ORIGINAL ARTICLE

EARLY CHILDHOOD HEMOGLOBIN LEVEL IS A STRONG PREDICTOR OF HEMOGLOBIN LEVELS DURING LATER CHILDHOOD AMONG LOW-INCOME ALASKA CHILDREN

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ABSTRACT

Objectives. For unknown reasons, Arctic Indigenous children have iron deficiency and anemia prevalences up to 10 times higher than national reference populations. The current study sought to identify the importance of Alaska Native status, residence and hemoglobin (Hb) level at age 10 to 23 months for predicting Hb levels at age 24 to 59 months when controlling for potential confounders.

Study design. Retrospective cohort.

Methods. A birth certificate database was linked to a database containing hemoglobin levels determined through the U.S. Supplemental Nutrition Program for Women, Infants and Children (WIC) among Alaskan children age 10 to 59 months evaluated from 1999–2006.

Results. Of children with a birth certificate matched to WIC data, Alaska Native status and residence in western and northern Alaska were associated strongly with anemia at both ages. Nevertheless, of 5,796 children with Hb levels determined at both ages, the single strongest predictor of Hb level at age 24 to 59 months was Hb level at age 10 to 23 months. The community-level anemia prevalence among children age 10 to 23 months was predictive of community-level anemia prevalence among children age 24 to 59 months.

Conclusions. The early onset of anemia and the strong association between earlier and later Hb levels or anemia at both the individual and community levels suggest a role for prenatal effects that remain until at least age 5 years. This is true particularly of Yupik and Inupiat children, who make up the primary residents of western and northern Alaska.

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Keywords: Alaska, Alaska Native, anemia, iron deficiency, iron deficiency anemia, nutrition
INTRODUCTION

Anemia and specifically iron deficiency anemia have been highly prevalent in Alaska and the Canadian Arctic for at least the past 50 years (1–13), and possibly for much longer (14). Rural and Indigenous Yupik and Inuit children in particular have iron deficiency and anemia prevalence up to 10 times higher than national U.S. and Canadian norms and this disparity persists into later childhood and adulthood (2,3,8,10,11). While most of this anemia occurs in association with iron deficiency, nutritional iron deficiency does not appear to be responsible, as groups with high prevalence have iron intakes that meet or exceed recommended intakes (1,4,5,14–16) and anemia is prevalent as early as 2 months of age (11).

The current study sought to determine risk factors for anemia among Alaskan children age 10 to 23 months and children age 24 to 59 months enrolled in the Special Supplemental Nutrition Program for Women, Infants and Children (WIC), with a focus on the independent contribution of Alaska Native status, rural residence and birth characteristics available on infant birth certificates. Additionally, a study in Chile evaluated predictors of iron and hemoglobin (Hb) status at age 12 months (17) and found that the strongest predictor of iron deficiency and iron deficiency anemia at age 12 months was lower Hb at age 6 months. These data suggested that early iron deficiency might have long-lasting effects on later hematological parameters. The study was limited in that children were not followed at later ages to see if the influence of infant anemia persisted. Based on this earlier study, the current study also determined if infant Hb levels predicted later Hb levels to age 5 years.

MATERIAL AND METHODS

Much of the methodology for the current study has been previously published (2), including descriptions of WIC both nationally (http://www.fns.usda.gov/wic/aboutwic/wicataglance.htm, last accessed March 6, 2008) and in Alaska (http://www.hss.state.ak.us/dpa/programs/nutri/WIC/default.htm, last accessed March 6, 2008). In brief, the income limit for WIC eligibility for a family of 4 in Alaska during 2007 was less than $47,767 annually. Alaska WIC did not provide prenatal vitamins, and no data existed on iron supplementation among pregnant women in Alaska. For women electing not to breastfeed, WIC supplied iron-fortified formula.

