

The Biocultural Context of Anemia in the Ancient Indus Valley

Nancy C. Lovell

*Department of Anthropology, 13-15 Tory Building, University of Alberta, Edmonton
Alberta T6G 2H4, Canada*

Fax : (403)492-5273 e-mail: Nancy.Lovell@ualberta.ca

KEY WORDS Mohenjo-Daro. Harappa. Harappan Civilization. Malaria. Porotic Hyperostosis. Cribra Orbitalia.

ABSTRACT The Harappan civilization is considered by many scholars to be among the earliest and most developed ancient states, flourishing some 4,000 to 5,000 years ago in the Indus Valley and peripheral areas. At the type site of Harappa, two of 29 crania recovered during excavations of the Harappan Period cemetery reveal cranial lesions indicating chronic anemia. Since no postcranial lesions consistent with the effects of genetic anemias, such as thalassemia or sickle cell anemia, were observed, anemia at Harappa is most likely an acquired iron deficiency. The precise cause is uncertain since the material exhibits low frequencies of skeletal indicators of chronic infection and nutritional deficiency, two contributing factors to the etiology of anemia. The low prevalence of anemia at Harappa may be linked to a good nutritional base in a diverse ecological setting, and to few gastrointestinal and other infections due to high standards of personal hygiene. A higher frequency of anemia at Mohenjo-Daro may be best explained by a genetic anemia because the environmental zone in which Mohenjo-Daro is located supports endemic malaria. These conclusions should be considered tentative, however, due to the small skeletal samples available for analysis from these and other South Asian sites.

INTRODUCTION

Anemia long has been considered a major health problem since there is compelling evidence that anemia impairs growth, delays sexual maturation, affects work performance and exercise capacity, and may lead to irreversible deficits in mental development, such as attention span and conceptual learning (Pollitt, 1987; Scrimshaw, 1991). The relative importance of different factors in its pathogenesis and the relative costs and benefits of iron deficiency, however, are the focus of much debate (see, for e.g., Stuart-Macadam and Kent, 1992). One line of evidence that

may be brought to bear on this debate is the geographic prevalence and patterning of anemia in antiquity, particularly in the context of different cultural and environmental settings. Although the interpretation of anemia lesions in South Asian skeletal samples is hampered by the absence of preserved soft tissues, artistic representations, and texts¹, it is clear that anemia existed in ancient populations and is detectable in archaeological skeletal remains (Ortner and Putschar 1981; Steinbock, 1976; Stuart-Macadam 1987a, b, 1989a). In healthy individuals, a circulating supply of iron in the blood as well as iron stores in the bone marrow, spleen, and liver ensure the transport of oxygen throughout the body. Iron is normally excreted in the urine, feces, and sweat, and is lost in the death of skin cells, and therefore is usually replaced through ingestion of iron in food. If the rate of loss is greater than the rate of replacement, stored iron can be used to maintain the required levels of hemoglobin in the blood stream. In unhealthy individuals, however, the body's iron stores have been depleted and the circulating hemoglobin has been reduced, which stimulates the bone marrow to increase red blood cell production. In the skull, increased red blood cell production leads to expansion of trabecular bone at the expense of the outer table of compact bone, and ultimately to a porous appearance on the parietal bones and orbital roofs that is called "porotic hyperostosis" by palaeopathologists (Angel, 1964; Palkovich, 1987; Stuart-Macadam, 1985). This paper therefore presents data on porotic hyperostosis in ancient populations of South Asia, particularly at Harappa and Mohenjo-Daro in the Indus Valley,

and evaluates the roles of cultural and environmental variables in the etiology of anemia in this part of the world.

Harappa is the type site of the Harappan, or Indus Valley, civilization, which flourished some 4,000 to 5,000 years ago in the Indus River valley of South Asia. The civilization apparently possessed a functionally integrated economy, numerous craft specializations, its own writing system, a system of weights and measures, and a richly symbolic iconography. The subsistence economy was based largely on wheat and barley agriculture, but also included cattle, sheep, and goat husbandry. A large population was settled in a few large urban centres and many villages, all apparently connected in some way to river systems throughout the Indus River drainage and peripheral areas. The sites of Harappa, in the north, and Mohenjo-Daro, in the south, long were considered the "twin capitals" of this cultural phenomenon, although more recent interpretations recognize instead the number and variety of Harappan settlements and their geographic extent, and the lack of concrete evidence for centralized bureaucratic or religious functions at either of these two sites.

SKELETAL MANIFESTATIONS OF ANEMIA

Porotic hyperostosis lesions may range in appearance from scattered fine foramina to linked cribrotic patterns, the latter most commonly seen in the roofs of the orbits and called "cribra orbitalia". Although vault lesions occur in association with orbital lesions in the majority of cases, particularly when severe (Stuart-Macadam, 1989b), there is considerable variability in the patterns and severity of lesions and there is as yet no evidence that the severity of bone lesions is correlated with the severity of clinical anemia. Radiographic features of anemia, such as "hair-on-end" trabeculation of the cranium, are well documented and have demonstrated that externally visible lesions are indicative of anemia (Reynolds, 1965; Stuart-Macadam, 1987a, b). Indeed, macroscopic lesions may provide a more accurate picture of the prevalence of the condition in a skeletal sample since, at most, only 50 to 75 per cent of clinical patients with anemias

show changes that can be seen on x-rays (Stuart-Macadam, 1985).

It has been suggested that porotic hyperostosis lesions indicate childhood episodes of anemia in which the resultant bone lesions did not completely heal (Stuart-Macadam 1985, 1991). Many studies indicate a greater number of subadults than adults with cribra orbitalia, which may mean that for most individuals the lesions had completed healed by adulthood; as well, several studies indicate that orbital lesions are most common from approximately six months of age to perhaps five years, and that the most severe orbital lesions are found in subadults (reviewed in Stuart-Macadam, 1985). In cases of sickle cell anemia, orbital roof thickening is characteristically found to develop in children under the age of four, while in later years changes are more likely to occur in the skull vault. In contrast to these age differences in the frequency of orbital lesions, sex differences in the frequency of cribra orbitalia are either small or not significant (Stuart-Macadam, 1985).

Unfortunately, it is only recently becoming clear that various anemias, including thalassemia, sickle cell anemia, and iron deficiency anemia, have discernibly different patterns of bone lesions (see, for *e.g.*, Hershkovitz et al., 1997). These skeletal changes and mortality patterns are summarized in table 2. According to the clinical literature, the most severe skeletal changes occur in the anemia of thalassemia major, which is characterized by a limited ability to synthesize the beta-chain of the hemoglobin molecule. This syndrome affects mainly central and eastern Mediterranean populations in modern times, as well as those of South and Southeast Asia. Skeletal changes in the disease include extensive tissue hypertrophy in the frontal and facial bones and sinuses, coarse trabeculation of the ribs, hands, feet, and long bones, as well as joint necrosis in the postcrania (Hershkovitz et al., 1997; Ortner and Putschar, 1981), but the most characteristic feature is "hair-on-end" trabeculation of the cranial vault. Growth deformity, due to premature epiphyseal union and the widening of epiphyses and metaphyses, and dental maleruption may occur, the former most pronounced in young children and again at puberty (Laor et al., 1982), and dental malocclusion is not uncommon. Since

there is a very high mortality in infants and children with thalassemia major, it may be difficult to identify the disease in subadults. Diagnosis may be easier in adults, since skeletal alterations tend to persist and adults have a characteristically reduced life span. Heterozygotes show thalassemia minor with little or no clinical manifestations and no skeletal effects. Moderately severe cases, referred to as thalassemia intermedia, may show skeletal lesions but this condition is poorly understood (Ortner and Putschar, 1981; Pearson et al., 1959).

