoning (102); conversely, 70-90% of children with lead poisoning give a history of pica (15, 28, 30, 184).

ETIOLOGY AND MECHANISM OF PICA

The causation of pica has been the subject of speculation since ancient times, and several hypotheses from that era have been mentioned above. Hypothe-

ses currently advanced include nutritional, psychological, cultural, pharmacologic, and disease (74, 161).

Nutritional Hypothesis

Pica has been hypothetized to be a craving generated by nutrient deficiency. The "salt lick" of wild animals is widely considered a response to a deficiency (17). Osteophagia in cattle, reported in many countries (71, 123, 209), is associated with phosphorus deficiency (209). Pica has also been described in pellagrous animals (54). Animals deprived of specific nutrients

described in pellagrous animals (54). Animals deprived of specific nutrients such as potassium (138), thiamin (92, 177, 179), and iron (65, 138, 224) often lick or selectively ingest items high in the depleted nutrient (58, 92, 176). However, this animal model of deficiency-induced pica has not always been confirmed (53, 213).

Davis (44, 45) tried to prove that children will without external guidance select a nutritionally complete diet. However, since the foods provided experimentally to children by Davis were mostly balanced in nutrients, these studies failed to test this hypothesis. On the basis of information from rat studies, Snowdon & Sanderson (197) proposed that a child deficient in calcium may discover that lead ingestion (pica) relieves some of the deficiency symptoms. Specific nutrient deficiencies, such as those of vitamin D (106), phosphorus (104), and vitamin C (79), have been thought to prompt the consumption of nonfood substances. However, pica for nonfood items did not decline in children given supplements of vitamins and minerals (unfortunately not including iron) (81). Hunter (99) hypothesizes that the ingestion of iron and calcium-rich clays by iron- and calcium-deficient individuals in Ghana represents diet supplementation. Similarly, it was postulated that consumption of clay rich in calcium and magnesium was to fulfill a physiologic deficit in Nigerian pregnant women (216).

Attempts to link pica with nutritional states have concentrated on iron (7). Several studies agree that anemia associated with pica for nonfood substances in children (119, 139, 151) and adults (33, 175) can be cured by administering iron. Case reports indicate a similar effect of iron on food pica (32, 39, 40, 166, 183). Unfortunately, no control groups were included in these studies. A special form of pica associated with iron deficiency is pagophagia, in which the pregnant woman consumes large amounts of ice (averaging 700 g daily). Controlled studies by Coltman (33–35) and Reynolds et al (175) demonstrated that the subnormal hemoglobin levels and the low concentrations of serum iron in such cases respond to iron therapy, following which the pagophagia disappears. In one series, parenteral administration of iron was effective within 5 days, while oral administration required 11 days to stop the pica (175). Whether the ice induces iron deficiency remains unknown.

Results supporting the hypothesis that iron deficiency causes pica and that such pica can be cured by giving iron have not always been obtained (79, 81, 164, 165). The occurrence of nutrient deficiencies and pica in the same subject does not prove a causal relationship. The disappearance of pica after iron therapy in subjects with very low hemoglobin values suggests that in some cases there may be a causal relationship. However, despite the high incidence of pica associated with anemia (39, 40), only a small percentage of individuals with anemia exhibit pica and vice versa. In cases of food pica (39, 40), the substance craved is rarely a good source of iron, nor does food pica during pregnancy always cease after delivery (2, 131).

Psychological Hypothesis

Pica has been explained as a persistence of the infantile hand-to-mouth behavior pattern (178). Lourie et al (131) determined the psychological status of the mother and child in cases of children with pica. The mother was often found to have personality disturbances and to relate poorly to the child, while the child sometimes had emotional problems, suffered from abnormal dependence and anxiety, and exhibited neurotic and depressive patterns. These authors suggest that pica is an expression of oral fixation (146), and Cooper (37) has noted that pica occurs more frequently in children with feeding problems such as anorexia or refusal of certain foods. Neumann (159) suggested that pica in both children and adults expresses a vestigial instinct related to the need to chew something solid. Others (5, 41, 122, 133) have also reported that texture, color, odor and taste are important components of the craving in pica. Specific neurological changes may be associated with pica results from lead poisoning but evidence indicates that the pica encourages the child to consume sources of lead and not the reverse (14). Several specific brain lesions have been associated with pica. Lesions of the left temporal lobe in monkeys (94) and the analogous Klüver-Bucy syndrome in humans (116) are accompanied by pica, as is damage to the amygdala of the cat (63). Mentally retarded individuals with seizures may have severe pica (13, 41). In instances of pica associated with specific brain lesions, the eating dysfunction seems confined to nonfood substances.

In addition to the individuals with seizures referred to above, the entire population of mentally retarded adults shows a high incidence of pica, which varies with the degree of retardation. In our series (41), the incidence of pica varied from 10% in mild mental deficiency to 33% in severe mental deficiency. However, incidence of pica for food items only was not correlated with severity of mental deficit.

Cultural Hypothesis

Pica has been associated with cultural and familial factors. In antiquity, clay lozenges were prepared on the Greek island of Lemnos, stamped with religious symbols, and exported throughout the Mediterranean area (74). Clay eating was encouraged among the male youths of Greece because it was believed to produce the desirable 'leucophlegmatic' skin and a slender, effeminate body (211). Symbolic geophagy occurs in many cultures (5). Earth-eating, irrespective of cravings, has frequently been associated with religious belief. Clay lozenges bearing Christian symbols are sold today in the Mexican city of Oaxaca (74). It has been noted that when Muslims erase sentences from the Koran by rubbing chalk from the board they sometimes consume the chalk dust out of respect for the book (74).

In parts of Africa it is believed that magical properties of the soil promote well-being. This belief results in the consumption of earth upon entering a territory, to promote fertility in women, and during pregnancy to increase lactation (5, 122, 216, 217). The consumption of earth during the first trimester of pregnancy is believed to suppress nausea, and in some African cultures young girls are taught in childhood that during pregnancy the consumption of earth as desirable (5, 56).

