Guidelines for the Identification and Management of Pregnant Women with Elevated Lead Levels in New York City

Recommendations from a Peer Review Panel

Convened by:

The New York City Department of Health and Mental Hygiene
Lead Poisoning Prevention Program

And

The Mount Sinai Center for Children's Health and the Environment

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I. COMMONLY USED ABBREVIATIONS

ACOG	American College of Obstetrics and Gynecology
BLL	Blood Lead Level
CDC	Centers for Disease Control and Prevention
DOHMH	New York City Department of Health and Mental Hygiene
LPPP	Lead Poisoning Prevention Program
PIH	Pregnancy Induced Hypertension
PROM	Premature Rupture of Membranes
SGA	Small for Gestational Age
UCLL	Umbilical Cord Blood Lead Level

II. EXECUTIVE SUMMARY:

1. Introduction:

Abundant scientific evidence accumulated over the past four decades indicates that lead in a child's body can adversely affect the developing brain. The consequences seen in children are loss of intelligence, shortening of attention span and disruption of behavior. This damage can occur at blood lead levels (BLLs) less than 10 μg/dL, concentrations previously thought to be safe. Lead freely crosses the placenta from the maternal to the fetal circulation, and elevated blood lead levels during pregnancy can affect the development of the infant. In addition to cognitive and developmental delays in the offspring, elevated BLLs in pregnant women are associated with spontaneous abortion, premature birth and pregnancy-induced hypertension.

In New York City (NYC), exposure to lead in pregnant women and their offspring has not been fully described as a public health problem. Pediatricians, obstetricians and public health authorities have not systematically evaluated the scope of maternal lead exposure or the effectiveness of current approaches to screening and intervention. It is estimated that between 0.5% and 2% of women giving birth in the United States today have Blood Lead Levels (BLLs) greater than or equal to (≥) 10 μg/dL, the Centers for Disese Control and Prevention's level of concern for children. In 2003, of the 36,319 tests reported on adult women of all ages in NYC, the Department of Health and Mental Hygiene's (DOHMH) Lead Poisoning Prevention Program (LPPP) identified 199 women with BLLs 10-19 μg/dL and 43 women with a BLL ≥ 20 μg/dL. Of the 43 women with a BLL ≥ 20 μg/dL, 31 were pregnant. Extensive screening of BLLs in pregnant women

has not been undertaken and the proportion of pregnant women that are tested each year is unknown. Thus, pregnant women may go undetected with elevations of lead in blood at levels potentially harmful for the fetus.

The health effects of lead can be seen in both pregnant women and their children. Lead exposure plays a role in the epidemiology of spontaneous abortion and hypertension in women. The offspring of lead exposed women may be born prematurely or manifest deficits in growth and development. There is increasing evidence that the adverse effects on neurodevelopment occur at BLLs < 10 μg/dL in children and accumulating evidence that this may apply to fetal exposure. Additionally, the unborn fetus can accumulate a body burden of lead that they carry with them into infancy. It is unclear to what extent this contributes to the epidemiology of childhood lead poisoning.

Prevention of lead poisoning in pregnant women and their offspring has been a growing area of concern for the New York City Department of Health and Mental Hygiene's Lead Poisoning Prevention Program. For several years, the DOHMH has been providing services for lead-poisoned pregnant women. In response to the lack of available guidance on the identification and management of pregnant women with elevated BLLs, the DOHMH engaged the Mount Sinai School of Medicine's Center for Children's Health and the Environment to convene a panel of experts to develop evidence-based recommendations on lead poisoning and pregnancy for health care providers. The panel also was charged with assessing the current services provided for lead-poisoned pregnant women by the DOHMH and making recommendations for areas of further development.

This report summarizes the findings and provides recommendations from this collaborative effort. The report is organized around six Charge Questions. Each response addresses the current practice or knowledge of the LPPP and the scientific community, the evidence from an extensive review of the literature, the experience of the LPPP and the expert panelists and the recommendations of the expert panel. A complete report of supporting information follows the executive summary. Please refer to the main text of the document for references. This text is meant to be a living document that may be refined in response to new scientific information and changing needs in New York City.

2. Summary of Charge Question Responses, Literature Review and Recommendations:

#1. Which pregnant women need to be tested for lead poisoning?

- **1.a. What subgroups of pregnant and lactating women are at greatest risk of lead poisoning?**
    - Current understanding of the risk factors for elevated BLLs in New York City women is limited by the lack of a prevalence study, particularly in high-risk communities.
    - The literature, as well as experience in New York City, indicates that women born outside of the United States are at highest risk for elevated BLLs in pregnancy and indicates further that women with severely elevated BLLs (≥ 45 µg/dL) are likely to engage in pica behavior.
    - No population-based assessment of BLLs in foreign-born versus native-born women and no epidemiological assessment of the prevalence of pica among pregnant women in New York City has, thus far, been undertaken.

Recommendations

The expert panel recommends a systematic population-based assessment of BLLs in suspected high-risk groups of pregnant women in New York City.

The panel recommends further that this epidemiological assessment be coupled with an in-depth assessment of the risk factors for elevated BLLs in these high-risk groups.

The expert panel recommends that the LPPP continue to investigate and track pregnant women with elevated BLLs in New York City.

#2. What, if any, questions should be asked by medical providers of all pregnant women to determine whether they are at risk and need testing?

- Current law in New York State requires that prenatal health care providers assess each pregnant woman for "high-dose" lead exposure at the initial prenatal visit using a questionnaire-based risk assessment tool.
- The literature suggests that the following risk factors are highly associated with elevated BLLs in pregnant women:
    - Pica – especially dirt or soil, clay, crushed pottery (Tierra) and paint chips.
    - Use of lead-glazed ceramics.
    - Consumption of imported spices or foods.
    - Folk remedies and cosmetics – see appendix D
    - Country of origin and number of years in the United States.
    - Home Renovations – recent, ongoing or planned especially in older housing.
    - Occupational Exposures – See Appendix E

- Certain Hobbies – See Appendix E

Additional factors that have been associated with BLLs higher than the general population of pregnant women include:

- Alcohol consumption
- Cigarette smoking
- No history of breast feeding
- General Poor Nutrition
  - Low Calcium Intake
  - Iron deficiency anemia

Recommendations

The expert panel recommends that prenatal health care providers consider the possibility of lead exposure in every pregnant woman in New York City, as is required by New York State Law (Part 65-1.5, effective December 22, 1993).

To standardize the clinical assessment of possible maternal exposure to lead, the panel recommends that providers ask all pregnant woman questions at the initial visit to ascertain exposure and obtain a BLL if they:

- ***Were born outside of the United States,***
- ***Engage in pica behavior,***
- ***Use imported spices, foods, cosmetics, ceramics or folk remedies,***
- ***Live in a home where there are any recent or ongoing renovations,***
- ***Work in an occupation which places them at risk for lead exposure.***

#3. What is the current evidence on the health effects of various degrees of overexposure to lead in pregnant women, lactating women, fetuses and neonates?

- **3.a. What are the signs or symptoms of lead poisoning in pregnant women?**
  - The signs and symptoms of acute lead toxicity in adults arise typically only at BLLs ≥ 60 µg/dL. Adults with highly elevated BLLs may complain of headaches, crampy abdominal pain, anorexia, constipation, fatigue, malaise, myalgias and arthralgias.
  - The literature records cases where these symptoms have occurred at much lower BLLs (≥ 25 µg/dL) when the exposure is chronic.
  - It is important to note that in the great majority of adult cases, no symptoms are associated with elevations in BLLs. In such circumstances toxicity can still occur, and there may still be sufficient lead in the maternal circulation to cross the placenta and cause fetal brain damage. *Presence or absence of symptoms is not a reliable guide to the presence or absence of exposure to lead or of an elevated BLL.*

- **3.b. What is the relationship between BLLs and pregnancy-induced hypertension (PIH)?**

    - The literature suggests that high-dose exposure to lead (BLL ≥ 40 µg/dL) is associated with increases in blood pressure and with PIH. This same relationship may hold true at lower BLLs, even < 10 µg/dL, especially if the exposure is chronic.
    - The expert panel concluded that an association between maternal BLL, blood pressure and PIH does exist.
    - The panel concluded that it is uncertain whether the increases in blood pressure due to lead exposure at the levels currently seen in New York City are sufficiently large to be clinically significant.

- **3.c. What is the clinical impact on spontaneous abortion of elevated maternal BLLs?**

    - It has been recognized for decades that lead exposure at high levels is associated with an increased incidence of spontaneous abortion. Lead was used historically as an abortifacient.
    - One recent study found a significantly increased risk of spontaneous abortion at BLLs as low as 5 µg/dL in a chronically exposed population.
    - The literature provides evidence that the risk of spontaneous abortion increases with increasing BLLs.
    - The panel concluded that the risk of spontaneous abortion is probably directly related to the BLL of pregnant women at lower BLLs.

- **3.d. What is the clinical impact on birth weight of *in utero* exposure to lead?**

    - The literature has shown an inverse relationship between bone lead and birth weight. Even though bone lead and blood lead are related, studies that used BLL alone or placental lead levels did not demonstrate an inverse relationship with birth weight.
    - The expert panel concluded that the evidence that lead exposure is associated with a decrease in birth weight is mixed and a single BLL cannot be used to measure risk.
    - The panel concluded that although it is likely that decreases in birth weight are not clinically significant at maternal BLLs < 20 µg/dL, the scientific evidence is limited.

- **3.e. What is the clinical impact on preterm birth of *in utero* exposure to lead?**

    - The expert panel concluded that the evidence is limited, but does suggest a relationship between lead exposure and increased rates of preterm birth.
    - More recent studies support an association between preterm birth **(**gestational age < 37 weeks**)** and exposure to lead, even at BLLs < 10 µg/dL. Studies that measure placental lead, support this finding.

- **3.f. What is the clinical impact on other pregnancy outcomes of *in utero* exposure to lead?**

    - The literature suggests, though not consistently, that lead increases the risk of premature rupture of membranes (PROM).
    - The literature suggests that there is no association between lead exposure and Apgar Scores, rates of small for gestational age (SGA) births or birth defects.
    - The literature suggests that lead exposure *in utero* is associated with a decrease in head circumference.

- **3.g. What is the clinical impact on neurodevelopment and behavior of *in utero* exposure to lead?**

    - The literature clearly demonstrates a correlation between *childhood* exposure to lead and decrements in **central neurological function, including diminished intelligence, shortened attention span, slowed reaction time and antisocial behavior**. The literature on *prenatal* exposure to lead demonstrates similar, albeit not as conclusive evidence.
    - Recent data suggest that the greatest decrements in IQ per unit increase in BLL in children occur at the lowest BLLs. This same relationship has been recently demonstrated for prenatal exposure.
    - The expert panel stressed that the fetus is susceptible to the toxic effects of lead on the central nervous system and that these effects may be lifelong.
    - The panel concluded that *in utero* exposure to lead is associated with decrements in neurocognitive and behavioral function. These effects have been seen at BLLs < 10 µg/dL, the CDC's current level of concern for children (a similar standard for pregnant women does not exist).

#4. At what maternal blood lead level should education and other interventions be provided to pregnant women? What should be the content of this intervention?

- **4.a. By the New York City LPPP?**

    - The current practice of the LPPP is to provide proactive educational and investigative intervention and encourage follow-up testing to any pregnant woman found to have a BLL ≥ 20 µg/dL on a single occasion.

- Whenever BLLs of 10-19 µg/dL are encountered, the LPPP mails educational material to the pregnant woman and her health care provider.
- LPPP is currently developing a plan to provide proactive educational and investigative intervention and follow-up testing to any pregnant woman found to have a BLL ≥ 15 µg/dL on even a single occasion.

Recommendations

The expert panel concurs with the LPPP's evolving plan to provide proactive educational and investigative intervention to any pregnant woman found to have a BLL ≥ 15 µg/dL on even a single occasion. This action is justified by the short duration of pregnancy and the susceptibility of the fetal brain to injury similar to children.

The expert panel recommends that the LPPP collaborate with prenatal health care providers and their professional organizations, such as ACOG, to create handouts to be given to all pregnant women.

- **4.b. By Health Care Providers?**

  - The current required practice of health care providers caring for pregnant women is to provide each pregnant woman anticipatory guidance on lead poisoning prevention during pregnancy. This is consistent with the "New York State Lead Poisoning Screening Requirements for Pregnant Women" (New York State Law Part 65-1.5, effective December 22, 1993). How frequently such guidance and education are actually given to pregnant women by their providers is unknown.
  - The current required practice of prenatal health care providers is to provide each pregnant woman, who has a confirmed BLL ≥ 10 µg/dL of whole blood, risk reduction counseling in accordance with guidelines recommended by the State Commissioner of Health.
  - The current required practice of prenatal health care providers is to provide anticipatory guidance to each woman at her postpartum visit on the prevention of childhood lead poisoning.
  - The literature suggests a number of educational messages about lead that should be provided to all pregnant women. These include a comprehensive list of possible sources of exposure to lead, nutritional advice, especially in regard to calcium and iron supplementation, and ways in which women can identify and reduce their exposure.
  - The literature suggests that maternal BLLs greater than 5 µg/dL are unusual and may be associated with identifiable exposures. Childhood BLLs in this range have been associated with adverse neurodevelopmental health outcomes. Although the evidence is limited, prenatal exposure at this level appears to have similar effects.

Recommendations

The expert panel agreed that an educational message concerning the hazards of lead exposure during pregnancy be provided by health care providers to all pregnant women in New York City and that it should include discussion of lead sources, proper nutrition and exposure prevention.

The panel recommends that prenatal health care providers attempt to identify the source of lead exposure by interviewing the pregnant woman and provide counseling on source reduction if her BLL is found to be ≥ 5 µg/dL. Based on the results of this investigation, the health care provider's message should focus on the likely source of the lead poisoning. The key message to convey is exposure reduction.

The panel was of the opinion that the current New York State brochure, "If You're Pregnant, Get Ahead Of Lead" (Publication Number 2511), provides a good foundation for the education of pregnant women, but recommended that the brochure be expanded to include discussion of more recently recognized exposure sources such as pica, use of imported pottery, and use of imported herbs, spices and remedies. The panel also recommended that this brochure be printed in multiple languages.

The expert panel recommends that the LPPP identify organizations for partnership. This may include existing agencies that provide services to high-risk populations of pregnant women within NYC, such as WIC, to create systematic screening for lead exposure risks and ensure universal distribution of educational materials.

Since clinics that deal mainly with patients receiving Medicaid benefits undergo regular audits and these groups are often at higher risk for lead exposure the LPPP should explore partnering with program such as the Prenatal Care Assistance Program (PCAP)/Medicaid program to improve the ways in which these clinics screen for lead exposure during pregnancy.

The expert panel recommends that a checklist for assessing lead exposure risk be incorporated into the forms used for all prenatal care visits. This will promote compliance with NYS law, improve the detection and identification of women at risk and focus risk reduction messages to individual pregnant women.

The panel expressed the view that additional consultation with cultural anthropologists and the formation of focus groups is recommended to explore how to optimally and appropriately communicate the risk of adverse neurodevelopmental effects of lead in various communities and to develop strategies for primary prevention.

- **4.c. What is the role of health care providers in coordinating environmental risk assessment and intervention with the LPPP for women found to have elevated BLLs?**

- The current role of the health care provider in documenting BLLs and in coordinating environmental risk assessment and intervention is dependent upon the individual provider's degree of knowledge.
- Prenatal health care providers are rarely trained in how to perform an exposure history.
- The LPPP is actively engaged in the education of health care providers on issues of lead poisoning in children.
- The LPPP supervises and coordinates the investigation, treatment and referral of the pregnant woman and other household members when her BLL is ≥ 20 µg/dL.

Recommendations

The expert panel recommends that prenatal health care providers document the results of either a risk factor questionnaire or a blood lead level for every pregnant woman in New York City.

The expert panel stated that any woman found by questionnaire to be at risk for lead exposure should have a blood lead level measured as soon as possible.

The expert panel stated further that it is the responsibility of prenatal health care providers to attempt to identify potential sources of lead exposure in a pregnant woman with a BLL ≥ 15 µg/dL by interview.

Consultation with an expert in the management of pregnant women with elevated lead levels (such as those listed in appendix O) is recommended when the BLL is ≥ 15 µg/dL.

The expert panel recommends that environmental risk assessment and intervention for pregnant women with BLLs ≥ 15 µg/dL should be a coordinated effort involving both health care providers and the LPPP.

- **4.d. What nutritional counseling should be provided to lead-poisoned pregnant and lactating women? Specifically, what are the benefits of calcium and iron supplementation?**

    - Health care providers currently recommend that pregnant women with elevated BLLs increase their intake of calcium and iron.
    - The literature indicates that, in general, poor nutrition can result in increased lead absorption.
    - The literature suggests that calcium may decrease gastrointestinal absorption of lead and that it may also reduce bone resorption during pregnancy. If bone resorption is reduced, release of lead from bone stores is diminished.
    - The current Adequate Intake of Calcium for women aged 19 to 50 years is 1000 mg/day. This value does not change with pregnancy status.

- Prenatal health care providers usually prescribe a prenatal multivitamin that contains 200-400 mg of Calcium. Dietary sources, dairy products in particular, supply the remainder.
- The literature suggests that iron deficiency anemia potentiates the adverse effects of lead and that iron supplementation would reduce this effect.
- The current practice is to start iron supplementation in pregnant women with iron deficiency anemia.
- The literature shows that a relationship exists between Vitamin C and BLLs in adults and children. It does not demonstrate causality. Therefore it is unclear whether Vitamin C supplementation provides a beneficial effect.

Recommendations

The expert panel emphasized counseling all pregnant women on good nutrition as part of routine prenatal care. It is important that this counseling emphasize that good nutrition is beneficial in cases of lead poisoning; however, it is not a substitute for exposure reduction.

The expert panel recommends that calcium supplementation be reinforced in pregnant women with elevated BLLs. The current recommended amount of calcium supplementation for pregnant and lactating women is summarized below. Dietary and supplemental sources of calcium are listed in the appendices J and K.

The expert panel recommends that the importance of iron supplementation be reinforced in the presence of a BLL ≥ 5 µg/dL in iron deficient pregnant women.

The Current Dietary Reference Intake (DRI) Values for Calcium	
Life Stage Group	**Adequate Intake (mg/day)**
Pregnancy	
≤18 years	1,300
19 through 50 years	1,000
Lactation	
≤18 years	1,300
19 through 50 years	1,000

Estimated Average Requirement (EAR) and Recommended Dietary Allowance (RDA) of Iron for Pregnant and Lactating Women	
Life Stage	**(mg/day)**
EAR for Pregnancy	
14-18 years	23
19-50 years	22
RDA for Pregnancy	
14-50 years	27
EAR for Lactation	
14-18 years	7
19-50 years	6.5
RDA for Lactation	
14-18 years	10
19-50 years	9

The expert panel concluded that further investigation is required before Vitamin C supplementation can be recommended for the purpose of limiting fetal exposure to lead

- **4.e. What should be the frequency of re-testing for BLLs in pregnant and lactating women and in neonates?**

  - **Pregnant and lactating women**
    - Currently, standardized guidelines for the frequency of re-testing BLLs by health care providers do not exist.
    - The LPPP's most current proposed protocol is based on the maternal BLL;
      - ≥ 20 µg/dL, repeat BLL monthly,
      - 10-19 µg/dL, repeat BLL every two months.
    - The literature does not adequately address the issue of re-testing or the physiological mechanisms that would help to determine the frequency of re-testing in pregnant and lactating women.
    - The current practice of the LPPP is to recommend a Free Erythrocyte Protoporphyrin level on all pregnant women with elevated BLLs.

- The literature suggests that protoporphyrin levels are helpful in differentiating between chronic and acute exposure. Many other conditions can cause alterations in protoporphyrin levels, such as iron deficiency anemia.

Recommendations

The expert panel recommends, mainly from clinical experience, that the frequency of re-testing be based upon the pregnant woman's initial BLL, chronicity of exposure, risk factors for continued, repeat or future exposure, and possible clinical interventions.

For the recommended schedule of follow-up testing refer to Appendix M, Table 2.

Certain risk factors for exposure, especially pica, may also warrant increased follow-up or counseling, regardless of the patient's blood lead level.

The expert panel recommends that protoporphyrin levels be considered when the BLL is ≥ 25 µg/dL to help differentiate between an acute and a chronic exposure in the absence of iron deficiency anemia.

- **Infants less than 6 months of age**

  - The LPPP's most current proposed protocol is to contact health care providers one month prior to expected delivery date to remind them to obtain maternal and cord blood lead test for mother and infant after delivery.
  - The literature provides anecdotal evidence that cord BLLs aid in the management of neonates born to lead poisoned mothers. Umbilical cord BLLs (UCLL) correlate closely with maternal BLLs.

Recommendation

The expert panel recommends that, since they are highly correlated, either a maternal BLL or an UCLL be obtained at the time of delivery when the mother's BLL has been ≥ 15 µg/dL at any time during pregnancy. Follow-up of this level by the pediatric health care provider is critical.

- **4.f. When should chelation be provided for pregnant and lactating women and for the neonate?**

  - The current practices of health care providers regarding chelation of pregnant and lactating women are not standardized, but instead are based on consultant recommendations and their own clinical experiences.
  - Based on animal studies, all of the chelating agents mentioned below have the potential to be teratogens.

- The literature contains anecdotal evidence describing instances in which pregnant women in their 3rd or late 2nd trimester of pregnancy and neonates less than 28 days of age were chelated without grossly obvious adverse effects. The most commonly used agent was Calcium Disodium Edetate ($CaNa_2EDTA$). Other agents used were British Anti-Lewisite in Oil (BAL in Oil or Dimercaprol) and Dimercaptosuccinic Acid (DMSA or Succimer).
- The US FDA classifies these medications as pregnancy risk category C. (Animal studies have shown that the drug exerts teratogenic or embryocidal effects, and there are no adequate, well-controlled studies in pregnant women.)

Recommendation

The expert panel recommends that when the maternal BLL are ≥ 45 µg/dL in the late 2nd or 3rd trimester, consideration be given to chelation in order to reduce the body lead burden of the mother. Chelation should always be undertaken with great caution in consultation with an experienced specialist (see appendix O) and the patient should be hospitalized. The agent with which there is the most clinical experience is $CaNa_2EDTA$. Chelation prior to the late 2nd or 3rd trimester is strongly discouraged and should be reserved for life threatening intoxications.

- **4.g. What postpartum hospital discharge plans should be recommended?**

  - The current recommended practice of obstetrical health care providers is to follow-up the mother as per the guidelines for lead poisoned adults. The neonate is treated as per the guidelines for childhood lead poisoning.
  - The literature has demonstrated that maternal BLLs correlate very closely with umbilical and neonatal BLLs.
  - According to the literature, lead exposure accounts for a very small amount of variance in cognitive ability (1-4%), whereas social and parenting factors account for 40% or more.

Recommendations

The expert panel recommends that the frequency of follow-up blood lead testing of the newborn (0-6 months of age) exposed in utero be based on the CDC recommended schedule for children. This is done in conjunction with anticipatory guidance and distribution of educational materials.

For the recommended schedule of follow-up testing in the newborn refer to appendix M, table 3.

The expert panel recommends re-testing of the mother 1 month postpartum with follow-up testing as dictated by the results of that BLL measurement.

The expert panel urges prenatal health care providers to contact the pediatric health care provider responsible for the follow-up of the neonate to coordinate care when the maternal or umbilical cord blood lead levels are elevated.

The expert panel recommends that pediatricians caring for prenatally exposed infants offer the parents guidance on ways to provide an intellectually nourishing environment to the child. In cases, where this may be difficult, referral to available services such as Early Intervention or Head Start may be warranted.

- **4.h. What is the recommendation on breastfeeding by women with elevated BLLs?**
  - The literature on the levels of lead in breast milk is limited and conflicting, but one important study showed a close relationship between BLL and milk LL when the mother's BLL was ≥ 40 µg/dL.
  - The current recommendation of the Academy of Breastfeeding is to stop breastfeeding when the mother's BLL ≥ 40 µg/dL.

Recommendations

The expert panel recognizes that the benefits of breastfeeding greatly outweigh the risks of lead poisoning when the mother's BLL is < 40 µg/dL.

Although there is some evidence indicating that it is safe to continue breastfeeding at BLLs ≥ 40 µg/dL, the recommendation of the expert panel is to temporarily stop breastfeeding in such cases until a repeat BLL is obtained and is found to be < 40 µg/dL. All efforts should be made to maintain the mother's milk supply during this time.

For the recommended actions at different BLLs refer to appendix M, table 1.

#5. What are the appropriate LPPP intervention activities for pregnant women with various degrees of elevation of BLLs (e.g., 10-19 µg/dL, ≥ 20 µg/dL), including environmental assessment of the home and risk reduction for pregnant women and other family members?