Sickle cell anemia has a slightly different geographic distribution, since the genes responsible for this disease occur throughout tropical Africa and in a very limited distribution in southern Mediterranean populations (Lehmann, 1984). Sickle cell anemia is characterized by an error in the sequence of amino acids on the beta chains of the hemoglobin molecule, and is designated HbS. There are several different genetic variants, or haplotypes, that are responsible for sickle cell anemia and the mutation that gave rise to the sickle cell trait is thought to have originated in at least three separate locations in west and central Africa, with further loci identified in Saudi Arabia and India (Pagnier et al., 1984). More than 20 haplotypes have been discovered in the Old World and may be variations of the three most common.

Individuals who are homozygous for the sickle cell trait suffer from excessive sickling of red blood cells and severe anemia, with a resulting increased demand for red cell production to replace those lost in hemolysis. In addition to skeletal changes that may result from increased marrow activity, the misshapen cells cause blockage of small blood vessels, hampering the transfer of nutrients in the blood, and often leading to the death of bone and other tissue cells. These ischemic infarctions occur most commonly in the hip but also are found in the shoulder and temporomandibular joints (El-Sabbagh and Kamel, 1989). Impaired circulation also may cause leg ulcers, particularly at the ankles, and these can leave skeletal evidence in the form of localized inflammation (periostitis). Premature epiphyseal fusion and distortion of small bones in the hands and feet also are not uncommon (Serjeant, 1974). The first and most noticeable skeletal changes in persons with sickle cell anemia, however, are widening of the diploic space and thinning of the inner and outer tables of the cranium (Hershkovitz, 1997; Moseley, 1974; Ortner and Putschar, 1981); in contrast to skeletal changes in thalassemia, "hair-on-end" trabeculation is not a common finding in clinical cases of sickle cell anemia.

Table 1: Frequencies of porotic hyperostosis in South Asian crania

Cultural Period	Site	Affected individuals			Reference
		n*	N	(%)	
Iron Age	Raigir	3	5	(60)	Kennedy, 1990b
Chalcolithic	Inamgaon	4	22 ¹	(18)	Lukacs and Walimbe, 1986
Harappan	Harappa	2	29	(7)	Lovell, 1997
	Mohenjo-daro	7	40	(18)	Kennedy, 1984b
	Chanhudaro	1	1	(100)	Krogman and Sussman, 1943
Mesolithic	Baghai Khor	1	1	(100)	Kennedy, 1990a
	Sahar Nahar Rai	0	6	0	Kennedy et al., 1986
	Mahadaha	0	30	0	Kennedy et al., 1992
Upper Pleistocene	Beli Iena Kitulgala	1	1	(100)	Kennedy et al., 1986a, 1987

*n = the number of individuals exhibiting porotic hyperostosis;

(%) = the percentage of the observable individuals that exhibit porotic hyperostosis

¹ The total number of burials at Inamgaon was 243, but from the excavation report I have determined that only 22 of these contained cranial remains sufficiently well preserved for observation of evidence of porotic hyperostosis.

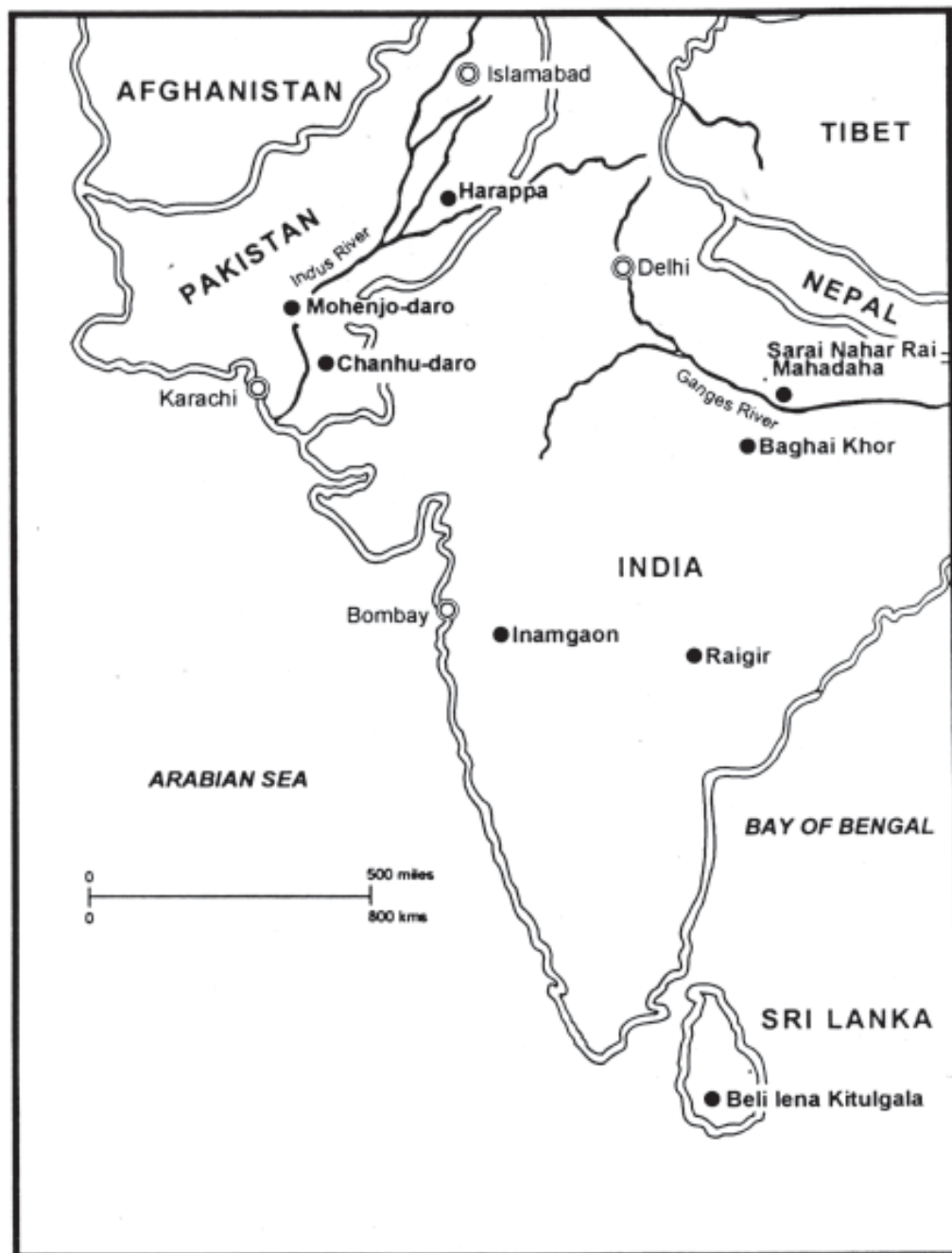


Fig. 1. Map of South Asia, showing the locations of sites referred to in the text

Table 2 : Mortality profiles and skeletal changes commonly associated with acquired and inherited anemias