Vermeer & Frate (218, 219) consider the eating of clay to be deeply ingrained in Southern black society. There clay is fed as a pacifier for the infant, a practice also observed in Africa (5). Geophagy occurs among the adults (151), and it may be practiced at group social functions (131). Given the deeply ingrained geophagy of the African cultures that supplied the bulk of slaves to the New World, it is not surprising that the practice persists in the black subculture of the United States (5, 218, 219). On the other hand, geophagy is historically recorded both from Europe and the indigenous Indian population in the New World, individuals in the United States could also have acquired the practice from either.

Other Hypotheses

Pica may sometimes manifest itself in a person's effort to medicate himself. For example, medicinal properties against anemia have been attributed to clay (5, 55, 211). Individuals who consume extraordinarily large amounts of ground coffee (caffeine), cigarette butts (nicotine), oak leaves (tannins), and so forth, may be seeking pharmacological effects (20, 41, 67, 69, 120, 158, 168, 205). It has been reported (41) that 59 individuals who consumed such substances pathologically tended to exhibit behavior characteristic of addiction (83, 130, 148), increasing both the frequency and volume of ingested material. Such obsessive pica has been associated with nocturnal searching for (41), and constant dreams about (125), the craved substance.

Other physiological factors that have been thought to cause pica include gastrointestinal malaise (5, 56, 72, 97, 99, 122, 148, 216), stress and inflammatory processes (13, 21, 117), toxicosis (149), parasitic infestations (56, 66, 156), disease states (122, 172, 190), and hunger (5, 122, 201).

CLINICAL DESCRIPTION OF PICA

Pica is widely thought to be age-related, with the majority of reported cases occurring in children and pregnant women. Recent data [(41) and case reports cited below] indicate that pica is not limited to any age, sex, or racial group; it can occur anywhere.

Geophagia is the most commonly reported and reviewed form (5, 37, 75, 85, 122). However, the substances eaten in pica are almost limitless and their benefits or hazards vary with the amount and type consumed (42).

Metabolic Associations

Most metabolic changes associated with pica have been observed in case studies and interpretation in terms of cause and effect frequently is clouded by the concurrent conditions.

Pica in children has been primarily associated with lead poisoning; as early as 1927 Ruddock (182) described this association. As recently as the early 1950s blood lead levels were not universally available, and the diagnosis of lead poisoning was primarily a clinical one. Despite the continuing controversy over what constitutes lead toxicity, diagnosis is now based on biochemical, gastrointestinal, and neurological parameters. Mahaffey (132) has provided an excellent critique of current knowledge of nutritional factors in lead poisoning.

Symptoms reported in children with pica and lead toxicity include altered hematological values (12, 83, 106, 128, 199), increased serum and urine Δ-aminolevulinic acid (83, 106), elevated protoporphyrin in erythrocytes (106), excretion of coproporphyrin II in the urine (83, 106), high blood lead (13, 14, 31, 127, 152, 163, 192, 199), high dental lead (46), and response to calcium EDTA-lead excretion tests (13, 14, 31, 83). The range of blood lead levels diagnostic for lead toxicity remains debated (36, 76, 127, 128, 199). These changes can occur before the appearance of clinical symptoms such as vague abdominal pain, constipation, anorexia, nonspecific gastroenteritis, and recurrent emesis (83, 106). The most serious manifestations of pediatric plumbism are those involving the central nervous system (drowsiness, coma, grand mal seizures, permanent brain damage) and the renal system (83, 106). Excessive lead ingestion can impose further brain damage and behavioral problems upon the mentally retarded (14, 31, 220, 223). Death rates associated with severe lead toxicity have been as high as 25% (83).

As in adults, pica in childhood has frequently been linked to iron deficiency anemia. Geophagia has been associated with low hemoglobin levels (79, 119, 139, 151), low serum iron (151), hypokalemia (142), low ascorbic acid (30), normal serum protein (119), low albumin (119), high incidence of respiratory infections (79), and normal anthropometric measurements including height and weight (79). Two children thought to have potassium craving secondary to Bartter's syndrome, a potassium wasting disease, consumed over a kilo of potatoes daily (70 mEq potassium/kg body weight) and had persistent hypokalemia (172). Fulton (62) reported a case of pica for beetles, slugs, and invertebrates that stopped suddenly without intervention at the age of 14. In another case (108) a boy who consumed Comet cleanser and had zinc deficiency was cured of his pica following oral zinc sulfate. A patient with pica for metal (88), exhibiting poor growth and appetite and low hair- and serum-zinc levels, improved following zinc therapy.

In many cultures pregnant women are expected to practice pica (5, 118). An extensive list of the varieties of pica in pregnancy emerged from a British Broadcast Corporation program (91) that generated 514 letters from listeners reporting 820 pregnancies (366 cravings for fruits and vegetables, and 187 cravings for nonfood substances such as coal, soap, and paper). In the United States geophagia, amylophagia, and pagophagia are the most commonly reported types of practices in pregnant women. With all three forms association with anemia (33-35, 85, 109-113, 160, 185, 187, 203, 207) has been observed. Bronstein & Dollar (18) observed iron/total-iron binding capacity ratios under 16% in pregnant women with amylophagia. Parotid enlargement has been reported in association with starch-eaters' anemia (144, 191), although it was not found by Roselle (181). Other documented effects of pica during pregnancy include gastric obstruction (4), increased incidence of toxemia (165) [not verified by Keith (113)], delivery complications (78, 95), successive picas (180), and repeated pica during multiple pregnancies (5, 56, 118). One young pregnant woman developed an appetite for blocks of toilet-bowl freshener (para-dichlorobenzene). She presented with anemia and was treated with iron and folic acid. This treatment improved neither her hemoglobin level nor her pica (23).