- **5.a. What type of environmental risk assessment of paint and non-paint lead hazards (e.g., pica, pottery, food sources, traditional remedies, cosmetics, etc) is appropriate at different BLLs?**
  - The LPPP currently provides case management to any pregnant woman with a BLL ≥ 20 µg/dL. Case management includes:
    - Assessment to identify potential sources of lead exposure with information obtained through an interview.
    - Recommendations for eliminating or reducing lead exposure

- Consultations with the women's medical providers to ensure follow-up BLL monitoring for the women and postnatal testing of their babies
- As of August 2004, the NYC DOHMH LPPP has provided case management of any pregnant women with a venous BLL of ≥ 15 µg/dL. This includes a plan to provide proactive educational and investigative intervention.

- When BLLs of 10-19 µg/dL are encountered, the DOHMH Adult Lead Program mails educational material to the pregnant woman and her health care provider.
- The literature indicates that there exists an extensive list of the possible sources of lead (see above, appendices D and E and the text of the supporting documents). Women presenting to the clinic with any elevation of their BLL should have a comprehensive history taken of their exposure to lead.
  - According to case reports, severe lead poisoning (BLL ≥ 45 µg/dL) in pregnant women seems to be more likely to occur because of intentional pica ("Tierra," soil or paint chips). Home renovations, folk remedies, retained bullets; occupational exposure and the use of crushed boned meal are additional sources of severe lead poisoning.
  - Anecdotal reports of pregnant women with BLLs ≥ 20 µg/dL identified many of the same sources as mentioned above adding the use of imported spices and lead-glazed ceramics to the list.

Recommendations

The expert panel recommends that the investigation start with an interview of the pregnant woman with a BLL ≥ 15 µg/dL, followed by a home and/or workplace investigation with direct observation. Lead-based paint risk assessment should be done in the home by a certified risk assessor to address issues of primary prevention of lead poisoning in the newborn.

The expert panel advises that investigators always be alert for new, previously unidentified sources of lead exposure for pregnant women.

For recommended actions at different BLLs refer to appendix M, table 1.

#6. What interventions should be recommended by LPPP to eliminate or reduce sources of lead? When should lead-based paint hazard reduction be recommended? How should cultural practices among cultural and immigrant groups (e.g., pica, use of pottery, consumption of foods or consumption of supplements) be addressed in a culturally competent way?

- The LPPP addresses both the primary and secondary prevention of lead poisoning in pregnant women.
- Primary prevention includes, but is not limited to, the development and distribution of educational materials and handouts, distribution of materials to the health care providers and pregnant women, dissemination of information on newly discovered sources of lead in the community and identification of the major sources in New York City.
- Primary prevention of lead exposure from lead-based paint hazards, if present, includes elimination of those hazards in the woman's home environment using procedures in the most current edition of the HUD Guidelines for the Evaluation and Control of Lead-Based Paint Hazards in Housing.
- The most appropriate way to elicit the practice of behaviors which increase the risk of lead poisoning is to ask specific neutral questions using language which is understandable and not confrontational.

Recommendations

The expert panel recommends that the LPPP further assess the issue of pica behavior. There is a need to identify which cultural/ethnic groups in New York City engage in pica behavior of lead-containing materials. Focus groups could help to better understand the beliefs that lead to this behavior and the possible methods to intervene and change cultural practices. These groups will also be able to derive the language needed to effectively elicit responses about actual behaviors.

When a lead based paint hazard is identified, the expert panel recommends that safe remediation be undertaken when:

- ***There are planned or ongoing renovations in the home,***
- ***There are young children living in the home,***
- ***The family is planning to stay in the home after the child is born,***
- ***Lead-based paint hazards are identified as the source of the lead poisoning.***

Any lead-based paint hazard reduction must be undertaken in full compliance with New York City, HUD and EPA guidelines and regulations. Pregnant women should not be in the area where lead-based paint hazard reduction work is being done. Where possible the woman should leave the home to avoid exposure. In some cases, this may mean temporary relocation.

Additional recommendations for risk reduction in the home are mentioned in the text of this report and include removal of shoes when entering the home, wet cleaning techniques, dust testing to ensure cleanup was adequate and removal of lead containing products from the home.

- **6.a. What counseling should the LPPP provide to lead-poisoned pregnant and lactating women?**

- The current practices of the LPPP include providing educational materials that address the following areas;
  - risk of adverse outcomes for the fetus,
  - possible sources of exposure,
  - good nutrition,
  - steps for follow-up.
- The literature contains information similar to that outlined in the materials distributed by the LPPP.
- The literature has demonstrated the importance of several factors on IQ in children such as socioeconomic status, parental IQ and the quality of the home environment.

Recommendation

The expert panel recommends that parents of children who were exposed to lead prenatally should be made aware of the positive influence on intelligence of an intellectually nourishing environment. In addition to efforts to reduce exposure, suggestions should be made on ways to provide positive developmental stimulation to the child that may counter the detrimental effects that lead has on intelligence.

The expert panel recommends that educational materials be updated to reflect the findings of this project.

- **6.b. How should the LPPP coordinate with medical providers who are serving lead poisoned pregnant and lactating women?**

  - The current practices of the LPPP include educational information for both the health care provider and the lead-poisoned woman. Telephone contact is required in certain cases.
  - The literature does not address this issue for lead exposure in pregnant women.

Recommendations

The expert panel recommends that the LPPP increase its role in educating health care providers, particularly those caring for women from the high-risk groups, on risk factors and source investigation, including information on the appropriate management of lead poisoned women.

- **6.c. How can LPPP best reach out to medical providers to promote systematic risk assessment and testing of pregnant women at high risk of lead poisoning?**

  - The current practices of prenatal health providers are not uniform. In some medical practices various lead screening questions are asked,

whereas other practices obtain a BLL as part of the routine screening laboratory exams at the first prenatal visit.
- The experience of the LPPP suggests that medical provider interest exists but evidence-based guidance on prevention, risk assessment and medical management is required.

Recommendation

The expert panel suggests that the LPPP explore the best method to communicate with providers such as email alerts from the DOHMH LPPP. These can be sent to key contact persons in professional organizations, such as ACOG, and institutions that can then further distribute the materials.

The expert panel recommends a mailing and outreach to all prenatal health care providers.

- **6.d. What are the barriers that prevent health care providers from systematically assessing risk, testing, providing case management and coordinating care for pregnant and lactating women and newborns?**

    - The current understanding of barriers to health care delivery in NYC is hampered by the enormous diversity of the population; each group has its own expectations of health care and the health paradigm.
    - The literature does not address this issue specifically.
    - The expert panelists identified that the main barrier to the systematic assessment of pregnant women for lead exposure is the lack of time during a typical prenatal office visit.
    - Additionally, women may not want to acknowledge behaviors that their health care provider perceives as dangerous or wrong. This includes pica behavior and the use of folk remedies.
    - Prenatal health care providers may not be familiar enough with the common sources of lead to ask the appropriate questions.

Recommendation

The expert panel recommends that the most effect way to overcome the time constraint of an office visit would be to develop a written questionnaire to be incorporated into existing standard prenatal visit forms. This must be geared toward the particular community being addressed. The language should be clear and translated appropriately. Alternatively, health care providers may benefit from a brief, perhaps laminated card, describing the main sources of lead for pregnant women.

The expert panel recommends that the LPPP partner with existing community organizations to assess the cultural barriers to effective screening and case management. The formation of focus groups may assist in this process. An additional goal of this approach would be to empower members of the community.

- **6.e. What are the cultural, ethnic and linguistic issues that LPPP staff and health care providers need to be aware of in order to reach and intervene with lead-poisoned pregnant women?**
  - The current approaches to these issues are based on understanding the patient's expectation of care and the health paradigm. This is embedded in the culture of each affected community.
  - The literature does not specifically address these issues.
  - The experience of the LPPP suggests that working with community-based organizations familiar with the particular cultural, ethnic and linguistic issues might be a productive way to build trust and find culturally sensitive alternatives.
  - The expert panel noted that little is currently known of the cultural barriers that exist within the communities being targeted.

- **6.f. What information should medical providers give all pregnant women about lead poisoning prevention and, specifically, women at high risk of lead poisoning?**

  - The current New York State Law requires all prenatal health care providers to provide each pregnant woman anticipatory guidance on lead poisoning prevention during pregnancy.
  - The literature suggests that certain risk factors place women of childbearing age at increased risk of lead poisoning. (see text)

Recommendations

The expert panel recommends that the LPPP develop, and publicize widely, a comprehensive list of possible sources of lead for pregnant women with a focus on those suspected to be the most common. The LPPP should indicate which sources of exposure are pertinent to which ethnic groups.

The expert panel recommends that the LPPP further assess the issues of cultural, ethnic and linguistic barriers to communication and intervention. There is a need to identify which cultural/ethnic groups of women in New York City are at the highest risk for lead poisoning during the childbearing years. Once identified, focus groups could provide information to be used to formulate questionnaires, design interventions and communicate risk.

LPPP should publicize widely information on proper nutrition during pregnancy, stressing adequate dietary sources of calcium and iron emphasizing that it is not a substitute for source identification and elimination.

LPPP should develop guidance documents for household members engaged in occupations that could result in exposure to lead. People who work in these trades

should be encouraged to change their clothing and, if possible, to shower prior to, or immediately after, returning home.

In conclusion, the information and recommendations that have resulted from this collaborative undertaking between the Center for Children's Health and the Environment of the Mount Sinai School of Medicine and the Lead Poisoning Prevention Program of the New York City Department of Health and Mental Hygiene are intended to be directly applicable to the practices of the LPPP and of health care providers who care for pregnant women. It is hoped that implementation of the recommendations of this report will reduce the adverse health impact of prenatal exposure to lead on pregnant women and their offspring in NYC.

3. Summary of Peer Review Panel Recommendations:

a. Recommendations for the DOHMH LPPP:

Education and Communication:

- **The LPPP should increase its role in educating prenatal health care providers, particularly those caring for women from high-risk groups, about risk factors for lead exposure in pregnant women, environmental history taking and the appropriate management and referral of pregnant women with elevated BLLs.**
- **The educational materials used by the LPPP for pregnant women should be updated to reflect the findings of this report, particularly in the areas of risk factors and nutrition.**
- **The LPPP should distribute a lead risk assessment questionnaire to all prenatal health care providers and provide education regarding its proper use.**
- **The LPPP should develop and disseminate a comprehensive list of possible sources of lead for pregnant women with a focus on the risk factors suspected to be the most common and the ethnic groups most likely to be affected.**
- **The LPPP should distribute information on proper nutrition during pregnancy, stressing adequate dietary sources of calcium and iron emphasizing that it is not a substitute for lead source identification and elimination.**
- **The LPPP should develop guidance documents for household members engaged in occupations that could result in exposure to lead. People who work in those trades should be encouraged to change their clothing and, if possible, shower prior to, or immediately after, returning home.**
- **The current New York State brochure*, "If You're Pregnant, Get Ahead Of Lead" (Publication Number 2511),* provides a good foundation for the education of pregnant women, but the brochure should be expanded to include discussion of more recently recognized exposure sources such as pica, use of imported pottery, and use of imported herbs, spices and remedies that may be from overseas and it should be printed in multiple languages.**
- **The LPPP should refer the parents of children who were prenatally exposed to lead to resources that can provide suggestions on ways to foster a developmentally stimulating environment.**

Investigation and Intervention:

- **The LPPP should continue with its plan to provide proactive educational and investigative intervention to any pregnant woman found to have a BLL ≥ 15 µg/dL on even a single occasion.**
- **In these cases the LPPP's investigation should start with an interview of the woman, followed by a home and/or workplace investigation with direct observation.**
- **LPPP investigators should be alert for new, previously unidentified sources of lead exposure for pregnant women.**

- **Lead-based paint risk assessment should be done in the home by an EPA certified risk assessor to address issues of primary prevention of lead poisoning in the newborn or other at-risk individuals.**
- **Safe lead-based paint hazard remediation should be undertaken when:**
    - **There are planned or ongoing renovations in the home,**
    - **There are young children living in the home,**
    - **The family is planning to stay in the home after the child is born,**
    - **Lead-based paint hazards are identified as the source of the lead poisoning.**
  - **Lead-based paint hazard reduction should be undertaken in full compliance with New York City, HUD and EPA guidelines and regulations.**
  - **Pregnant women should not be in the area where lead-based paint hazard reduction work is being done. Where possible the woman should leave the home to avoid exposure. In some cases, this may mean temporary relocation.**

b. Recommendations for Partnership and Collaboration between Health Care Providers and the DOHMH LPPP:

- **Environmental risk assessment and intervention for pregnant women with elevated BLLs should ideally be a coordinated effort involving both the health care providers and the LPPP.**
- **The LPPP should continue to coordinate the investigation and referral of pregnant women when the BLL obtained by the health care provider is ≥ 15 µg/dL.**
- **The LPPP should collaborate with prenatal health care providers and their professional organizations, such as ACOG, to create educational materials to be given to all pregnant women with detectable BLLs.**
- **The LPPP should partner with existing agencies that provide services to low income and immigrant groups of pregnant women within NYC, such as WIC, to foster a systematic approach to screening for lead exposure risks and ensure wide distribution of educational materials to these high risk populations.**
- **Since clinics that deal mainly with patients receiving Medicaid benefits undergo regular audits and these groups are often at higher risk for lead exposure the LPPP should explore partnering with programs such as the Prenatal Care Assistance Program (PCAP)/Medicaid program to improve the ways in which these clinics screen for lead exposure during pregnancy.**

c. Recommendations For Health Care Providers:

Screening and Education:

- **Prenatal health care providers should consider the possibility of lead exposure in every pregnant woman in New York City, as is required by New York State law. (Part 65-1.5, effective December 22, 1993).**

- **To standardize the clinical assessment of possible maternal exposure to lead, the panel recommends that providers ask <u>all</u> pregnant woman questions at the initial visit to ascertain exposure and obtain a BLL if they:**
  - **Were born outside of the United States,**
  - **Engage in pica behavior,**
  - **Use imported spices, foods, cosmetics, ceramics or folk remedies,**
  - **Live in a home where there are any recent or ongoing renovations,**
  - **Work in an occupation which places them at risk for lead exposure.**
- **As part of routine primary prevention of lead poisoning and its adverse effects, prenatal health care providers should provide all pregnant women in New York City with an educational message concerning the hazards of lead exposure during pregnancy that includes discussion of lead sources, exposure prevention, and proper nutrition. It is important that this counseling emphasizes that good nutrition is not a substitute for exposure reduction.**
- **The current New York State brochure*, "If You're Pregnant, Get Ahead Of Lead" (Publication Number 2511),* provides a good foundation for the education of pregnant women, but the brochure should be expanded to include discussion of more recently recognized exposure sources such as pica, use of imported pottery, and use of imported herbs, spices and remedies that may be from overseas and it should be printed in multiple languages.**
- **A checklist for assessing lead exposure risk should be incorporated into forms used for prenatal care visits. This will promote compliance with NYS law, improve the detection and identification of women at risk, assist in focusing risk reduction messages to individual pregnant women, and likely be an effective way to overcome the time constraints of an office visit.**
- **Prenatal health care providers should document the results of either a risk assessment questionnaire or a blood lead level for every pregnant woman in New York City.**
- **Prenatal health care providers should obtain a blood lead level as soon as possible on any woman found by questionnaire to be at risk for lead exposure.**

<u>Intervention and Follow-Up:</u>

- **<u>Maternal BLLs greater than 5 µg/dL</u> are unusual and are likely to be associated with identifiable exposures. Childhood BLLs in this range <u>have been associated with adverse neurodevelopmental health outcomes</u>. Although the evidence is limited, prenatal exposure at this level appears to have similar effects. Thus, the prenatal health care provider should attempt to identify potential sources of lead exposure interviewing the pregnant woman and provide counseling on source reduction if her BLL is found to be ≥ 5 µg/dL.**
- **The frequency of re-testing should be based upon the pregnant woman's initial BLL, the chronicity of exposure, risk factors for continued, repeat or future exposure, and possible clinical interventions (see table 2 below).**
- **When the maternal BLL is ≥ 45 µg/dL in the late 2nd or 3rd trimester, consideration should be given to chelation in order to reduce the body lead burden of the mother. Chelation should always be undertaken with great**

caution in consultation with an experienced specialist and the patient should be hospitalized. The agent with which there is the most clinical experience is $CaNa_2EDTA$. Chelation prior to the late 2nd or 3rd trimester is strongly discouraged and should be reserved for life threatening intoxications.

- **Certain risk factors for exposure, especially pica, may also warrant increased follow-up or counseling, regardless of the patient's blood lead level.**
- **Protoporphyrin levels should be considered only when the BLL is ≥ 30 µg/dL to help differentiate between an acute and a chronic exposure in the absence of iron deficiency anemia.**
- **Since they are highly correlated, either a maternal BLL or an UCLL should be obtained at the time of delivery when the mother's BLL has been ≥ 15 µg/dL at any time during pregnancy. The pediatric health care provider should obtain a follow-up BLL on the infant. The schedule of follow-up testing is adapted from the CDC's recommendations for children.**
- **Calcium supplementation should be advised for all pregnant women at the level recommended by the Institutes of Medicine (1,000 - 1,300 mg/day depending on age) but particularly stressed in pregnant women with BLLs ≥ 5 µg/dL because it may decrease mobilization of maternal bone lead stores.**
- **Any woman with iron deficiency anemia should be started on iron supplementation. The importance of this treatment should be reinforced in the presence of a BLL greater than the threshold for intervention.**
- **Additional scientific evidence is required before Vitamin C supplementation can be recommended for the purpose of limiting fetal exposure to lead.**
- **The expert panel recommends re-testing of the mother 1 month postpartum with follow-up testing as dictated by the results of that BLL measurement.**
- **The expert panel urges prenatal health care providers to contact the pediatric health care provider responsible for the follow-up of the neonate to coordinate care when the maternal or umbilical cord blood lead levels are elevated.**

Breastfeeding:

- **The benefits of breastfeeding greatly outweigh the risks of lead poisoning when the mother's BLL is < 40 µg/dL.**
- **Although there is some evidence indicating that it is safe to continue breastfeeding at BLLs ≥ 40 µg/dL, the recommendation of the expert panel is to temporarily stop breastfeeding until a repeat BLL is obtained and is found to be < 40 µg/dL. All efforts should be made to maintain the mother's milk supply during this time.**

d. Recommendations for Pediatric Providers:

- **The frequency of follow-up blood lead testing of the neonate exposed in utero should be based on the CDC recommended schedule for children (see table 3 below). This should be done in conjunction with anticipatory guidance and distribution of educational materials.**

- **The parents of prenatally exposed infants should be given guidance on ways to provide an intellectually nourishing environment to the child. In cases, where this may be difficult, referral to available services such as Early Intervention or Head Start may be warranted.**

e. Recommendations for Further Research and Discussion:

- **A systematic population-based assessment of BLLs in suspected high-risk groups of pregnant women in New York City should be undertaken.**
- **This epidemiological assessment should be coupled with an in-depth assessment of the risk factors for elevated BLLs in these high-risk groups.**
- **Additional consultation with cultural anthropologists and the formation of focus groups is recommended to explore how to optimally and appropriately communicate the risk of adverse neurodevelopmental effects of lead in various communities and to develop strategies for primary prevention.**

Table 1: Actions and Time Frames According to a Pregnant Woman's Blood Lead Level

Perform a risk assessment for all pregnant women at the first prenatal visit. Obtain a BLL when risk factors are present.		
Blood Lead Level (µg/dL)	**Actions**	**Time Frame for Beginning Intervention**
0-4	**By Prenatal Health Care Providers:** Provide anticipatory guidance and patient education	First Prenatal Visit
5-10	Above actions, plus: **By Prenatal Health Care Providers**: Administer risk reduction counseling Attempt source identification by interview Provide nutritional assessment and counseling Provide follow-up testing	Within 30 Days
10-14	Above actions, plus: **By Prenatal Health Care Providers**: Notify the LPPP within 24 hours **By LPPP:** Provide educational materials to exposed pregnant woman	Within 30 Days
15-45	Above actions, plus: **By Prenatal Health Care Providers**: Emphasize Source Reduction Provide clinical evaluation and care Provide follow-up testing Provide appropriate referrals Consider obtaining a protoporphyrin level when the BLL ≥ 25 µg/dL to distinguish between acute and chronic exposure in the absence of iron deficiency anemia Recommend temporary cessation of breastfeeding in lactating women when BLL ≥ 40 µg/dL **By LPPP:** Provide coordination of care, education and counseling emphasizing source reduction (case management) Provide environmental investigation and control of lead sources	Within 2 weeks
≥45	Above actions, plus: **By Prenatal Health Care Providers in collaboration with LPPP and an experienced specialist**: Hospitalize and consider chelation therapy upon confirmation of BLL	Within 48 hours

Table 2: Frequency of Maternal BLL Follow-Up Testing

Initial Venous Blood Lead Level (µg/dL)	Perform a follow-up test:
5-14	Once at least 30 days from the initial test to assess the trend, efficacy of education, investigation, and interventions. Repeat test only if the BLL is rising.
15-44	Within 2 weeks and then monthly to assess the efficacy of investigation and interventions. Obtain a BLL at delivery (maternal or UCLL).
≥45	Within 24 hours and then at frequent intervals depending on clinical interventions and trend in BLLs. Consultation with a clinician experienced in the management of pregnant women with BLLs in this range is strongly advised. Obtain a BLL at delivery (maternal or UCLL).

Table 3: Follow-Up Blood Lead Testing of the Newborn (0-6 months of age) Exposed In Utero

Maternal or Umbilical Cord Blood Lead Level at or around the time of delivery (µg/dL)	Initial Post-Partum Venous Blood Lead Testing in the Newborn	Frequency of Retesting In the Newborn Based on Initial Post-Partum BLL
5-14	< 1 month	Every 3 months[a]
15-24	< 1 month	Every 1-3 months[a]
25-44	< 2 weeks	2 weeks – 1 month
>45	As soon as possible	Depends on Clinical Intervention[b]

a. Repeat blood lead testing at these BLLs is performed mainly to assess the trend. Once the BLL of the newborn is declining, repeat testing may be unnecessary.
b. The frequency of retesting should be based on the clinical interventions performed in consultation with a specialist.

III. MAIN REPORT:

1. Project Description:

In New York City, exposure to lead in pregnant women and their offspring has not been fully described as a public health problem. Pediatricians, obstetricians and public health authorities have not systematically evaluated the scope of maternal lead exposure or the effectiveness of current approaches to screening and intervention. It is estimated that between 0.5% and 2% of women giving birth in the United States today have BLLs greater than or equal to (≥) 10 μg/dL, the CDC's current level of concern for children (Appendix C). Moreover, there is increasing evidence in children that adverse effects occur at BLLs < 10 μg/dL (Canfield et al. 2003). Extensive screening of BLLs in pregnant women has not been undertaken, and the number of pregnant women tested each year is neither known nor fully compiled. Thus, there may be a number of pregnant women with undetected elevations of lead in blood at levels that can potentially harm the fetus.

Pregnant women in New York City with elevated BLLs represent a unique population both in terms of demographics and exposure pathways. New York State surveillance data for BLLs in women of childbearing age (18-45 years) found that statewide, 2% had BLLs ≥ 10 μg/dL in 1996. There were 124,023 live births in 2001 in New York City. If 2% of these neonates were born to pregnant women who had elevated BLLs, this would translate into 2,480 lead-exposed fetuses. In 2003, there were approximately 36,319 tests in adult women in NYC. 242 (0.7%) had BLLs ≥ 10 μg/dL. The recent upsurge of immigrants to New York City adds a further dimension to the issue

of lead exposure during pregnancy. According to the 1998 Medicaid Births File, Medicaid financed 35,643 births in NYC to foreign-born women in that year. The New York City Department of Health and Mental Hygiene (DOHMH) reported that in 2000, 50% of all NYC women giving birth were foreign born. Since women of foreign origin may be at higher risk of elevated lead levels due to environmental exposures in their countries of origin and cultural practices that may involve the ingestion of lead, the true number of pregnant women in New York City with BLLs ≥ 10 μg/dL may be higher than the above estimate based on statewide data.

Current New York State Law requires assessment of pregnant women for lead risks and screening of those determined to be at risk. However, there are many unanswered questions about the effectiveness of this approach to identify affected mothers and children and ensuring appropriate intervention and follow-up. These questions include:

- How rigorously are obstetricians following the current prenatal lead assessment and screening guidelines in NYC? Is there variation by practice type or population served?
- What is the actual number of lead exposed pregnant women in NYC? Many lead exposed mothers and newborns may currently be unidentified and thus suffer potentially preventable adverse health effects.
- Do sub-populations at high-risk such as foreign-born pregnant women require a specialized approach?
- What are the unique cultural characteristics that place certain sub-populations at increased risk of lead exposure?

- What does the current evidence demonstrate regarding health effects of various degrees of overexposure to lead in this population?
- What is the benefit of calcium supplementation?
- What type of environmental investigation is appropriate at different BLLs?
- At what lead levels is chelation appropriate for the mother or the newborn?
- What types of primary and secondary prevention initiatives would be effective in the NYC population? What special cultural considerations need to be addressed in order to ensure a successful prevention strategy?