Hemoglobin determination

The Alaska WIC program obtained blood for Hb testing during the initial visit for each child enrolled. Infant testing was supposed to begin at age 9 months, but on occasion children received an evaluation as young as age 6 months. Hb levels were determined at community-based WIC clinics using a portable hemoglobinometer (HemoCue). No information was available regarding standardization of machines or the methods used by WIC staff at any particular location. However, all WIC staff received standard training on hemoglobinometer use. Anemia was defined as an Hb level <110 g/L for children under age 2 years and <111 g/L for children age 2 to 4 years (18). Severe anemia was defined as <90 g/L for all children, consistent with Alaska WIC guidelines. Only Hb levels obtained at age 6 to 59 months were included in the study, and only Hb levels from 40 to 169 g/L were considered valid (levels outside this range constituted 0.2% of the total sample).
Analysis

The Alaska Bureau of Vital Statistics linked the WIC database for 1999–2006 to birth certificates based on child name, date of birth and community of residence. All evaluated independent variables were derived from the birth certificate except for residence, Alaska Native status, sex and age, which were derived from the WIC database. WIC assigns race based on the client's (or guardian’s) report, and allows for more than one race per individual. Individuals were placed in the category of Alaska Native if Alaska Native/American Indian was the only identifying race reported; inclusion of children with any mention of Alaska Native/American Indian race would have increased the total size of this group by 3%. Alaska’s Indigenous peoples include several distinct racial groups, including Yupik and Inupiat Eskimos, Athapascan Indians and Aleuts; however, birth certificates did not include this level of detail and consequently Alaska Native was used as a unifying designation of all Alaskan Indigenous peoples.

Residence at the time of the most recently documented Hb level was used for all analyses, as this was the only residence provided in the WIC database. Ninety-six percent of children with rural residence and 97% with non-rural residence from the WIC database were categorized similarly based on the mother’s residence from the birth certificate. Residence was categorized into 3 regional groups. “Rural” encompassed south-western and northern Alaska, populated predominantly by Yupik or Inuit Eskimos, and which contained most of Alaska’s small, rural communities, including all communities previously reported to have high iron deficiency and anemia prevalences. “Urban” encompassed Anchorage (Alaska’s largest city), the adjacent Matanuska-Susitna region in south-central Alaska and interior Alaska, populated by a diverse mix of non-Native and Alaska Native peoples, the latter including Yupik and Inuit Eskimos, Athapascan Indians and Aleuts. “Coastal” areas encompassed the Gulf Coast and south-east Alaska and contained mainly small, rural communities from the Aleutian Islands and south-eastern Alaska that were also a diverse mix of Alaska Native and non-Native populations.

The primary goal of the study was to evaluate risk factors for low Hb level at ages 10 through 23 months, and compare these to risk factors for low Hb level at ages 24 through 59 months. These age groups were determined based on the ages at which the Alaska WIC program determined Hb levels (few levels were determined earlier than age 10 months) and to provide approximately equal representation in each age strata. To achieve this goal, for each outcome a base linear regression model was created that contained Alaska Native status, rural versus non-rural residence and age at Hb determination (the latter because of the observed increase in Hb with age). Birth certificate variables were included if, when added to the base model for either outcome, they were associated with Hb status at the 95% confidence level. Tested birth certificate variables included maternal previous pregnancies, prenatal tobacco use, prenatal alcohol use, marital status, education, age and weight gain; infant birth weight, gestation and sex; Caesarian section delivery; and prenatal care as measured by the Kessner index. Some children had more than one Hb level determined within evaluated age groups. To magnify the effects of age-related risk factors, for ages 10 to 23 months the first valid Hb was used, while for ages 24 to 59 months the last was used.
To identify any association between Hb level at age 10 to 23 months and Hb level at age 24 to 59 months, the former variable was added to the final linear regression model for the latter outcome. The presence of anemia at age 10 to 23 months was associated with Hb testing at age 24 to 59 months. While the strength of this association was high, the magnitude of the effect was small. Among 5,796 children with anemia and 10,247 without it at age 10 to 23 months, 40% versus 35% had a Hb determination at age 24 to 59 months (p<0.001); the mean Hb levels at age 10 to 23 months of those with and without anemia were 116.3 versus 117.5 g/L (p<0.001). Analyses were conducted with SPSS version 13.0 statistical software (SPSS Inc., Chicago, IL).

**Ethical issues**
The current study evaluated 2 linked administrative databases housed within the Alaska Department of Health and Social Services, and was conducted by an employee with legal access to this database for the purpose of developing public health recommendations. No persons were contacted. Consequently, institutional review board approval was neither sought nor obtained.

**RESULTS**
Overall, 27,953 (55%) of the 50,964 children in the WIC database were matched to a birth certificate. Among those who matched to a birth certificate, 46% were Alaska Native children and 26% were rural residents, while among those who did not match 18% were Alaska Native children and 7% were rural residents; these differences likely reflected the lower migration rates among Alaska Native and rural children. Children with and without a match to a birth certificate had anemia prevalences at age 10 to 23 months of 27% and 23%, respectively, versus 17% and 14% at age 24 to 59 months. At age 10 to 23 months, severe anemia occurred in 3.3% of children that matched to a birth certificate and 2.7% that did not; at age 24 to 59 months these values were 0.72% and 0.52%, respectively.

