

Anemia and Elevated Lead Levels in Underimmunized Inner-city Children

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ABSTRACT. *Objective.* Underimmunized children are less frequently screened for anemia and elevated lead levels than those who are up-to-date (UTD). However, the association between underimmunization and actual disease (hemoglobin [Hgb] <11 g/dL or blood lead level [PbB] ≥ 10 $\mu\text{g/dL}$) has not been reported. The objective of this study was to evaluate the association between underimmunization, anemia, and elevated lead levels among children attending an inner-city clinic.

Study Design. Data from a computer-based immunization tracking system were integrated with primary care-based laboratory data. Cross-sectional data for immunization coverage, anemia, and elevated lead levels were evaluated for children who were 1, 2, 3, and 4 years of age. The first Hgb or PbB values obtained within 6 months of the child's birthday were used.

Setting. An inner-city hospital-affiliated pediatric primary care center.

Patients. A child was considered to be a pediatric primary care center patient if he/she had at least 3 immunizations in the immunization tracking system and at least 1 Hgb or PbB screening test during February 1993 through February 1996.

Results. A total of 4045 Hgb tests from 2672 children were available for analysis (1198, 1102, 945, and 800 at 1, 2, 3, and 4 years of age, respectively). Anemia was common during the first 4 years of life (21.2%, 15.8%, 11.0%, and 10.3% at 1, 2, 3, and 4 years of age, respectively). At 2 and 3 years of age, underimmunized children were significantly more likely to be anemic compared with UTD children (relative risk [RR] = 1.49, 95% confidence interval [CI] = 1.24–1.79 at 2 years of age; RR = 1.43, 95% CI = 1.12–1.83 at 3 years of age). Underimmunized children with anemia at 1 year of age were less likely than UTD children to resolve their anemia by 2 years of age (52.5% vs 20.8%, RR = 2.39; 95% CI = 1.47–3.87). Underimmunized children were also significantly more likely to have elevated lead levels at 2 years of age (RR = 1.24; 95% CI = 1.03–1.5).

Conclusion. Underimmunized children in the inner city are at especially high risk for anemia and elevated lead levels. These children need routine preventive health services, as well as immunization. Integrating laboratory screening data with immunization tracking systems would be an important step toward improving the health of inner-city children. *Pediatrics* 1998;101(3). URL: <http://www.pediatrics.org/cgi/content/full/101/3/e6>; *ane-*

mia, iron deficiency, elevated lead levels, immunization, tracking system.

ABBREVIATIONS. UTD, up-to-date; PACC, Pediatric Ambulatory Care Center; BMC, Boston Medical Center; WIC, Women, Infants, and Children (program); Hgb, hemoglobin; PbB, blood lead level; DPT, diphtheria-tetanus-pertussis vaccine; Polio, oral or inactivated polio vaccine; Hib, *Haemophilus influenzae* type b vaccine; HepB, hepatitis B vaccine; MMR, measles-mumps-rubella vaccine; MCV, mean corpuscular volume; IDA, iron deficiency anemia; SD, standard deviation; RR, relative risk; CI, confidence interval.

Immunization is cost-effective and prevents serious morbidity and mortality in childhood.^{1,2} However, underimmunization continues to be a problem in the United States, especially among inner-city children.^{3–6} In addition to the risk of vaccine-preventable diseases, underimmunized children are also at risk for decreased screening for iron deficiency, lead poisoning, and tuberculosis.^{7,8} These children also have fewer preventive maintenance and illness visits, as well as more missed preventive care appointments than children who are up-to-date (UTD) on their immunizations.⁷

Iron deficiency and elevated lead levels are also common among urban children and have the potential for long-term morbidity. Iron deficiency is associated with lower cognitive function and behavioral problems.^{9–11} Anemia is a late manifestation of iron deficiency and is frequently used as an indication for iron therapy. Most anemia in inner-city children is due to iron deficiency.¹² Elevated lead levels have been associated with decreased IQ, impaired attention and speech performance, increased school failure, hyperactivity, and disturbed social behavior.^{13–15} Early detection and treatment of both of these conditions is important.

Although underimmunized children are under-screened for anemia and elevated lead levels, whether they are at higher risk for actual disease is unknown. The purpose of this study was to evaluate the association between immunization status, anemia, and elevated lead levels in children attending an inner-city pediatric clinic.