Along with the NYC DOHMH's Lead Poisoning Prevention Program (LPPP) we proposed to address these issues when starting this project. Our strategy was to begin with an intense scrutiny of the medical literature. The review of the literature was designed to assess the impact of lead exposure during pregnancy on maternal, fetal and infant health and development. The further objectives of the review were to address issues related to the identification and management of lead exposed pregnant women. The "Charge Questions," modified to ask specific clinical questions, were used as a guide to direct the search. Included in the review were original articles, epidemiological surveys, meta-analyses, systematic and critical reviews. Where the literature lacked any information on a particular subject, case reports were included. The bibliographies of the articles were checked for missing studies. The majority of the articles were found through the PUBMED database. Additional databases used were The Cochrane Library and Wilson OmniFile Full Text Mega. The searches were limited to the English language, studies of humans, studies that used an actual measure of lead exposure (such as a BLL) and recent publications (1980-). Articles that were not relevant were

eliminated from the review by reading the abstract. To fill gaps in the literature of lead poisoning during pregnancy in humans, some animal studies were included. Data were extracted by a group of reviewers and each article was critiqued. The assessments made on the overall impact of lead on the clinical outcome measured were based on a critical analysis of studies. The literature review was presented to the expert panelists prior to the first meeting.

The panel convened twice in October 2003 to reach a consensus on the answers to the "Charge Questions." These guidelines have undergone multiple revisions and once approved by the expert panelists, these recommendations will be submitted to the NYC DOHMH and subsequently shared with other professional organizations. The ultimate goals of this project were to improve the identification and management of exposed pregnant women and their offspring.

The expert panel was chosen based on the following criteria:

1. National reputation for scholarship in the treatment and epidemiology of lead poisoning.
2. Persons nominated function strictly independent of the lead and lead paint industry.

Specific Areas included in the expert panel:

1. Expertise in treatment of low-dose lead poisoning in children.
2. Clinical experience in chelation therapy for lead poisoned pregnant women and children.
3. Expertise in the epidemiology of lead poisoning.
4. Expertise in the area of high-risk obstetrical care, obstetrical toxicology, and clinical care of pregnant women.
5. Expertise in the area of cultural anthropology to better understand culturally-related behaviors during pregnancy and to focus on issues of culturally sensitivity in screening guidelines.

2. Introduction:

Even with the great advances that have been achieved in the prevention of lead exposure, including the removal of many important sources in the environment, lead poisoning is still a significant public health problem in New York City and throughout the world. Women exposed to lead at any point in their lives can carry a lead burden in their bones that subsequently becomes mobilized into the bloodstream during pregnancy. Direct lead exposure during pregnancy can also occur as a result of certain cultural practices or environmental contamination. Lead in the maternal bloodstream freely crosses the placenta and can affect the fetus with its unique susceptibilities to developmental toxins. Moreover, scientific evidence is accumulating that levels of lead in the blood previously thought to be harmless can have adverse effects on maternal health and pregnancy outcomes, as well as on infant development, cognition and behavior. Lead has been known to be toxic for centuries, but only recently have actions been taken to protect individuals from relatively low lead levels and their chronic effects.

3. Prevalence:

With the phase-out of leaded gasoline, which began in 1976 in the United States, the average lead levels in the populations decreased dramatically. According to the National Health and Nutrition Examination Survey (NHANES) II (1976-1980), 88% of the population 6 months to 74 years of age had BLLs > 10 μg/dL and 1.9% had levels > 30 μg/dL (Mahaffey et al. 1982). This suggests that 86% of the population had levels between 10 and 30 μg/dL. The average BLL for the population studied was 12.8 μg/dL. These levels are now known to have adverse effects on health and development. A report

to the U.S Congress in 1990 estimated that the prevalence of BLLs > 10 μg/dL among women of childbearing age was between 8.2% and 19.7%, depending on age and race (Crocetti et al. 1990). This would indicate that approximately 4.4 million U.S women of childbearing age had a BLL > 10 μg/dL in 1984. Of these, an estimated 403,200 would have been pregnant at the time (Ventura et al. 2001).

Over the past 2 or 3 decades, the average BLLs of the U.S. population declined dramatically. This decrease closely paralleled the removal of lead from gasoline, canned foods and other consumer products. The average BLL in all age groups (1-74 years of age) declined from 12.8 μg/dL to 2.8 μg/dL from the late 1970's to the early 1990's. The mean BLLs in females aged 20-49 declined to 2.0-2.6 and only 3.3% of this group had levels ≥ 10 μg/dL (Brody et al. 1994, Pirkle et al. 1998). Therefore, present cases of pregnant women presenting with elevated BLLs will, for the most part, have risk factors specific to their environmental or cultural situations.

A few recent small studies and reports are specific to the BLLs in the City of New York. New York State Heavy Metal Registry (NYS HMR) data from 1999 concluded that 1.6% of the women tested had levels ≥ 10 μg/dL (Fletcher et al. 1999). This retrospective study included many women who were identified secondary to workplace screening, and the sample included women from all over NYS. 35% of the women were pregnant at the time of testing. In 2001, 40 lead poisoned pregnant women with BLL ≥ 20 μg/dL were identified by the New York City Department of Health and Mental Hygiene's Lead Poisoning Prevention Program (NYC DOHMH LPPP) (Leighton et al. 2002). In 2003, of the 36,319 tests on adult women reported to the NYC DOHMH, 242 had BLLs ≥ 10 μg/dL. The lack of data on the prevalence of elevated lead levels in New

York City points to the need for a thorough study. Please refer to Appendix C for additional information on prevalence.

4. Sources Of Lead:

Lead exposure pathways for pregnant women are unique and often differ from those of children and other adults. The primary exposure pathways for non-pregnant adults are occupational. For pregnant women, particularly in certain ethnic groups, an additional significant pathway involves pica behavior, the intentional ingestion of nonfood substances. A few studies have examined the characteristics or behaviors associated with the severity of lead poisoning. Severe lead poisoning (BLL $\geq$ 45 µg/dL) in pregnant women seems more likely to occur because of intentional pica (Shannon 2003, Klitzman et al. 2002). Most of the women identified with these very elevated BLLs ingested soil, clay or pottery ("tierra"), although cases of paint chip ingestion have been documented. According to this analysis of 15 case reports, home renovation and the use of crushed bone meal were additional sources of lead exposure (Shannon 2003). Of the 40 pregnant women identified to the NYC LPPP in 2001 with BLLs of 20 µg/dL or greater, 95% were foreign born, 60% were from Mexico, and 20% reported pica behavior during their pregnancy (Leighton et al. 2002). An analysis of women in Pittsburgh, PA where the average BLLs were less than 5 µg/dL, concluded that BLLs increase with age, smoking, lower educational level and African-American race and decrease with a positive history of breastfeeding and higher calcium intake (Hertz-Picciotto et al. 2000).

Other sources of lead exposure in immigrant populations include the consumption of contaminated imported spices and foods, lead-glazed ceramics, botanica products and cosmetics. Many immigrant women have elevated endogenous bone lead stores due to

prior exposures in their countries of origin, such as lead-glazed ceramics, leaded gasoline, battery recycling and contaminated food. These maternal bone lead levels tend to decline over time upon immigration to the United States (Rothenberg et al. 1999b). Seasons may also play a role in BLLs. The observed BLLs in a population of 316 pregnant women in New York State were highest in December through March (Schell et al. 1997). However, a similar analysis in Los Angeles found the BLLs to be highest from April through June (Rothenberg et al. 2001). In addition to the other innumerable health effects of cigarette smoking and alcohol consumption, both were found to independently increase UCLLs (Rhainds and Levallois. 1997, Ernhart et al. 1985).

According to reports from the NYC Department of Environmental Protection, drinking water is not a major source of lead. In addition, orthophosphate is added to the water supply to decrease the likelihood that lead soldered pipes will leach lead. Additional analysis specific to the population in NYC needs to be conducted in order to ascertain the association between these risk factors and BLLs.

a. Pica:

Pica is the behavior of ingesting nonfood substances. This behavior has been noted more commonly in children and in pregnant women. Poor nutrition and mineral deficiency have been suspected to precipitate the pica behavior (Hamilton et al. 2001). This has not been confirmed and the exact cause may vary in different individuals. Geophagia is the intentional ingestion of earths and is usually associated with cultural practices. The ingested clay is typically harvested from 2-3 feet below the surface. Geophagical clays are primarily from known, and usually uncontaminated sources (ATSDR 2000). Soil-pica is the recurrent ingestion of surface soil. Soil-pica is an

important source of lead exposure whereas geophagia is unlikely to place women at risk for lead poisoning. These practices are common among African Americans in the southeastern US. Geophagia has also been observed among Mexicans and West Africans who have immigrated to the US (Simpson et al. 2000, Sule and Madugu. 2001).

Another important source of lead is pica of crushed pottery, whether from the clay itself or in the glaze that is applied to the finished product. Other lead containing substances that have been ingested include paint chips and crushed calcium supplements derived from bone. Pica of ice (pagophagia) and starch (amylophagia) is also common, but has not been associated with lead exposure. They are important in cases of lead poisoning because they have been found to be associated with anemia, which can worsen the effects of lead (Rainville, 1998). Other less commonly ingested materials include bean stones, magnesium carbonate, ashes, battery acid, fabric softener, shampoo, soap, thread, paint thinner, laundry bluing, spearmint leaves, bricks, eggshells, salt and lipstick (Simpson et al. 2000).

The incidence of pica in New York City is unknown but specific groups are at higher risk. One study of Mexican American women living in California reported a 31% prevalence (Simpson et al. 2000). A summary of older research indicated that the groups at highest risk for pica were more likely to be black, to live in rural areas and to have a positive childhood and family history of pica. This article did not include any studies of immigrant populations (Horner et al. 1991). Cases of women ingesting surface soils in NYC have occurred. Most women in urban areas, however, would likely not dig and process their own geophagical clays, but would likely purchase them or obtain them from areas where they were reared when relatives come to visit (ATSDR. 2000). Studies have

not been conducted to determine the extent to which pregnant women exhibit soil-pica behavior.

More information needs to be gathered in order to understand certain cultural behaviors during pregnancy. Pica needs to be understood as it occurs among various cultural groups. The issues which need to be explored in terms of pica include the nature of its usage, generationally taught or peer influenced, types of material ingested, availability of the materials and cultural attitudes towards pica within particular communities.

The incidence of soil-pica or geophagia is probably underestimated. When asked, many women who do practice pica may not admit to engaging in this behavior. It is important for the practitioner to screen all pregnant women for pica. The most appropriate way to elicit the practice of this behavior is to ask specific and neutral questions using language which is understandable and not confrontational. It is clear, however, that there may be social stigma related to the behavior which prevents women from sharing this information. Research on pica usage is needed in order to understand women's experience of pica behavior and the best ways to ascertain that behavior. Women who do admit to pica should be screened for lead and anemia. Conversely, any pregnant woman that presents with an elevated lead level should be asked about pica behavior and educated on the risks to themselves and their unborn child.

b. Folk Remedies:

The use of folk remedies and alternative medicines is prevalent among women of childbearing age. In 1993, a representative survey of Complementary and Alternative Medicine (CAM) use in the general US population documented that approximately one

third of all US adults used CAM for treatments for a defined disorder (Eisenberg et al. 1993). A follow-up to this survey indicated that the use of CAM had increased to approximately 42% of the US adult population by 1997. Indeed, nearly half (49%) of women were using CAM (Eisenberg et al. 1998). The types of CAM used most often by women living in New York City were medicinal teas, herbs and vitamins. This study population consisted of 300 women, 100 from each of the following groups: White, Hispanic/Latina and African American. Racial and ethnic differences in CAM use were minimal (Factor-Litvak et al. 2001). However, there are many lead containing remedies specific to certain ethnic or cultural groups which are more likely to contain lead. In a Boston Hospital, 7.1% of the 734 parturients surveyed reported the use of herbal medications during pregnancy. Only 14.6% of users considered them to be medications (Hepner et al. 2002). A list of folk remedies which have been shown to be occasionally contaminated with lead is included in appendix D. In many of these products, lead is an occasional contaminant, however, it is the main ingredient in a few. For the provider, it may be more productive to ask the patient how they treat their symptoms than asking directly about their use of traditional or folk remedies. It is also advisable to interview them in their own language using culturally-specific vocabulary. For instance, a provider seeing Mexican women may ask how they treat "empacho" rather than asking if they give an herbal remedy to treat gastrointestinal problems.

c. Occupational And Take Home Exposures:

A large number of occupations put workers at risk for lead exposure (see Appendix E). Job activities known to involve using or disturbing lead include: handling lead-containing powders, liquids or pastes; processes that produce dust or fumes by melting, burning, cutting, drilling, machining, sanding, scraping, grinding, polishing, etching, blasting, torching, or welding lead-containing solids; as well as dry sweeping lead-containing dust and debris. It is not necessary for pregnant women to be directly involved in the activity to be exposed. Reports have shown that employees, such as clerical staff, are also at risk for exposure (Nunez et al. 1993). According to an analysis of 1996 NYS HMR data, however, most occupationally exposed women with elevated lead levels were directly involved in processes which use lead (Fletcher et al. 1999). In addition, there is a risk to household members of workers in these industries. In a study of automobile radiator repair workers in NYC, children in the household were found to have elevated lead levels. This was possibly due to lead dust in their parent's work clothes (Nunez et al. 1993). A meta-analysis of 10 studies dating from 1987 to 1994 showed that children of lead-exposed workers are at an increased risk for having elevated BLLs (Roscoe et al. 1999). While the data are inconclusive, secondary risk to pregnant women probably exists if other household members are exposed to lead at work. Therefore, it is important for employees to be encouraged to change their clothing and shower prior to, or immediately after, returning home.

Currently, there are no occupational standards or regulations with provisions for pregnant women. The current OSHA standards set for women are the same as applied to men. The standards sets a permissible exposure limit (PEL) of thirty micrograms of lead

per cubic meter of air (30 μg/m^3), averaged over an 8-hour work-day. Biological monitoring under this standard consists of measuring whole BLL and zinc protoporphyrin levels at least every 6 months after the initial blood lead test. Continued monitoring, however, is limited to whole blood lead measurements. If a worker's whole blood level exceeds 40 μg/100g, the monitoring frequency must be increased to at least every 2 months until two consecutive BLLs are < 40 μg/100g. (For practical purposes, the units of measurement used by New York State for enforcement are μg/dL where it is assumed 1 μg/dL is approximately 1 μg/100g.) The employer is obligated to notify an employee within five working days of the receipt of abnormal test results. The employer must also inform the employee that the standard requires temporary medical removal from the exposure with economic protection if the BLL exceeds certain criteria. This removal criterion is 50 μg/100g averaged over 6 months. Anytime the BLL exceeds 50 μg/100g averaged over 6 months the employer must make available to the employee a prompt follow-up blood lead test. If the repeat test exceeds 50 μg/100g and the employee is temporarily removed, then the employer must make successive BLL tests on a monthly basis during the period of removal. The employee may not be returned to work until the BLL declines to at least 40 μg/100g (Commerce Clearing House and United States. Occupational Safety and Health Administration. 2001). In addition, it has been noted elsewhere that small family-owned businesses are more likely to be out of compliance with OSHA standards and will not be likely to undergo monitoring (Nunez et al. 1993).

d. Lead In Bone:

As much as 90% of the total body lead burden is deposited in the adult skeleton. Lead enters the body mainly through the gastrointestinal tract. Once absorbed, it circulates through the bloodstream and gets deposited in all of the tissues of the body, including the brain, kidney and bone. While the half-life of lead in the bloodstream is approximately 3 weeks, lead can remain in bone for decades, where its excretion becomes dependent on many factors. During times of physiological stress, such as pregnancy and lactation, this lead can be increasingly mobilized into the bloodstream (Silbergeld 1991, Gulson et al. 2003, Tellez-Rojo et al. 2002, Moline et al. 2000, Rothenberg et al. 2000, Osterloh and Kelly. 1999). It is then free to cross the placenta and affect the fetus.

Women who have been exposed to lead, for example, in their countries of origin or through occupations that put them at risk, can carry this burden with them for years. The chronicity of the exposure is an important factor in the amount of lead deposition. Once removed from those exposures the BLLs decline slowly over time. The decline in bone lead levels is even more gradual (Rothenberg et al. 2000, Brown et al. 2000, Hernandez-Avila et al. 1996). Looking at pregnant women who had immigrated to Los Angeles from Latin America, Rothenberg et al. found that increased bone lead was related to lead-glazed ceramic ware use, use of folk remedies, daily number of hours spent in bed during the pregnancy, higher maternal age and fewer years resident in the US. Bone lead was also positively associated with third trimester and maternal post-natal blood lead (Rothenberg et al. 2000). The majority of women in the study had no ongoing exposure to lead. They had relatively low BLLs, mean BLL = 2.3 μg/dL, and moderately

high bone lead levels. This is consistent with the current understanding that blood lead is a marker of current exposures and bone lead is a marker of past exposures.

e. Lead Exposure In Countries Of Origin:

For many of the women with lead in their skeleton, the exposure may have occurred in their country of origin. In 2001, there were 124,023 live births in New York City (NYC); 53% of these mothers were born outside of the United States. Therefore, lead exposure in countries of origin may be a major factor in the epidemiology of elevated lead levels within the city. Innumerable sources of potential lead exposure exist for women living in developing nations. In addition to the persistent use of leaded gasoline, many focal sources can lead to lead poisoning such as flour mills, lead-glazed ceramics, mining and smelting and battery repair and recycling (Falk 2003). By the end of 1999, only 36 countries had completely phased-out the use of leaded gasoline and 22% of all gasoline sold worldwide was leaded (Earth Summit Watch 1999). Internationally, leaded gasoline still remains a major source of lead exposure. Lead-glazed ceramic ware is also fairly common in many countries. Mexico is just one example where its manufacture and use are common (Hernandez-Avila et al. 1996, Azcona-Cruz et al. 2000, Romieu et al. 1997, Hernandez-Avila et al. 1991). Preparation of spices or foods in these "lead containing" house wares can contaminate the food. Acidic foods promote the leaching of lead from the glaze. Pica, in particular geophagia, is a culturally accepted, and at times encouraged, practice among a diversity of African, Latin American and African-American cultures. The ingested earth can be contaminated with lead. Consideration of past exposures to lead is important when evaluating immigrant women for prenatal care.

4. Laboratory Assessment Of Lead Exposure:

a. Blood Lead

The most widely used laboratory test for lead is whole blood lead concentration, a well studied and reliable indicator of the amount of lead in circulation at the time of the test. BLLs do not, however, completely reflect the total body burden of lead, particularly in bone. In children, 90 % of lead in the body is found in bone, < 2% in blood, and the remainder is distributed in both the soft and hard tissues of the body (Markowitz 2000). Blood lead concentrations are a reflection of both exogenous exposure and endogenous release from tissue and bone stores. The half life of lead in the blood is approximately 3 weeks in adults based on radioisotope studies (Gulson et al. 2003). Thus, blood lead concentrations demonstrate that an exposure has occurred, but do not necessarily discriminate between recent or remote exposure. If the BLL decreases rapidly over time, the exposure was probably acute and the patient is likely no longer exposed to the source. When the level is stable, it may represent an ongoing exposure, the slow release from endogenous stores, or a combination of both.

As a predictor of fetal exposure, maternal blood lead concentration is fairly well correlated to umbilical cord blood lead concentrations at delivery (Chuang et al. 2001, Rothenberg et al. 1996). Therefore, the two appear interchangeable as measures of the newborn's BLL around the time of delivery. However, the cord blood levels are generally lower than simultaneously measured maternal BLL (Chuang et al. 2001, Cooney et al. 1989, Ernhart et al. 1987). The relationship between blood lead concentration and clinical outcome has generally been based on levels that result from subacute or ongoing chronic lead exposure, and not on transiently high values that may

occur immediately after acute exposure (Ford 2001). The availability and low cost of the blood lead test makes it the most practical tool for assessment of lead exposure in pregnant women and children. When interpreting the results of the test it is important to assess whether the exposure was acute or chronic and whether it was recent or remote.

b. Protoporphyrins

Elevations in erythrocyte protoporphyrins (EP) or zinc protoporphyrin (ZPP) (a subset of EP) may reflect lead-induced inhibition of heme synthesis. The synthesis of heme occurs in developing red blood cells and not circulating, mature erythrocytes. The mature erythrocyte has a lifespan of about 120 days. Hence, there is a lag time between lead exposure and increases in protoporphyrin concentrations. This is between 2-6 weeks. If a patient has an elevated lead level and the EP or ZPP level is low, this indicates recent exposure. Accordingly, when both levels are elevated this is evidence of an ongoing chronic or continuing exposure. Of note, the ZPP and EP levels can also be elevated in some chronic conditions, such as iron deficiency anemia and anemia of chronic disease. Protoporphyrin levels are not sensitive as a screening tool for lead exposure at low BLLs (less than 30 μg/dL). Therefore, they are not recommended as a screening test for low level exposure (Ford 2001).

c. Plasma Lead

Recently, measurement of plasma lead has been has been suggested to be an alternative and possibly more accurate measure of the amount of lead in the blood that is actually biologically available to tissues. BLLs are a measure of the amount of lead in the red blood cell and the plasma. The portion of lead that is in the plasma is less than 3% of the total BLL. Plasma lead may be the portion that freely crosses the placenta and

can have adverse effects on the fetus. This level has been shown to fluctuate with changes in binding proteins, concentrations of competitors and other yet undefined physiological processes (Chuang et al. 2001, Hernandez-Avila et al. 1998). It may be that the average concentration of plasma lead over time is the better predictor of fetal outcomes. A way to estimate this may be by measuring the bone lead which is a fairly constant value that decreases very slowly over the period of gestation. Once mobilized from bone into plasma there may be no detectable change in whole blood lead. Moreover, plasma lead has been shown to have a positive correlation with levels of lead in bone (Hernandez-Avila et al. 1998, Cake et al. 1996). If measuring plasma lead becomes less expensive and more practical it may be possible to further evaluate this alternative biological measure of lead exposure.

d. Bone K X-Ray Fluorescence (K-Xrf)

K-XRF is a noninvasive diagnostic method for measuring the concentration of lead in bone. K-XRF is finding increasing utility in research as a biomarker of long-term, cumulative lead exposure. It has been increasingly used in some studies of health effects associated with total body lead burden. Lead that is deposited in bones may remain there for years to decades and may be released during pregnancy and lactation because of increased rates of bone turnover (Gulson et al. 2003, Tellez-Rojo et al. 2002, Rothenberg et al. 2000, Osterloh and Kelly 1999, Landrigan and Todd 1994).

In a population with exposure to lead from significant background environmental sources, tibial lead concentration has been highly correlated with age. This is probably a reflection of relatively higher environmental lead exposure in years past (Kosnett et al. 1994). With this in mind, immigrant women from areas of the world where lead

poisoning is widespread are more likely to have elevated body lead burdens. Most of this lead is stored in their bones and studies of pregnant women that have been removed from their exposures have shown that the level declines slowly over time (Rothenberg et al. 2000, Brown et al. 2000, Hernandez-Avila et al. 1996).

Even though K-XRF is relatively safe, the risk for radiation exposure to the fetus, albeit small, prevents its use during pregnancy. There is a technique that limits this exposure (L-XRF) but it is rarely employed. In a pilot study conducted in the Bronx that employed L-XRF only 2 of the 53 women studied had bone lead measurements above the minimum threshold of detection (Markowitz and Shen 2001). This may reflect the fact that the maternal exposure was remote in their childhood and their bone lead was diluted by later bone mineral accumulation or that L-XRF was not sensitive enough in this population.