Type of Anemia	Skull Lesions	Postcranial Lesions
Iron Deficiency Anemia - not usually life-threatening - increased mortality risk due to associated infection	- osteoporosis - diploic space widening - porotic hyperostosis of cranial vault and orbits - possible hypertrophy of facial bones in adults	- coarse trabeculation, especially in infants - thinned cortices - widened medullary spaces - demineralization
Thalassemia major (homozygotes) - high mortality in infants and children - reduced adult life span	- "hair-on-end" trabeculation - calvarial thickening - hypertrophy of frontal and facial bones and sinuses - dental retardation - malocclusion - mandibular infarction	- coarse trabeculation - enlarged nutrient foramina - pathological fractures - widening of metaphyses and epiphyses - premature epiphyseal union and growth deformity
Sickle cell anemia (homozygotes) - reduced life expectancy - usually fatal in children - 50 % risk of maternal death in child birth	- osteoporosis - diploic space widening - delayed pneumatization of all but frontal sinuses - localized calvarial "ballooning" - thinned inner and outer tables - coarse trabeculation in mandible	- coarse trabeculation - thinned cortices - widened medullary spaces - enlarged nutrient foramina - pelvic demineralization and sclerosis - osteomyelitis - periostitis from leg ulcers, especially at ankles - joint necrosis - long bone bowing - biconcave vertebrae ("step" deformity) - distortion of hands and feet, especially in children - posterior iliac surface foramina and disruptions - articular surface lesions on metacarpals

Children with sickle cell anemia are generally underweight, slow to mature, and subject to painful swellings caused by blood vessel blockage. Congestion of the spleen with sickled cells impairs the spleen's usual function of cleaning bacteria from the bloodstream and hence the afflicted child is prone to infection. Without medical care, the average life expectancy of persons afflicted with sickle cell anemia is 20 years. Those who survive past the age of six have much improved survival rates but may have permanent damage to tissues and are predisposed to strokes. Females with sickle cell anemia have a 50% chance of dying in childbirth, even with modern medical care (McElroy and Townsend, 1989). Individuals who carry the sickle cell trait in heterozygous form produce hemolysis and infarctions only under extreme hypoxemic stress (such as strenuous physical activity or conditions of low oxygen density) and therefore typically show no skeletal lesions.

In contrast to the genetic anemias, acquired iron-deficiency anemia does not commonly result in bone changes. When these do occur they are usually mild and localized, such as the porotic lesions and diploic thickening of the cranial vault and orbital roofs. Osteoporosis, thinned cortices, widened medullary spaces, coarse trabeculation, and some facial hypertrophy in adults also have been noted (Ortner and Putschar, 1981).

EVIDENCE FOR ANEMIA IN THE ANCIENT INDUS VALLEY

The analysis reported here is based on published and unpublished data on the prevalence of porotic hyperostosis at eight South Asian sites (Table 1, Fig. 1) and on data obtained from the author's observation of skeletal remains excavated at Harappa in 1987 and 1988 from the Harappan period cemetery, traditionally known as Cemetery R-37. Although the remains of 92 individuals were recovered in those excavations at Harappa, a high water-table and alkaline soils at the site resulted in very poor preservation of some skeletons and consequently only 29 crania could be adequately assessed for the presence of porotic hyperostosis. All crania and cranial fragments were examined visually and with the aid of a 10-power hand lens.

Nearly one-third of the 92 individuals at Harappa displayed pathological lesions, but the most common conditions were arthritis and trauma, as is typical of most archaeological samples. Although porotic hyperostosis was first noted in a Harappan skull by Dutta (1969, cited in Kennedy, 1984b), only two adults in the recently excavated sample exhibit lesions suggestive of anemia: a young female with cribra orbitalia and an adult of unknown sex with ectocranial porosity (Lovell, 1989; 1997). The cranium of this second individual was highly fragmented and diploic expansion could not be confirmed, but the cortical resorption appears to be consistent with a diagnosis of porotic hyperostosis. Only five individuals displayed periosteal lesions, all on the long bones, and all healed or healing. None of the skeletons from Harappa exhibited evidence of specific nutritional deficiencies. Enamel hypoplasia was exhibited by 72 per cent of permanent dentitions, however, providing some evidence for childhood episodes of disease or malnutrition (Lukacs, 1992).

In addition to the data obtained from the skeletal remains excavated at Harappa, Kennedy has obtained data from several hundred individuals from Harappan civilization sites and has identified porotic hyperostosis in 25 per cent of the total sample, occurring predominantly on the frontal and parietal bones (Kennedy, 1982, 1984a). Seven individuals in a sample of 40 (18 per cent) from Mohenjo-Daro display porotic hyperostosis (Kennedy, 1984b) and both children and adults are affected (Kennedy, personal communication). Porotic hyperostosis also was observed on the single, female, skull recovered from Chanhu-Daro (Krogman and Sassman, 1943, cited in Kennedy, 1984a).

Evidence of anemia is very limited outside the Indus Valley cultural and geographic sphere. Possible porotic hyperostosis was observed on the frontal bone of a child from Upper Pleistocene levels (12, 260 $\pm$ 870 b.p.) at the Sri Lankan site of Beli lena Kitulgala, although the etiology of this condition is uncertain (Kennedy et al., 1986b, 1987). A skeleton from the Mesolithic Baghai Khor rockshelter exhibits porotic hyperostosis on the frontal and parietal bones (Kennedy, 1990a), but no lesions were observed

in skeletal samples of six and 30 individuals for the Mesolithic Gangetic sites of Sarai Nahar Rai and Mahadaha, respectively (Kennedy et al., 1986a, 1992). Although the skeletal remains were in some cases extremely fragmentary, vault lesions of porotic hyperostosis were recognized in four of 22 relatively complete adult crania from the Chalcolithic site of Inamgaon, and orbital lesions also were observed in one of a smaller number of individuals with observable orbits (Lukacs and Walimbe, 1986). Three of five crania from Iron Age Raigar display vault lesions of porotic hyperostosis (Kennedy, 1990b).

DISCUSSION

Anemia is caused by one or more of five underlying disturbances: hemorrhage, infection, nutritional deficiency, marrow failure, and excess hemolysis (Bickley, 1980; McKenzie, 1988; Stedman, 1982; Stuart-Macadam, 1991, 1992; Tver and Russell, 1989; Wadsworth, 1992). The inherited disorders, such as those involving hemoglobin defects, are called genetic anemias and are usually the most severe forms of the disease. The other forms of anemia, i.e., the acquired anemias, or iron deficiency anemias, are clinically the most common but tend to have less severe health effects. Since the diagnosis of the probable causes of anemia lesions in the Indus Valley requires an analysis of the relative probabilities of hemorrhage, infection, dietary deficiencies, and genetic anemias in the area, the physical, sociocultural, environmental and documentary evidence for these pathological conditions merit discussion.

Anemia of Hemorrhage

Hemorrhage is the condition in which blood elements, typically red blood cells, are found outside the vascular space. The effects of hemorrhage are negligible unless considerable amounts of blood are lost, and even with acute, serious hemorrhage, such as results from trauma, the body is usually capable of producing normal, replacement, red blood cells and eventually the blood picture returns to normal. With chronic, serious hemorrhage, however, the body is deprived of a significant amount of blood over a protracted period of time. The most common rea-

son for this, other than normal menstrual bleeding, is a lesion of the gastrointestinal tract, typically caused by a parasite, such as hookworm. Since iron is very slowly absorbed, transported, and processed, loss of blood to the outside of the body will lead ultimately to iron deficiency anemia. The amount of stored iron in the body at the time of parasitic infection, however, will influence the development of anemia (Wadsworth, 1992). Thus, individuals with other contributing factors that limit body stores (e.g., pre-existing infections or long-term dietary inadequacy) are more susceptible to anemia development. Young children whose iron stores are not yet at a maximum are at greatest risk.