METHODS

Data were collected for children attending the Pediatric Ambulatory Care Center (PACC) at the Boston Medical Center (BMC, formerly Boston City Hospital) between the years 1992 through 1996. BMC has over 16 000 pediatric primary care visits annually. The families of the children attending the clinic are primarily poor

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and from minority ethnic groups. In 1996, 55% of families received health insurance through Medicaid or other public assistance agencies, 32% did not have any health insurance, and 10% had private health insurance. Sixty-eight percent of the families defined themselves as African-American, 15% as Hispanic, 6% as white, 3% were from other ethnic groups, and 8% were from unspecified ethnic groups.

Most BMC-PACC patients are enrolled in the Women, Infants, and Children (WIC) program and children receive recommended hemoglobin (Hgb) and blood lead level (PbB) screening according to WIC guidelines. Children enrolled in WIC are required to undergo Hgb testing at least once a year for the first 3 years of life, or every 6 months after an abnormal result. Many BMC patients receive screening tests for WIC at BMC. However, some patients receive WIC screening outside BMC. These children's results were not available for this study.

Data Sources

The Immunization Database was created in 1993 as part of the City of Boston Immunization Action Plan. Initial chart review was performed for all children who were <8 years old in 1993. Data were then updated daily from clinic billing sheets by an immunization coordinator. Immunization status was evaluated using the American Academy of Pediatrics recommended schedule.¹⁶ Children were considered fully immunized (UTD) at 12 months of age if they had received 3 doses of diphtheria-tetanus-pertussis vaccine (DPT), 2 doses of either oral or inactivated polio vaccine (Polio), 3 doses of *Haemophilus influenzae* type b vaccine (Hib), and 3 doses of hepatitis B vaccine (HepB). Children were considered UTD at 24 to 48 months of age if they had received 4 doses of DPT, 3 doses of Polio, 4 doses of Hib (1 dose of Hib if given on or after 15 months of age), 1 dose of measles-mumps-rubella (MMR), and 3 doses of HepB vaccine. Immunization status was determined on each child's first, second, third, and fourth birthday. All children who were identified as not fully immunized (underimmunized) had a review of their medical record for confirmation of immunization status.

The Laboratory Database was created from all Hgb, mean corpuscular volume (MCV), and PbB sent for any children <7 years old attending BMC during 1993 through 1996. The first Hgb or PbB value obtained within 6 months of the child's birthday was used for study analysis. Hgb and PbB levels were evaluated near each child's first (the 1-year-old group), second (the 2-year-old group), third (the 3-year-old group), and fourth (the 4-year-old group) birthday. All laboratory specimens were venous samples obtained by a licensed phlebotomist. Hgb and MCV specimens were analyzed on a Sysmex NE-8000 (Long Grove, IL). Only laboratory values for samples sent from primary care-related areas were included in the analysis.

A child was considered to be a patient of the clinic and included in the study if he/she had at least 3 immunizations in the immunization database and was 12 to 48 months old during 1992 through 1996. A child was considered to have moderate anemia if Hgb was <10.5 g/dL, mild anemia if Hgb was 10.5 to <11.0 g/dL, and no anemia if Hgb was ≥11 g/dL. Anemia was considered to be very likely iron deficiency anemia (IDA) if MCV was <75fL and Hgb was <11 g/dL. A child was considered to have mildly elevated lead levels if PbB was ≥10 to <15 μg/dL, moderately elevated lead levels if PbB was 15 to <25 μg/dL, and severely elevated lead levels if PbB was ≥25 μg/dL.

Statistical Analysis

Statistical significance testing was performed using Yates corrected χ^2 test for comparison of categorical data and the *t* test for

comparison of continuous data. Differences were considered statistically significant for $P < .05$.

RESULTS

Immunization Status

A total of 2672 children had at least 1 Hgb or 1 PbB during the study period. At 1 year of age, 62.1% of these children were UTD compared with 65% at 2 years of age (Table 1). At 1 year of age, 19.7% more children would have been UTD if HepB vaccine were excluded. However, only 6.5% more children would have been UTD at 2 years of age with exclusion of HepB. By 3 and 4 years of age, this difference was even smaller (5.7% and 2.9%, respectively). The proportion of UTD children did not increase substantially with increasing age.