Finally, K-XRF instruments are currently available in only a handful of research settings and their high cost is not covered by insurance. Thus, although K-XRF appears to be an accurate measure of significant historical lead exposures, it cannot be recommended as a routine clinical tool and its lower radiation alternative, L-XRF, appears safe for use in pregnant women but may not be sensitive enough in women with remote lower background exposure and it too is expensive, not widely available, and not covered by insurance.

e. Hair And Urine Testing

Several laboratories provide analysis of heavy metals in the urine without the use of standardized reference values, identifying results as elevated, normal or low at arbitrary levels. Very often, these same tests can be sent to multiple laboratories with different

results and analyses. This is also true for hair analysis, which has been shown in several studies to be unreliable (Seidel et al. 2001). Some health care centers do have well controlled standardized tests for lead in the urine. Their use is limited to specific circumstances. Any patient that presents with results of this type of testing should have a confirmatory BLL

5. Health Effects Of Lead:

Lead has been shown to have adverse affects on multiple organ systems reflecting the diffuse cellular toxicity of this metal. These findings have been well documented in occupationally exposed adults and children. For pregnant women, the evidence is not as extensive. Lead exposures in pregnant women can be chronic or acute. Effects on health are dependent not only on the degree of exposure but the length of time those levels have been maintained. Even very low BLLs can produce health effects, especially if the exposure persists over many years. Moreover, the risk for health effects is difficult to estimate from a single BLL, since this reflects recent exposure. While studies have tried to account for both factors, this has led to inconsistent technique within the research, including the measurement of lead levels in bone, placental tissues, maternal venous blood and umbilical cord blood. These studies have shown that both the pregnant woman and her fetus can be affected. Lead plays a role in pregnancy induced hypertension, pre-eclampsia and spontaneous abortion. The fetus can manifest deficits in growth, development, gestational age and behavior as a child. The following is a summary of the medical literature on this subject as it pertains to pregnant women and their offspring.

a. Risks For The Mother:

i. Acute Toxicity:

Acute and chronic lead toxicity may present with similar clinical findings. Acute toxicity is relatively rare but may occur in the pregnant population. Adults with extremely high concentrations of lead in their blood (generally >60 µg/dL or 70 µg/dL) may complain of headaches, crampy abdominal pain, anorexia, constipation, fatigue, malaise, myalgias and arthralgias. Lead colic is characterized by paroxysmal bouts of pain in a rigid, retracted abdomen. The blood lead concentration in overtly encephalopathic adults is almost always in excess of 100 µg/dL. Delirium, ataxia, seizures, stupor and coma characterize this medical emergency. Microcytic anemia with basophilic stippling can be seen on blood smear. Adults with chronic lead exposure may experience some of the nonspecific constitutional complaints cited above when levels are maintained in the range of 25-60 µg/dL, such as, irritability, fatigue, headache, anorexia, sleep disturbance and depressed mood. These patients are also at risk for hypertension and subclinical neurotoxic effects (Ford 2001). In one review of 15 cases involving only pregnant women with lead levels ≥ 45 µg/dL, all patients complained of malaise, fatigue, and all were found to be anemic, two had basophilic stippling on peripheral smear (Shannon 2003). Most pregnant women with BLLs ≥ 5 µg/dl, however, can experience the toxic effects of lead without overt symptoms.

ii. Pregnancy Induced Hypertension:

The prevalence of pregnancy induced hypertension (PIH) has been found to be increased even at BLLs lower than 5 µg/dL. In a cohort of 705 pregnant women aged 12-34 in New Jersey where the average BLL was 1.2 µg/dL (s.e. +/-0.03), the investigators

found that maternal blood lead concentrations varied significantly among women with PIH, compared to women without PIH. The conclusion that low level maternal blood lead concentrations were significantly associated with PIH remained valid after adjusting for age, ethnicity and calcium intake (Sowers et al. 2002). A study of 1006 pregnant women living in Los Angeles attempted to quantify the relationship between bone lead levels and third trimester hypertension. The authors concluded that for every 10 μg/g increase in calcaneus (trabecular) bone lead level, the odds ratio for third trimester hypertension (systolic BP ≥ 140 mmHg or diastolic BP ≥ 90 mmHg) was 1.86 (95% CI: 1.04, 3.32) (Rothenberg et al. 2002). Since bone lead reflects past exposure, the significant association between bone lead and blood pressure may result from the nephrotoxic effects of long-term lead exposure. A BLL may not be an adequate measure to assess a patient's risk in this situation. In a cross-sectional study of occupationally exposed non-pregnant female workers, BLLs above 40 μg/dL were associated with increases in both systolic and diastolic blood pressure. In addition, the prevalence of hypertension (systolic >125 mmHg) was significantly higher in women with BLLs > 40 μg/dL (Nomiyama et al. 2002). It is uncertain whether the increases in blood pressure due to exposure to lead are large enough to be clinically significant. In conclusion, the evidence suggests that exposure to lead is associated with increases in blood pressure and with pregnancy induced hypertension, especially if that exposure is chronic. This is true even at very low levels of exposure. Additional studies confirm these findings and are summarized in appendix I.

iii. Spontaneous Abortion:

Reports from a period spanning more than a century support an increased rate of pregnancy loss due to high maternal lead levels in occupationally exposed women. Nevertheless, most studies conducted among populations with low to moderate exposures provide little evidence for an association between BLLs and pregnancy loss, in particular spontaneous abortions (Hertz-Picciotto 2000). Most of these studies suffer from small sample sizes, problems in definition or ascertainment of outcome, lack of control for confounding, and or deficiencies in the exposure assessment. One prospective study which overcame most of these deficiencies had enrolled pregnant women in Mexico City with low to moderate level lead exposures, collected blood specimens during their first trimester, and ascertained rates of spontaneous abortions. For each woman who had a spontaneous abortion two controls were randomly selected from women with normal pregnancies at the time that the case occurred. The mean BLLs were 12.03 μg/dL for cases and 10.09 μg/dL for controls (p=0.02). After multivariate adjustment, the odds ratio for spontaneous abortion was 1.8 (95% CI: 1.1, 1.3) for every 5 μg/dL increase in blood lead. In addition, the study used a referent range of <5 μg/dL and generated odd ratios comparing 5-9 μg/dL, 10-14 μg/dL, and ≥15 μg/dL. The odds ratio based on matched sets were 2.3, 5.4 and 12.2, respectively (test for trend, p=0.03) (Borja-Aburto et al. 1999). In this study the risk for spontaneous abortion was increased in women with BLLs ≥ 5 μg/dL. A comparable population in NYC would consist of women who have maintained BLLs ≥ 5 μg/dL for an extended period of time.

b. Risks For The Fetus:

i. Neurodevelopment and Behavior:

To assess the neurodevelopmental toxicity of lead in infants and children, extensive research has sought to determine whether lead causes asymptomatic impairment of the central nervous system at doses insufficient to produce clinical encephalopathy. The most important of these studies have been a series of prospective analyses of neurological and behavioral development in newborn children conducted in the United States, Mexico, Australia, and Yugoslavia (Gomaa et al. 2002, Wasserman et al. 2000, Dietrich et al. 1987, Bellinger et al. 1991, Baghurst et al. 1987). In each of these investigations, correlations have been examined between intellectual and behavioral performance in young children and prenatal lead exposure. All of these studies have found sub-clinical decrements in central neurological function. These decrements correlate quantitatively with increasing BLLs and cannot be explained by potentially confounding biological or social factors. This dysfunction is characterized by diminished intelligence, shortened attention span and slowed reaction time. It appears to be permanent and irreversible.

Studies on the neurological toxicity of prenatal lead exposure estimate fetal dose by a variety of biological markers. Each of the studies summarized in appendix G of this report attempted to quantify the degree of prenatal exposure by maternal BLLs, maternal bone lead levels, placental lead levels and/or UCLLs. In addition, these studies have employed a variety of different developmental and behavioral scales used in the assessment of the children. These examinations are time consuming, difficult to administer and very expensive. Extensive follow-up is needed to properly assess the long

term affects of neurotoxic substances. In spite of these differences and limitations, the conclusions are fairly consistent and support the contention that prenatal exposure to lead causes damage to the central nervous system at levels too low to cause obvious clinical symptoms in the mother.

The evidence that lead causes changes in the developing central nervous system of animals on both the cellular and sub-cellular level is substantial (Antonio and Leret 2000, Flora and Seth 2000, Loikkanen et al. 2003, Reddy et al. 2003, Schneider et al. 2003, Goyer 1996). Whether these changes are also present in the children of mothers exposed to lead is currently being investigated. As a proxy to this cellular damage, the studies on humans have found differences in the scores on developmental and behavioral testing scales. A summary of this research is in appendix G. An early study in Cincinnati showed no effect of fetal lead exposure on the Bayley Physical Developmental Index (PDI). However, multiple linear regression analysis showed a decrease in Mental Developmental Index (MDI) by 0.34 points for each increase of 1 µg/dL of maternal BLL. For umbilical cord lead levels, this decrease was 0.6 points for each 1 µg/dL increase (Dietrich et al. 1987). In Mexico City, the population studied had a mean UCLL of 6.7 µg/dL and the range was 1.2-21.6 µg/dL. The authors found that a 2 fold increase in UCLL was associated with a 3.1 point decrement in adjusted MDI scores at 24 months of age. In other words, an increase in UCLL from 5 to 10 µg/dL would result in a decrease of 3.1 points. This was not influenced by postnatal BLLs (at 12 and 24 months of age), even when forced into the model (Gomaa et al. 2002). The women studied were noted to have higher bone lead levels than women in studies in the United States. Chronic exposure would explain this. Looking at women from a town with a lead smelter

compared to a control group in a nearby city, a study reported similar findings. With adjustments for covariates, children from the exposed group had a significant decrement of 6.05 points in IQ for each log unit increase in prenatal BLL. This translates into a decrease in IQ by 1.07 points for every 50% increase in prenatal BLL. According to the model in this study, a child whose mother had a prenatal BLL of 3 µg/dL and then had 12 and 24 month BLLs of 5 and 5 µg/dL, would have an expected IQ decrement of 5.6 points between ages 3 and 7 years. Of this, 2.9 points would be attributable to prenatal BLL (Wasserman et al. 2000). These studies also illustrate that the association between prenatal BLL and IQ is not linear. The strongest postnatal effects are noted at the lower levels of prenatal exposure. This nonlinear trend was demonstrated in a recent study of children looking at postnatal BLLs (Canfield et al. 2003). This evidence suggests that the greatest damage per unit increase in BLL to the developing brain occurs at the lowest BLLs.

A prospective longitudinal study confirmed earlier clinical observations and recent retrospective studies linking lead exposure with antisocial behavior in children and adolescents. In this cohort, prenatal exposure to lead was significantly associated with a covariate-adjusted increase in the frequency of parent-reported delinquent and antisocial behaviors. Prenatal and postnatal exposure to lead was significantly associated with a covariate-adjusted increase in frequency of self-reported delinquent and antisocial behaviors, including marijuana use (Dietrich et al. 2001). The prenatal BLLs in this study were low (mean = 8.9, S.D. = 3.9).

From a summary of the scientific evidence there is a clear negative relationship between BLLs and neurodevelopment. These adverse effects have been documented for

both pre- and post-natal exposures, although the evidence is clearer when looking at post-natal BLLs. These effects are seen in both cases at levels below 10 μg/dL. In fact, more recently acquired evidence has shown that lead appears to have a greater relative impact on these neurocognitive outcomes at the lowest lead levels (< 10 μg/dL). Moreover, there is no threshold level below which adverse neurocognitive effects have not been clearly demonstrated.

The findings on the developmental neurotoxicity of lead exposure in children are highly credible. They have been reviewed critically and accepted by the U.S. Centers for Disease Control and Prevention (CDC). They provide the intellectual foundation for CDC's lead poisoning prevention program. They have also been reviewed and accepted by the U.S. National Academy of Sciences (Landrigan et al. 2000). The body of proof supporting the neurotoxic effects of prenatal lead exposure is not as clear-cut but the evidence is accumulating (see appendix G). Considered along with the fact that lead freely crosses the placenta at a time of critical neuronal development the evidence suggests that the effects of prenatal lead exposure are likely to be similar to those seen in children.

An additional implication of the finding that lead causes insidious injury to the central nervous system is the possibility that some yet unknown fraction of chronic neurological or psychopathic disease in adults may be caused by early life exposure to lead. One recently completed study looked at the relationship between maternal BLLs and rates of schizophrenia. δ-Aminolevulinic Acid levels were used as a proxy measure in samples of banked blood from a cohort of pregnant women enrolled in the Prenatal Determinants of Schizophrenia Study in Oakland, California. The results are suggestive

of a relationship highlighting the pressing need for further research in this area (Opler et al. 2004). Additionally, epidemiological and clinical studies are needed to assess possible connections between early life exposure to lead and such chronic neurological conditions as Parkinson's Disease, amyotrophic lateral sclerosis and dementia (NRC 1992).

ii. Birth Weight:

Birth weight is a strong predictor of survival and developmental outcomes in childhood including growth, morbidity, and cognitive performance. A review of the literature revealed, in general, well-controlled and executed studies with mixed results for lead exposure's effect on birth weight. The studies vary mainly by the methods utilized for measuring prenatal exposure. Those studies predicting a significant negative correlation used bone lead levels as a measure of in utero exposure. Although the best biomarker for in utero lead exposure is uncertain, bone lead may be the best available means of estimating the true exposure. As the lead that has been stored in bone is released slowly into the blood it becomes bioavailable to the developing fetus. This release is fairly steady with minimal fluctuations over short periods of time. The BLL may not accurately reflect the bioavailable portion of lead since it is likely to be transported in the plasma, contributing very little to the BLL value (Hernandez-Avila et al. 1998, Cake et al. 1996).

A review of the literature in 1994 concluded that there is a possible association with decreased birth weight. Many of the studies included were done on high risk populations with no direct measurement of lead levels (Andrews et al. 1994). From the baseline data of a study in Mexico City to assess the benefit of calcium supplementation,

maternal tibial bone lead burden was inversely related to birth weight. In the highest quartile, neonates were on average, 156 grams lighter than those in the lowest quartile. Maternal and UCLLs and patellar bone lead burden were not associated with a decrease in birth weight (Gonzalez-Cossio et al. 1997). The one recent study that predicted a decrease in birth weight using maternal BLL compared two distinct populations, one in Russia and the other in Norway. They could not control for this significant "country factor" in their statistical models (Odland et al. 1999). The most recent study looking at a variety of outcomes used placental lead as a predictor of in utero exposure. The measurements were performed on areas of the placenta unlikely to have calcification and they found good correlation within specimens. The authors concluded that, in general, higher placental lead levels were not related to lower birth weight (Falcon et al. 2003). One study looking at women in New Jersey and another study from Kosovo in the former Yugoslavia agreed that maternal BLLs as high as 20 µg/dL did not correlate with a decrease in birth weight (Sowers et al. 2002, Factor-Litvak et al. 1993). The evidence that lead exposure is associated with a decrease in birth weight is mixed and thus there is no conclusive evidence that elevated BLLs are associated with reduced birth weight.

iii. Preterm Birth:

Preterm birth, as defined in one study as a gestational age < 37 weeks, places the newborn at serious risk for adverse health outcomes. The findings with respect to prenatal lead exposure and preterm birth are inconsistent. Some studies have found an inverse correlation between BLLs and the frequency of preterm birth (Falcon et al. 2003, Torres-Sanchez et al. 1999, Baghurst et al. 1991). This was supported by a review of the literature from 1971-1991 (Andrews et al. 1994). Other studies have reported no such

association (Sowers et al. 2002, Factor-Litvak et al. 1991). A recent study looking at UCLL found that primiparous women had a frequency of preterm birth that was almost 3 times higher when the UCLLs were ≥ 5.1 μg/dL. This was not true for multiparous women (Torres-Sanchez et al. 1999). A study in Spain which looked at placental lead levels found a significant negative correlation between lead levels and gestational age and preterm pregnancies (Falcon et al. 2003). Unfortunately, the levels reported are in ngPb/g dry tissue and this is difficult to correlate with any blood lead values. Pregnant women in a population surrounding a lead smelter in Kosovo, Yugoslavia were compared with women in a non-exposed town, Pristina, Albania. In this study there was no difference in the length of gestation or rates of preterm birth between the two groups. The BLLs were 5.6 μg/dL for the control group in Pristina and 19 μg/dL for the exposed group in the town with the lead smelter (Factor-Litvak et al. 1991). However, in this same study population, when the results are reported by town, the exposed group had an unadjusted odds ratio of 1.6; (95% CI 1.3-1.9) (Murphy et al. 1990). This can suggest that the increased rate of preterm delivery is due to a factor other than lead or that a BLL is not an adequate biomarker for overall exposure. In conclusion, the more recent studies support the statement that lead exposure in utero increases the risk for preterm birth. This finding, if true, can occur at BLLs < 10 μg/dL.

iv. Additional Outcomes:

Additional pregnancy outcomes that have been evaluated include premature rupture of membranes (PROM), Apgar Scores, rates of small for gestational age newborns, rates of congenital anomalies and head circumference. According to a review of the literature from 1971-1991 lead was unlikely to increase the risk of PROM

(Andrews et al. 1994). Since then, one study was able to associate the two. However, this study used placental lead as a predictor of in utero exposure (Falcon et al. 2003).

The scientific literature supports the conclusion that there is no association between lead exposure and Apgar Scores, rate of SGA or birth defects (Sowers et al. 2002, Falcon et al. 2003, Baghurst et al. 1991). A number of anthropomorphic measurements have been investigated. Data from the Cincinnati Cohort where the BLLs were generally low (<10µg/dL) showed no statistically adverse effect on head circumference, weight or stature (Greene and Ernhart. 1991). An additional study that also used BLLs showed a small negative association between the 6 month head circumference and maternal BLL at 36 weeks (Rothenberg et al. 1999). The most recent study was done in Mexico City using bone lead measurements: patellar lead was negatively associated with head circumference. Tibia lead was associated with decreased birth length (Hernandez-Avila et al. 2002). Drawing a conclusion from this literature is difficult. If lead exposure in utero is associated with a decrease in head circumference, that risk is quite small at the levels generally seen today in NYC.

6. Interventions By Health Care Providers:

The expert panel has concluded that lead exposure is found among women throughout New York City. Since a systematic analysis of the population has not been undertaken, the subgroups of pregnant women with the highest risk for lead poisoning remain unidentified. Many women who are exposed may not be screened either by risk factor questionnaires or blood tests. However, little is known about what actually takes place during the prenatal care visits. The current practices of health care providers are not standardized. The panelists have agreed on the following evidence-based recommendations for interventions by the health care providers involved in prenatal care.

At this time, the prevalence of elevated BLLs in the population of pregnant women in NYC is presumed to be sufficiently low enough not to recommend universal blood lead screening. As mandated by New York State Law (see appendix A) all prenatal health care providers should be providing anticipatory guidance on the hazards of lead poisoning to each pregnant woman. The expert panel agrees with this and added that the educational message should include discussion of lead sources, exposure prevention and proper nutrition. The law also dictates that they should be assessing patients presenting at their initial prenatal visit for high dose lead exposure. The panel recommends that our practices should expand this to include any lead exposure, not just high dose. **In compliance with NYS law, the recommendation of the expert panel is to have prenatal health care providers assess each pregnant woman for lead exposure using the suggested risk assessment tool (see text box below). Any woman found to be at risk for lead exposure should have a BLL measured as soon as possible. Additionally, the expert panel noted that the standard of care for prenatal**

health care providers should be to document the results of either a risk factor questionnaire or a BLL for every pregnant woman in New York City.

Recommended risk factor questions to ask all pregnant women.

To standardize the clinical assessment of possible maternal exposure to lead, the panel recommends that providers ask <u>all</u> pregnant woman questions at the initial visit to ascertain exposure potential and obtain a BLL if they:

- ***Were born outside of the United States,***
- ***Engage in pica behavior,***
- ***Use imported spices, foods, cosmetics, ceramics or folk remedies,***
- ***Live in home where there are any recent or ongoing renovations,***
- ***Work in an occupation which places them at risk for lead exposure.***

Additional sources are listed in appendices D and E and discussed on pages 42-50.

A barrier to the task of screening in the office or clinic setting is the time constraint of the prenatal care visit. Health care providers already assume a large number of responsibilities that need to be addressed during the initial prenatal visit. To overcome this, the panel recommends that a checklist for assessing lead exposure risk be incorporated into existing standard prenatal care forms. These questions may be integrated into forms that are filled out in the waiting room or they may be added in as a mandatory section of the patient's chart. This will ensure compliance with NYS law, improve the detection and identification of women at risk and assist focusing risk reduction messages to individual pregnant women.

Over the past several years, at least four peer-reviewed scientific studies have demonstrated an association between lead exposure in children and cognitive impairments at BLLs below 10 µg/dL, the current "level of concern" as defined by the CDC (Canfield et al. 2003, Lidsky and Schneider 2003, Schwartz 1994, Lanphear et al.

2000, NYS DOH 2004). The most rigorous of these studies, a prospective longitudinal analysis of BLLs and IQ between the age of 6 and 60 months, found a non-linear inverse relationship between BLLs and IQ, with the greatest decrements occurring at the lowest BLLs (Canfield et al. 2003). It is accepted that lead can readily cross the placenta. The exposed fetus undergoes critical periods of neurodevelopment and the brain may be uniquely vulnerable to the diffuse cellular toxicity of lead. Consistent with this, there is now a growing body of evidence that prenatal exposure to lead causes poorer performance on scales of mental development and decrements in IQ in the same non-linear fashion seen in children exposed to lead postnatally (Wasserman et al. 2000, Gomaa et al. 2002). These studies demonstrated effects at BLLs < 10 µg/dL. Although, the effects appear small, the public health implications of these effects may be significant. At a population level, a shift in the population curve even a few IQ points to the left will notably increase the number of children at risk for problematic outcomes, and in need of special services. Collectively, the studies on the health and neurodevelopmental effects of lead demonstrate that there is no discernible threshold for the toxic effect of lead (Canfield et al. 2003, Schwartz 1994, Fulton et al. 1987, Pocock et al. 1994). However, it would be of unclear benefit in reducing the source of the lead exposure to require that any pregnant woman with a detectable BLL receive interventions beyond what is recommended for all pregnant women. Therefore, a BLL must be chosen at which there is an indication of exposure, a risk for adverse effects, and available effective interventions. The expert panel has reached the conclusion that **any pregnant woman with a BLL ≥ 5 µg/dL should receive counseling and a follow-up blood lead**

test. Additional steps may be necessary depending on the BLL (see Appendix M, Table 1).

Health care providers with access to women of childbearing age should take advantage of opportunities to educate them on the risks of lead poisoning during pregnancy. Providers with these opportunities include, but are not limited to, pediatricians, internists, obstetricians and family practitioners. Efforts should be made to train these health care providers how to perform an exposure history.

In general, the reduction of lead in the general environment means that most women will have lead levels below the panel's recommended concentration for intervention (< 5 μg/dL). Women presenting to the clinic with a BLL ≥ 5 μg/dL will have a history of exposure to lead. **It is the health care provider's responsibility to attempt to identify the source of the lead exposure by interview.** To assist them in this task, they must be provided with a comprehensive list of possible sources. Once identified, steps to limit further exposure and to treat the patient should be implemented. Resources exist to assist the provider in these tasks (See appendix O). This exposure could be past, recent or ongoing. In most cases, the source can be teased out by a thorough history. In the case of immigrants, the source may be in their country of origin. However, these patients still warrant a thorough investigation for ongoing exposures since they may have brought contaminated products from their country of origin, use folk remedies or lead containing cosmetics, engage in pica, use imported spices or lead-glazed ceramics, live in older housing, or engage in occupations with exposure risks. Questioning patients about the risk factors is an important part of education. This should be done in their primary language, whenever possible. When translators are used they

should be unbiased assistants in the process. It is also important that culturally appropriate terms be used. In the cases where no source is identified and the patient is properly informed of potential sources, close monitoring for changes in BLLs should be carried out. The frequency of re-testing is dependent upon the initial BLL (see table). In cases where a source is clearly identified, the scheduling of blood lead measurements may be modified by anticipated or ongoing exposure. Certain risk factors for exposure may also warrant increased follow-up or counseling, regardless of the patient's BLL. This is particularly relevant in cases of acute lead exposure where there is only a transient elevation which is not accurately reflected by a one-time blood test.

The maternal BLL at or around the time of delivery or an UCLL is considered a good estimate of the BLL of the neonate. One of these should be obtained if the mother's BLL has been ≥ 15 μg/dL at any time during the pregnancy. Follow-up of this level by the pediatric health care provider is critical. The expert panel recommends that the frequency of follow-up blood lead testing of the neonate exposed in utero be based upon the CDC recommended schedule for children (see Appendix M, table 3). This is done in conjunction with anticipatory guidance and distribution of educational materials. To ensure appropriate follow-up, the prenatal health care provider is urged to contact the pediatric health care provider responsible for the follow-up of the neonate to coordinate care.

Pediatric health care providers routinely follow the development of their patients. The neurodevelopmental deficits from prenatal lead exposure are subtle in the majority of cases and are difficult to detect. There is increasing interest in the ability of other factors to blunt the destructive effects of lead on the central nervous system. From an analysis of

the Boston cohort of lead exposed infants and children, the prenatally exposed 2 year old children (UCLL 6-7 μg/dL) showed impaired cognitive development only if they were from the lower social class stratum (Bellinger 2000). The report on the Port Pirie cohort at 11-13 years of age supports the hypothesis that children from socially disadvantaged backgrounds are apparently more sensitive to the effects of lead than children from higher SES families (Tong et al. 2000). An animal study demonstrated that rats raised in an enriched environment were significantly protected against the behavioral and neurochemical toxicity of lead (Schneider 2001). The conclusion of a recent review of the epidemiologic research concluded that "efforts should continue to reduce childhood lead exposure. However, from a public health perspective, exposure to lead should be seen within the many other risk factors impacting on normal childhood development, in particular the influence of the learning environment itself" (Koller et al. 2004). Confounders common to all of the epidemiologic studies are SES, parental IQ and the quality of the home environment. It is estimated that current lead exposure accounts for a very small amount of variance in cognitive ability (1-4%), whereas social and parenting factors account for 40% or more (Koller et al. 2004). These findings suggest that interventions that enrich the child's educational environment may be beneficial for children exposed prenatally to lead. **Therefore, the recommendation for pediatric health care providers is to offer the parents guidance on ways to provide an intellectually nourishing environment to the child. In cases, where this may be difficult, referral to available services such as Early Intervention or Head Start, may be warranted.**

To help delineate between an acute and a chronic exposure, it is advised to measure Erythrocyte Protoporphyrin (EP) or Zinc Protoporphyrin (ZPP) levels when the BLL is ≥ 30 µg/dL. An elevated lead level with a normal EP or ZPP would indicate that the exposure was recent, within the last 2-6 weeks. An elevated lead level with an elevated EP or ZPP is indicative of a chronic or ongoing exposure. Protoporphyrin levels are not sensitive to low levels of lead in blood (less than 30 µg/dL), and are not recommended as a screening test for low level exposure. In addition, EP or ZPP levels can be elevated in other medical conditions such as anemia of chronic disease and iron deficiency anemia. These can be ruled out with a complete blood count and red blood cell indices, a part of the routine prenatal labs.