A variety of intestinal parasitic diseases may contribute to anemia through hemorrhage, including several which are endemic in modern South Asia. These include amebiasis, giardiasis, ascariis, schistosomiasis, and hookworm infection (Abou Gareeb, 1982; Chaudhuri, 1962). The transmission of these intestinal parasites between individuals is usually by the fecal-oral route, and thus is usually related to the nature of settlement, water supply, and waste disposal. Fortunately, there exists sociocultural and environmental evidence pertaining to the transmission of intestinal parasites in the Indus Valley. Impressive features of water supply and waste disposal have been documented at both Mohenjo-Daro and Harappa. Fresh water was supplied by wells made of wedge-shaped bricks, sunk in some cases more than ten metres deep. It has been estimated that the citizens of Mohenjo-Daro constructed one well for each three houses, and it appears that some of their water consumption was related to personal hygiene since bathing platforms, with sloping floors leading to gutters and outlets to the street drain, were installed inside private houses (Jansen, 1989). A latrine was often incorporated in the outside wall of the bathing platforms, and allowed sewage to fall into the street drain or into a cesspit.

Drainpipes are visible in the outside of household walls at Mohenjo-Daro, permitting waste from upper storeys to be channeled into covered drains that ran along one side or down the middle of the streets. The drains were built of fired bricks set in clay mortar, with covers of loose bricks and flagstones, and perhaps also wooden

boards. In spite of the prevalence of fresh water wells and drains in the Indus Valley, recent evidence from Harappa points to a short period of relative urban decay during the mature Harappan phase; the street drains were clogged, permitting sewage to run in the streets, and animal carcasses were left in the street or dumped into abandoned rooms (Kenoyer, 1991). In general, however, there is good evidence for a generally high level of personal, household, and community hygiene in the Indus Valley for most of the Harappan period.

Anemia of Infection

Anemia of infection results when the body reduces the amount of iron available to invading pathogens, thus diminishing their growth. In areas where pathogens such as bacteria, fungi, and parasites are common, iron deficiency is advantageous to the human host but may deteriorate to clinically apparent anemia in poorly nourished or otherwise biologically stressed individuals (Stuart-Macadam, 1992). When combined with the physiological requirements of growth in infancy and early childhood, the demands of infection may outstrip the bioavailable dietary sources of iron, resulting in anemia (Mensforth et al., 1978).

Anemia of chronic infection is one of the most common forms of anemia and in areas where the pathogen load is high it may develop as a result of an overwhelmed iron deficiency adaptive response (Stuart-Macadam, 1992). The pathogen load of any population depends upon a variety of factors in the physical environment, such as climate and geography. Micro-organisms are more viable, for example, in the warm, humid conditions found near the equator, and less viable in the cold, dry conditions of high altitude. Pathogen load also depends upon factors in the social environment, such as population size and density, hygiene, and subsistence. A greater pathogen load is a function of increased sedentism and population density, where infectious agents can be exchanged more easily between people in close contact and where human wastes and other refuse accumulate in and around the settlement. Conversely, proper sanitation and personal hygiene can moderate these effects. In addition to the gastrointestinal parasitic diseases

described in an earlier section, respiratory infectious diseases are the most common diseases associated with increased sedentism and population density.

In spite of the apparent value placed on sanitation in the Indus Valley civilization, the degree of urban development and high population density at Mohenjo-Daro and Harappa would be conventionally interpreted as favourable to the spread of chronic infectious disease. No skeletal evidence of tuberculosis or any similar infection has been identified in Indus Valley samples, however, and frequencies of nonspecific infectious disease, represented by periosteal lesions, are low. Only five individuals in the recently excavated Harappa sample exhibit periostitis (Lovell, n.d.). Since several researchers have observed marked correlations of porotic hyperostosis and periosteal lesions (Palkovich, 1987; Carlson et al., 1974), the parallel low frequencies of porotic hyperostosis and periostitis seem to indicate a generally low pathogen load among the group of people buried in the Harappan cemetery.

Dietary Deficiencies and Anemia

Most marrow failure results from nutritional deficiency and is usually traceable to a shortage of vitamin B12, folic acid, protein, or iron². Vitamin B12 is needed by bone marrow to complete the maturation of red blood cells, and without it the cells are poorly developed and short-lived. Vitamin B12 is obtained primarily from striated muscle tissue, liver, kidneys, fish, milk, and eggs. Plant foods do not supply Vitamin B12 and deficiencies of this nutrient commonly occur in strict vegetarians (Pike and Brown, 1984; Garrison and Somer, 1985; Smith, 1962). Folic acid deficiency is based on a dietary shortage of folic acid or of ascorbic acid (Vitamin C). Ascorbic acid prevents oxidation of folic acid and thus maintains folic acid levels adequate for metabolic needs. Excellent dietary sources of folic acid are liver, kidney, and dark green leafy vegetables, as well as other meats, eggs, and whole grain cereals to a lesser extent. Ascorbic acid sources include fruits and many vegetables. Protein is also essential to red blood cell formation and protein deficiency diseases, such as kwashiorkor, may be linked to anemia. A dietary shortage of iron,

however, is by far the most common of the nutritional causes of anemia.

Shortages of iron intake often can be linked to the relative proportions of animal and plant foods in the diet, since these two food types supply different types of iron. Heme iron is derived from animal sources and is easily absorbed by the body. Nonheme iron, found in plants, is absorbed at only 10 per cent to 25 per cent of the rate of heme iron absorption, although nonheme iron absorption may be enhanced by ingesting plant foods with animal foods. Thus, a reliance on agricultural products, such as grains, may translate into a high degree of iron deficiency anemia in a population. Deficient iron intake also may occur in cultures in which infants are maintained for too long on milk, which is a poor source of iron when compared to liver and other organ meats, red meat, legumes, shellfish, and dark green leafy vegetables. Even with adequate dietary intake, deficiencies can result from impaired absorption of nutrients.

One anemia associated with impaired nutrient absorption is pernicious anemia, an autoimmune anemia. It results from a lack of intrinsic-factor, a glycoprotein, which is normally synthesized in the stomach and which is required for the absorption of Vitamin B12. Pernicious anemia often develops as a consequence of aging, when the production of intrinsic-factor lags, but also results from a hereditary lack of intrinsic-factor. Inadequate absorption of Vitamin B12 also is caused by damage to the lining of the gastrointestinal tract, or by infestation with a fish tapeworm, *Diphyllobothrium spp.*, which consumes a great deal of the vitamin in the intestine. Decreased absorption of iron also results from heavy metal poisoning or phytates in the diet, disorders of the gastrointestinal tract such as chronic diarrhea, or acute or chronic infectious diseases.

Maize dependent diets have been widely cited as the principal instigators of iron-deficiency anemia since they subject infants and children to both iron and protein/calorie deficiencies (El-Najjar, 1976). Maize diets can be ruled out as causative factors of anemia in the Indus Valley, however, since the primary agricultural foodstuffs in this area were wheat and barley, and, later, millets. Maize was unknown in the Old World

until the 16th century AD. The presence of phytates, which inhibit the absorption of dietary iron and other minerals, also is a factor in iron deficiency, however, and is a more plausible culprit in these regions since phytates are found in the bran of cereal grains. The consumption of leavened bread minimizes the problem, since yeast fermentation destroys much of the phytate present in whole meals.

The most common nutritional deficiencies in modern South Asia are those of energy, calcium, and certain vitamins (beta-carotene, B-complex, and ascorbic acid) (Ryan et al., 1984), and these vitamin deficiencies could be linked to anemia by impairing red blood cell development. It is clear, however, that nutritional deficiencies today are the result of inadequate purchasing power and hence food consumption experienced by some segments of the population (Rao, 1982). Such status differentiation in ancient South Asian skeletal samples has yet to be demonstrated archaeologically. Recent analysis of skeletal remains from the urban phase cemetery at Harappa did not reveal evidence of micronutrient deficiencies, although radiographs of long bones documented lines of arrested growth in two of the 12 individuals for which skeletal x-rays were taken (Lovell, 1989; n.d.).