Of the 27,953 children with a valid Hb level that matched to a birth certificate, the mean Hb levels by age group were for 6 to 11 months 116±11.8 g/L (mean±SD, n=3,798), for 12 to 23 months 117±11.4 g/L (n=13,250), for 24 to 35 months 118±11.7 g/L (n=8,562), for 36 to 47 months 120±11.2 g/L (n=120), and for 48 to 59 months 122±11.1 g/L (n=5,851). There were 7,381 (26%) children from rural communities, 13,551 (49%) females, and 12,758 (46%) Alaska Native children.

Of these 27,953 children, 16,043 had a valid Hb at age 10 to 23 months (mean age, 15±3.6 months), 16,894 had a valid Hb at age 24 to 59 months (mean age, 42±10 months), and 5,796 had a valid Hb at both ages. The mean Hb at age 10 to 23 months was 117±11.5 g/L while the mean at age 24 to 59 months was 121±11.3 g/L. Among the 5,796 children with a valid Hb at both ages, the means at ages 10 to 23 and 24 to 59 months were 116±11.8 g/L versus 120±11.4 g/L.

Alaska Native status was associated with an increased risk of anemia at both ages (Table I). This was true even when analysis was stratified by region of residence. Residence in the rural south-west and northern regions increased the risk of anemia for Alaska Native children at both ages, but only at age 24 through 59 months among non-Native children.
Anemia in Alaskan children

Anemia in Alaska’s rural areas was pervasive. Among communities in these areas with at least 20 children tested at both ages, at age 10 to 23 months all but 3 communities had anemia prevalence higher than the average for the remainder of the state, and all but 2 had anemia prevalence higher at age 24 to 59 months (Fig. 1).

Initial linear regression base models that included Alaska Native status and rural residence (while controlling for age at Hb test) (Table II) had $R^2$ values of approximately 0.05. In the full model that included birth certificate variables, the number of previous pregnancies the mother had had was associated with Hb levels at both ages, while prenatal tobacco use was associated with Hb level at age 10 to 23 months and maternal education was associated with Hb level at age 24 to 59 months. Nevertheless, the addition of these variables did not substantially improve the predictive

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**Table 1.** Relative risk of anemia among Alaska Native (AN) versus non-Native (NN) children enrolled in the Supplemental Nutrition Program for Women, Infants and Children (WIC), by age group and region of residence: Alaska, 1999–2006.

| Group analysed | Age 10–23 months (n=16,043) | Age 24–59 months (n=16,894) |
|----------------|-----------------------------|-----------------------------|
|                | AN vs. NN anemia prevalence | AN vs. NN anemia prevalence |
|                | Prevalence ratio (95% CI)    | Prevalence ratio (95% CI)    |
| All residents  | 35% vs. 21%                 | 22% vs. 12%                 |
|                | 1.7 (1.6 to 1.7)            | 1.9 (1.8 to 2.0)            |
| Region of residence |                     |                             |
| Rural          | 41% vs. 23%                 | 25% vs. 20%                 |
|                | 1.8 (1.3 to 2.5)            | 1.3 (0.88 to 1.8)           |
| Coastal        | 27% vs. 21%                 | 18% vs. 13%                 |
|                | 1.3 (1.1 to 1.5)            | 1.4 (1.2 to 1.7)            |
| Urban          | 28% vs. 21%                 | 17% vs. 11%                 |
|                | 1.3 (1.2 to 1.4)            | 1.5 (1.3 to 1.7)            |

*Hb <110 g/L at age <10–23 months and 111 g/L at age 24–59 months

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Figure 1. Anemia prevalences within individual communities by age group, among WIC-enrolled children residing in southwest or northern Alaska, by age group; Alaska, 1999–2006. Only communities with at least 20 data points for each age group were included. For comparison, among WIC-enrolled children residing elsewhere in Alaska, anemia prevalences at ages 10 to 23 and 24 to 59 months were, respectively, 23% and 13%.