Although, it is important for prenatal health care providers to be aware of the presentation of acute lead poisoning, in the great majority of adult cases, no symptoms are associated with elevations in BLLs. The signs and symptoms of acute lead toxicity in adults typically arise only when the BLL ≥ 60 µg/dL. Adults with highly elevated BLLs may complain of headaches, crampy abdominal pain, anorexia, constipation, fatigue, malaise, myalgias and arthralgias. The literature records cases, including pregnant women, where these symptoms have occurred at much lower BLLs (≥ 25 µg/dL) when the exposure is chronic (Rosenman et al. 2003, Shannon 2003). Toxicity can still occur in the absence of these symptoms as there may still be sufficient lead in the maternal circulation to cross the placenta and cause damage to the fetal brain. **The presence or absence of symptoms is not a reliable guide to the presence or absence of exposure to lead or its adverse health effects.**

Refer to the algorithm in appendix L for specific information on actions by health care providers based on BLL.

7. Chelation:

At BLLs ≥ 45 µg/dL in the late 2nd or 3rd trimester of pregnancy, health care providers should consider chelation to reduce the total body lead burden of the mother. This recommendation is made for pregnant women regardless of the presence or absence of symptoms or signs of toxicity. Due to the paucity of scientific literature which shows chelation to be beneficial in asymptomatic pregnant women, this recommendation is based on empiric evidence. Since the agents used are potentially harmful to the developing fetus, it is imperative that chelation of pregnant women be performed in consultation with an experienced specialist. The agent with which there is the most documented clinical experience is Calcium Disodium Edetate ($CaNa_2EDTA$).

The most comprehensive documentation of pregnant women treated for lead poisoning included 15 pregnant women of whom 5 underwent chelation with $CaNa_2EDTA$, dimercaprol or succimer. In 4 of the cases, $CaNa_2EDTA$ was the agent used. All of the women were in the 3rd or late 2nd trimester. No adverse effects on either the mother or fetus were observed during chelation. 13 of the neonates underwent chelation therapy, all within the first 28 days of life, using the same agents. No immediate or short term adverse effects of chelation were observed. Neurodevelopmental monitoring is ongoing (Shannon 2003). There are no known dangers of chelation therapy to pregnant women. Fetal effects are also uncertain as there are no reports of chelation-associated birth defects in humans in the relatively small number of infants who have been treated (Gardella 2001). A number of in vitro and in vivo animal studies have shown EDTA to be embryotoxic or teratogenic under the conditions in the study (REPROTEXT® Database). However, a study of metal-chelating

agents suggests that all materials used as chelating agents be administered with mineral supplements to prevent potential teratogenic effects due to induced trace element deficiencies (Domingo 1998). It is unlikely that these data are generalizable to humans. As a precaution, chelation should be avoided during particularly sensitive periods of development. In particular, the first half of pregnancy. Use of chelation during the 1st and early 2nd trimester should be limited to life threatening circumstances only. As with all medications administered during pregnancy, unnecessary exposure should be avoided. Breastfeeding should be temporarily stopped until the maternal BLL falls below 40 µg/dL.

The common side effects of intravenous therapy with $CaNa_2EDTA$ include headache, myalgias, nausea and vomiting. Serious adverse effects of this medication include a histamine-like reaction, low blood pressure, thrombophlebitis, nephrotoxicity and a systemic febrile reaction. There are no documented cases of serious reactions when used in pregnant women.

8. Calcium Supplementation and Nutritional Intervention:

The first step in intervention once a woman has been recognized as having an elevated BLL should be to identify and eliminate the source of lead. Nutritional assessment and advice based on this assessment should be given to attempt to minimize the impact of the toxin and to decrease the absorption of lead into the blood. These recommendations should be consistent with the nutritional recommendations for all pregnant women. The following evidence is a review of the benefits of good nutrition in cases of lead exposure.

As discussed earlier, lead that enters the body is stored in the bone. During pregnancy and lactation there is a marked increase in maternal bone turnover. Some studies have shown that calcium supplementation may decrease bone loss during lactation. These findings suggest that increasing maternal calcium through dietary supplementation could reduce bone resorption and therefore bone lead release. Another possible mechanism may involve decreased lead absorption in the intestine. A study to investigate the impact of dietary calcium supplements to lower BLLs in lactating women was conducted in Mexico City. The women were randomly assigned to receive either calcium carbonate (1200 mg of elemental calcium daily) or placebo in a double-blind trial. Among the subgroup of compliant women with high patella bone lead there was an estimated reduction in mean blood lead of 1.16 μg/dL (95% CI: -2.08, -0.23), an overall reduction of 16.4% (Hernandez-Avila et al. 2003). A study that supports this conclusion was conducted in Pittsburg, PA on a population of pregnant women with low exposure to lead. The authors found that high intakes of calcium (>2000 mg/day) decreased the BLL, which could potentially minimize fetal exposure to lead. This is nearly twice the amount of calcium recommended for women during pregnancy and approaches the upper limit for calcium intake of 2,500 mg/day (Hertz-Picciotto et al. 2000, Johnson. 2001). Research which has looked at the diets of women during pregnancy confirm that the association exists between BLLs and calcium intake. A cross-sectional study which surveyed women giving birth in Mexico City suggested that increased milk intake decreases maternal and umbilical cord lead levels (Hernandez-Avila et al. 1997). In a study of mother-infant pairs from lower socioeconomic circumstances living in Albany County, New York, the influences of maternal iron and vitamin D intake on neonatal

lead levels was clear. A two standard deviation increase in the intake of iron and calcium resulted in a decrease in neonatal BLL of 0.77 μg/dL or 45% of the mean neonatal BLL (Schell et al. 2003). It is the recommendation of the panel that pregnant women with BLLs above the level of intervention should have additional counseling on the need for calcium supplementation. The current dietary reference intake (DRI) for calcium is outlined in the table below. Refer to appendices J and K for a list of supplements and dietary sources of calcium.

The current Dietary Reference Intake (DRI) Values for Calcium	
Life Stage Group	**Adequate Intake (mg/day)**
Pregnancy	
≤18 years	1,300
19 through 50 years	1,000
Lactation	
≤18 years	1,300
19 through 50 years	1,000

(IOM 1997)

The DRIs are a set of four reference values: Estimated Average Requirements (EAR), Recommended Dietary Allowances (RDA), Adequate Intakes (AI), and Tolerable Upper Intake Levels, (UL) that have replaced the 1989 Recommended Dietary Allowances (RDAs) (IOM 1997, IOM 2002). The DRIs are nutrient-based reference values for use in planning and assessing diets and for other purposes. They are being determined by the Standing Committee on the Scientific Evaluation of Dietary Reference Intakes of the Food and Nutrition Board, Institute of Medicine (IOM), National Academy of Sciences, with help from Health Canada.

1. Estimated Average Requirement (EAR): The intake that meets the estimated nutrient need of 50% the individuals in a specific group. This figure will be used

as the basis for developing the RDA and can be used by nutrition policy-makers to evaluate the adequacy of nutrient intakes for population groups.

2. Recommended Dietary Allowance (RDA): The intake that meets the nutrient need of almost all (97 to 98%) of the healthy individuals in a specific age and gender group. The RDA should be used in guiding individuals to achieve adequate nutrient intake aimed at decreasing the risk of chronic disease. It is based on estimating an average requirement plus an increase to account for the variation within a particular group. If individual variation in requirements is well defined, the RDA is set at 2 standard deviations above the EAR, which means it should be high enough to meet the needs of at least 97% of the population. If sufficient data are not available, the RDA is set at 1.2 x EAR.

3. Adequate Intake (AI): When sufficient scientific evidence is not available to estimate an average requirement, Adequate Intakes (AIs) are set. These are derived though experimental or observational data that show a mean intake which appears to sustain a desired indicator of health, such as calcium retention in bone. The AIs should be used as a goal for individual intake where no RDAs exist.

Like lead, iron deficiency anemia can adversely affect neurodevelopment. Lead may produce an anemia by shortening red blood cell survival time and by inhibiting heme synthesis. Although hemolysis may be seen after acute or subacute high-dose exposure, the more common pattern is a slowly developing, hypochromic anemia with normocytic or microcytic indices, with the latter being a possible consequence of coexistent iron deficiency. In most cases seen in the U.S. population, the anemia is more likely the result of poor nutrition rather than the direct effect of lead. The proposed

mechanism for lead absorption is similar to that for other essential elements, in particular calcium and possibly iron. These competitive pathways result in increased lead absorption when dietary mineral intake is inadequate. In general, poor nutrition can result in increased lead absorption (Markowitz 2000). Therefore, it is the recommendation of this panel that all pregnant women should be counseled on good nutrition as part of the primary prevention of lead poisoning and its adverse effects. In addition, any women with a BLL greater than the threshold for intervention and iron deficiency anemia should be started on iron supplementation as per current management guidelines. Dietary sources of iron can be found in appendices J and K.

Estimated Average Requirement (EAR) and Recommended Dietary Allowance (RDA) of Iron for Pregnant and Lactating Women	
Life Stage	**(mg/day)**
EAR for Pregnancy	
14-18 years	23
19-50 years	22
RDA for Pregnancy	
14-50 years	27
EAR for Lactation	
14-18 years	7
19-50 years	6.5
RDA for Lactation	
14-18 years	10
19-50 years	9

(IOM 2002)

Some animal studies suggest that orally administered ascorbic acid may chelate lead and decrease the risk of the toxic effects of lead. However, results from several small studies in humans have yielded inconclusive evidence of a beneficial effect (Hsu and Guo 2002). Ascorbic acid blood levels have been found to have an inverse association with BLLs in pregnant women (West et al. 1994). In a study based on NHANES III, researchers found that youths in the highest serum ascorbic acid tertile had

an 89% decreased prevalence of elevated BLLs compared with youths in the lowest serum ascorbic acid tertile, OR=0.11 (95% CI: 0.04-0.35). Adults were found to have similar results (Simon and Hudes 1999). From this study it still remains unclear whether dietary supplementation is beneficial because dietary intake of ascorbic acid (from a 24 hour dietary recall) was substituted. In the study they did not find a statistically significant relationship between vitamin C intake and BLL. This is an area that requires further investigation before vitamin C supplementation can be recommended for the purpose of limiting fetal exposure to lead.

9. **Breastfeeding:**

Extensive research, especially in recent years, documents diverse and compelling advantages to infants, mothers, families and society from breastfeeding and the use of human milk for infant feeding. These include health, nutritional, immunologic, developmental, psychological, social, economic and environmental benefits (AAP 1997). As a result, pediatricians are encouraging mothers to breastfeed their babies. To establish a level of concern for the safety of the newborn or infant, regarding lead poisoning and breastfeeding, two points must be considered. The first one is how much lead is actually found in the breast milk of lead exposed women. The second is whether that dose contributes to an increase the total body lead burden of the child.

Any studies that measure the amount of lead in human milk should be viewed with caution. Methodological factors that may affect the reported results include the high potential for contamination of samples, inaccuracy of laboratory analytic methods and study design issues such as inconsistent sampling and analysis protocols, incomplete reporting of sampling methods, nonrepresentative sampling, timing and duration of

sampling and small numbers of study subjects (LaKind et al. 2001). Breast milk production is a dynamic process and the contents of the milk change from moment to moment.

Several studies have attempted to quantify the amount of lead in breast milk of lead exposed women. In Boston, as part of a longitudinal study of the sources and developmental effects of current urban lead exposure, lead was measured in tap water, breast milk and infant formulas. Blood lead was measured in the umbilical cord and at 6 months. The study found that overall milk lead accounted for only 10% of the variance in infant BLLs and the lead content of the milk correlated very well with their 6-month BLL ($r=0.42$, $P=0.0003$) (Rabinowitz et al. 1985). A later study looked at lead levels in the breast milk and blood of lactating mothers living in close vicinity to 3 lead smelters. This was a population with much higher average BLLs. 56% of the women had detectable milk lead levels. The mean BLL was 45.88 µg/dL (SD 19.88). Above 40, there was a very tight relationship between BLL and milk LL ($r=0.88$) (Namihira et al. 1993). The Academy of Breastfeeding currently recommends not to breastfeed when the mother's BLL is ≥ 40 µg/dL. Most recently, in a study of 310 lactating women in Mexico City, Mexico, breast milk lead was significantly correlated with umbilical cord lead (Spearman coefficient (r_s)=0.36, $p<0.0001$) and maternal blood lead at delivery ($r_s=0.38$, $p<0.0001$) and with maternal blood ($r_s=0.42$, $p<0.0001$) and patella lead ($r_s=0.15$, $p<0.01$) at 1 month postpartum. Mother's age, years living in Mexico city, and use of lead-glazed ceramics, all predictive of cumulative lead exposure, were not significant predictors of breast milk lead levels. The BLLs ranged from 1.8 to 29.9 µg/dL and the breast milk lead levels ranged from 0.21 to 8.02 ppb (Ettinger et al. 2004).

The results of this study indicate that even among a population of women with relatively high lifetime exposure to lead, levels of lead in breast milk are low. The values in this study agree with results from additional studies which estimate the lead concentration of milk to be 0.6 to 3% of the maternal BLL (Gulson et al. 2001, Manton et al. 2000).

There are no standards for the maximum daily permissible intake of lead for children. The limits suggested for adults are based on approximately 10% absorption from the digestive tract. The availability for infants is probably closer to 50%, depending on age and maturity. Any permissible limits must be much stricter for infants and children. At the time when the suggested standard for adults was 300 µg/d, literature suggested that the limit be set at 100 µg/d (Mahaffey. 1977). Additional evidence, based on theoretical not observational data, estimated that a maternal BLL of 20 µg/dL would lead to an increase of 3.4 µg/dL in the infant's BLL (Abadin et al. 1997). The scientific knowledge in this area is very limited.

The relationship of lead levels in breast milk to the infant's BLLs is not completely investigated or understood. At this time there are only estimates of the effect of maternal blood lead on the BLL of a breastfed infant. Lead does not concentrate in the breast milk because it does not attach to fat; thus, levels of lead are generally higher in a mother's blood than in her milk. In addition, the lead that is found in the breast milk is probably a reflection of the plasma concentration and not that of whole blood (Gulson et al. 1998). It is theoretically, only the lead in the plasma that crosses into the milk and not the lead sequestered in the red blood cells. This portion has been reported to range between 0.6% and 3% of the maternal BLL (Gulson et al. 2001, Manton et al. 2000).

In light of this limited and conflicting knowledge and the known public and personal health benefits of breastfeeding, it is recommended that breastfeeding be continued at lead levels less than 40 µg/dL. Above a maternal BLL of 40 µg/dL it is recommended to temporarily stop breastfeeding until a repeat level is below 40 µg/dL. During this interval, all efforts should be made to help the mother maintain her milk supply. For breastfed babies with mothers who have an elevated BLL it is recommended to check the infant's venous BLL. The results of this test dictate the schedule for follow-up which is adapted from the CDC's guidelines for childhood lead poisoning (see appendix M, Table 3) (CDC 2002). Above 6 months of age, follow-up is dictated by those guidelines. However, decisions should be made on an individual case basis. Whenever a breastfed infant has an elevated lead level, an evaluation of the home environment should be carried out to identify other, more likely, sources of the lead. In general, if the infant's BLL remains below 10 µg/dL and human milk is thought to be the source, the advantages of breastfeeding greatly outweigh the risks of lead exposure. Only upon the detection and elimination of all other suspected lead sources without corresponding reduction of the infant's BLL should the clinician recommend the cessation of breastfeeding.

10. Current Practices Of The LPPP:

Since 1992, the NYC Health Code has defined a BLL of 10 µg/dL or greater to be elevated. Medical signs and symptoms are more likely to be evident as the level of lead in the blood increases. Because lead can easily cross the placenta, women of child-bearing age with BLLs greater than 10 µg/dL are at risk of delivering a child with a BLL over 10 µg/dL – the level of concern in Public Health pediatric guidelines. For both men and women, BLLs should be as low as possible. At the time of that this report was developed, the LPPP was investigating cases of pregnant women with elevated BLLs when there is one venous BLL ≥ 20 µg/dL. As of August 2004, the NYC DOHMH has provided case management to any pregnant women with a venous BLL of ≥15 µg/dL. Case management includes assessment through interview to identify potential sources of exposure, source reduction counseling, and consultation with the woman's health care provider to ensure follow up BLL monitoring for the women and postnatal of their infants. Refer to appendix L for additional information.

11. Interventions by the LPPP:

The New York City Department of Health and Mental Hygiene's Lead Poisoning Prevention Program has responsibilities in both the primary and secondary prevention of lead poisoning in pregnant women. Primary prevention includes, but is not limited to, the development and distribution of educational materials and handouts to health care providers and pregnant women, dissemination of information on newly discovered sources of lead in the community and identification of the major sources in New York City. The materials prepared by the LPPP should be updated to reflect the findings of this report.

Periodically, a new source of lead is discovered within communities. It is recommended that the LPPP create an accessible list that other public health agencies can access and continually update when new sources are identified. The LPPP should develop and widely publicize a comprehensive list of possible sources of lead for pregnant women with a focus on the risk factors suspected to be the most common and the ethnic groups most likely to be affected.

Good nutrition is important for a healthy pregnancy. Proper nutrition, in particular the adequate intake of calcium and iron, has the potential to reduce the absorption of lead into the body. Information on proper nutrition during pregnancy should be reinforced when a women is identified as being at risk for lead exposure. This is not a substitute for lead source identification and elimination.

Individual case investigations and management are an additional responsibility of the LPPP. This includes educating the patient and supervising medical management. In these cases, the investigation should start with an interview of the woman followed by a

home and/or workplace investigation with direct observation. The current plan of the LPPP is to provide this educational and investigative intervention to any pregnant woman found to have a BLL ≥ 15 μg/dL on even a single occasion. Prenatal health care providers need to be active partners in this endeavor, particularly those caring for women at high-risk for lead poisoning. For this to be successful, they need to be educated on the risk factors for exposure and trained to take an environmental history.

It is the recommendation of the panel that the level at which prenatal health care providers attempt to identify lead sources with more than routine questions, provide risk reduction counseling, and provide follow-up testing be lowered to a BLL ≥ 5 μg/dL. The level of intervention for the LPPP which includes source identification, elimination and close follow-up to the end of pregnancy should be modified to a single BLL ≥ 15 μg/dL once at any time during pregnancy. The need to retest quickly is important in pregnant women because of the unique susceptibility of the fetus and the short time frame of gestation. At BLLs from 10 to 15 μg/dL, the patient should receive an educational packet. This material sent to the patient should stress the need for close follow up, discuss some of the possible sources of lead and include information on nutrition during pregnancy.

The LPPP should work closely with health care providers to assess and limit the exposure of pregnant women to lead. Identification of women at risk for lead exposure is the first step. The LPPP should distribute a lead risk assessment questionnaire to prenatal health care providers and provide education regarding its proper use. This can be integrated into already existing forms that are either filled out in the waiting area or by the provider seeing the patient. Since clinics that deal mainly with patients receiving Medicaid benefits undergo regular audits and these groups are often at higher risk for

lead exposure, the LPPP should work in partnership with the Prenatal Care Assistance Program (PCAP)/Medicaid program to improve the ways in which these clinics screen for lead exposure during pregnancy. To lower the prevalence, the LPPP should use identified sources from individual cases to focus public health campaigns within the appropriate communities. Each source, once identified, could be the target of a public health campaign with the appropriate communities. Focus groups are a way to find out more about the cultural groups with the highest prevalence of elevated lead levels.

IV. APPENDICIES

Appendix A

New York State Lead Poisoning Screening Requirements for Pregnant Women

Effective Date: December 22, 1993

Part 67-1.5 Lead Screening and follow-up of pregnant women by prenatal care providers.

(a) Prenatal health care providers shall provide each pregnant woman anticipatory guidance on lead poisoning prevention during pregnancy, and shall assess each pregnant woman at the initial prenatal visit for high dose lead exposure using a risk assessment tool. A risk assessment tool shall be recommended by the State Commissioner of Health.

(b) Prenatal health care providers shall screen or refer for blood lead screening each pregnant woman found to be at risk for current high dose lead exposure.

(c) Prenatal health care providers shall provide each pregnant woman, who has a confirmed BLL equal to or greater than 10 µg/dL of whole blood, risk reduction counseling in accordance with guidelines recommended by the State Commissioner of Health.

(d) Prenatal Care providers shall refer each pregnant woman, who has a confirmed BLL $\geq$ 10 µg/dL of whole blood and who may have been occupationally exposed to lead, to an occupational health clinic for individual guidance.

(e) Prenatal care providers shall provide anticipatory guidance to each woman at her postpartum visit on the prevention of childhood lead poisoning.

Appendix B

Charge Questions

1. What does the current evidence demonstrate regarding the health effects of various degrees of overexposure to lead in pregnant or lactating women and in neonates?

    a. What is the clinical impact on pregnancy outcomes of elevated lead levels?
        i. Stillbirths
        ii. Preterm delivery and gestational age
        iii. Spontaneous abortion
        iv. Birth weight
    b. What is the relationship between BLLs and Pregnancy induced hypertension?
    c. What is the clinical impact on neurodevelopment and behavior of prenatal lead exposure?
    d. What is the clinical impact of prenatal lead exposure on head circumference?
    e. What are the BLLs at which adverse clinical outcomes are seen?

2. At what blood lead level should minimal intervention such as education or follow-up testing be provided?

    a. By medical providers?
    b. By LPPP?

3. What are the appropriate intervention activities at different BLLs (e.g., 10-19 mcg/dL, ≥20 mcg/dL) for health care providers treating lead poisoned women during and after pregnancy?

    a. What educational messages should be provided to lead poisoned pregnant and lactating women?
    b. What is the role of medical providers in coordinating environmental risk assessment and intervention with the LPPP?
    c. What nutritional counseling should be provided to lead poisoned pregnant and lactating women. Specifically, what are the benefits of calcium and iron supplementation?
    d. What should the frequency of re-testing be for pregnant and lactating women and for the neonate?
    e. When should chelation be provided for pregnant and lactating women and for the neonate?
    f. What postpartum hospital discharge plans should be recommended?

4. What are the appropriate LPPP intervention activities for pregnant women at various BLLs (e.g., 10-19 mcg/dL, ≥20 mcg/dL), including environmental assessment of home and risk reduction for pregnant women and other family members?

    a. What type of environmental risk assessment of paint and non-paint lead hazards (e.g., pica, pottery, food sources, folk remedies, cosmetics, etc) is appropriate at different BLLs?
    b. What interventions should be recommended to eliminate or reduce sources of lead? When should lead-based paint hazard reduction be recommended? How should cultural practices among cultural and immigrant groups (e.g., pica, use of pottery, consumption of foods or consumption of supplements) be addressed in a culturally sensitive way?
    c. What counseling should the LPPP be providing to lead poisoned pregnant and lactating women?
    d. How should the LPPP coordinate with medical providers who are serving lead poisoned pregnant and lactating women?

5. Which pregnant women need to be tested for lead poisoning?

    a. What subgroups of pregnant and lactating women are at greatest risk of lead poisoning?
    b. What, if any, questions should be asked by medical providers of all pregnant women to determine whether they are high risk and need testing?
    c. How can LPPP best reach out to medical providers to promote systematic risk assessment and testing of pregnant women at high risk of lead poisoning.

6. What are the barriers that prevent health care providers from systematically assessing risk, testing, providing case management and coordinating care for pregnant and lactating women and newborns?

7. What are the cultural, ethnic and linguistic issues that LPPP staff and health care providers need to be aware of in order to reach and intervene with lead-poisoned pregnant women in NYC?

    What are the unique cultural characteristics that place these sub-populations at increased risk of lead exposure?

8. What information should medical providers be giving all pregnant women about lead poisoning prevention and, specifically, women at high risk of lead poisoning?