Pica also occurs in nonpregnant adult females and in adult males. Case reports of nonpregnant adult females include: anemia and olive consumption that ceased upon oral treatment with ferrous sulfate (27); pagophagia in a diabetic who started consuming heads of lettuce when she was prevented from eating ice and whose hematocrit then decreased from 27 to 23% (153); consumption of tomato seeds that ceased following parenteral administration of iron (32); and consumption of burned matches (167, 184). A study of a mentally retarded adolescent who consumed up to two pack-

ages of cigarettes a day and had low plasma zinc levels, elevated copper levels, and wounds that would not heal, showed a reversal of all signs after oral administration of zinc sulfate (43). A 74 year-old black woman presenting with severe microcytic hypochromic anemia without blood loss was consuming 60–180 g of magnesium carbonate daily (125). Other cases of pica in nonpregnant women have involved cigarette ash, peanuts (gooberphagia), hair (trichophagia) and lettuce (lectophagia) (49, 134, 157, 164, 195).

The clinical phenomena associated with pica in males has not been well studied. However, in one study of mentally retarded adults the men suffered more severe anemia than did their female counterparts (43). This appeared to be a result of the higher consumption of the craved substance among the males.

In an institutionalized, mentally retarded, primarily adult population, pica was observed in both sexes (41–43). Clinical symptoms varied with the type of pica. Some types of pica (geophagia, cigarette tobacco, coprophagia, paper, string, metal/paint, and twigs) were associated with low hematocrit, low hemoglobin, low plasma iron, elevated total-iron binding saturation, low plasma ferritin, low plasma zinc, elevated plasma copper, normal hair zinc, and some abnormal hair copper and magnesium (43). Other types of pica (cravings for grass, leaves, and insects) were associated with normal plasma values of metals and minerals (43). Five cases of geophagia with hyperkalemia (attributed to the potassium content of the clay) have been reported in male and female individuals with chronic renal failure (67).

Geographic

The combination of a diet high in phytate and fiber and the consumption of clay and soil that can chelate metals has resulted in numerous cases of iron and zinc deficiency in Middle Eastern populations (reviewed in 85). The first descriptions of a syndrome characterized by geophagia, iron deficiency anemia, hepatosplenomegaly, and hypogonadism appeared in the Turkish literature in 1942 (208). Subsequently, the syndrome has been reported in Turkey (26, 162, 186) and Iran (86, 87, 170, 171, 187). Prasad et al (170) first described the same syndrome (nutritional dwarfism) in male Iranians consuming clay and subsequently demonstrated that the dwarfism was due to zinc deficiency (171). This syndrome has been reported more recently in females (180). Many biochemical parameters have been evaluated in populations with pica and zinc-deficient dwarfism, including low hemoglobin (7, 26, 86, 162, 170, 183, 186), pallor (26, 186), low serum iron (7, 26, 73, 86, 87, 170, 180, 186), low hematocrit (26, 86, 180), elevated serum TIBC (7, 26, 86, 186), low transferrin saturation (7), increased erythrocyte fragility (26), no stainable iron in bone marrow (26, 186), reduced hemoglobin A₂ (26); low serum zinc (7, 26, 87, 170), low and elevated serum copper (26, 186), low serum magnesium (26), low serum phosphorus (26), high alkaline phosphatase (86), achlorhydria (86), elevated or normal SGOT, SGPT, BSP, CCF (26, 186); abnormal glucose tolerance (186), decreased vitamin A absorption (26), increased iron absorption test (26), decreased plasma zinc tolerance (7), decreased total protein (26), low albumin (26, 186), elevated globulin (186), low PBI (180, 186), decreased folic acid (186); hepatosplenomegaly (7, 26, 73, 86, 186), liver biopsy changes (86, 186, 187), histological changes with peroral intestinal biopsy (7, 186), retarded bone age (7, 26, 86, 87, 186), growth retardation (26, 73, 87, 170), delayed secondary sex characteristics (7, 73, 86, 170, 186). Essentially normal findings include cholesterol (26), calcium (26), prothrombin time (26), alkaline phosphatase (26), total protein (87, 186), erythrocyte glucose-6-phosphate (26), and d-xylose absorption (186).

Complications

Complications of pica repeatedly encountered include bezoars (22, 42, 107, 195, 214), intestinal perforation (48, 70), dental injury (1), intestinal obstruction (42, 93, 155, 214), achlorhydria (23, 64), parasitic infection (50, 55, 66, 136, 151, 189), and constipation (4, 42, 59, 106). Isolated examples of conditions such as ulcerative colitis (50) and urinary retention (189) are reported. Plain abdominal radiography that can visualize, depending on their mineral content, certain of the substances consumed in pica (42, 64, 114, 119, 133, 142, 219) has been proposed as a diagnostic tool (30).

NUTRITIONAL CONSEQUENCES OF PICA

Because pica is associated with and in some cases may be caused by nutritional deficiencies, the nutrient intakes of individuals with pica have been studied. As mentioned above, Gutelius (80) found that individuals with pica consumed less meat and milk, fewer vitamin C-rich sources, and a smaller variety of foods than normal subjects. Geophagia has been associated with diets low in iron-rich foods (52, 56), calories (56), thiamine (56), and niacin. Sand eating has been encountered in children with excessive milk intake who refuse solid food (25). In the Middle East the diets of individuals with geophagia rarely include animal-protein foods but rather consist of bread, rice, and a few vegetables; however, such diets are not uncommon in the region (170). Danford et al (43) calculated the nutrient intakes of 66 mentally retarded adults (15–71 years old) with and without pica. Dietary intakes of calories, protein, vitamin D, ascorbic acid, thiamin, riboflavin, niacin, calcium, phosphorus, iron, and zinc were within the amounts specified by the Recommended Dietary Allowances. Low intakes of vitamin A,

magnesium, and copper were noted in both individuals with and without pica. Thus pica did not appear to interfere with total food intake in this population. Individuals with pica consumed more coffee and water than those without (42, 69, 205).

Dietary factors that may influence a child's susceptibility to lead toxicity are poorly understood. Johnson (103) found an inverse correlation between children's blood-lead levels and their calcium and milk intake. This relationship had previously been shown in an animal model (173). Three-day food records revealed intakes low in calcium, iron, magnesium, pantothenic acid, and zinc in this population (103). Mooty (154) found no dietary intake differences between children with high and low blood lead levels. Several studies in animals have suggested that nutritional inadequacies may potentiate the toxic effects of lead. These relationships have been comprehensively reviewed (106, 126, 128, 132, 198, 204). Sources of lead ingested by children with pica continue to be identified (10, 74, 90, 103, 105, 115, 193, 194, 198, 200).