To evaluate immunization trends among children continuously enrolled at the BMC-PACC, we compared the proportion of UTD children in the group of children who had a screening Hgb at both 1 and 3 years of age. In this group, 240 children had a screening test at both ages. The proportion of UTD children (including HepB) in this group was 62.9%, 68.3%, and 77.1% at 1, 2, and 3 years, respectively.

Anemia

A total of 4045 Hgb tests were available for the 2672 study children. In the 1-year-old group there were 1198 children who met the study criteria (at least 1 Hgb at 6–18-month-old and at least 3 immunizations recorded). In the 2-year-old, 3-year-old, and 4-year-old groups there were 1102, 945, and 800 children, respectively, who met the study criteria.

Anemia was common in the study population (Fig 1). In the 1-year-old group there were 140 (11.7%) children who had mild anemia and 114 (9.5%) who had moderate anemia. In the 2-year-old group, 72 (6.5%) of the children had mild anemia and 102 (9.3%) of the children had moderate anemia. In the 3-year-old group, 33 (3.5%) of the children had moderate anemia and 71 (7.5%) of the children had mild anemia. In the 4-year-old group, 31 (3.9%) of the children had moderate anemia and 51 (6.4%) of the children had mild anemia.

Prevalence of anemia was compared between children who were UTD and those who were underimmunized (Table 2). In the 1-year-old group, underimmunized children were more likely to be anemic compared with UTD children. However, this difference did not reach statistical significance. In the 2-year-old group, underimmunized children were significantly more likely to be anemic compared with UTD children. Underimmunized children in the

TABLE 1. Percent of Children* With Recommended Immunization by Age

Age Group	DPT	OPV	Hib	MMR	HepB	Overall	
						w/o HepB	w/HepB
1 y (n = 1367)	86.3	93.3	88.8	—	69.2	81.8	62.1
2 y (n = 1289)	80.5	86.2	85.8	91.7	85.8	71.5	65.0
3 y (n = 1159)	86.1	89.8	84.8	93.4	89.7	74.4	68.7
4 y (n = 997)	85.2	88.8	81.0	92.8	95.0	70.8	67.9

* Study children had received at least 1 Hgb or PbB during each time period.

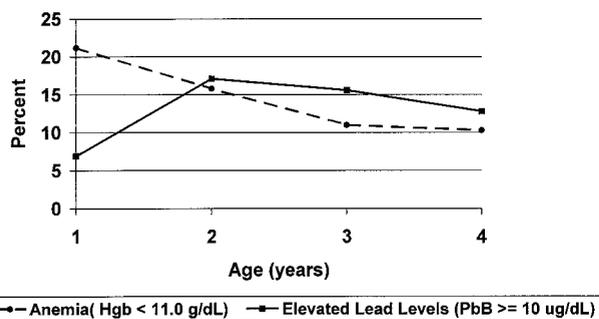


Fig 1. Percent of children with anemia or elevated lead levels by age.

TABLE 2. Prevalence of Anemia by Age and Immunization Status

Age Group	Hgb <11.0 g/dL		RR (95% CI)
	UTD	Underimmunized	
1 y	187 (20.1)	67 (24.9)	1.23 (0.97–1.57)
2 y	91 (12.6)	83 (21.8)	1.49 (1.24–1.79)
3 y	60 (9.2)	44 (15.0)	1.43 (1.12–1.83)
4 y	56 (10.3)	26 (10.2)	1.00 (0.71–1.40)

3-year-old group were less likely than underimmunized children in the 2 year-old group to be anemic, however, these children were significantly more likely than UTD children of similar age to be anemic. By 4 years of age, anemia was much less common and the prevalence of anemia in UTD and underimmunized children was nearly identical.

In the 1-year-old group, mean Hgb was similar in UTD (Hgb = 11.64 g/dL, standard deviation [SD] = 0.92) and underimmunized (Hgb = 11.60 g/dL, SD = 0.95) children ($P = .51$). In the 2-year-old group, mean Hgb for UTD children was 11.90 g/dL (SD = 0.89) and 11.66 g/dL (SD = 1.02) for underimmunized children ($P = .003$). In the 3-year-old group, mean Hgb for UTD children was 11.97 g/dL (SD = 0.87) and 11.89 g/dL (SD = 0.95) for underimmunized children ($P = .08$). In the 4-year-old group, mean Hgb for UTD children was 12.03 g/dL (SD = 0.89) and 12.01 g/dL (SD = 0.92) for underimmunized children ($P = .52$).