Appendix C

Table of Prevalence Data

Title	Survey	Sample Selection	Ages/Sex	Race	Geography	Sample Size	Lead standard	Survey Years	Prevalence

Table of Prevalence Data

1. Lead poisoning among pregnant women in New York City: risk factors and screening practices (Klitzman et al. 2002)	NYSDOH lead registry	Levels reported to the NYCDOH	15+ Pregnant women only	90% foreign born 57% from Mexico	New York City	33 total # of women with elevated BLLs unknown	BLL > of 20 µg/dl or higher	Sept 1996 and June 1999	33 women denominator unknown
2. Adult blood lead epidemiology and surveillance--United States, 1998-2001 (Roscoe et al. 2002)	Adult Blood Lead Epidemiol. And Surveillance (ABLES) program	Cases reported by 25 states during 1998-2001	16+ All adults, M + F workers	Not specified	25 states AL, AZ, CT, IA, MD, MA, MI, MN, NJ, NY, NC, OH, OK, OR, PA, RI, SC, TX, WA, WI, and WY, CA, (NE), NH, UT.	National sample, denominator is all persons 16+employed in the state, the year in question	>25 mcg/dL	1998-2001	13.4/100,000 employed adults vs. 15.2/100,000 for 1994-97 13.8 (1998) 12.9 (1999) 14.3 (2000) 12.5 (2001) 2.9/ 100,000 adults BLL >40mcg/dL 3.9/100,000 for 1994-97. 3.3 (1998) 2.5 (1999) 2.9 (2000) 2.8 (2001)
3. Adult Blood Lead Epidemiology and Surveillance--United States, second and third quarters, 1998, and annual 1994-1997 (Anonymous 1999)	Adult Blood Lead Epidemiology and Surveillance (ABLES) program	27 states reported surveillance data to ABLES	Ages 16+ M + F Gender or pregnancy status not known workers	Not specified	27 states Maine, NM, VT, not Nebraska	20,000 denominator for 94-97 are the population figures aged 16-64 of the individual participating states.	>25 mcg/dL	1998 vs 1997	4000/20,000
4. Reasons for testing and exposure sources among women of childbearing age with moderate BLLs (Fletcher et al. 1999)	NYS heavy metals registry	31,585 reported 197 levels 10-25 135 women interviewed via telephone	18-45 women only 35% pregnant	76% white 14% black 10% other	New York State 51% urban	31,585	10-25	1999	1.6% levels >10 197/31,585 levels b/tw 10-25

Title	Survey	Sample Selection	Ages/Sex	Race	Geography	Sample Size	Lead standard	Survey Years	Prevalence
5. Lead exposure among young urban women (Moline et al. 1999)	Study population	Women attending a NYC health care center were eligible. Participants recruited by MDs, the study coordinator and the participants themselves.	18-25 women only	62% African American 33% Hispanic 5% Caucasian or Asian.	New York City	239	Mean BLLs ascertained	1995-1998	mean blood lead level among study participants is 2.1 +/- 1.7 mcg/dl
6. Maternal blood lead level during pregnancy in South Central Los Angeles (Rothenberg et al. 1999b)	Study population	enrolled 1932 pregnant women	Women only	79.6 % Latino 19.3% AA 1.1% Other	South Central LA	1932 women 1428 immigrants 504 non-immigrants	> or = 10	1999	Pregnant immigrants mean = 2.3 mcg/dl pregnant nonimmigrants mean = 1.9 mcg/dl 25 out of the 30 cases ≥ 10 mcg/dl occurred in the immigrant group. The odds ratio (95% CI) for having elevated BLLs: (a) 9.3 (1.9, 45.8) if the immigrant engaged in pica; (b) 3.8 (1.4, 10.5) if the immigrant had low dietary calcium intake during pregnancy (c) 0.65 (.43, .98) for every natural log unit increase of years of residence in US.
7. Adult Blood Lead Epidemiology and Surveillance in New Jersey (Gerwel et al. 1998)	ABLES data	ABLES data for NJ workers	16+ 98% were male, w/ mostly occupational exposures	31% were minoritie 13% black 11% Hispanic 7% other	New Jersey	25021 reports of BLL> 25 on 5009 individuals	BLL> or = 25 µg/dL	January 1, 1986 to December 31, 1996	4011new cases
8. Exposure of the U.S. population to lead, 1991-1994 (Pirkle et al. 1998)	NHANES III	13,642 persons participated in Phase 2 of NHANES III	U.S. M + F population aged 1 year and older	National sample also targeted Mexican American	US	13,642 persons	Mean BLLs ascertained	1991 through 1994	The mean blood lead level of persons aged 1 to 74 years was 2.8 mcg/dL.

Title	Survey	Sample Selection	Ages/Sex	Race	Geography	Sample Size	Lead standard	Survey Years	Prevalence
9. Evolution of a state occupational lead exposure registry: 1986-1996 (Roche et al. 1998)	NJ lead registry	New Jersey adult lead registry	M + F	Not specified	New Jersey	23,456 reports of occupational lead toxicity	BLL> or = 25 µg/dL	January 1, 1986, through December 31, 1996	4011 new cases
10. Levels of lead in blood and bone of women giving birth in a Boston hospital (Hu et al. 1996)	Study population	223 women who gave birth in a Boston hospital obstetrical service	17-47yo Women only	62% white 23% black 5% Latino 5% Asian 6% other	Boston, MA	223	Mean umbilical cord BLLs ascertained	1990	umbilical cord BLLs were very low mean of 1.19 mcg/dL median of 1.0 mcg/dL
11. BLLs in the US population. Phase 1 of the Third National Health and Nutrition Examination Survey (NHANES III, 1988 to 1991) (Brody et al. 1994)	NHANES III	13,201 persons participated	15-45 women of childbearing age and pregnant women	Caucasian African - American	Standardized Metropolitan Statistical Areas (big urban areas) United States	13201	>10, 15, 20, and 25 mcg/dL. Looked at lead exposures sufficiently elevated to pose an intrauterine toxicity risk	1980 Census data 1984 census projections	Only 0.5% of women aged 12-49 had BLLs > 10 and this varied very little by race/ethnicity. Mean BLL in females 20-49 was 2.0 - 2.6 and in Mex American women was 2.0 3.3% of BLLs in the 20-49 age group were >10
12. The decline in BLLs in the United States. The National Health and Nutrition Examination Surveys (NHANES) (Pirkle et al. 1994)	NHANES II NHANES III HHANES Hispanic Health and Nutrition Examination Survey	NHANES data	M + F	nationally representative survey and another representing Mexican Americans in the southwestern US.	National data	n = 9832 n = 12,119 n=5682	Mean BLLs ascertained	1976 to 1980 1988 to 1991 1982-1984	Aged 1-74 BLL average was 2.8 mcg/L down from 12.8
13. Umbilical cord BLLs in the Quebec City area (Rhainds and Levallois. 1993)	Study population	823 live newborns in two hospitals from the Quebec City area	Newborns	Mostly French Canadian: 96.2% No Hispanic	Quebec City area Non-industrialized Suburban>rural>urban	823	Mean umbilical cord BLLs ascertained	spring 1990	The mean cord blood lead levels was 1.96 mcg/dL or 0.094 µmol/l ([95% CI] = 0.088-0.099). Less than 1% (95% CI = 0.2-1.7) of the babies had cord BLLs at 10 µg/dL (0.48

Title	Survey	Sample Selection	Ages/Sex	Race	Geography	Sample Size	Lead standard	Survey Years	Prevalence
									µmol/l) or greater. We estimate that each year in the Quebec City area between 150 and 200 newborns are at risk for developing psycho-neurological problems during their first years of life.
14. Studies on lead exposure in patients of a neighborhood health center: Part II. A comparison of women of childbearing age and children (Flanigan et al. 1992)	Study population	Not specified	541 pregnant women and 351 non-pregnant women of childbearing age	African American only	St Louis University School of Medicine, MO	892 total	greater than or equal to 10	1988-89	Mean PbB and prevalence rates at > than or equal to 10 and > than or equal to 15 mcg/dL were higher in the nonpregnant women of the than in the pregnant women The women showed mean PbB and prevalence that were not only higher than in white women but also higher than in black women nationally.
15. Lead levels among pregnant women in Hennepin County (Fredeen et al. 1992)	Study population	women receiving prenatal care from seven Minneapolis clinics and one suburban Hennepin County clinic	pregnant women	White 37.4% AA 32.9% Am Indian 16.6% Hmong 6.4% Laotian/ Cambodian/Vietnamese 2.2% Hispanic 0.8% Other 3.7%	Minneapolis area women	n = 1,055 resampled 1/3 in second half of pregnancy = 375	Mean BLLs ascertained	1988-1990	The mean Pb-B level of the first sample was 1.83 +/- 1.83 mcg/dL; of the second sample 1.99 +/- 1.92 mcg/dL. Only one woman had a Pb-B level > 12.0 mcg/dL, which was occupational
16. Patterns of BLLs in US black and white women of childbearing age (Geronimus and Hillemeier. 1992)	NHANES II	NHANES data	US women of childbearing age, 15-44 years	black and white women excluded pregnant women	National sample	1397 White 206 black	Mean BLLs ascertained	1976-1980	Black women tend to have higher lead levels than white women, and the magnitude of this difference is larger among older compared to younger age-groups of reproductive-age women.

Title	Survey	Sample Selection	Ages/Sex	Race	Geography	Sample Size	Lead standard	Survey Years	Prevalence
17. Determination of numbers of lead-exposed women of childbearing age and pregnant women: an integrated summary of a report to the U.S. Congress on childhood lead poisoning (Crocetti et al. 1990)	NHANES II	NHANES data to generate projected prevalence	women of childbearing age, ages 15 to 19 and 20 to 44.	white and black women	National sample	Census data	Estimates of mean BLLs ascertained	projected 1984 prevalence of PbB levels	Caucasian Women: 15-19: 9.2% 20-44:9.7% African American 15-19: 8.2% 20-44: 19.7% 4.4 million U.S. women of childbearing age estimated to have had PbBs > than 10 mcg/dL 403,200 pregnant women were estimated to have levels > 10 mcg/dL.
18. National estimates of BLLs: United States, 1976-1980: association with selected demographic and socioeconomic factors (Mahaffey et al. 1982)	NHANES II	NHANES data	6 months through 75 years old M + F	White, Black or other (Am Indians, Chinese, Japanese, and all other races not white or black.) Mexican were included with whites.	National sample	27801	greater than or equal to 30 mcg/dl	1976 – 1980	22% of popn 6mo to 74y had BLLs under 10 mcg/dL 1.9% had levels >30 mcg/dL. Suggests that 86% of population had levels between 10 and 30 mcg/dL. Mean levels of blood lead were higher in blacks than white, among young children living in urban and rural areas, and among members of low-income, moderate-income, and higher-income families. Young children from families w/ incomes under $6,000 had higher prevalence of elevated lead levels.

Appendix D
Folk Remedies or Cosmetics that Have Been Found To Contain Lead

Al Murrah	Used as a remedy for colic, stomach aches and diarrhea in Saudi Arabia
Albayalde or albayaidle	Used by mainly by Mexicans and Central Americans to treat vomiting, colic, apathy and lethargy.
Alkohl (also known as kohl, surma or saoott)	A black powder used within Middle Eastern, African and Asian cultures as an eye cosmetic and umbilical stump remedy.
Anzroot	A remedy from the Middle East used to treat gastroenteritis.
Ayurevedic Remedies	A number of these may contain lead: o Guglu o Sundari Kalp o Jambrulin
Azarcon (also known as reuda, liga, coral, alarcon and maria luisa)	A bright orange powder used within Hispanic cultures to treat gastrointestinal upset and diarrhea.
Ba Bow Sen (Ba-Baw-Sen)	Used to detoxify "fetus poisoning" and treat colic, hyperactivity and nightmares in children in China.
Bali goli	A round, flat black bean which is dissolved in "gripe water" and used within Asian Indian cultures for stomach ache.
Bint al dahab, bint or bent	Used as a remedy for diarrhea, colic, constipation and general neonatal uses in Oman, Saudi Arabia and India.
Bokhoor (and noqd)	Burned on charcoal to produce pleasant fumes and calm infants in Saudi Arabia.
Cebagin	Used in the Middle East as a teething powder.
Chuifong tokuwan	A pill imported from Hong Kong used to treat a wide variety of ailments.
Cordyceps	Used in China as a treatment for hypertension, diabetes and bleeding.
Deshi Dewa	A fertility pill used in Asia and India.
Farouk	A teething powder from Saudi Arabia.
Ghazard (Ghasard)	A brown powder used within Asian Indian cultures to aid digestion.
Greta	A yellow-orange powder used within Hispanic cultures to treat digestive problems.
Hai Ge Fen (Concha cyclinae sinensis)	A Chinese herbal remedy derived from crushed clam shells.

Henna	Used as a hair dye and for temporary tattoos in the Middle East and India that may contain lead.
Jin Bu Huan	From China.
Kandu	A red powder from Asia and India used to treat stomachache.
Koo Sar Pills	Red pills from China used to treat menstrual cramps.
Kushta	Used for diseases of the heart, brain, liver, and stomach and as an aphrodisiac and tonic in India and Pakistan
Litargirio	A yellow or peach-colored powder used as a deodorant, a foot fungicide and a treatment for burns and wound healing particularly by people from the Dominican Republic.
Pay-loo-ah	An orange red powder used within Southeast Asian cultures to treat rash or fever.
Poying Tan	General Chinese remedy.
Santrinj	Used as a teething powder in Saudi Arabia.

Appendix E

Lead Related Occupations and Industries

Ammunition/explosives production
Automotive repair shops
Battery manufacturing and recycling
Brass, bronze, copper or lead foundries
Bridge, tunnel and elevated highway/subway construction
Cable/wire stripping, splicing or production
Ceramic manufacturing
Firing range work
Glass recycling, stained glass and glass manufacturing
Home renovation/restoration
Lead Abatement
Lead production or smelting
Machining or grinding lead alloys
Manufacturing and installation of plumbing components
Manufacturing of industrial machinery and equipment
Metal scrap yards and other recycling operations
Motor vehicle parts and accessories
Occupations using firearms
Plastics manufacturing
Pottery making
Production and use of chemical preparations
Rubber manufacturing
Sandblasting, sanding, scraping, burning or disturbing lead paint
Use of lead based paints
Welding or torch-cutting painted metal

Hobbies and Activities That May Cause Lead Exposure

Making stained glass and painting on stained glass
Copper Enameling
Bronze Casting
Making pottery and ceramic ware with lead glazes and paints
Casting ammunition, fishing weights or lead figurines
Collecting, painting or playing games with lead figurines
Jewelry making with lead solder
Electronics with lead solder
Glassblowing with leaded glass
Print making and other fine arts
Liquor distillation
Hunting and target shooting

Appendix F - Lead Exposure and Pregnancy Outcomes

Study	Lead Level(s) Measured	Outcome(s)	Lead Levels	Results
Placental Lead and outcome of Pregnancy (Falcon et al. 2003)	Placental Lead Level	PROM; Preterm birth; birth weight; anthropometric measurements; Apgar Scores	N=89; mean=113.4 ngPb/g dry tissue; S.D.=58.0	significant negative correlation between lead levels and gestational age, preterm pregnancies and early membrane ruptures. Higher placental lead levels, in general, were not related to smaller weight, head and abdominal circumference or shorter length at birth.
Blood Lead Concentrations and Pregnancy Outcomes. (Sowers et al. 2002)	Maternal BLLs	Apgar scores; birth weight; gestational age; SGA	Average BLL = 1.2 µg/dL (se = +/- 0.03)	No association was found between the listed outcomes and BLLs
BLLs Measured Prospectively and Risk of Spontaneous Abortion (Borja-Aburto et al. 1999)	Maternal BLLs	Spontaneous Abortion	Cases: 12.0 µg/dL (range 3.1-29 µg/dL) Controls: 10.1 µg/dL (range 1.3-26 µg/dL)	OR = 1.8 (CI = 1.1-3.1) for each 5 µg/dL
Blood Lead and Cadmium and Birth Weight Among Sub-Arctic and Arctic Populations of Norway and Russia (Odland et al. 1999)	Maternal BLLs	Birth Weight and BMIC	Mean BLLs were 3.8 µg/dL exposed and 1.6 µg/dL nonexposed	Maternal blood lead was recognized as a negative explanatory variable ($p<0.05$) for birth weight and child's body mass index (BMIC), with or without adjustment for gestational age
Intrauterine Lead Exposure and Preterm Birth (Torres-Sanchez et al. 1999)	Umbilical Cord Blood Lead Level	Preterm Birth	Cases: 9.77 µg/dL +/- 2.0 Controls: 8.24 µg/dL +/- 2.15	In primiparous women only the frequency of preterm birth was almost 3 times higher among women who had UCL levels ≥ 5.1 µg/dL

Study	Lead Level(s) Measured	Outcome(s)	Lead Levels	Results
Decrease in Birth Weight in Relation to Maternal Bone-Lead Burden (Gonzalez-Cossio et al. 1997)	Maternal and Umbilical Cord BLLs and Maternal tibia and patella lead	Birth Weight	Mean, Median and SD Maternal Blood: 8.9, 9.1 and 4.1 µg/dL UCL: 7.1, 6.2 and 3.5 µg/dL Tibia: 9.8, 9.1 and 8.9 µgPb/g bone mineral Patella: 14.2, 13.8 and 13.2 µgPb/g bone mineral	Tibial (cortical) bone-lead burden is inversely related to birth weight
Prenatal Lead Exposure in Relation to Gestational Age and Birth Weight: A Review of Epidemiologic Studies (Andrews et al. 1994)	Studies from 1971-1991	PROM, Preterm birth; gestational age; birth weight	Many of the studies were done on high risk populations with no direct measurement of lead levels	Increased risk of preterm delivery. Unlikely to increase the risk of PROM. Possible association with decreased birth weight.
A Prospective Study of Birth weight and Length of Gestation in a Population Surrounding a Lead Smelter in Kosovo, Yugoslavia (Factor-Litvak et al. 1991)	Maternal Blood Lead Level	Birth weight; Length of Gestation; Preterm Birth	Exposed: 19 µg/dL +/- 7.9 Control: 5.6 µg/dL +/- 1.9	No difference in Birth weight or length of gestation.
Lead in the Placenta, Membranes, and Umbilical Cord in Relation to Pregnancy Outcome in A Lead-Smelter Community. (Baghurst et al. 1991)	Umbilical Cord Blood and Placental Tissue Concentrations	Stillbirth; Preterm Birth; PROM	Avg. Maternal BLL Preterm Births: 11.9 µg/dL Controls, PROM and Late Fetal Death: between 8 and 9 µg/dL	The authors conclude that a correlation was found between placental tissue lead levels and stillbirth rate and preterm birth but not PROM.

Appendix G
Neurodevelopment

Study	Lead Level(s) Measured	Outcome(s)	Lead Levels	Results
Low-Level Environmental Lead Exposure and Intellectual Impairment in Children: An International Pooled Analysis (Lanphear et al. 2004)	Blood Lead	Full Scale IQ score	Geometric mean BLL peaked at 17.8 mg/dL and declined to 9.6 mg/dL by 5 to 7 years of age; 240 (18%) children had a maximum BLL that never met or exceeded 10 mg/dL and 103 (7.7%) children had a maximum BLL that never met or exceeded 7.5 mg/dL.	Using a log-linear model, there was a 9.2 point IQ decrement associated with an increase in concurrent BLL from 1 mg/dL to 30 mg/dL. The model estimated an IQ decrement associated with an increase in blood lead for the ranges 1 mg/dL to 10 mg/dL, 10 mg/dL to 20 mg/dL and 20 mg/dL to 30 mg/dL of 6.2, 1.8 and 1.1 points, respectively.
Intellectual Impairment in Children with Blood Lead Concentrations Below 10 µg/dL. (Canfield et al. 2003)	Blood Lead	Stanford-Binet Intelligence Scale	*For children with complete data* Lifetime avg: 7.4+/-4.3 Peak: 11.1+/-7.1 Concurrent: 5.8+/-4.1 Avg in infancy: 7.0+/-3.8	In a nonlinear model, IQ declined by 7.4 points as lifetime average blood lead concentrations increased from 1 to 10 µg/dL.
Maternal Bone Lead as an Independent Risk Factor of fetal Neurotoxicity: A Prospective Study. (Gomaa et al. 2002)	Umbilical and Maternal Blood Lead; Tibia and Patella Bone Lead	Bayley Mental Development Index and Psychomotor Development Index(BSID-II)	Mean(SD) Range Umb. 6.7(3.4) 1.2-21.6 Pat. 17.9(15.2) <1-76.6 Tib. 11.5(11.0) <1-85.9	In relation to the lowest quartile of trabecular bone lead, the 2nd, 3rd, and 4th quartiles were associated with 5.4, 7.2 and 6.5 point decrements in adjusted MDI scores. A 2-fold increase in cord blood lead level was associated with a 3.1 point decrement in MDI Score.

Study	Lead Level(s) Measured	Outcome(s)	Lead Levels	Results
Early exposure to lead and juvenile delinquency. (Dietrich et al. 2001)	Maternal (prenatal) and Child Blood Lead	Antisocial and delinquent behaviors by self and parental reports	Prenatal BLL: Mean(SD) = 8.9(3.9) Range was not reported	Prenatal exposure to Pb was significantly associated with a covariate-adjusted increase in the frequency of parent-reported delinquent and antisocial behaviors, while prenatal and postnatal exposure to Pb was significantly associated with a covariate-adjusted increase in frequency of self-reported delinquent and antisocial behaviors.
Brainstem Auditory Evoked Response at Five Years and Prenatal and Postnatal Blood Lead. (Rothenberg et al. 2000)	Maternal and Child Blood Lead	BAER and Head Circumference	Mean (SD) 20 Week 8.1(+8.1/-4.0) Cord 8.7(+8.4/-4.3)	The nonlinear model showed I-V and III-V interpeak intervals decreased as 20 week blood lead rose from 1 to 8 µg/dL, and then increased as blood lead rose from 8 to 30.5µg/dL.
The Yugoslavia Prospective Lead Study: Contributions of Prenatal and Postnatal Lead Exposure to Early Intelligence. (Wasserman et al. 2000)	Maternal and Child Blood Lead	McCarthy GCI (ages 3 and 4); Wechsler Preschool and Primary Scale of Intelligence-Revised (age 5), Wechsler Intelligence Scale for Children-version III (age 7)	Means Mid-pregnancy Exposed: 18.2 µg/dL Controls: 5.25 µg/dL Umbilical Exposed: 20.4 µg/dL Controls: 5.01 µg/dL Prenatal Exposed: 19.5 µg/dL Controls: 5.13 µg/dL	With adjustment for covariates, they detected a significant decrement of 6.05 points in IQ for each log unit increase in prenatal BLL. A 50% rise in prenatal BLL was associated with a 1.07 point decrement in IQ (95% CI:0.60, 1.53). The association between prenatal BLL and IQ is not linear; the strongest postnatal effects are noted at the lower levels of prenatal exposure.

Study	Lead Level(s) Measured	Outcome(s)	Lead Levels	Results
Low-Level Prenatal Lead Exposure and Neurobehavioral Development of Children in the First Year of Life: A Prospective Study in Shanghai. (Shen et al. 1998)	Cord Blood Lead	Bayley MDI	Geometric Mean for all cord blood: 9.2 µg/dL High Pb group: 13.4µg/dL (SD=2.0) Low Pb group: 5.3µg/dL (SD=1.4)	After adjusting for confounders Infants who had higher cord BLLs had lower MDI scores at all three visits during the first year ($P \leq 0.25$). The difference in PDI was only seen at the 3 month visit.
Results of Lead Research: Prenatal Exposure and Neurological Consequences. (Goyer. 1996)	General Review Article	NA	NA	There is limited evidence that prenatal lead exposure leads to neurodevelopmental deficits in spite of the demonstrated morphological and pharmacological effects in the maturing brain.
Pre- and Postnatal Lead Exposure and Behavior Problems in School-Aged Children. (Bellinger et al. 1994)	Umbilical Cord Blood and Tooth Lead	Teacher Report Form (Child Behavior Checklist) which yielded a Total Problem Behavior Score	Means Cord Blood: 6.8 µg/dL, SD=3.1 (all <15) Tooth: 3.4 µg/g, SD=2.4	The risk of behavior problems was unrelated to children's prenatal Pb exposure.
A Critical Review of Low-Level Prenatal Lead Exposure in the Human: 2. Effects on the Developing Child (Ernhart. 1992)	Critical Review Article	Based on scientific literature available at the time of this report.	Prenatal lead exposure from several studies.	There is little consistency in the evidence of behavioral effects of prenatal lead exposure. If there are effects at the levels described in these studies, those effects are small and, apparently, not persistent in the massive milieu of other conditions that influence children.

Study	Lead Level(s) Measured	Outcome(s)	Lead Levels	Results
Low-Level Lead Exposure In the Prenatal and Early Preschool Periods: Language Development. (Ernhart and Greene. 1990)	Maternal and Cord Blood Lead; Child Blood Lead	Bayley MDI (6m, 1y, 2y); Stanford-Binet (3y); WPPSI (4y 10m); Sequency Inventory of Communication Development (1,2,3y); Recorded Speech Sample for Medium Length Utterance (2y)	Source: Arithmetic Mean(SD) Range Maternal: 6.56 (1.81) 2.7-11.8 Cord: 6.03 (2.12) 2.8-14.7 Source: Geometric Mean (SD) Maternal: 6.30 (1.33) Cord: 5.69 (1.41)	MLU at 2 y was significantly correlated with cord blood lead; otherwise, there were no statistically significant associations between prenatal (cord) lead exposure and Language development after correcting for cofactors.
Neurobehavioral Consequences of Prenatal Low Level Exposures to Lead. (Cooney et al. 1989)	Maternal and Cord Blood Lead	Bayley MDI and PDI at 6, 12 and 24 months, McCarthy GCI motor subscale at 36 months	Range: 0-29 µg/dL with the majority below 15	Did not find an association between maternal and cord BLLs and developmental deficits in young children to the age of three years.
Low Level Lead Exposure in the Prenatal and Early Preschool Periods: Intelligence Prior to School Entry. (Ernhart et al. 1989)	Maternal and Cord Blood Lead	Wechsler Preschool and Primary Scales of Intelligence (4y10m); Stanford-Binet (for 2 children with MR)	Source: Arithmetic Mean(SD) Range Maternal: 6.56 (1.81) 2.7-11.8 Cord: 6.03 (2.12) 2.8-14.7 Source: Geometric Mean (SD) Maternal: 6.30 (1.33) Cord: 5.69 (1.41)	Fetal BLL was significantly correlated with decrements in full scale, verbal and performance IQs at 4 years 10 months of age.
Neurobehavioral Deficits After Low Level Lead Exposure in Neonates: The Mexico City Pilot Study. (Rothenberg et al. 1989)	Maternal and Neonatal Blood Lead	Neonatal Behavioral Assessment Scale (NBAS) at 48 hrs, 15 and 30 days of life.	Source: Mean (SD) Range (µg/dL) Maternal @ 36 wks: 15.0(6.4) 5.5-42 Maternal @ birth: 15.5(5.7) 6.0-33.5 Umbilical Cord: 13.1(6.0) 3.0-33.5	The change in lead in the mother between 36 weeks and birth predicted NBAS regulation of state as identified by the neonatal behavioral assessment scale at 15 days (p=0.049), regulation of state at 30 days (p=0.055) and autonomic regulation at 30 days (p=0.073).