Nutritional status may be influenced by pica in several ways. First, the consumption of the craved substance can reduce the intake of normal dietary sources of nutrients. For instance, large intakes of laundry starch have been reported to depress intake of regular foods (6, 18, 110, 181, 185, 207). However, amylophagia may not interfere with appetite (43, 56), and can cause obesity (133). Second, pica can reduce the bioavailability of minerals. To geophagia has been attributed reduced absorption of iron (7, 26, 43, 143, 147), zinc (7, 26, 43), and potassium (146), perhaps due to chelation. Others have observed high phytate diets in geophagic populations which could potentially decrease absorption of iron and zinc (174). Starch has been shown to reduce iron absorption (15, 207, 210), and magnesium carbonate was reported to interfere with iron absorption (125). On the other hand, some clays can be a source of such minerals as magnesium (216), potassium (67), iron (99), zinc (196), and calcium (99, 216).

THERAPY FOR PICA

Two major treatment modalities—the nutritional and the behavioral—are recommended in the literature. Many early references advocate the use of iron and "nutritious" food (37). The anemia and low plasma zinc of individuals with pica (especially geophagia) indicate appropriate mineral therapy.

Iron and zinc supplementation may result in improvements in the clinical picture. This is illustrated by cases of Middle Eastern dwarfism, wherein oral zinc administration (26, 58, 87, 170, 180) for pica-induced zinc deficiency resulted in sexual maturation and improved growth rates and iron therapy reversed anemia (7, 26, 86). Many instances of apparent responses

to treatment with iron (11, 26, 104, 119, 139, 151) and zinc (88, 108) can be cited. More rapid disappearance of the pica following parenteral iron has been claimed (25, 28, 151, 175). Not all nutrient therapies affect pica. In the series studied by Gutelius et al (81), the oral administration of fat-soluble vitamins, B-vitamins and ascorbic acid supplements raised the plasma ascorbic acid levels of children with pica, but failed to cure the pica. Cure rates have rarely been evaluated over a long period. In a double-blind controlled trial McDonald & Marshall (139) observed a relapse of pica in individuals after 6 months of iron therapy (this was accompanied by a decrease in hemoglobin).

The sporadic success of iron therapy for pica has been postulated to be related to whether the therapy causes critical threshold levels of hemoglobin (139) or serum iron levels (175) to be exceeded. Others hypothesize that the defect behind pica involves iron-dependent tissue enzymes (35, 101, 175). Pica tends to disappear with age. Even double-blind iron therapy studies in young children have not accounted for this (80). Caution must therefore be exercized in evaluating and accepting the results of treatment, notably in the numerous single case reports in the literature.

Pica has in the past been, and is still being, "treated" by physical restraint of its practitioners/sufferers with masks and other devices. However, since individuals with pica persistently seek the specific substances they crave (42, 131, 178)—sometimes, for example, traveling great distances to obtain clay from special areas (5, 218, 219), a behavior also observed in lower animals (60) and primates (B. Marriott, personal communications)—attempts to restrain them are often unsuccessful.

Modern psychotherapy has concentrated on overcorrection techniques in which the pica practitioner is punished with mouth wash-outs (negative reinforcement) for indulgence of the craving and rewarded for the absence of pica with pleasant foods (positive reinforcement). A series of behavioral treatments (8, 20, 59, 61), has resulted in some regression of pica, even in the mentally retarded individuals in whom little spontaneous change was likely. Reviewing the literature on behavioral treatment, Albin (3) notes that experimental conditions are poor, follow-up data inadequate, and thus conclusions difficult.

CONCLUSIONS

The medical and nutritional implications of certain types of pica have been grossly underestimated. Despite extensive investigation, few studies present a comprehensive nutrition picture and none elucidate the etiology of pica. A review of the literature reveals that pica appears to have multiple etiologies. One may not be able to compare the results of one study to another,

particularly if the two studies consider different forms of pica. Thus the type of pica should be elucidated, the significant preceding events determined.

Like alcoholism, the consumption of nonfood items is difficult to diagnose by means of an interview. Often the condition is first revealed when the sufferer is X-rayed for other reasons. Identification of individuals at risk is extremely important, especially children and pregnant women who present with anemia and/or other nutrient deficiencies.

In populations habituated to geophagia, amylophagia, and other types of pica associated with iron deficiency, trace element and mineral status should be evaluated. Trace element levels in the body may be subnormal, with consequences that are as yet unknown but perhaps nutritionally significant. Heavy metal toxicity can still be a problem for individuals ingesting substances containing metals such as lead. Treatment modalities vary with the type of pica. Nutritional therapy should be instituted when appropriate and the effects of such intervention systematically documented.

Literature Cited

- Abbey, L. M., Lombard, J. A. 1973. J. Am. Dent. Assoc. 87:885-87
- Aetius-Aëtios of Amida. 1542. The Gynecology and Obstetrics of the VIth Century. (Transl. from the Latin edition of Coronarius by J. V. Ricci). Cited in Ref. 37
- Albin, J. B. 1977. Ment. Retard. 15:14–17
- Allan, J. D., Woodruff, J. 1963. N. Engl. J. Med. 268:776-78
- Anel, B., Lagercrantz, S. 1958. Geographical Customs. Stud. Ethnogr. Upsaliensia 17:1-84
- Ansell, J. E., Wheby, M. S. 1972. VA Med. Mon. 99:951-54
- Arcasoy, A., Cavdar, A., Babacan, E. 1978. Acta Haematol. 60:76-84
- Ausman, J., Ball, T. S., Alexander, D. 1974. Ment. Retard. 12:16-18
- Barltrop, D. 1966. Am. J. Dis. Child. 112:116-23
- Barltrop, D., Stehlow, C. D., Thorton, I., Webb, J. S. 1974. Environ. Health Perspect. 7:75-82
- 11. Ber, R., Valero, A. 1961. Harefuah 61:35-39
- Betts, P. R., Astley, R., Raine, D. N. 1973. Br. Med. J. 1:402-6
- Bicknell, D. J. 1975. Pica A Childhood Symptom. Southampton, England: Camelot Press. pp. 191
- Bicknell, J., Clayton, B. E., Delves, H. T. 1968. J. Ment. Defic. Res. 12:282-93
- Blum, M., Orton, C. G., Rose, L. 1968. Ann. Intern. Med. 68:1165