Strict vegetarianism also may be implicated in iron and other nutrient deficiencies, and it has been inferred on religious grounds that the antecedents of classical Hindu culture may be found in a vegetarian Indus Valley Civilization. Vegetarian laws in the Hindu tradition do not appear until much later than Hinduism's proposed links to the Indus Valley, however, and there is no archaeological evidence for vegetarianism in the Indus Valley in the time periods of interest. There is good evidence for an agricultural economy based on wheat and barley as well as use of a variety of fruits and legumes in the Indus Valley (Kajale, 1991), but animal bones from Harappan period levels at a variety of sites in the Indus Valley and peripheral areas indicate that a broad spectrum of faunal resources also were being utilized, with an apparent emphasis on cattle, sheep, goats, and fish (Belcher, 1991; Meadow, 1989, 1991).

A finding similarly suggestive of dietary deficiencies is that of high frequencies of enamel

hypoplasia, which may represent childhood episodes of physiological stress, including malnutrition, at Harappa (Lukacs, 1992) and at Mohenjo-Daro (Kennedy, 1981). Several studies of South Asian skeletal remains have documented evidence of deficiency syndromes, including rickets at Iron Age Adittanalur and Mahujhari (Kennedy, 1984a) and scurvy at Inamgaon (Lukacs and Walimbe, 1986). It is generally agreed that micronutrient deficiency syndromes such as rickets and scurvy rarely occur in populations with access to a diverse range of food items, except where some foods may be culturally restricted or where methods of food preparation reduce a food's nutrient content. Overall underconsumption of food, as in famine, however, usually results in vitamin and mineral deficiencies as well as protein and calorie deficiencies.

A contribution to the lack of skeletal evidence for malnutrition may be the lack of postcranial material in collections of ancient South Asian human remains. This prevents the study of skeletal growth in children as well as the observation of long bone and thoracic deformity caused by rickets. Scurvy may be identified in the skull when it affects the alveolar bone, but this may have been confused with periodontal disease in early reports.

Genetic Anemias

Most genetic anemias are attributed to abnormal hemoglobins, including sickle hemoglobin (HbS) and hemoglobins C, D, and E, and a number of less common forms. As a general rule, HbS and HbC are distributed in Africa and elsewhere in the world among individuals of African ancestry, while HbD and HbE are prevalent in South and Southeast Asia and in those of Asian ancestry. Beta thalassemia is the most common thalassemia, but other variants also exist. These include alpha thalassemia, alpha-beta thalassemia, hereditary persistence of fetal hemoglobin, and the abnormal fusion of the alpha and beta chains of hemoglobin. Both alpha and beta thalassemia occur widely in the Mediterranean area as well as the Middle and Far East. Alpha thalassemia is also commonly found in people of African ancestry. The clinical severity

of all of these abnormal hemoglobins varies considerably and there may be interaction between different forms that occur simultaneously in the same individual (Huntsman, 1987; McKenzie, 1988).

Sickle cell anemia and thalassemia are often thought to underlie the lesions of porotic hyperostosis (Angel, 1966, 1967; Kennedy, 1984b). Angel suggested that infants and children exhibiting porotic cranial and/or orbital lesions were homozygotes for one of the thalassemias or sickle cell anemia and that the adults represent a spectrum of heterozygotes who were variably affected by the disease. Given the serious health consequences of these genetic anemias, they would be eliminated from human gene pools by natural selection were it not for the advantage of their heterozygous expression in endemic malaria regions. The protozoan parasite that causes malaria lives in red blood cells, and the errors in the genetic coding for the hemoglobin molecule that characterize the genetic anemias result in a less favorable environment for the parasite. In the case of sickle cell anemia, an error in the synthesis of the amino acid at the sixth position on the beta chains of the hemoglobin molecule reduce the molecules' oxygen affinity, with the result that they clump together and distort the red blood cell into an irregular or sickled shape. This inhibits the metabolism and reproduction of the malaria parasite in the red blood cell; a normal red blood cell lasts about 120 days, while a red blood cell with normal and abnormal hemoglobin may last only two to three weeks, insufficient time for the parasite to reproduce. Since the sickling trait possessed by heterozygotes is disadvantageous for the parasite, the severity of the infection is reduced and heterozygotes are unlikely to suffer greatly from malaria. Persons homozygous for sickling also resist malaria, but their red cells contain only abnormal hemoglobin, resulting in excessive sickling and severe anemia. Without medical care, homozygotes rarely survive long enough to reproduce.

Thus, one aspect of the argument pertaining to the presence of genetic anemias in the Indus Valley is the evidence, direct or circumstantial, for malaria, particularly the evidence for the

mosquito vector of the disease. Although no mosquito remains have been identified in archaeological contexts in the Indus Valley region, the fossilized remains of several genera of blood-sucking mosquito, including *Anopheles*, document their existence in the Old World for over 60 million years (Capasso, 1991). Mosquitoes lay eggs on the surface of stagnant water, or on the damp mud near the water's edge. Sunlight and warmth are needed during the larval stage of the mosquito life cycle. The adult mosquitoes emerge 12 to 15 days after the eggs were laid, and will be infected with the malaria parasite, *Plasmodium spp.*, if the eggs were laid by an infected female. The parasite will then be passed on to the first human that the mosquito bites: while ingesting human blood, the mosquito injects saliva, which contains malaria protozoa. The malaria protozoa need both mosquitoes and human or other mammalian hosts to survive since they undergo part of their life cycles in each. Some 56 species of anopheline mosquitoes have been identified worldwide. These share similar life cycles and behavior, but have adapted to slightly different environments.

Based on the observed frequency and patterning of porotic hyperostosis in remains from Mohenjo-Daro, it has been argued that the Harappan population possessed an adaptive polymorphism with the capacity to act as a malarial prophylaxis (Kennedy, 1981, 1982, 1984b). Kennedy cited Harappan irrigation practices and the ponding of water following Indus River flooding as being conducive to the formation of breeding places for malaria-bearing mosquitoes, and proposed that endemic malaria may have followed from the commencement of Neolithic technologies of food production in South Asia. Mohenjo-Daro lies now in a semi-arid climate, and the agricultural cycle is traditionally dependent on the annual inundations of the Indus River. Flooding of the Indus results from the melting of glacier ice in the northern mountains and from the monsoon rains, both of which are summer phenomena. Although the antiquity of these is not precisely known for all of the Indian subcontinent, geoarchaeological evidence for Indus flooding is clear, and there are possible descriptions of monsoon rains in the Rig Veda, which may date to earlier than the second millennium

BC (Das, 1988). Although details are contested, much of the greater Indus Valley may have been significantly wetter immediately before and during the Harappan period, perhaps due to increased winter precipitation (reviewed in Meadow, 1989).

Malaria in the Mohenjo-Daro area is dependent presently on the mosquito vector *A. culicifacies*. This mosquito feeds primarily on cattle, but may feed on humans should they be in close proximity or the cattle be unavailable. In urban areas, therefore, the source of food is principally humans, as demonstrated in malaria epidemics in the Pakistani state of Sind, where Mohenjo-Daro is located and where the mosquito breeds in pools of water in river beds, ditches, and village tanks, as well as in irrigation canals (Macdonald, 1957). In the hills and foothill regions, *A. fluviatilis* is the more common malaria vector. It thrives in moving water in streams and rivers, and also occurs in standing water such as irrigated fields. There are two other species of anopheline mosquito which are known to transmit malaria in South Asia, although both have smaller regions of influence than the two main species described above (Macdonald, 1957). The epidemiological characteristics of malaria are dependent upon the seasons, climate, and local availability of breeding grounds for the mosquito (Thakur et al., 1993), but malaria in the Punjab, where Harappa is located, has been characterized as both endemic and epidemic in this century (Macdonald, 1957). Thus, in the absence of major environmental changes during the five thousand years since the occupation of Harappa, there is circumstantial evidence for malaria in this more northerly region as well as at Mohenjo-Daro.