Study	Lead Level(s) Measured	Outcome(s)	Lead Levels	Results
The Port Pirie Cohort Study: Lead Effects on Pregnancy Outcome and Early Childhood Development. (Baghurst et al. 1987)	Maternal and Cord Blood Lead	Bayley Scales of Infant Development MDI and PDI at 24 months of age.	Mean Maternal Lead Level Exposed: 9.9-10.4 µg/dL Control: <3 µg/dL	No association was found between prenatal or at birth BLLs and the Bayley MDI and PDI.
Longitudinal Analyses of Prenatal and Postnatal Lead Exposure and Early Cognitive Development. (Bellinger et al. 1987)	Umbilical Cord Blood Lead	Bayley Scales of Infant Development MDI at 6 months then semiannually	Low <3ug/dL Medium 6-7 µg/dL High ≥10ug/dL	At all ages, infants in the high prenatal exposure group scored lower than infants in the other two groups.
Low-Level Fetal Lead Exposure Effect on Neurobehavioral Development in Early Infancy. (Dietrich et al. 1987)	Maternal, Cord and Newborn Blood Lead	Bayley Scales of Infant Development MDI and PDI at 3 and 6 months	Source: Mean (SD) Range (µg/dL) Prenatal: 8.0 (3.7) 1-27 Umbilical: 6.4 (4.5) 1-28	In multiple regression analysis, prenatal Pb decreased MDI by 0.34 for each increase of 1 µg/dl of Pb and umbilical cord Pb decreased MDI by 0.6 for each increase of 1 µg/dl of Pb.
Low Level Lead Exposure in the Prenatal and Early Preschool Periods: Early Preschool Development. (Ernhart et al. 1987)	Maternal, Cord and Child Blood Lead	Several Developmental Measures	Sample: Mean (SD) Range (µg/dL) Maternal: 6.4 (1.8) (3.0-11.8) Cord: 5.7 (2.0) (2.6-14.7)	With statistical control of covariate measures as well as potentially confounding risk factors most statistically significant associations of PbB with concurrent and later development were completely attenuated.

Study	Lead Level(s) Measured	Outcome(s)	Lead Levels	Results
Intrauterine Exposure to Low Levels of Lead: The Status of the Neonate (Ernhart et al. 1986)	Maternal and Cord Blood Lead	Routine newborn assessments; Examination for Minor Anomalies; The Brazelton Neonatal Behavioral Assessment; The Graham/Rosenblith Behavioral Examination	Sample: Mean (SD) Range (µg/dL) Maternal: 6.4 (1.8) (3.0-11.8) Cord: 5.7 (2.0) (2.6-14.7)	In regression analyses, seven behavioral scales were unrelated to either maternal or UCLL. Three scales, the NBAS Abnormal Reflexes, the G/R Neurological Soft Sign, and the G/R Muscle Tonus Scales, were related minimally to either UCLL or maternal BLL.

Appendix H
Head Circumference

Study	Lead Level(s) Measured	Outcome(s)	Lead Levels	Result
Effect of Maternal Bone Lead on Length and Head Circumference of Newborns and 1 Month Old Infants. (Hernandez-Avila et al. 2003)	Tibia and Patella Bone Lead Levels	Length and Head Circumference	Mean bone lead levels Tibia: 9.8 µgPb/g bone mineral Patella: 14.4 µgPb/g bone mineral	Tibia lead associated with decreased birth Length (OR 1.79; 95% CI = 1.10, 3.22) Patella lead negatively associated with head circumference [Risk = 1.02 per µgPb/g bone mineral (95% CI = 1.01, 1.04)]
Pre- and Postnatal Lead Effect on Head Circumference: A Case for Critical Periods. (Rothenberg et al. 1999)	Maternal Blood Lead Level	Head Circumference	Range of Median BLLs = 7.5-9.0 µg/dL during pregnancy and 7.0-10.0 µg/dL for in children from birth to 48 months	Negative association between 6-month head circumference and 36-week maternal BLL
Prenatal and Preschool Age Lead Exposure: Relationship with Size. (Greene and Ernhart. 1991)	Maternal and Umbilical cord BLLs	Head Circumference; Weight; Stature	Maternal: Mean = 6.22 SD=1.35 Umbilical: Mean = 5.63 SD=1.41 (µg/dL)	No Statistically adverse effects were seen.

Appendix I
Hypertension

Study	Lead Level(s) Measured	Outcome(s)	Lead Levels	Results
Lead Induced Increase of Blood Pressure in Female Lead Workers. (Nomiyama et al. 2002)	Blood Lead	Blood Pressure	Exposed: Mean 44.42, SD 13.52, Range 22.5-99.4 Control: Mean 6.42, SD 1.55, Range 3.8-11.4 (µg/dL)	BLLs were positively correlated to Systolic and diastolic blood pressure, as well as, pulse pressure
Increases in Hypertension and Blood Pressure During Pregnancy with Increased Bone Lead Levels. (Rothenberg et al. 2002)	Tibia and calcaneus bone lead Maternal Blood Lead	Third Trimester Blood Pressure	Tibia: Mean 8.0 µg/g, SD 11.4 Calcaneus: Mean 10.7 µg/g, SD 11.9 Prenatal BLL: mean 1.9 µg/dL, SD +3.6/-1.0 Postnatal BLL: mean 2.3 µg/dL, SD +4.3/-1.2	For each 10 µg/g increase in calcaneus (trabecular) bone lead level, the odds ratio for HTN was 1.86 (95% CI: 1.04, 3.32), the increase in sys bp was 0.70 mmHg (95% CI: 0.04, 1.36), and dias bp was 0.54 mmHg (95% CI: 0.01, 1.08)
Blood Lead Concentrations and Pregnancy Outcomes (Sowers et al. 2002)	Blood Lead	Presence of Pregnancy Induced Hypertension	Avg. = 1.2 µg/dL (s.e. = +/- 0.03	Revealed an association at very low levels of blood lead.
Blood Cell Lead, Calcium, and Magnesium Levels Associated with Pregnancy-Induced Hypertension and Preeclampsia (Dawson et al. 2000)	Red Blood Cell Lead	Systolic and diastolic blood pressure; presence of preeclampsia	Normal: 1.35 +/- 0.27 Mild PE: 1.71 +/- 0.35 Severe PE: 1.79 +/- 0.22	Revealed a direct relationship at very low levels of blood lead.
Blood Lead Level and Blood Pressure During Pregnancy in South Central Los Angeles (Rothenberg et al. 1999a)	Blood Lead	Systolic and Diastolic Blood Pressure	Immigrant: 2.3 µg/dL SEM: +/- 0.04 Nonimmigrant: 1.9 µg/dL SEM: +0.06/-0.04	From the 5^{th} to 95^{th} blood lead percentiles (0.9-6.2 µg/dL) in immigrants, systolic blood pressure increased 2.8 mmHg and diastolic blood pressure increased 2.4 mmHg.

Study	Lead Level(s) Measured	Outcome(s)	Lead Levels	Results
Increased Risk of Proteinuria among a Cohort of Lead-exposed Pregnant Women (Factor-Litvak et al. 1993)	Blood Lead	Proteinuria	Means Exposed: 17.1 µg/dL Non-exposed: 5.1 µg/dL	Comparing the women in the upper 10^{th} %ile with those in the lowest 10^{th}, the adjusted odds ratio for ≥ 1+ proteinuria was 4.5 (95% CI 1.5, 13.6)
Review of the Relation Between Blood Lead and Blood Pressure. (Hertz-Picciotto and Croft. 1993)			Studies from 1980-1992 representing occupational or population based cohorts	The evidence suggests a small dose response though the range of blood led values up to about 30 or 40 µg/dL.
Pregnancy Hypertension, Blood Pressure During Labor and BLLs. (Rabinowitz et al. 1987)	Umbilical Cord Lead	Systolic and Diastolic Blood Pressure; Presence of PIH	Mean: 6.9 +/- 3.3	Lead levels correlated with both systolic and diastolic blood pressures during labor. The incidence of PIH increased with lead level. No association with preeclampsia.

Appendix J

Multivitamins for Women

Brand Name	Calcium	Iron	Folic Acid
Centrum	162mg	18mg	400mcg
Centrum Complete Performance	100mg	18mg	400mcg
Centrum Silver	200mg	none	400mcg
One-A-Day Today for Active Women	240mg	none	400mcg
One-A-Day Women's Tablets	450mg	18mg	400mcg

Prenatal Vitamins

Brand Name	Calcium	Iron	Folic Acid
Estroven	150mg	none	400mcg
Obegyn Prenatal	455mg	18mg	1mg
Pre-Care Chewables	250mg	40mg	1mg
Pre-Care Conceive	200mg	30mg	1mg
Pre-Care Prenatal Caplets	250mg	40mg	1mg
Premesis Rx	200mg	none	1mg
Prenate GT	200mg	90mg	1mg
Primacare GM	250mg	30mg	1mg
Natachew	None	29mg	1mg

Calcium Supplements

Brand Name	Calcium
Active Calcium Usana (4 per day)	200mg
Caltrate 600	600mg
Citracal (1-2 BID)	200mg
D-Cal Chewable (1 BID)	300mg
Extra Strength Rolaids	675mg
Rolaids	550mg
Florical (1 QD)	145mg
OsCal (1 BID-TID)	500mg
Tums	500mg
Tums E-X	750mg
Tums Ultra	1000mg

Iron Supplements

Brand Name	Iron
Feosol	45mg
Fergon	27mg
Nu-Iron	150mg

Appendix K

Foods that contain iron

The best way to get iron is from foods such as those listed below (along with the amount of iron they contain). If you have anemia, you may need more iron, and your doctor may prescribe a supplement. Do not take an iron supplement unless your doctor advises you to do so.

Liver, 4 oz cooked	9 mg
Beef, 4 oz	3 mg
Turkey, 4 oz dark meat	2 mg
Pork, 4 oz	1 mg
Shrimp, 12 large	2 mg
Chicken breast, 4 oz	1 mg
Fish/tuna, 4 oz	1 mg
Egg, 1 large	1 mg
Prune juice, 8 oz	3 mg
Apricots, 5 halves dried	0.8 mg
Dates, 10 dried	1 mg
Raisins, 1/3 cup	1 mg
Refried beans, 1 cup	4.5 mg
Spinach, 2 cups cooked	3 mg
Peas, 2 cups	1 mg
Broccoli, 2 cups	1 mg
Milk, 1 cup skim	0.1 mg
Cheddar cheese, 1 oz	0.2 mg
Total cereal, 1 cup	18 mg
Raisin Bran, 3/4 cup	18 mg
Cream of Wheat, 1 cup	9 mg
Cheerios, 1 cup	4.5 mg*
Quaker flavored instant oatmeal, 1 serving	2 mg
Pasta, 1 cup cooked, enriched	1 mg
Bread, 1 slice enriched	1 mg
Brown rice, 1 cup cooked	1 mg
Brewer's yeast, 1 oz (homemade bread)	5 mg
Molasses, 1 tablespoon blackstrap (found in some dark breads and can be used to sweeten oatmeal)	3.5 mg
Wheat germ, 1/4 cup (can be mixed into a smoothie)	2 mg

* Most cereals are fortified with 4 to 5 mg iron/serving

Foods that contain calcium

Factors that can interfere with your body's ability to absorb calcium and use it to build strong bones include:

- a high-phosphorus diet (large amounts of meat and soda)
- caffeine (more than two cups of coffee or soda a day)
- alcohol
- cigarette smoking
- a low estrogen level (irregular or absent menstrual periods) in adolescent girls

Milk	
Whole, 8 oz	291 mg
Skim, 8 oz	302 mg
Yogurt	
Low fat plain, 8 oz	415 mg
Low fat with fruit, 8 oz	343 mg
Frozen (fruit), 8 oz	240 mg
Ice cream, soft serve, 1 cup	274 mg
Milk shake	
McDonald's 15 oz (vanilla)	320 mg
Burger King, 10 oz	240 mg
Cheese	
Muenster, 1 oz	203 mg
Cheddar, 1 oz	204 mg
Ricotta, part skim (1 cup)	167 mg
Mozzarella, part skim (1 oz)	207 mg
Cottage, 1û2 cup	100 mg
Fortified orange juice, 8 oz	300 mg
Salmon, 3 oz	167 mg
Shrimp, 3 oz	100 mg
Collards, cooked from raw (1 cup)	252 mg
Broccoli, cooked, 1 cup	100-136 mg
Spinach, cooked, (1/2 cup)	122 mg
Tofu in oriental foods (stir fry and soups), 4 oz	150-250 mg

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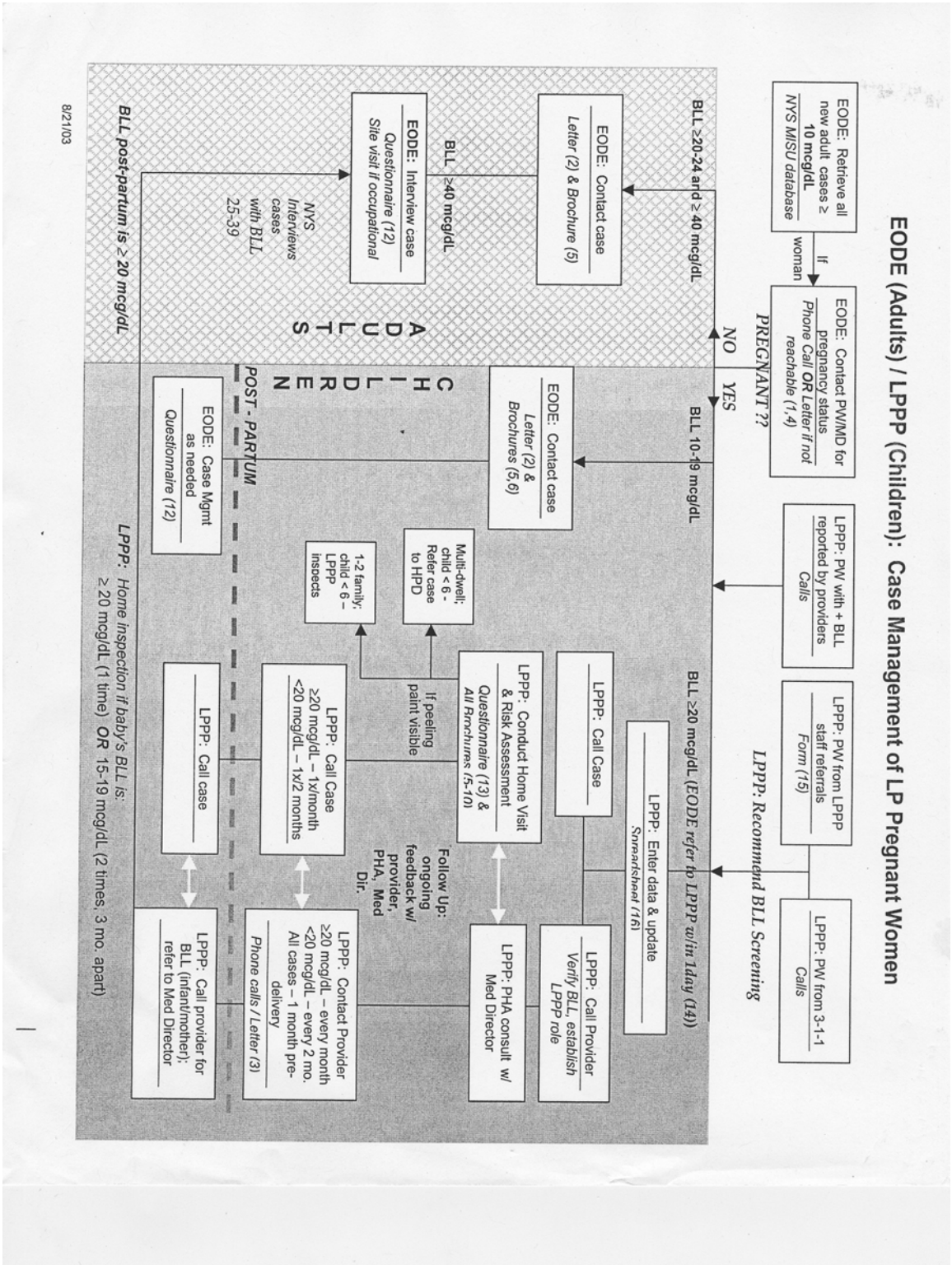
Appendix L
Flow Chart for Activities of the LPPP prior to August 2004



Appendix M

Table 1: Actions and Time Frames According to a Pregnant Woman's Blood Lead Level

Perform a risk assessment for all pregnant women at the first prenatal visit. Obtain a BLL when risk factors are present.		
Blood Lead Level (µg/dL)	**Actions**	**Time Frame for Beginning Intervention**
0-4	**By Prenatal Health Care Providers:** Provide anticipatory guidance and patient education	First Prenatal Visit
5-10	Above actions, plus: **By Prenatal Health Care Providers**: Administer risk reduction counseling Attempt source identification by interview Provide nutritional assessment and counseling Provide follow-up testing	Within 30 Days
10-14	Above actions, plus: **By Prenatal Health Care Providers**: Notify the LPPP within 24 hours **By LPPP:** Provide educational materials to exposed pregnant woman	Within 30 Days
15-45	Above actions, plus: **By Prenatal Health Care Providers**: Emphasize Source Reduction Provide clinical evaluation and care Provide follow-up testing Provide appropriate referrals Consider obtaining a protoporphyrin level when the BLL ≥ 25 µg/dL to distinguish between acute and chronic exposure in the absence of iron deficiency anemia Recommend temporary cessation of breastfeeding in lactating women when BLL ≥ 40 µg/dL **By LPPP:** Provide coordination of care, education and counseling emphasizing source reduction (case management) Provide environmental investigation and control of lead sources	Within 2 weeks
≥45	Above actions, plus: **By Prenatal Health Care Providers in collaboration with LPPP and an experienced specialist**: Hospitalize and consider chelation therapy upon confirmation of BLL	Within 48 hours

Table 2: Frequency of maternal BLL follow-up testing

Initial Venous Blood Lead Level (µg/dL)	Perform a follow-up test:
5-14	Once at least 30 days from the initial test to assess the trend, efficacy of education, investigation, and interventions. Repeat test only if the BLL is rising.
15-44	Within 2 weeks and then monthly to assess the efficacy of investigation and interventions. Obtain a BLL at delivery (maternal or UCLL).
≥45	Within 24 hours and then at frequent intervals depending on clinical interventions and trend in BLLs. Consultation with a clinician experienced in the management of pregnant women with BLLs in this range is strongly advised. Obtain a BLL at delivery (maternal or UCLL).

Table 3: Follow-Up Blood Lead Testing of the Newborn (0-6 months of age) Exposed In Utero

Maternal or Umbilical Cord Blood Lead Level at or around the time of delivery (µg/dL)	Initial Post-Partum Venous Blood Lead Testing in the Newborn	Frequency of Retesting In the Newborn Based on Initial Post-Partum BLL
5-14	< 1 month	Every 3 months[a]
15-24	< 1 month	Every 1-3 months[a]
25-44	< 2 weeks	2 weeks – 1 month
>45	As soon as possible	Depends on Clinical Intervention[b]

a. Repeat blood lead testing at these BLLs is performed mainly to assess the trend. Once the BLL of the newborn is declining, repeat testing may be unnecessary.
b. The frequency of retesting should be based on the clinical interventions performed in consultation with a specialist.

Consultation Services

New York Lead Poisoning Prevention Resource Center
Montefiore Medical Center
Division of Environmental Sciences
Albert Einstein College of Medicine
111 East 210th Street
Bronx, NY 10467
Director: John Rosen, MD
Tel: (718) 920-5016
Fax: (718) 920-4377

Pediatric Environmental Health Specialty Unit
Region II
Mount Sinai Medical Center
One Gustave Levy Place
Box 1512
New York, NY 10029
Director: Joel Forman, MD
Tel: (866) 265-6201
Fax: (212) 241-4309

New York City Department of Health and Mental Hygiene's Lead Poisoning Prevention Program
253 Broadway
11th Floor, Box CN58
New York, NY 10007
Director: Deborah Nagin, MPH
Medical Director: Jacqueline Ehrlich, MD, MPH
Tel: (212) 676-6100
Fax: (212) 676-6122

V. REFERENCES

Anonymous (1999) Adult Blood Lead Epidemiology and Surveillance--United States, second and third quarters, 1998, and annual 1994-1997. M*MWR Morb. Mortal. Wkly. Rep. , 4*8, 213-6, 223.

AAP (1997) Breastfeeding and the use of human milk. American Academy of Pediatrics. Work Group on Breastfeeding. P*ediatrics, 1*00, 1035-1039.

Abadin, H.G., Hibbs, B.F. and Pohl, H.R. (1997) Breast-feeding exposure of infants to cadmium, lead, and mercury: a public health viewpoint. T*oxicol. Ind. Health, 1*3, 495-517.

Andrews, K.W., Savitz, D.A. and Hertz-Picciotto, I. (1994) Prenatal lead exposure in relation to gestational age and birth weight: a review of epidemiologic studies. A*m. J. Ind. Med. , 2*6, 13-32.

Antonio, M.T. and Leret, M.L. (2000) Study of the neurochemical alterations produced in discrete brain areas by perinatal low-level lead exposure. L*ife Sci. , 6*7, 635-642.

ATSDR (2000) Summary Report for the ATSDR Soil-Pica Workshop. 205-95-0901,

Azcona-Cruz, M.I., Rothenberg, S.J., Schnaas, L., Zamora-Munoz, J.S. and Romero-Placeres, M. (2000) Lead-glazed ceramic ware and blood lead levels of children in the city of Oaxaca, Mexico. A*rch. Environ. Health, 5*5, 217-222.

Baghurst, P.A., Robertson, E.F., McMichael, A.J., Vimpani, G.V., Wigg, N.R. and Roberts, R.R. (1987) The Port Pirie Cohort Study: lead effects on pregnancy outcome and early childhood development. N*eurotoxicology, 8, 395-401*.

Baghurst, P.A., Robertson, E.F., Oldfield, R.K., King, B.M., McMichael, A.J., Vimpani, G.V. and Wigg, N.R. (1991) Lead in the placenta, membranes, and umbilical cord in relation to pregnancy outcome in a lead-smelter community. E*nviron. Health Perspect. , 9*0, 315-320.

Bellinger, D.C. (2000) Effect modification in epidemiologic studies of low-level neurotoxicant exposures and health outcomes. *Neurotoxicol. Teratol.,* **22,** 133-140.

Bellinger, D., Leviton, A., Allred, E. and Rabinowitz, M. (1994) Pre- and postnatal lead exposure and behavior problems in school-aged children. E*nviron. Res. , 6*6, 12-30.

Bellinger, D., Leviton, A., Waternaux, C., Needleman, H. and Rabinowitz, M. (1987) Longitudinal analyses of prenatal and postnatal lead exposure and early cognitive development. N. *Engl. J. Med. , 3*16, 1037-1043.

Bellinger, D., Sloman, J., Leviton, A., Rabinowitz, M., Needleman, H.L. and Waternaux, C. (1991) Low-level lead exposure and children's cognitive function in the preschool years. P*ediatrics, 8*7, 219-227.

Borja-Aburto, V.H., Hertz-Picciotto, I., Rojas Lopez, M., Farias, P., Rios, C. and Blanco, J. (1999) Blood lead levels measured prospectively and risk of spontaneous abortion. A*m. J. Epidemiol. , 1*50, 590-597.

Brody, D.J., Pirkle, J.L., Kramer, R.A., Flegal, K.M., Matte, T.D., Gunter, E.W. and Paschal, D.C. (1994) Blood lead levels in the US population. Phase 1 of the Third National Health and Nutrition Examination Survey (NHANES III, 1988 to 1991). J*AMA, 2*72, 277-283.

Brown, M.J., Hu, H., Gonzales-Cossio, T., Peterson, K.E., Sanin, L.H., de Luz Kageyama, M., Palazuelos, E., Aro, A., Schnaas, L. and Hernandez-Avila, M. (2000) Determinants of bone and blood lead concentrations in the early postpartum period. O*ccup. Environ. Med. , 5*7, 535-541.