- Boezo, M. H. 1638. De Pica. Sm. Lipsiae. Cited in Ref. 37
- Bott, E., Denton, D. A., Goding, J. K., Sabine, J. R. 1964. *Nature* 202:461-63
- Bronstein, E. S., Dollar, J. 1974. J. Med. Assoc. Ga 63:332-35
- Bruhn, C. M., Pangborn, R. M. 1971.
 J. Am. Diet. Assoc. 58:417-20
- Bucher, B., Reykdal, B., Albin, J. B. 1976. J. Behav. Ther. Exper. Psychol. 2:137-40
- Burchfield, S. R., Elich, M. S., Woods,
 S. C. 1977. Psychol. Behav. 19:265-67
- 22. Butterworth, W. W. 1909. J. Am. Med. Assoc. 53:617
- Campbell, D. M., Davidson, R. J. L. 1970. J. Obstet. Gynecol. Br. Commonw. 77:657-59
- Carpenter, W. M. 1844. New Orl. Med. Surg. J. 1:146-68
- 25. Catzel, P. 1963. Pediatrics 31:1056
- Cavdar, A. O., Arcasoy, A. 1972. Clin. Pediatr. 11:215-23
- Chandra, P., Rosner, F. 1973. Ann. Intern. Med. 78:973-74
- Chisholm, J. J., Kaplan, E. 1968. J. Pediatr. 73:942-50
- Christopherson, J. B. 1910. J. Trop. Med. 13:3-7
- Clayton, R. S., Goodman, P. H. 1955.
 Am. J. Roentgenol. 73:203-7
- Cohen, D. J., Johnson, W. T. 1976. Am. J. Dis. Child. 130:47-48
- Coleman, D. L., Greenberg, C. S., Ries,
 C. A. 1981. N. Engl. J. Med. 304:848
- Coltman, C. A. 1969. J. Am. Med. Assoc. 207:513-16

- 34. Coltman, C. A. 1969. Nutr. Rev. 27:244
- 35. Coltman, C. A. 1971. Arch. Intern. Med. 128:472-73
- 36. Committee on Biologic Effects of Atmospheric Pollutants. 1972. Lead. Washington DC: Nat. Acad. Sci. 330 pp.
- 37. Cooper, M. 1957. Pica. Springfield, IL: Charles C. Thomas. 109 pp. 38. Craigin, F. W. 1835. Am. J. Med. Sci.
- 17:365–74
- 39. Crosby, W. H. 1976. J. Am. Med. Assoc. 235:2765
- Crosby, W. H. 1971. Arch. Intern. Med. 127:960-61
- 41. Danford, D. E., Huber, A. M. 1981. Appetite. 2:281-92
- 42. Danford, D. E., Huber, A. M. 1982. Am. J. Ment. Defic. In press
- 43. Danford, D. E., Smith, J. C., Huber, A. M. 1982. Am. J. Clin. Nutr. In press
- 44. Davis, C. M. 1928. Am. J. Dis. Child. 36:651-79
- 45. Davis, C. M. 1939. Can. Med. Assoc. J. 41:257–61
- 46. de la Burdé, B., Shapiro, I. M. 1975. Arch. Environ. Health 30:281–84
- 47. Dehne, T. 1698. Inauguralis Medica Appetiti Ventriculi Depravato in Pica et Malacia. Disertatio. Jenae: Literis Christophori Krebsii. Cited in Ref. 37
- 48. Delaitre, B., Lemaigre, G., Acar, J. F., Atsamena, M., Bouhroum, A. 1976. Nouv. Presse Med. 5:1743-46
- 49. DeSilva, R. A. 1974. Ann. Intern. Med. 80:115-16
- 50. DiCagno, L., Castello, D., Savio, M. T. 1974. Minerva Pediatr. 26:1768-77
- 51. Dickens, G., Trethowan, W. H. 1971. J. Psychosom. Res. 15:259–68
- 52. Dickins, D., Ford, R. N. 1942. Am. Sociol. Rev. 7:59-65
- 53. Donhoffer, S. 1960. *Triangle* 4:233–39
- 54. Dupont. 1959. Union Med. Gironde, Bordeaux 4:400, 498, 545. Cited in Ref. 37
- 55. Duprey, A. J. B. 1900. Lancet 2:1192
- 56. Edwards, C. H., McDonald, S., Mitchell, D., Jones, S., Mason, L., Kemp, A. M., Laing, D., Trigg, L. 1959. J. Am. Diet. Assoc. 35:810-15
- 57. Ferguson, J. H., Keaton, A. G. 1950. New Orleans Med. Surg. J. 102:460-63
- 58. Foster, J. W. 1927. E. African Med. J. 4:63-76
- 59. Foxx, R. M., Martin, E. D. 1975. Behav. Res. Ther. 13:153-62
- 60. French, M. H. 1945. E. African Med. J. 22:103-10
- 61. Friedin, B. D., Johnson, H. K. 1979. J. Ment. Defic. Res. 23:55-61