Should this evidence be extrapolatable to Indus Civilization times, the much lower frequency of porotic hyperostosis, if due to genetic anemia, at Harappa compared to Mohenjo-Daro (Table 1) is curious. Physical and social environmental factors, however, may play a role in the discrepancy. For example, the geographic and topographic particulars of the location of Mohenjo-Daro may have made it more susceptible than was Harappa to widespread flooding. The construction of massive platforms in much of Mohenjo-Daro and the extent of the surrounding

alluvium suggest that flooding was indeed pronounced. In addition, there was a presumed larger settlement and greater population density at Mohenjo-Daro. These factors combined suggest that the environmental setting at Mohenjo-Daro may have been more favorable than that at Harappa to malarial disease, with a consequent higher frequency of genetic anemia.

Kennedy also has suggested that sickle cell anemia or thalassemia may have been the primary etiological factor at Mesolithic Baghai Khor. Malaria may have been endemic in the Neolithic communities that became established in this area and may also have affected the hunting-gathering bands that lived in areas peripheral to the cultivated river valleys and plains. The acquisition of abnormal hemoglobins by the Mesolithic peoples would have been by gene flow between the nomadic hunter-gatherers and their settled agricultural neighbors (Kennedy, 1990a).

The interpretation of skeletal lesions in ancient South Asians as resulting from genetic anemia is plausible, given the unquestioned presence of the genetic defect in modern populations (Narahari, 1991; Ramana and Naidu, 1992). The sickle cell gene, in various forms, is present in 5-10 per cent of inhabitants of the subcontinent's central peninsula and in 15-20 per cent of those in southern India (Kennedy, 1984a; Rucknagel, 1966). The identification of the causative disorder, *i.e.*, thalassemia or sickle cell anemia, is difficult, however. Kennedy's reliance on the different anatomical distributions of cranial lesions in different genetic anemia syndromes has not been substantiated in the more recent clinical or paleopathological literature (*e.g.*, Ortner and Putschar, 1981; Stuart-Macadam, 1985, 1987a, 1987b, 1989b, 1992), for example. Further, the pathognomonic postcranial evidence of thalassemia (*e.g.*, HersHKovitz, 1991) is unfortunately lacking in South Asian skeletal series. In many cases this may result from the fact that almost all studies have focused on the crania (Kennedy, 1984b), although excavations at Harappa in 1987 and 1988 produced no examples of postcranial bone lesions resembling those expected in cases of thalassemia major or sickle cell anemia (Lovell, 1989, in prep; Lovell and Kennedy, 1989).

CONCLUSIONS

As is clear from the discussions above, the etiology of anemia is not simple, and is best explained by considering multiple factors in each physical and social context, which leads to the following conclusions. First, circumstantial evidence supports Kennedy's suggestion that anemia lesions in South Asian samples may represent genetic anemias that resulted as an adaptation to endemic malaria, perhaps linked to irrigation practices. Postcranial evidence of genetic anemias will be necessary, however, to confirm this interpretation. The pronounced difference in anemia prevalence at Mohenjo-Daro and Harappa may be due to physical environmental differences related to Indus flooding.

Second, urbanization usually results in high frequencies of infectious diseases that are caused by contaminated water supplies and high population densities, but although there is a possibility that acute infectious diseases related to urbanism existed in the Indus civilization, the attention to personal and public hygiene seems to have minimized the risks of chronic infectious diseases (particularly gastro-intestinal parasitism) that can lead to anemia. The identification of systemic stress indicators, such as enamel hypoplasia and Harris' lines, at Harappa suggest that nutritional or acute infectious disease stresses may be involved but since these are not associated with high frequencies of anemia lesions or periostitis they appear to reflect acute rather than chronic stress. Further, there is presently no reliable evidence for chronic infectious conditions, such as tuberculosis or fungal diseases, in South Asian skeletal samples. Therefore, in spite of the high population density in the Indus Valley civilization, high levels of personal and community hygiene may have minimized potential health risks.

Finally, although nutritional deficiencies have been inadequately studied, overall malnutrition during times of famine or during weaning may have been a contributor to anemia, and impaired absorption of iron due to diarrhea caused by gastrointestinal parasites may have been an additional factor. There is limited skeletal evidence for micronutrient deficiencies, in the form of rickets and scurvy, in South Asia but given the varied dietary items that have been documented,

nutritional deficiencies are not likely to have affected large segments of the populations. Enamel hypoplasia, rickets and scurvy all affect children, and the inadequacy of subadult skeletal samples prevents elaboration of the nature of possible nutritional stress and its relationships to the development of anemia lesions. The paucity of well-preserved postcranial remains from South Asian sites also limits the study of nutritional stress.

ACKNOWLEDGMENTS

The Harappan period cemetery was excavated under the field direction of J. Mark Kenoyer (University of Wisconsin, Madison). Human remains were excavated at Harappa in 1987 and 1988 with Brian E. Hemphill, Kenneth A. R. Kennedy, and John R. Lukacs. Since the death in 1992 of George F. Dales (University of California, Berkeley), the Harappa Archaeological Research Project continues under the co-direction of Richard H. Meadow (Harvard University) and J. Mark Kenoyer (University of Wisconsin, Madison), with Rita P. Wright (New York University) as assistant project director. Funding for this research was provided by the Social Sciences and Humanities Research Council of Canada, the Support for the Advancement of Scholarship Fund (Faculty of Arts) and the Central Research Fund, University of Alberta, and by the University of California (Berkeley) Harappa Project. This paper has benefited greatly from the comments made on a earlier draft by Kenneth A. R. Kennedy, Richard Meadow, and Patty Stuart-Macadam.

NOTES

1. Soft tissue from human remains has unfortunately not survived since the methods of disposal of the dead as well as the burial environment were not conducive to natural mummification practices. Further, although the Indus Civilization had a script, known examples are restricted to seals and sealings of only a few characters and proffered translations of the characters have not yet met with widespread acceptance. It was only much later in South Asia that the system of medicine that was eventually called "Ayur Veda" appeared (Desai, 1989; Keswani, 1974; Kapoor, 1990). This developed from the lore contained in one of the four sacred Sanskrit books, and appeared as two treatises, one on surgery (the Sushruta Samhita) and the other on medicine (the Charaka Samhita), which combine magic and religion with

a scientific approach. Although the dates and original authorship of these literary works is uncertain, it is likely that the medical science exemplified in the early Vedic treatises dates to the first centuries of the second millennium BC (Allchin and Allchin, 1982; Desai, 1989; Keswani, 1974), and thus the Indus Valley civilization itself has no written records by which to identify medical problems of ancient times (in contrast, for example, to the medical papyri of ancient Egypt).

2. Various pharmaceuticals, chemicals, radiation, marrow-displacing conditions (e.g., tumours), and metabolic disorders may suppress red blood cell production and lead to marrow failure, but since these were not factors in the ancient environment, are difficult to ascertain, or tend to be of individual rather than populational significance, they will not be discussed further in this paper.