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Anemia in Alaska’s rural areas was pervasive. Among communities in these areas with at least 20 children tested at both ages, at age 10 to 23 months all but 3 communities had anemia prevalence higher than the average for the remainder of the state, and all but 2 had anemia prevalence higher at age 24 to 59 months (Fig. 1).

Initial linear regression base models that included Alaska Native status and rural residence (while controlling for age at Hb test) (Table II) had $R^2$ values of approximately 0.05. In the full model that included birth certificate variables, the number of previous pregnancies the mother had had was associated with Hb levels at both ages, while prenatal tobacco use was associated with Hb level at age 10 to 23 months and maternal education was associated with Hb level at age 24 to 59 months. Nevertheless, the addition of these variables did not substantially improve the predictive
value of the model with $R^2$ values, remaining at approximately 0.05. For Hb level at age 24 to 59 months, a last model was created by adding Hb level at age 10 to 23 months as a risk factor (of the 16,043 children with a Hb level at age 10 to 23 months, 5,796 [36%] had a Hb level at age 24 to 59 months and 5,424 had values for all included variables). This model had approximately twice the predictive value of other models ($R^2$, 0.096), indicating that earlier Hb levels were among the most important predictors of Hb levels at later ages.

Table II. Multivariate linear regression analysis of the independent effects of risk factors for hemoglobin (Hb) levels (in g/L) at 2 different ages among Alaskan children enrolled in the Supplemental Nutrition Program for Women, Infants and Children (WIC); Alaska, 1999–2006. Two separate regression models are presented for children age 10 to 23 months, while 3 models are presented for children age 24 to 59 months, as the latter age group includes a final model with Hb level at age 10 to 23 months included as a risk factor.

| Risk factors | Age 10 through 23 months (n=16,043) | Standardized beta | Age 24 through 59 months (n=16,894) | Standardized beta |
|--------------|-----------------------------------|-------------------|-----------------------------------|-------------------|
| **Base model** | | | | |
| Age at test (in months) | 0.13 (0.082 to 0.18) | 0.041 | 0.041 (-0.035 to 0.12) | 0.014 |
| Alaska Native | 1.7 (1.3 to 2.2) | 0.074 | 1.3 (0.86 to 2.4) | 0.090 |
| Rural residence | 4.2 (3.7 to 4.7) | 0.16 | 3.9 (0.86 to 2.4) | 0.16 |
| Model fit: $R^2$ | 0.046 | | 0.045 | |
| **Overall model** | | | | |
| Age at test (in months) | 0.14 (0.088 to 0.19) | 0.044 | 0.040 (-0.039 to 0.12) | 0.013 |
| Alaska Native | 1.7 (1.2 to 2.2) | 0.074 | 1.3 (0.59 to 2.2) | 0.060 |
| Rural residence | 4.2 (3.6 to 4.7) | 0.16 | 3.7 (2.9 to 4.5) | 0.16 |
| Number of previous pregnancies | -0.22 (-0.31 to -0.14) | -0.043 | -0.15 (-0.28 to -0.015) | -0.031 |
| Birth weight <2500 g | -1.2 (2.0 to -0.38) | -0.023 | -1.2 (-2.6 to 0.25) | -0.022 |
| Maternal prenat al tobacco use | -0.52 (-0.94 to -0.10) | -0.021 | 0.31 (-0.37 to 0.98) | 0.103 |
| Caesarian section delivery | -0.048 (-1.0 to 0.08) | -0.013 | -0.73 (-1.7 to 0.24) | -0.020 |
| Mother married | 0.30 (-0.095 to 0.69) | 0.013 | 0.18 (-0.47 to 0.83) | 0.008 |
| Maternal education (in years) | 0.058 (-0.053 to 0.17) | 0.009 | 0.21 (0.018 to 0.41) | 0.030 |
| Female | 0.54 (0.19 to 0.90) | 0.024 | -0.35 (-0.94 to 0.25) | -0.015 |
| Model fit: $R^2$ | 0.050 | | 0.050 | |
| **Overall model with addition of Hb level at age 10 to 23 months** | | | | |
| Hb level at age 10 to 23 months (in g/L) | 0.22 (0.19 to 0.24) | 0.22 | | |
| Age at test (in months) | 0.027 (-0.050 to 0.10) | 0.009 | | |
| Alaska Native | 0.94 (0.16 to 1.7) | 0.041 | | |
| Rural residence | 2.9 (2.1 to 3.7) | 0.12 | | |
| Number of previous pregnancies | -0.11 (-0.24 to 0.024) | -0.022 | | |
| Birth weight <2,500 g | -0.85 (-2.2 to 0.55) | -0.016 | | |
| Maternal prenatal tobacco use | 0.31 (-0.34 to 0.97) | 0.013 | | |
| Caesarian section delivery | -0.49 (-1.4 to 0.46) | -0.013 | | |
| Mother married | 0.12 (-0.52 to 0.75) | 0.005 | | |
| Maternal education (in years) | 0.21 (0.017 to 0.40) | 0.029 | | |
| Female | -0.41 (-0.99 to 0.17) | -0.018 | | |
| Model fit: $R^2$ | 0.097 | | | |