In all age groups, the mean age (in months) of testing was significantly ($P < .05$) higher for the underimmunized group compared with the UTD group. Mean ages for UTD and underimmunized children in the 1-, 2-, 3-, and 4-year-old groups were 11.2 and 11.7 months, 22.9 and 23.2 months, 34.7 and 35.6 months, and 46.7 and 47.5 months, respectively. Mean age differences for all groups were <1 month.

MCV has been shown to be a sensitive, although not very specific, measure for IDA. The prevalence of likely IDA (Hgb <11 g/dL, MCV <75 fL) was compared between UTD and underimmunized children. At 2 years of age, 57/380 (15.0%) of underimmunized children were likely IDA compared with 48/722 (6.7%) of UTD children (relative risk [RR] = 1.68; 95% confidence interval [CI] = 1.47–2.29). At 3 years of age, 18/293 (6.1%) of underimmunized children were likely IDA compared with 27/652 (4.1%) of UTD children (RR = 1.48; 95% CI = 0.83–2.65). At 4

years of age, 9/254 (3.5%) of underimmunized children were likely IDA compared with 28/546 (5.1%) of UTD (RR = 0.69; 95% CI = 0.33–1.44).

Severity of anemia was compared between UTD and underimmunized children. In the 2-year-old group, 37/380 (9.73%) children in the underimmunized group had moderate anemia compared with 35/722 (4.85%) children in the UTD group (RR = 2.01; 95% CI = 1.29–3.13). In the 1-, 3-, and 4-year-old groups, RR of moderate anemia was similar to that seen for any anemia; however, the results did not reach statistical significance.

Anemic children in the 1-year-old group were also less likely to resolve their anemia by 2 years of age if they were underimmunized at 2 years of age. In the 1-year-old group a total of 254 children were anemic. Of these children, 117 (46.1%) had a Hgb test in the 2-year-old group also. Anemia was still present in 21/40 (52.5%) underimmunized children compared with 17/77 (20.8%) of UTD children (RR = 2.39; 95% CI = 1.47–3.87).

Elevated Lead Levels

A total of 4403 PbB tests were available for the 2672 study children. In the 1-year-old group there were 1244 children who met the study criteria. In the 2-, 3-, and 4-year-old groups, there were 1190, 1089, and 897 children, respectively, who met the study criteria.

Elevated lead levels were common among children in this study (Fig 1). In the 1 year-old group, 58 (4.7%) children had mildly elevated lead levels, 23 (1.9%) had moderately elevated lead levels, and 5 (0.4%) had severely elevated lead levels. In the 2-year-old group, 142 (11.9%) children had mildly elevated lead levels, 51 (4.3%) had moderately elevated lead levels, and 11 (0.9%) had severely elevated lead levels. In the 3-year-old group, 129 (11.9%) children had mildly elevated lead levels, 43 (4.0%) had moderately elevated lead levels, and 3 (0.3%) had severely elevated lead levels. In the 4-year-old group, 83 (9.3%) children had mildly elevated lead levels, 31 (3.5%) had moderately elevated lead levels, and 1 (0.1%) had severely elevated lead levels.

Prevalence of elevated lead levels was compared between children who were UTD and those who were underimmunized (Table 3). In the 1-year-old group, underimmunized children were slightly more likely to be have elevated lead levels compared with UTD children, however, the difference was not statistically significant. In the 2-year-old group, underimmunized children were significantly more likely to have elevated lead levels compared with UTD

TABLE 3. Prevalence of Elevated Lead Levels by Age and Immunization Status

Age Group	PbB $\geq 10 \mu\text{g/dL}$		RR (95% CI)
	UTD	Underimmunized	
1 y	61 (6.3)	25 (9.1)	1.35 (0.95–1.91)
2 y	120 (15.4)	84 (20.4)	1.24 (1.03–1.50)
3 y	111 (14.7)	56 (16.7)	1.10 (0.87–1.40)
4 y	78 (12.6)	37 (13.2)	1.04 (0.78–1.38)

children. Children in the 3-year-old group were slightly less likely than children in the 1- and 2-year-old groups to have elevated lead levels, and differences in PbB levels were not significantly different between UTD and underimmunized children. By 4 years of age, elevated lead levels were less common and a similar proportion of UTD and underimmunized children had elevated lead levels.