REFERENCES

- Abou Gareeb, A.H.: Bilharziasis in India, pp 235-236. In: *First International Symposium on Bilharziasis*. Government Printing Office, Cairo (1962).
- Allchin, B., and Allchin R.: *The Rise of Civilization in India and Pakistan*. Cambridge University Press, Cambridge (1982).
- Angel, J.L.: Porotic Hyperostosis, Anemias, Malaras, and the Marshes in Prehistoric Eastern Mediterranean. *Science*, 153: 760-763 (1966).
- Angel, J.L.: Porotic Hyperostosis or Osteoporosis Symmetrica, pp 378-389. In: *Diseases in Antiquity*. D. Brothwell and A.T. Sandison (Eds.). CC Thomas Publishers, Springfield IL (1967).
- Belcher, W.R.: Fish Resources in an Early Urban Context at Harappa, pp 107-120. In: *Harappa Excavations 1986-1990*. R.H. Meadow (Ed.). Monographs in World Archaeology No. 3. Prehistory Press, Madison WI (1991).
- Bickley, H.C.: *Practical Concepts in Human Disease*, 2nd ed. Williams and Wilkins Publishers, Baltimore (1980).
- Capasso, L.: Fossil mosquitoes and the spread of infectious diseases in man's ancestors. *Journal of Paleopathology*, 3: 171-201 (1991).
- Carlson, D., Armelagos, G., and Van Gerven, D.: Factors Influencing the Etiology of Cribra Orbitalia in Prehistoric Nubia. *Journal of Human Evolution*, 3: 405-410 (1974).
- Chaudhuri, R.N.: Bilharziasis in India, pp 131-136. In: *First International Symposium on Bilharziasis*. Government Printing Office, Cairo (1962).
- Das, P.K.: *The Monsoons*. National Book Trust, New Delhi (1988).
- Desai, P.N.: *Health and Medicine in the Hindu Tradition*. Crossroad, New York (1989).
- El-Najjar, M.Y.: Maize, Malaria and the Anemias in the Pre-Columbian New World. *Yearbook of Physical Anthropology*, 20: 329-337 (1976).
- El-Sabbagh, A.M., and Kamel, M.: Avascular Necrosis of Temporomandibular Joint in Sickle Cell Disease. *Clinical Rheumatology*, 8: 393-397 (1989).
- Garrison, R.H., and Somer, E.L.: *The Nutrition Desk Reference*. Keats Publishing, New Canaan, CT (1985).
- Hershkovitz, I., Ring, B., Speirs, M., Galili, E., Kislev, M., Edelson, G., and Hershkovitz, A.: Possible Congenital Hemolytic Anemia in Prehistoric Coastal Inhabitants

- of Israel. *American Journal of Physical Anthropology*, 85: 7-13 (1991).
- Hershkovitz, I., Rothschild, B.M., Latimer, B., Dutour, O., Léonetti, G., Greenwald, C.M., Rothschild, C., and Jellema, L.M.: Recognition of sickle cell anemia in skeletal remains of children. *American Journal of Physical Anthropology*, 104: 213-226 (1997).
- Huntsman, R.G.: *Sickle-cell Anemia and Thalassemia: A Primer for Health Care Professionals*. Canadian Sickle Cell Society, St. John's, NF (1987).
- Jansen, M.: Water Supply and Sewage Disposal at Mohenjodaro. *World Archaeology*, 21: 177-192 (1989).
- Kajale, M.D.: Current Status of Indian Palaeoethnobotany: Introduced and Indigenous Food Plants With a Discussion of the Historical and Evolutionary Development of Indian Agriculture and Agricultural Systems in General, pp 155-189. In: *New Light on Early Farming*. J.E. Renfrew (Ed.). Edinburgh University Press, Edinburgh (1991).
- Kapoor, L.D.: *CRC Handbook of Ayurvedic Medicinal Plants*. CRC Press, Boca Raton FL (1990).
- Kennedy, K.A.R.: Skeletal Biology: When Bones Tell Tales. *Archaeology*, 34: 17-24, 51 (1981).
- Kennedy, K.A.R.: Skulls, Aryans and Flowing Drains: The Interface of Archaeology and Skeletal Biology in the Study of the Harappan Civilization, pp 289-295. In: *Harappan Civilization: A Contemporary Perspective*. G.L. Possehl (Ed.). Aris and Phillips, Warminster (1982).
- Kennedy, K.A.R.: Growth, Nutrition, and Pathology in Changing Paleodemographic Settings in South Asia, pp 169-192. In: *Paleopathology at the Origins of Agriculture*. M.N. Cohen and G.J. Armelagos (Eds.). Academic Press, Orlando (1984a).
- Kennedy, K.A.R.: Trauma and Disease in the Ancient Harappans, pp 425-436. In: *Frontiers of the Indus Civilization*. B.B. Lal and S.P. Gupta (Eds.). Books and Books, New Delhi (1984b).
- Kennedy, K.A.R.: Porotic Hyperostosis on Human Remains from Mesolithic Baghai Khor. *Bulletin of the Deccan College Post-Graduate and Research Institute*, 49: 183-194 (1990a).
- Kennedy, K.A.R.: Skeletons in the Closet: Recent Recovery of Lost Human Remains from Iron Age Raigir, Andhra Pradesh. *South Asian Studies*, 6: 201-226 (1990b).
- Kennedy, K.A.R., Lovell, N.C., and Burrow, C.B.: *Mesolithic Human Remains from the Gangetic Plains: Sarai Nahar Rai*. Occasional Papers and Theses No. 10. Cornell University South Asia Program, Ithaca NY (1986a).
- Kennedy, K.A.R., Disotell, T., Roertgen, W.J., Chiment, J., and Sherry, J.: Biological Anthropology of Upper Pleistocene Hominids from Sri Lanka. *Ancient Ceylon*, 6: 68-168 (1986b).
- Kennedy, K.A.R., Deraniyagala, S.U., Roertgen, W.J., Chiment, J., and Disotell, T.: Upper Pleistocene Fossil Hominids from Sri Lanka. *American Journal of Physical Anthropology*, 72: 441-461 (1987).
- Kennedy, K.A.R., Lukacs, J.R., Pastor, R.F., Johnston, T.L., Lovell, N.C., Pal, J.N., Hemphill, B.E., and Burrow, C.B.: *Human Skeletal Remains from Mahadaha: a Gangetic Mesolithic Site*. Occasional Papers and Theses No. 11. Cornell University: South Asia Program, Ithaca NY (1992).
- Kenoyer, J.M.: Urban Process in the Indus Tradition: A Preliminary Model From Harappa, pp 29-60. In: *Harappa Excavations 1986-1990*. R.H. Meadow (Ed.) Monographs in World Archaeology No. 3. Prehistory Press, Madison WI (1991).
- Keswani, N.H.: Medical Heritage of India, pp 3-49. In: *The Science of Medicine and Physiological Concepts in Ancient and Medieval India*. N.H. Keswani (Ed.). All-India Institute of Medical Sciences, New Delhi (1974).
- Krogman, W.M., and Sassman, W.H.: Skull Found at Chanhudaro, pp 252-264. In: *Chanhudaro Excavations 1935-1936*. J.H. Mackay (Ed.). American Oriental Society, New Haven, CT (1943).
- Laor, E., Garfunkel, A., and Koyumdjisky-Kaye, E.: Skeletal and Dental Retardation in Beta Thalassemia Major. *Human Biology*, 54: 85-92 (1982).
- Lehmann, H.: Sickle cell anemia 35 years ago. *American Journal of Pediatric Hematology/Oncology*, 6: 72-76 (1984).
- Lovell, N.C.: Paleopathology in the Mature Phase of the Indus Valley Civilization. Paper presented at the annual meeting of the American Association for Physical Anthropology, San Diego. *American Journal of Physical Anthropology*, 78: 263-264 (1989).
- Lovell, N.C.: Anaemia in the ancient Indus Valley. *International Journal of Osteoarchaeology*, 7: 115-123 (1997).
- Lovell, N.C.: Lifestyle and Pathology at Harappa. In: *Harappa Human Remains*. R.H. Meadow (Ed.) Manuscript in preparation (n.d.).
- Lovell, N.C., and Kennedy, K.A.R.: Society and Disease in Prehistoric South Asia, pp 89-92. In: *Old Problems and New Perspectives in the Archaeology of South Asia*. J.M. Kenoyer (Ed.). Wisconsin Archaeological Reports, Vol. 2., Madison WI (1989).
- Lukacs, J.R.: Dental paleopathology and agricultural intensification in South Asia: New Evidence from Bronze Age Harappa. *American Journal of Physical Anthropology*, 87: 133-150 (1992).
- Lukacs, J.R., and Walimbe, S.R.: *Excavations at Inamgaon: Vol II: The Physical Anthropology of Human Skeletal Remains. Part I: An Osteobiographical Analysis*. Deccan College Postgraduate and Research Institute, Pune (1986).
- Macdonald, G.: *The Epidemiology and Control of Malaria*. Oxford University Press, London (1957).
- McElroy, A. and Townsend, P.K.: *Medical Anthropology in Ecological Perspective*, 2nd Edition. Westview Press, Boulder CO (1989).
- McKenzie, S.B.: *Textbook of Hematology*. Lea and Febiger, Philadelphia (1988).
- Meadow, R.H.: Continuity and Change in the Agriculture of the Greater Indus Valley: The Palaeoethnobotanical and Zooarchaeological Evidence, pp 61-74. In: *Old Problems and New Perspectives in the Archaeology of South Asia*. J.M. Kenoyer, (Ed.). Wisconsin Archaeological Reports, Vol. 2., Madison WI (1989).
- Meadow, R.W.: Faunal Remains and Urbanism at Harappa, pp 89-106. In: *Harappa Excavations 1986-1990*. R.H. Meadow, (Ed.). Monographs in World Archaeology No. 3. Prehistory Press, Madison WI (1991).
- Mensforth, R., Lovejoy, C., Lallo, H., and Armelagos, G.: The Role of Constitutional Factors, Diet and Infectious Disease in the Etiology of Porotic Hyperostosis and Periosteal Reactions in Prehistoric Infants and Children. *Medical Anthropology*, 2: 1-59 (1978).
- Moseley, J.E.: Skeletal changes in the anemias. *Seminars in Roentgenology*, 9: 169-184 (1974).
- Narahari, S.: Red Cell G-6PD and Sickle Cell Haemoglobin