- 62. Fulton, J. 1979. Aust. Med. J. Melbourne 1:257
- 63. Ganong, W. F. 1977. Review of Medical Physiology. Los Altos, CA: Lange Med. Publ. pp. 178, 362
- 64. Gardner, J. E., Tevetoglu, F. 1957. J. Pediatr. 51:667-71
- 65. Garretson, F. D., Conrad, M. E. 1967. Proc. Soc. Exp. Biol. Med. 126:304-8
- 66. Gelfand, M. 1945. E. African Med. J. 22:98–103
- 67. Gelfand, M. C., Zarate, A., Knepshield, J. H. 1975. J. Am. Med. Assoc. 234:738–40
- 68. Gould, A. N. 1876. Boston Med. Surg. J. 94:417
- 69. Graham, D. M. 1978. Nutr. Rev. 36:97-
- 102 70. Graham, P. W. 1976. Med. J. Aust. 2:385-86
- 71. Green, H. H. 1925. Physiol. Rev. 5: 336-48
- 72. Green, J., Jones, A. 1968. Los Panecitos Benditos: Clay eating in Oxaca. Ethnic Techn. Notes No. 2. San Diego, CA: San Diego Museum of Man, Balboa Park
- 73. Griscelli, C., Raux, M., Attal, C., Barthelemy, C., Mozziconacci, P. 1970. Ann. Pediatr. (Paris) 17:214-19
- 74. Grivetti, L. E. 1978. BioScience 28: 172-73
- 75. Grivetti, L. E. 1981. Ann. Rev. Nutr. 1:47-68
- 76. Guinee, V. F. 1971. Nutr. Rev. 29: 267-69
- 77. Gumilla, J. 1791. Historia Natural, Civil y Geographica de Rio Orinoco, Barcelona. Cited in Ref. 37
- 78. Gusdon, J. P., Tunca, C. 1974. Obstet. Gynecol. 43:197-99
- 79. Gutelius, M. F., Millican, F. K., Layman, E. M., Cohen, G. J., Dublin, C. C. 1962. Pediatrics 29:1012-17
- 80. Gutelius, M. F., Millican, F. K., Layman, E. M., Cohen, G. J., Dublin, C. C. 1962. Pediatrics 29:1018-23
- 81. Gutelius, M. F., Millican, F. K., Layman, E. M., Cohen, G. J., Dublin, C. C. 1963. Am. J. Nutr. 12:388-93
- 82. Hale, M., Lepow, M. L. 1971. Conn. Med. 35:492-97
- 83. Haley, T. J. 1971. Clin. Toxicol. 4:11-29
- 84. Haller, J. S. 1972. Med. Hist. 16:238-53
- 85. Halsted, J. A. 1968. Am. J. Clin. Nutr. 21:1384-93
- Halsted, J. A., Prasad, A. S. 1960. Trans. Am. Clin. Climatol. Assoc. 72: 130 - 49
- 87. Halsted, J. A., Ronaghy, H. A., Abadi, P., Haghshnass, M., Amirhakemi, G.

- H., Barakat, R. M., Reinhold, J. G. 1972. Am. J. Med. 53:277-83
- 88. Hambidge, K. M., Silverman, A. 1973. Arch. Dis. Child. 48:567-68
- 89. Hancock, J. 1831. Edinburgh Med. Surg. J. 35:67-73
- 90. Hankin, L., Heichel, G. H., Botsford, R. A. 1973. Clin. Pediatr. 12:654-55
- 91. Harries, J. M., Hughes, T. F. 1957. Proc. Nutr. Soc. 16:20-21
- 92. Harris, L. J., Clay, J., Hargreaves, J., Ward, A. 1933. Proc. R. Soc. Lond. Biol. Sci. 113:161-90
- 93. Henderson, F. F., Gaston, E. A. 1938.
- Arch. Surg. 36:66-95 94. Holden, C. 1979. Science 204:1066-68
- 95. Holt, W. A., Hendricks, C. H. 1969. Obstet. Gynecol. 34:502-4
- 96. Hook, E. B. 1978. Am. J. Clin. Nutr. 31:1355-62
- 97. Hooper, D., Mann, H. H. 1906. Mem. Asiatic Soc. Bengal 1:249-70
- 98. Hubrigkt, J. F. 1562. De Appetitu Depravato Pica Dicto, Altdorff. Cited in Ref. 37
- 99. Hunter, J. M. 1973. Geog. Rev. 63: 170-95
- 100. Imray, J. 1843. Edinburg Med. Surg. J. 59:304-21
- 101. Jacobs, A. 1961. Lancet 2:1331-33
- 102. Jacobziner, H., Raybin, H. W. 1962. Arch Pediatr. 79:72–76
- 103. Johnson, N. E., Tenuta, K. 1979. *Envi*ron. Res. 18:369-76
- 104. Jolly, H. L. 1963. Practitioner 191: 417-25
- 105. Joselow, M. M., Bogden, J. D. 1974. Am. J. Public Health 64:238–40
- 106. Kalisz, K., Ekvall, S., Palmer, S. 1978. Pediatric Nutrition in Developmental Disorders, pp. 150-55. Springfield, IL: Charles C. Thomas
- 107. Kanner, L. 1937. Child Psychiatry, pp. 340-53. Springfield, IL: Charles C. Thomas
- 108. Karayalcin, G., Lanzkowsky, P. 1976. Lancet 2:687
- 109. Keith, L., Brown, E. R., Rosenberg, C. 1970. Perspect. Biol. Med. 13:626-32
- 110. Keith, L., Evenhouse, H., Webster, A. 1968. Obstet. Gynecol. 32:415-18
- 111. Keith, L. G., Rosenberg, C. D., Brown, E. 1969. J. Am. Med. Assoc. 208:535
- 112. Keith, L., Rosenberg, C., Brown, E. Webster, A. 1969. Chicago Med. Sch. Q. 28:109-14
- 113. Keith, L., Rosenberg, C., Brown, E. Webster, A. 1969. Proc. Soc. Exp. Biol. Med. 131:1285-87
- 114. Kennedy, R. S. 1935. Brit. Med. J. 1:1262-64