*Of the 16,043 children with a Hb level at age 10–23 months, 5,796 had a Hb level at age 24–59 months, and of these, 5,424 had values for all appropriate variables and were included in the final model.
The correlation between earlier and later Hb levels existed for both Alaska Native and non-Native children; although for the former, the distribution of Hb levels was shifted to the lower end (Fig. 2). In bivariate linear regression models, Hb at age 10 to 23 months predicted Hb at age 24 to 59 months among Alaska Native children (beta, 2.2 [95% CI: 1.9, 2.6]; R², 0.052) to almost the same degree as among non-Native children (beta, 2.3 [95% CI: 2.0, 2.7]; R², 0.059).

This relationship was seen more dramatically at the community level. Among 102 Alaskan communities with at least 20 children tested at both ages, anemia prevalence among children age 10 to 23 months predicted anemia prevalence among children age 24 to 59 months (beta, 0.48 [95% CI: 0.38, 0.58]; R², 0.47) (Fig. 3).

Figure 3. Among Alaskan communities, the correlation between anemia prevalences among WIC-enrolled children age 10 to 23 months and age 24 to 59 months, Alaska, 1999–2006. Only communities with at least 20 data points for each age group were included.
DISCUSSION

The current study and other evidence provide support for a prenatal influence on iron metabolism that persists well into childhood. First, while the current study evaluated anemia, previous studies have documented that anemia among arctic populations occurs primarily in association with iron deficiency, rather than Hb disorders or chronic disease (3–5,7,10–12). Second, consistent with results from the current study, investigators in Chile found that lower Hb at age 6 months was the only consistent predictor of iron deficiency and iron deficiency anemia at age 12 months, and was a more important predictor than dietary iron intake (17). In the current study this effect was similar among both Alaska Native and non-Native children, despite the higher anemia risk among Alaska Native children, and effects were seen at both the individual and community levels. Third, anemia occurs at an early age: at least as early as 10 months in the current study and as early as 2 months in other studies among arctic children (2,11). Fourth, maternal prenatal anemia has been associated with early infancy anemia in other settings (19). Lastly, a study of 7 to 11 year-old Alaska Native children with iron deficiency found extremely high recidivism rates following iron replacement therapy (20).

It could be argued that the above results are consistent with nutritional iron deficiency,
and the strong effect of residence on anemia prevalence may indicate an environmental effect. However, nutritional micronutrient deficiency seems an unlikely primary factor for several reasons. Alaska Native children have substantially higher anemia prevalences than non-Native children, despite high meat content in traditional Alaska Native diets and numerous studies documenting iron intake at least as high among Alaska Native persons as among U.S. reference populations (1,4,5,14–16). While reliance on subsistence diets has declined recently (21,22), high anemia prevalences have been documented among Alaska Native people since at least 1955 (9), and anthropological evidence pushes this date back hundreds of years earlier (10).

During infancy, nutritional iron deficiency may be caused by prolonged breastfeeding or use of iron deficient formulas (11–13) (although other studies dispute this, at least in the U.S. [23]). It is true that breastfeeding prevalence at age 8 weeks in Alaska is relatively high at 70%. However, while anemia risk was substantially lower in urban and non-Native children, using the same categories as in the current paper the lowest breastfeeding prevalences have occurred among urban (61%) and rural (62%) Alaska Native infants (Alaska Pregnancy Risk Assessment Monitoring System, 2005; unpublished data). Moreover, the Alaska WIC program supplies iron fortified formulas to all infants not breastfed. Thus, breastfeeding and formula consumption differences seem unlikely to explain the observed epidemiological patterns.