In all age groups, the mean age of lead testing was significantly higher for the underimmunized group compared with the UTD group. Mean ages for UTD and underimmunized children in the 1-, 2-, 3-, and 4-year-old groups were 11.5 and 11.9 months, 22.9 and 23.8 months, 34.9 and 35.6 months, and 46.9 and 47.5 months, respectively. Mean age differences for all groups were <1 month.

DISCUSSION

These findings confirm that underimmunized inner-city children are at risk for more than just vaccine-preventable diseases. These children are more likely than UTD children to be anemic and to have elevated lead levels. Underimmunized children are also more likely to have more severe anemia and less likely to resolve anemia, once present. We are unaware of any other data that links underimmunization with health outcomes other than vaccine-preventable diseases. Anemia and elevated lead levels are both associated with long-term morbidity.

IDA continues to be a major problem for inner-city children. The problem has been well-described and iron therapy has proven efficacy, yet the problem persists. Several factors may explain the increase in anemia seen in underimmunized children. Underimmunization may be a marker for children more likely to have a diet containing inadequate amounts of iron. Underimmunized children may also live in families for whom screening is performed for WIC but contact with primary care providers is sporadic. Underimmunized children may also live in families who are difficult to contact after abnormal lab testing due to frequent address changes and a lack of a telephone. Finally, compliance with iron therapy may also be lower among these children. More studies are needed to determine which of these factors is responsible for the observed differences.

The children in this study also had persistently elevated lead levels throughout the first 4 years of life. Underimmunized children were more likely to have elevated lead levels throughout the first 3 years of life, although differences were only significant at 2 years of age. We hypothesize that factors contributing to elevated lead levels (ie, age of building, lack of ownership of housing) may be different than those contributing to iron deficiency, although still associated with factors leading to underimmunization.

Immunization levels in the population studied were similar to levels reported elsewhere. These levels are likely higher than in the overall population because these children had all received a screening test for either Hgb or PbB. Surprisingly, immunization levels for this population did not improve substantially after the second year of life. This may have

been due to the dynamic nature of the population attending this inner-city primary care center. Poor patients and families move frequently within a city as well as between cities and countries. New patients are common. Each study group was a cross-sectional sample and temporal trends do not reflect immunization trends in continuously enrolled patients. Patients with continuous enrollment as suggested by two separate lab tests 2 years apart were more likely than the overall group to be UTD at 2 years of age (68.3% vs 65%) and substantially more likely to be UTD by 3 years of age (77.5% vs 67.9%). Nonetheless, even in continuously enrolled patients immunization rates were well below the levels of the *Healthy People 2000* objectives (90% of children fully immunized by 2 years of age).

The findings from this study are limited by several factors. First, the study samples are cross-sectional and do not reflect health status measures of continuously enrolled patients. Furthermore, each cross-sectional sample includes values from multiple years. Second, the etiology of anemia (ie, hemoglobinopathies, α -thalassemia) is unknown. However, the prevalence of anemia decreased from 21.2% to 10.3% between the ages of 1 and 4 years of age, suggesting that at least half of anemia in infancy is from a reversible etiology such as IDA. Furthermore, because genetic causes of anemia are not likely to disproportionately affect immunization status, the presence of non-IDA anemia, if present, would bias toward the null. Finally, it is possible that children with a history of anemia would be oversampled at older ages, which could overestimate the prevalence of anemia at older ages. We chose to use the first laboratory value by each year period to minimize this problem.

The effort to increase immunization rates in this country is laudable, and for the most part has been successful. However, tracking systems offer new opportunities to improve the health of children beyond immunization. Substantial resources are being directed toward automated immunization tracking and outreach during a time when, fortunately, vaccine-preventable diseases are rare. Current tracking systems are successfully being used to identify children who are underimmunized and to recall these children for missing immunization. We need not settle for these modest goals. We are experimenting with adding the results of vision and hearing to the tracking system as well as computer-generated prescriptions for children with IDA.

Linking immunization tracking data to other data will lead to a better understanding of the epidemiology of pediatric primary care conditions and offers the potential to improve health outcomes. Routinely integrating laboratory screening data into immunization tracking systems is now possible and should form a cornerstone of pediatric information systems for inner-city primary care populations.

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