- 115. Klein, R. 1974. Pediatr. Clin. North Am. 21:277-84
- 116. Klüver, H., Bucy, P. C. 1939. Arch. Neurol. Psychiatr. 42:979-1000
- 117. Koptagel, G., Reimann, F. 1973. Psychother. Psychosom. 22:351-58
- 118. Lackey, C. J. 1978. The Anthropology of Health, pp. 121-29. St. Louis: C. V. Mosby
- 119. Lanzkowsky, P. 1959. Arch. Dis. Child. 34:140-48
- 120. Larson, P. S., Haag, H. B., Silvette, H. 1961. Tobacco-Experimental and Clinical Studies, pp. 491-501. Baltimore: Williams and Wilkins
- 121. Lasch, R. 1898. Mitt. Anthropol. Gesellsch. 28:214-22
- 122. Laufer, B. 1930. Field Mus. Natl. Hist. Publ. 280, Anthropol. Ser. 18:99
- 123. LeConte, J. 1846. Southern Med. Surg. J. 1:417-44
- 124. Ledelius, J. 1668. De Pica. Jenae. Cited in Ref. 37
- 125. Leming, P. D., Reed, D. C., Martelo, O. J. 1981. Ann. Intern. Med. 94:660
- 126. Levander, O. A. 1979. Environ. Health Perspect. 29:115-25
- 127. Lin-Fu, J. S. 1973. N. Engl. J. Med. 289:1229–89
- 128. Lin-Fu, J. S. 1973. N. Engl. J. Med. 289:1289-93
- 129. Livingstone, D. 1870. Last Journals, p. 346. Cited in Ref. 37
- 130. Lourie, R. S., Layman, E. M., Millican, F. K. 1958. Problems of Addiction and Habituation. NY: Grune and Stratton
- 131. Lourie, R. S., Layman, E. M., Millican, F. K. 1963. Children 10:143-46
- 132. Mahaffey, K. R. 1981. Nutr. Rev. 39(10):353-62
- 133. Maravilla, A. M., Berk, R. N. 1978. Am. J. Gastro. 70:94-99
- 134. Marks, J. W. 1973. Ann. Intern. Med. 79:612
- 135. Mason, D. 1833. Edinburgh Med. Surg. *J*. 34:289–96
- 136. Mathieu, J. 1927. Arch. de Med. d. Enf. 30:591-97
- 137. Maxwell, J. 1835. Jamaica Phys. J. 2:416-27
- 138. McCollum, E. V., Orent-Keiles, E., Gay, H. G. 1939. The Newer Knowledge of Nutrition. NY: Macmillan. pp. 577
- 139. McDonald, R., Marshall, S. R. 1964. Pediatrics 34:558-62
- 140. McGanity, W. J., Little, H. M., Fogelman, A., Jennings, L., Calhoun, E., Dawson, E. B. 1969. Am. J. Obstet. Gynecol. 103:773-88
- 141. Medhurst, W. H. 1838. China, Its State and Prospects, p. 38. Cited in Ref. 37

- Mengel, C. E., Carter, W. A. 1964. J. Am. Med. Assoc. 187:955-56
- Mengel, C., Carter, W. A., Horton, E.
 S. 1964. Arch. Intern. Med. 114:470-74
- 144. Merkatz, I. R. 1961. N. Engl. J. Med. 265:1304-6
- Millican, F. K., Layman, E. M., Lourie,
 R. S. Takahashi, L. Y., Dublin, C. C.
 1962. Clin. Proc. Child. Hosp. (Wash.)
 18:207-14
- 146. Millican, F. K., Layman, E. M., Lourie, R. S., Takahashi, L. Y. 1968. J. Am. Acad. Child. Psychiatr. 7:79-107
- 147. Minnich, V., Okçuoglu, A., Tarcon, Y., Arcasoy, A., Cin, S., Yörükoglu, O., Renda, F., Demirag, B. 1968. Am. J. Clin. Nutr. 21:78-86
- Mitchell, D., Laycock, J. D., Stephens,
 W. F. 1977. Am. J. Clin. Nutr. 30:147-50
- Mitchell, D., Wells, C., Hoch, N., Lind, K., Woods, S. C., Mitchell, L. K. 1976. *Physiol. Behav.* 17:691–97
- Mitra, S. C. 1904–7. J. Anthropol. Soc. Bombay 7:284–90
- Mohan, M., Agarwal, K. N., Bhutt, I., Khanduja, P. C. 1968. J. Indian Med. Assoc. 51:16-18
- 152. Moncrieff, A. A., Koumides, O. P., Clayton, B. E., Patrick, A. D., Renwick, A. G. C., Roberts, G. E. 1964. Arch. Dis. Child. 39:1-13
- Moss, J., Nissenblatt, M. J., Inui, T. S. 1974. Ann. Intern. Med. 80:425
- Mooty, J., Ferrand, C. F., Harris, P. 1975. *Pediatrics* 55:636-39
- Murty, T. V., Rao, N. N., Bopardikar,
 K. U. 1976. *Indian Pediatr*. 13:575-76
- 156. Mustacchi, P. 1971. J. Am. Med. Assoc. 218:229-32
- Nawalkha, P. L., Mehta, M. C. 1972.
 J. Assoc. Phys. India 20:339-41
- Neil, J., Horn, T. L., Himmelhoch, J. M. 1977. Dis. Nerv. Syst. 38:724-26
- 159. Neumann, H. H. 1970. *Pediatrics* 46: 441–44
- Nutrition Foundation. 1969. Nutr. Rev. 27:52-54
- 161. Ohara, T., Shibata, F. 1969. *Iryo* 23:1248-55
- Okcuóglu, A., Arcasoy, A., Minnich, V., Tarcon, Y., Cin, S., Yörükoglu, O., Bahtiyar, D., Renda, F. 1966. Am. J. Clin. Nutr. 19:125-31
- Oliver, B. E., O'Gorman, G. 1966. Develop. Med. Child. Neurol. 8:704-6
- O'Brien, W., Arkin, R. M. 1969. Ann. Intern. Med. 70:232
- O'Rourke, D. E., Quinn, J. G., Nicholson, J. O., Gibson, H. H. 1967. *Obstet. Gynecol.* 29:581–84