The common and sustained lack of access to fresh produce in rural Alaskan and other arctic villages make deficiencies of other micronutrients – such as vitamin A, which may act as a cofactor in iron deficiency (1) – a possibility, but this hypothesis requires verification. The young age at presentation and decreasing anemia prevalence with age indicate H. pylori infection is an unlikely etiology during early childhood, and the low ferritin levels documented to occur in association with anemia (3–5,7,10–12) suggest frequent or chronic infections are not responsible. More unusual etiologies such as idiopathic pulmonary hemosiderosis may contribute to iron deficiency and anemia; however, in general there is little evidence that these etiologies are important at a population level.

The precise mechanisms by which prenatal factors might influence iron metabolism for a prolonged period during childhood remain unknown. The in utero fetal environment could affect a postnatal iron set point, and thus maternal iron deficiency (including that related to nutritional vitamin A deficiency [24]) may play an important role. Evolutionarily, this could have occurred as a way of adjusting iron levels to the postnatal infectious disease context, since lower iron levels may be protective against some infections (25). Arguing against this hypothesis are the results from 4 controlled clinical trials (in Niger, Indonesia, Australia and India) that evaluated the effect of prenatal maternal iron on postnatal infant hematological status (26–29). Despite improvements in maternal hematological status during pregnancy, resultant changes in infant status were small or non-existent. None of these studies, though, implemented iron supplementation earlier than 18 weeks gestation, so it remains possible that the first trimester is the critical period. To date, no studies in Alaska have correlated maternal and early infant iron status at an individual level.
A second hypothesis is that genetic influences play a role in iron metabolism (30) even in the absence of clinical syndromes such as haemochromatosis (31). Genetically based differences in iron absorption and metabolism would explain the high prevalence during early infancy, correlation between infant and later childhood anemia, recidivism after iron replacement therapy, high prevalence in the south-west and northern areas of Alaska which are populated by the relatively genetically homogeneous Yupik and Inupiat Eskimos, high prevalence among other Inupiat populations in Canada, and studies documenting the importance of genotype on iron metabolism (30). It is also consistent with the current data showing no influence of residence on anemia prevalence among non-Native children until after age 2 years, when presumably environmental influences begin to have an important role. A corollary of this hypothesis is that results among the Alaska Native population reflect different standards of normal based on the specific historical environmental conditions experienced by this population. No normal values exist for Alaska Native children. Moreover, until it is known if the hematological status experienced by Alaskan subpopulations results in health outcomes, it is unclear how normal values would be defined.

The current study had several substantial limitations. The most problematic was that a defined population was not identified and followed systematically over time. Those children that presented for more than one WIC visit and Hb test may have done so for reasons directly related to hematological status such as known anemia, poor nutrition or persistent socio-economic disadvantage. Nevertheless, over 5,000 children had a Hb level evaluated at both ages and analysis found only a small influence of earlier anemia on later testing. Other limitations existed. The current study was conducted among an economically disadvantaged population that qualified for WIC, and results may not apply to other groups. However, at least in the United States, WIC enrollment did not predict iron deficiency (23). Persons identified as Alaska Native come from several distinct groups with different dietary practices, including those related to subsistence harvests. However, these groups all rely heavily on meat, and meat provides a rich source of bioavailable iron, whether marine or terrestrial. Childhood Hb levels were measured with field-based hemoglobinometers; while these give reliable results when properly maintained and used by trained personnel (32,33), this may not have been the case at all WIC sites.

Indigenous Arctic children have had greatly elevated iron deficiency and iron deficiency anemia prevalences documented for at least 50 years, and archeological evidence suggests the problem predates Western influences. The weight of evidence suggests that most of this anemia is not related to nutritional iron deficiency, *H. pylori* infection, intestinal parasitosis (34) or lead poisoning (35). The current study and previous data suggest that, at least to some extent, prenatal – possibly genetic – factors influence iron levels for years post-natally, and that these factors help explain differences in anemia prevalences between Alaska Native and non-Native children. Four evaluations would assist in differentiating potential mechanisms and thus in designing interventions, including (1) an evaluation of the correlation between maternal and infant
hematological status, followed by a clinical trial of iron supplementation of pregnant women during the first trimester, (2) postnatal iron absorption studies, (3) comprehensive dietary and serological surveys that emphasize the intake and deficiency prevalence of iron absorption cofactors, such as vitamin A, and (4) an evaluation of the clinical effects (if any) of relatively low iron and Hb levels among Alaska Native children.

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Anemia in Alaskan children

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