- Among Four Nomadic Isolates of Andhra Pradesh. *Journal of Human Ecology*, 2: 71-72 (1991).
- Ortner, D.J., and Putschar, W.G.J.: *Identification of Pathological Conditions in Human Skeletal Remains*. Smithsonian Institution Press, Washington (1981).
- Pagnier, J., Baudin, V., Beldjord, C., Nagel, R.L., and Labie, D.: Evidence for the Multicentric Origin of the Sickle Cell Hemoglobin Gene in Africa. *Proceedings of the National Academy of Sciences*, 81: 1771-1773 (1984).
- Palkovich, A.M.: Endemic Disease Patterns in Paleopathology: Porotic hyperostosis. *American Journal of Physical Anthropology*, 74: 527-537 (1987).
- Pearson, H.A., Gerald, P.S., and Diamond, L.K.: Thalassemia Intermedia Due to Interaction of Lepore Trait With Thalassemia Trait. *Journal of Diseases of Children*, 97: 463-472 (1959).
- Pike, R.L., and Brown, M.L.: *Nutrition: An Integrated Approach*, 3rd edition. John Wiley and Sons, New York (1984).
- Pollitt, E.: Effects of Iron Deficiency on Mental Development: Methodological Considerations and Substantive Findings, pp 225-254. In: *Nutritional Anthropology*. F.E. Johnston (Ed.). Alan R. Liss, New York (1987).
- Ramana, G.V., and Naidu, J. M.: Sickle Cell Haemoglobin and G-6PD Deficiency in Manne Dora Tribe of Andhra Pradesh. *Journal of Human Ecology*, 3: 155-156 (1992).
- Rao, V.K.R.V.: *Food, Nutrition and Poverty in India*. Vikas Publishing, New Delhi (1982).
- Reynolds, J.: *The Roentgenological Features of Sickle Cell Disease and Related Hemoglobinopathies*. CC Thomas Publishers, Springfield IL (1965).
- Rucknagel, D.L.: On the Geographical Distribution and Ethnic Origin of Thalassemia. *New Zealand Medical Journal*, 65: 826-832 (1966).
- Ryan, J.G., Bidinger, P.D., Rao, N. P., and Pushpamma, P.: *The Determinants of Individual Diets and Nutritional Status in Six Villages of Southern India*. ICRISAT Research Bulletin No. 7, India (1984).
- Scrimshaw, N.S.: Iron Deficiency. *Scientific American*, 265(4): 46-52 (1991).
- Serjeant, G.R.: *The Clinical Features of Sickle Cell Disease*. North-Holland Publishing Co., Amsterdam (1974).
- Smith, A.D.M.: Veganism: A Clinical Survey with Observations on Vitamin B12 Metabolism. *British Medical Journal*, 1: 1655-1658 (1962).
- Stedman, T.L.: *Stedman's Medical Dictionary*, 24th ed. Williams and Wilkins, Baltimore (1982).
- Steinbock, R.T.: *Paleopathological Diagnosis and Interpretation*. C.C. Thomas, Springfield IL (1976).
- Stuart-Macadam, P.: Porotic Hyperostosis: Representative of a Childhood Condition. *American Journal of Physical Anthropology*, 66: 391-398 (1985).
- Stuart-Macadam, P.: A Radiographic Study of Porotic Hyperostosis. *American Journal of Physical Anthropology*, 74: 511-520 (1987a).
- Stuart-Macadam, P.: Porotic Hyperostosis: New Evidence to Support the Anemia Theory. *American Journal of Physical Anthropology*, 74: 521-526 (1987b).
- Stuart-Macadam, P.: Nutritional Deficiency Diseases: A Survey of Scurvy, Rickets, and Iron-deficiency Anemia, pp 201-222. In: *Reconstruction of Life from the Skeleton*. K.A.R. Kennedy and M.Y. Iscan, (Eds.). Alan R. Liss, New York (1989a).
- Stuart-Macadam, P.: Porotic Hyperostosis: Relationship Between Orbital and Vault Lesions. *American Journal of Physical Anthropology*, 80: 1 87-193 (1989b).
- Stuart-Macadam, P.: Porotic Hyperostosis: Changing Interpretations, pp 36-39. In: *Human Paleopathology: Current Syntheses and Future Options*. D.J. Ortner and A.C. Aufderheide (Eds.) Smithsonian Institution Press, Washington (1991).
- Stuart-Macadam, P.: Porotic Hyperostosis: A New Perspective. *American Journal of Physical Anthropology*, 87: 39-47 (1992).
- Stuart-Macadam, P., and Kent, S. (Eds.): *Diet, Demography and Disease*. Aldine de Gruyter, New York (1992).
- Thakur, A., Verma, I.C., and Menon, P.S.N.: Seroepidemiology of Malaria in Bastar District, Central India. *Journal of Human Ecology*, 4: 125-129 (1993).
- Tver, D.F., and Russell, P.: *The Nutrition and Health Encyclopedia*, 2nd edition. Van Nostrand Reinhold, New York (1989).
- Wadsworth, G.R.: Physiological, Pathological, and Dietary Influences on the Hemoglobin Level, pp 63-104. In: *Diet, Demography, and Disease*. P. Stuart-Macadam and S. Kent (Eds.). Aldine de Gruyter, New York (1992).