- Patterson, E. C., Staszak, D. J. 1977. J. Nutr. 107:2020-25
- Perry, M. C. 1977. N. Engl. J. Med. 296:824
- Podboy, J. W., Mallory, W. A. 1977. Ment. Retard. 15:40
- 169. Postell, W. D. 1951. The Health of Slaves on Southern Plantations. Baton Rouge: Louisiana State Univ. Press
- Prasad, A. S., Halsted, J. A., Nadimi, M. 1961. Am. J. Med. 31:532-46
- Prasad, A. S., Miale, A., Farid, Z., Sandstead, H. H., Darby, W. J. 1963. Arch. Intern. Med. 11:407-27
- Pynoos, R. S., Charrow, J., Gribetz, D.
 1978. Am. J. Dis. Child. 132:420-21
- 173. Quarterman, J., Morrison, J. N. 1975. Brit. J. Nutr. 34:351-62
- 174. Reinhold, J. G., Nasr, K., Lahimgarzadeh, A., Hedayati, H. 1973. *Lancet* 1:283-88
- Reynolds, R. D., Binder, H. J., Miller, M. B., Chang, W., Horan, S. 1968. Ann. Int. Med. 69:435-40
- Richter, C. P. 1947. J. Comp. Physiol. Psychol. 40:129-41
- Richter, C. P., Holt, L. E., Barelare, B. 1937. Science 86:354
- 178. Robischon, P. 1971. Nurs. Res. 20:4-16
- 179. Rodgers, W., Rozin, P. 1966. J. Comp. Physiol. Psychol. 61:1-4
- Ronaghy, H. A., Halsted, J. A. 1975.
 Am. J. Clin. Nutr. 28:831-36
- Roselle, H. A. 1970. Arch. Intern. Med. 125:57–61
- 182. Ruddock, J. C. 1924. J. Am. Med. Assoc. 82:1682-84
- 183. Sachs, H. K., Blanksma, L. A., Murray, E. F. 1970. *Pediatrics* 46:389-96
- 184. Sacks, S., Tapia, A., Varela, N., Morales, A. 1971. Rev. Med. De Chile 99: 848-51
- 185. Sage, J. C. 1962. The practice, incidence and effect of starch eating in Negro woman at Temple University Medical Center. PhD thesis. Temple Univ. Med. Sch., Philadelphia
- 186. Say, B., Özsöylu, S., Berkel, I. 1969. Clin. Pediatr. 8:661-68
- Sayar, S. N., Sarlatti, R., Naficy, M. 1975. Acta Med. Iran 18:137-47
- Sayers, G., Lipschitz, D. A., Sayers, M., Seftel, H. C., Bothwell, T. H., Charlton, R. W. 1974. S. A. Med. J. 53:1655-70
- 189. Shrand, H. 1964. Lancet 1:1357-59
- Shrimali, R., Jain, A. M., Bhandari, B. 1971. J. Assoc. Physicians India 19: 285-86
- Silverman, M., Perkins, R. 1966. Ann. Intern. Med. 64:842
- 192. Sinclair, S., Mittal, S. K., Basu, N.,

- Ghai, O. P., Bhide, N. K. 1973. *Indian Pediatr.* 10:13-18
- Six, K. M., Goyer, R. A. 1970. J. Lab. Clin. Med. 76:933-42
- 194. Six, K. M., Goyer, R. A. 1972. J. Lab. Clin. Med. 79:128-36
- Small, A., Muehlbauer, M., Kleinhaus,
 S. 1968. Am. J. Gastroenterol. 50:297–302
- Smith, J. C., Halsted, J. A. 1970. N. Nutr. 100:973-80
- Snowdon, C. T., Sanderson, B. A. 1974.
 Science 183:92-94
- 198. Snowdon, C. T. 1977. Physiol. Behav. 18:885-93
- 199. Sobel, R. 1970. Pediatr. Clin. N. Am. 17:653-85
- Sohler, A., Pfeiffer, C. C. 1977. J. Am. Med. Assoc. 238:936-37
- 201. Solien, N. L. 1954. Fla. Anthropol. 7: 1-9
- 202. Spengler, O. 1851. Wochenschr. Ges. Heilk. Berlin 321-27
- Speirs, J., Jacobson, R. 1976. S. A. Med. Tydskrif. 58:1742
- Stephens, R., Waldron, H. A. 1975.
 Food Cosmet. Toxicol. 13:555-63
- Stephenson, P. E. 1977. J. Am. Diet. Assoc. 71:240-47
- 206. Taggart, N. 1961. Proc. Nutr. Soc. 20: 35-40
- Talkington, K. M., Gant, N. F., Scott, D. E., Pritchard, J. A. 1970. Am. J. Obstet. Gynecol. 108:262-67
- 208. Tayanc, M. M. 1942. Tip Diinyasi 15: 175-77
- 209. Theiler, A., Green, H. H., Dutoit, P. J. 1924. J. Dept. Agri. So. Africa 18:1-47

- Thomas, F. B., Falko, J. M., Zuckerman, K. 1976. Gastroenterology 71: 1028-32
- Thompson, G. J. S. 1913. 17th Intern. Med. Congr. Hist. Med. 23:433. Cited in Ref. 85
- Trew, C. J. 1742. Acta Acad. Nat. Curios. Norimb. 6:458-64
- Underwood, E. J. 1966. The Mineral Nutrition of Livestock. Scotland: The Central Press. pp. 237
- Uretsky, B. F. 1974. Arch. Surg. 109:123
- Verga, A. 1849. Gaz. Med. Lombarda 2:18-20
- Vermeer, D. E. 1966. Assoc. Am. Geog. Ann. 56:197-204
- Vermeer, D. E. 1971. Ethnology 10: 56-72
- Vermeer, D. E., Frate, D. A. 1975. Assoc. Am. Geog. Ann. 65:414-24
- Vermeer, D. E., Frate, D. A. 1979. Am. J. Clin. Nutr. 32:2129–35
- Vessal, K., Ronaghy, H. A., Zarabi, M. 1975. Am. J. Clin. Nutr. 28:1095-98
- 221. Volpato, S. 1848. Gaz. Med. Lombarda 2(1):49-52
- 222. Von Humboldt, A., Bonpland, A. 1821. Personal Narrative of Travels to the Equinoctial Regions of the New Continent During the Years 1799-1804. (Transl. H. M. Williams), London, 5:2. Cited in Ref. 37
- Wiener, G. 1970. Public Health Rep. 85:19-24
- Woods, S. C., Weisinger, R. S. 1970.
 Science 169:1334–36