Cake, K.M., Bowins, R.J., Vaillancourt, C., Gordon, C.L., McNutt, R.H., Laporte, R., Webber, C.E. and Chettle, D.R. (1996) Partition of circulating lead between serum and red cells is different for internal and external sources of lead. A*m. J. Ind. Med. , 2*9, 440-445.

Canfield, R.L., Henderson, C.R.,Jr, Cory-Slechta, D.A., Cox, C., Jusko, T.A. and Lanphear, B.P. (2003) Intellectual impairment in children with blood lead concentrations below 10 microg per deciliter. N. *Engl. J. Med. , 3*48, 1517-1526.

Centers for Disease Control and Prevention. Managing Elevated Blood Lead Levels Among Young Children: Recommendations from the Advisory Committee on Childhood Lead Poisoning Prevention. Atlanta: CDC; 2002.

Chuang, H.Y., Schwartz, J., Gonzales-Cossio, T., Lugo, M.C., Palazuelos, E., Aro, A., Hu, H. and Hernandez-Avila, M. (2001) Interrelations of lead levels in bone, venous blood, and umbilical cord blood with exogenous lead exposure through maternal plasma lead in peripartum women. E*nviron. Health Perspect. , 1*09, 527-532.

Commerce Clearing House and United States. Occupational Safety and Health Administration (2001) OSHA standards for general industry (29 CFR part 1910).

Cooney, G.H., Bell, A., McBride, W. and Carter, C. (1989) Neurobehavioural consequences of prenatal low level exposures to lead. N*eurotoxicol. Teratol. , 1*1, 95-104.

Crocetti, A.F., Mushak, P. and Schwartz, J. (1990) Determination of numbers of lead-exposed women of childbearing age and pregnant women: an integrated summary of a

report to the U.S. Congress on childhood lead poisoning. E*nviron. Health Perspect. , 8*9, 121-124.

Dawson, E.B., Evans, D.R., Kelly, R. and Van Hook, J.W. (2000) Blood cell lead, calcium, and magnesium levels associated with pregnancy-induced hypertension and preeclampsia. B*iol. Trace Elem. Res. , 7*4, 107-116.

Dietrich, K.N., Krafft, K.M., Bornschein, R.L., Hammond, P.B., Berger, O., Succop, P.A. and Bier, M. (1987) Low-level fetal lead exposure effect on neurobehavioral development in early infancy. P*ediatrics, 8*0, 721-730.

Dietrich, K.N., Ris, M.D., Succop, P.A., Berger, O.G. and Bornschein, R.L. (2001) Early exposure to lead and juvenile delinquency. N*eurotoxicol. Teratol. , 2*3, 511-518.

Domingo, J.L. (1998) Developmental toxicity of metal chelating agents. R*eprod. Toxicol. , 1*2, 499-510.

Earth Summit Watch (1999) The Global Phaseout of Leaded Gasoline: A Successful Initiative. w*ww.earthsummitwatch.org,*

*E*isenberg, D.M., Davis, R.B., Ettner, S.L., Appel, S., Wilkey, S., Van Rompay, M. and Kessler, R.C. (1998) Trends in alternative medicine use in the United States, 1990-1997: results of a follow-up national survey. J*AMA, 2*80, 1569-1575.

Eisenberg, D.M., Kessler, R.C., Foster, C., Norlock, F.E., Calkins, D.R. and Delbanco, T.L. (1993) Unconventional medicine in the United States. Prevalence, costs, and patterns of use. N. *Engl. J. Med. , 3*28, 246-252.

Ernhart, C.B. (1992) A critical review of low-level prenatal lead exposure in the human: 2. Effects on the developing child. R*eprod. Toxicol. , 6, 21-40.*

Ernhart, C.B. and Greene, T. (1990) Low-level lead exposure in the prenatal and early preschool periods: language development. A*rch. Environ. Health, 4*5, 342-354.

Ernhart, C.B., Morrow-Tlucak, M., Marler, M.R. and Wolf, A.W. (1987) Low level lead exposure in the prenatal and early preschool periods: early preschool development. N*eurotoxicol. Teratol. , 9, 259-270.*

Ernhart, C.B., Morrow-Tlucak, M., Wolf, A.W., Super, D. and Drotar, D. (1989) Low level lead exposure in the prenatal and early preschool periods: intelligence prior to school entry. N*eurotoxicol. Teratol. , 1*1, 161-170.

Ernhart, C.B., Wolf, A.W., Kennard, M.J., Erhard, P., Filipovich, H.F. and Sokol, R.J. (1986) Intrauterine exposure to low levels of lead: the status of the neonate. A*rch. Environ. Health, 4*1, 287-291.

Ernhart, C.B., Wolf, A.W., Sokol, R.J., Brittenham, G.M. and Erhard, P. (1985) Fetal lead exposure: antenatal factors. E*nviron. Res. , 3*8, 54-66.

Ettinger, A.S., Tellez-Rojo, M.M., Amarasiriwardena, C., Gonzalez-Cossio, T., Peterson, K.E., Aro, A., Hu, H. and Hernandez-Avila, M. (2004) Levels of lead in breast milk and their relation to maternal blood and bone lead levels at one month postpartum. E*nviron. Health Perspect. , 1*12, 926-931.

Factor-Litvak, P., Cushman, L.F., Kronenberg, F., Wade, C. and Kalmuss, D. (2001) Use of complementary and alternative medicine among women in New York City: a pilot study. J. *Altern. Complement. Med. , 7, 659-666.*

Factor-Litvak, P., Graziano, J.H., Kline, J.K., Popovac, D., Mehmeti, A., Ahmedi, G., Shrout, P., Murphy, M.J., Gashi, E. and Haxhiu, R. (1991) A prospective study of birthweight and length of gestation in a population surrounding a lead smelter in Kosovo, Yugoslavia. I*nt. J. Epidemiol. , 2*0, 722-728.

Factor-Litvak, P., Stein, Z. and Graziano, J. (1993) Increased risk of proteinuria among a cohort of lead-exposed pregnant women. E*nviron. Health Perspect. , 1*01, 418-421.

Falcon, M., Vinas, P. and Luna, A. (2003) Placental lead and outcome of pregnancy. T*oxicology, 1*85, 59-66.

Falk, H. (2003) International environmental health for the pediatrician: case study of lead poisoning. P*ediatrics, 1*12, 259-264.

Flanigan, G.D.,Jr, Mayfield, R. and Blumenthal, H.T. (1992) Studies on lead exposure in patients of a neighborhood health center: Part II. A comparison of women of childbearing age and children. J. *Natl. Med. Assoc. , 8*4, 23-27.

Fletcher, A.M., Gelberg, K.H. and Marshall, E.G. (1999) Reasons for testing and exposure sources among women of childbearing age with moderate blood lead levels. J. *Community Health, 2*4, 215-227.

Flora, G.J. and Seth, P.K. (2000) Alterations in some membrane properties in rat brain following exposure to lead. C*ytobios, 1*03, 103-109.

Ford, M.D. (2001) C*linical toxicology. W*.B. Saunders, Philadelphia ; New York.

Fredeen, D.J., Ehlinger, E.P., Cruikshank, S.H., Godes, J.R., Braun, J.E. and Deinard, A.S. (1992) Lead levels among pregnant women in Hennepin County. M*inn. Med. , 7*5, 29-32.

Fulton, M., Raab, G., Thomson, G., Laxen, D., Hunter, R. and Hepburn, W. (1987) Influence of blood lead on the ability and attainment of children in Edinburgh. L*ancet, 1, 1221-1226.*

Gardella, C. (2001) Lead exposure in pregnancy: a review of the literature and argument for routine prenatal screening. O*bstet. Gynecol. Surv. , 5*6, 231-238.

Geronimus, A.T. and Hillemeier, M.M. (1992) Patterns of blood lead levels in US black and white women of childbearing age. E*thn. Dis. , 2, 222-231.*

Gerwel, B., Pearson, M., Ramaprasad, R., Stanbury, M. and Valiante, D. (1998) Adult Blood Lead Epidemiology and Surveillance in New Jersey. R*eport to the New Jersey Department of Health and Human Services,*

*G*omaa, A., Hu, H., Bellinger, D., Schwartz, J., Tsaih, S.W., Gonzalez-Cossio, T., Schnaas, L., Peterson, K., Aro, A. and Hernandez-Avila, M. (2002) Maternal bone lead as an independent risk factor for fetal neurotoxicity: a prospective study. P*ediatrics, 1*10, 110-118.

Gonzalez-Cossio, T., Peterson, K.E., Sanin, L.H., Fishbein, E., Palazuelos, E., Aro, A., Hernandez-Avila, M. and Hu, H. (1997) Decrease in birth weight in relation to maternal bone-lead burden. P*ediatrics, 1*00, 856-862.

Goyer, R.A. (1996) Results of lead research: prenatal exposure and neurological consequences. E*nviron. Health Perspect. , 1*04, 1050-1054.

Greene, T. and Ernhart, C.B. (1991) Prenatal and preschool age lead exposure: relationship with size. N*eurotoxicol. Teratol. , 1*3, 417-427.

Gulson, B.L., Jameson, C.W., Mahaffey, K.R., Mizon, K.J., Patison, N., Law, A.J., Korsch, M.J. and Salter, M.A. (1998) Relationships of lead in breast milk to lead in blood, urine, and diet of the infant and mother. E*nviron. Health Perspect. , 1*06, 667-674.

Gulson, B.L., Mizon, K.J., Korsch, M.J., Palmer, J.M. and Donnelly, J.B. (2003) Mobilization of lead from human bone tissue during pregnancy and lactation--a summary of long-term research. S*ci. Total Environ. , 3*03, 79-104.

Gulson, B.L., Mizon, K.J., Palmer, J.M., Patison, N., Law, A.J., Korsch, M.J., Mahaffey, K.R. and Donnelly, J.B. (2001) Longitudinal study of daily intake and excretion of lead in newly born infants. E*nviron. Res. , 8*5, 232-245.

Hamilton, S., Rothenberg, S.J., Khan, F.A., Manalo, M. and Norris, K.C. (2001) Neonatal lead poisoning from maternal pica behavior during pregnancy. J. *Natl. Med. Assoc. , 9*3, 317-319.

Hepner, D.L., Harnett, M., Segal, S., Camann, W., Bader, A.M. and Tsen, L.C. (2002) Herbal medicine use in parturients. A*nesth. Analg. , 9*4, 690-3; table of contents.

Hernandez Avila, M., Romieu, I., Rios, C., Rivero, A. and Palazuelos, E. (1991) Lead-glazed ceramics as major determinants of blood lead levels in Mexican women. E*nviron. Health Perspect. , 9*4, 117-120.

Hernandez-Avila, M., Gonzalez-Cossio, T., Hernandez-Avila, J.E., Romieu, I., Peterson, K.E., Aro, A., Palazuelos, E. and Hu, H. (2003) Dietary calcium supplements to lower

blood lead levels in lactating women: a randomized placebo-controlled trial. E*pidemiology, 1*4, 206-212.

Hernandez-Avila, M., Gonzalez-Cossio, T., Palazuelos, E., Romieu, I., Aro, A., Fishbein, E., Peterson, K.E. and Hu, H. (1996) Dietary and environmental determinants of blood and bone lead levels in lactating postpartum women living in Mexico City. E*nviron. Health Perspect. , 1*04, 1076-1082.

Hernandez-Avila, M., Peterson, K.E., Gonzalez-Cossio, T., Sanin, L.H., Aro, A., Schnaas, L. and Hu, H. (2002) Effect of maternal bone lead on length and head circumference of newborns and 1-month-old infants. A*rch. Environ. Health, 5*7, 482-488.

Hernandez-Avila, M., Sanin, L.H., Romieu, I., Palazuelos, E., Tapia-Conyer, R., Olaiz, G., Rojas, R. and Navarrete, J. (1997) Higher milk intake during pregnancy is associated with lower maternal and umbilical cord lead levels in postpartum women. E*nviron. Res. , 7*4, 116-121.

Hernandez-Avila, M., Smith, D., Meneses, F., Sanin, L.H. and Hu, H. (1998) The influence of bone and blood lead on plasma lead levels in environmentally exposed adults. E*nviron. Health Perspect. , 1*06, 473-477.

Hertz-Picciotto, I. (2000) The evidence that lead increases the risk for spontaneous abortion. A*m. J. Ind. Med. , 3*8, 300-309.

Hertz-Picciotto, I. and Croft, J. (1993) Review of the relation between blood lead and blood pressure. E*pidemiol. Rev. , 1*5, 352-373.

Hertz-Picciotto, I., Schramm, M., Watt-Morse, M., Chantala, K., Anderson, J. and Osterloh, J. (2000) Patterns and determinants of blood lead during pregnancy. A*m. J. Epidemiol. , 1*52, 829-837.

Horner, R.D., Lackey, C.J., Kolasa, K. and Warren, K. (1991) Pica practices of pregnant women. J. *Am. Diet. Assoc. , 9*1, 34-38.

Hsu, P.C. and Guo, Y.L. (2002) Antioxidant nutrients and lead toxicity. T*oxicology, 1*80, 33-44.

Hu, H., Hashimoto, D. and Besser, M. (1996) Levels of lead in blood and bone of women giving birth in a Boston hospital. A*rch. Environ. Health, 5*1, 52-58.

Institute of Medicine . Panel on Micronutrients (2002) DRI *: dietary reference intakes for vitamin A, vitamin K, arsenic, boron, chromium, copper, iodine, iron, manganese, molybdenum, nickel, silicon, vanadium, and zinc : a report of the Panel on Micronutrients ... and the Standing Committee on the Scientific Evaluation of Dietary Reference Intakes, Food and Nutrition Board, Institute of Medicine. N*ational Academy Press, Washington, D.C.

Institute of Medicine . Standing Committee on the Scientific Evaluation of Dietary Reference Intakes (1997) D*ietary reference intakes : for calcium, phosphorus, magnesium, vitamin D, and fluoride. N*ational Academy Press, Washington, D.C.

Johnson, M.A. (2001) High calcium intake blunts pregnancy-induced increases in maternal blood lead. N*utr. Rev. , 5*9, 152-156.

Klitzman, S., Sharma, A., Nicaj, L., Vitkevich, R. and Leighton, J. (2002) Lead poisoning among pregnant women in New York City: risk factors and screening practices. J. *Urban Health, 7*9, 225-237.

Koller, K., Brown, T., Spurgeon, A. and Levy, L. (2004) Recent developments in low-level lead exposure and intellectual impairment in children. *Environ. Health Perspect.,* **112,** 987-994.

Kosnett, M.J., Becker, C.E., Osterloh, J.D., Kelly, T.J. and Pasta, D.J. (1994) Factors influencing bone lead concentration in a suburban community assessed by noninvasive K x-ray fluorescence. J*AMA, 2*71, 197-203.

LaKind, J.S., Berlin, C.M. and Naiman, D.Q. (2001) Infant exposure to chemicals in breast milk in the United States: what we need to learn from a breast milk monitoring program. E*nviron. Health Perspect. , 1*09, 75-88.

Landrigan, P.J., Boffetta, P. and Apostoli, P. (2000) The reproductive toxicity and carcinogenicity of lead: a critical review. A*m. J. Ind. Med. , 3*8, 231-243.

Landrigan, P.J. and Todd, A.C. (1994) Direct measurement of lead in bone. A promising biomarker. J*AMA, 2*71, 239-240.

Lanphear, B., Hornung, R., Khoury, J., Yolton, K., Baghurst, P., Bellinger, D., Bornschein, R., Canfield, R., Dietrich, K. and Graziano, J., et al (2004) Low-Level Environmental Lead Exposure and Intellectual Impairment in Children: An International Pooled Analysis. P*AS,*

*L*anphear, B.P., Dietrich, K., Auinger, P. and Cox, C. (2000) Cognitive deficits associated with blood lead concentrations <10 microg/dL in US children and adolescents. P*ublic Health Rep. , 1*15, 521-529.

Leighton, J., Nagin, D. and Steinsapir, C. (2002) Lead Poisoning Prevention Program, Annual Report 2001. N*ew York: New York City Department of Health and Mental Hygiene,*

*L*idsky, T.I. and Schneider, J.S. (2003) Lead neurotoxicity in children: basic mechanisms and clinical correlates. B*rain, 1*26, 5-19.

Loikkanen, J., Chvalova, K., Naarala, J., Vahakangas, K.H. and Savolainen, K.M. (2003) Pb2+-induced toxicity is associated with p53-independent apoptosis and enhanced by glutamate in GT1-7 neurons. T*oxicol. Lett. , 1*44, 235-246.

Mahaffey, K.R. (1977) Relation between quantities of lead ingested and health effects of lead in humans. P*ediatrics, 5*9, 448-455.

Mahaffey, K.R., Annest, J.L., Roberts, J. and Murphy, R.S. (1982) National estimates of blood lead levels: United States, 1976-1980: association with selected demographic and socioeconomic factors. N. *Engl. J. Med. , 3*07, 573-579.

Manton, W.I., Angle, C.R., Stanek, K.L., Reese, Y.R. and Kuehnemann, T.J. (2000) Acquisition and retention of lead by young children. E*nviron. Res. , 8*2, 60-80.

Markowitz, M. (2000) Lead poisoning. P*ediatr. Rev. , 2*1, 327-335.

Markowitz, M.E. and Shen, X.M. (2001) Assessment of bone lead during pregnancy: a pilot study. E*nviron. Res. , 8*5, 83-89.

Moline, J., Lopez Carrillo, L., Torres Sanchez, L., Godbold, J. and Todd, A. (2000) Lactation and lead body burden turnover: a pilot study in Mexico. J. *Occup. Environ. Med. , 4*2, 1070-1075.

Moline, J.M., Golden, A.L., Todd, A.C., Godbold, J.H. and Berkowitz, G.S. (1999) Lead exposure among young urban women. S*alud Publica Mex. , 4*1 Suppl 2, S82-7.

Murphy, M.J., Graziano, J.H., Popovac, D., Kline, J.K., Mehmeti, A., Factor-Litvak, P., Ahmedi, G., Shrout, P., Rajovic, B. and Nenezic, D.U. (1990) Past pregnancy outcomes among women living in the vicinity of a lead smelter in Kosovo, Yugoslavia. A*m. J. Public Health, 8*0, 33-35.

Namihira, D., Saldivar, L., Pustilnik, N., Carreon, G.J. and Salinas, M.E. (1993) Lead in human blood and milk from nursing women living near a smelter in Mexico City. J. *Toxicol. Environ. Health, 3*8, 225-232.

National Research Council . Committee on Neurotoxicology and Models for Assessing Risk (1992) E*nvironmental neurotoxicology. N*ational Academy Press, Washington, D.C.

Nomiyama, K., Nomiyama, H., Liu, S.J., Tao, Y.X., Nomiyama, T. and Omae, K. (2002) Lead induced increase of blood pressure in female lead workers. O*ccup. Environ. Med. , 5*9, 734-738.

Nunez, C.M., Klitzman, S. and Goodman, A. (1993) Lead exposure among automobile radiator repair workers and their children in New York City. A*m. J. Ind. Med. , 2*3, 763-777.

NYS DOH (2004) Eliminating Childhood Lead Poisoning in New York State by 2010 - Working Draft.

Odland, J.O., Nieboer, E., Romanova, N., Thomassen, Y. and Lund, E. (1999) Blood lead and cadmium and birth weight among sub-arctic and arctic populations of Norway and Russia. A*cta Obstet. Gynecol. Scand. , 7*8, 852-860.

Opler, M., Brown, A., Graziano, J., Desa, M., Zheng, W., Schaefer, C., Factor-Litvak, P. and Susser, E. (2004) Prenatal Lead Exposure, δ-Aminolevulinic Acid, and Schizophrenia. *EHP,*

Osterloh, J.D. and Kelly, T.J. (1999) Study of the effect of lactational bone loss on blood lead concentrations in humans. *Environ. Health Perspect. ,* 107, 187-194.

Pirkle, J.L., Brody, D.J., Gunter, E.W., Kramer, R.A., Paschal, D.C., Flegal, K.M. and Matte, T.D. (1994) The decline in blood lead levels in the United States. The National Health and Nutrition Examination Surveys (NHANES). *JAMA,* 272, 284-291.

Pirkle, J.L., Kaufmann, R.B., Brody, D.J., Hickman, T., Gunter, E.W. and Paschal, D.C. (1998) Exposure of the U.S. population to lead, 1991-1994. *Environ. Health Perspect. ,* 106, 745-750.

Pocock, S.J., Smith, M. and Baghurst, P. (1994) Environmental lead and children's intelligence: a systematic review of the epidemiological evidence. *BMJ,* 309, 1189-1197.

Rabinowitz, M., Bellinger, D., Leviton, A., Needleman, H. and Schoenbaum, S. (1987) Pregnancy hypertension, blood pressure during labor, and blood lead levels. *Hypertension,* 10, 447-451.

Rabinowitz, M., Leviton, A. and Needleman, H. (1985) Lead in milk and infant blood: a dose-response model. *Arch. Environ. Health,* 40, 283-286.

Rainville, A.J. (1998) Pica practices of pregnant women are associated with lower maternal hemoglobin level at delivery. J. *Am. Diet. Assoc. , 9*8, 293-296.

Reddy, G.R., Basha, M.R., Devi, C.B., Suresh, A., Baker, J.L., Shafeek, A., Heinz, J. and Chetty, C.S. (2003) Lead induced effects on acetylcholinesterase activity in cerebellum and hippocampus of developing rat. I*nt. J. Dev. Neurosci. , 2*1, 347-352.

REPROTEXT® Database: Calcium Edetate (REPROTEXT® Document). 2004,

Rhainds, M. and Levallois, P. (1997) Effects of maternal cigarette smoking and alcohol consumption on blood lead levels of newborns. *Am. J. Epidemiol. ,* 145, 250-257.

Rhainds, M. and Levallois, P. (1993) Umbilical cord blood lead levels in the Quebec City area. *Arch. Environ. Health,* 48, 421-427.

Roche, L.M., Ramaprasad, R., Gerwel, B., Valiante, D., Pearson, M., Stanbury, M. and O'Leary, K. (1998) Evolution of a state occupational lead exposure registry: 1986-1996. *J. Occup. Environ. Med. ,* 40, 1127-1133.

Romieu, I., Lacasana, M. and McConnell, R. (1997) Lead exposure in Latin America and the Caribbean. Lead Research Group of the Pan-American Health Organization. *Environ. Health Perspect. ,* 105, 398-405.

Roscoe, R.J., Ball, W., Curran, J.J., DeLaurier, C., Falken, M.C., Fitchett, R., Fleissner, M.L., Fletcher, A.E., Garman, S.J. and Gergely, R.M., et al (2002) Adult blood lead epidemiology and surveillance--United States, 1998-2001. *MMWR Surveill. Summ. ,* 51, 1-10.

Roscoe, R.J., Gittleman, J.L., Deddens, J.A., Petersen, M.R. and Halperin, W.E. (1999) Blood lead levels among children of lead-exposed workers: A meta-analysis. *Am. J. Ind. Med. ,* 36, 475-481.

Rosenman, K.D., Sims, A., Luo, Z. and Gardiner, J. (2003) Occurrence of lead-related symptoms below the current occupational safety and health act allowable blood lead levels. *J. Occup. Environ. Med.,* **45,** 546-555.

Rothenberg, S.J., Karchmer, S., Schnaas, L., Perroni, E., Zea, F., Salinas, V. and Fernandez Alba, J. (1996) Maternal influences on cord blood lead levels. *J. Expo. Anal. Environ. Epidemiol. ,* 6, 211-227.

Rothenberg, S.J., Khan, F., Manalo, M., Jiang, J., Cuellar, R., Reyes, S., Acosta, S., Jauregui, M., Diaz, M. and Sanchez, M., et al (2000) Maternal bone lead contribution to blood lead during and after pregnancy. *Environ. Res. ,* 82, 81-90.

Rothenberg, S.J., Kondrashov, V., Manalo, M., Jiang, J., Cuellar, R., Garcia, M., Reynoso, B., Reyes, S., Diaz, M. and Todd, A.C. (2002) Increases in hypertension and blood pressure during pregnancy with increased bone lead levels. *Am. J. Epidemiol. ,* 156, 1079-1087.

Rothenberg, S.J., Kondrashov, V., Manalo, M., Manton, W.I., Khan, F., Todd, A.C. and Johnson, C. (2001) Seasonal variation in bone lead contribution to blood lead during pregnancy. *Environ. Res. ,* 85, 191-194.

Rothenberg, S.J., Manalo, M., Jiang, J., Cuellar, R., Reyes, S., Sanchez, M., Diaz, M., Khan, F., Aguilar, A. and Reynoso, B., et al (1999a) Blood lead level and blood pressure during pregnancy in South Central Los Angeles. *Arch. Environ. Health,* 54, 382-389.

Rothenberg, S.J., Manalo, M., Jiang, J., Khan, F., Cuellar, R., Reyes, S., Sanchez, M., Reynoso, B., Aguilar, A. and Diaz, M., et al (1999b) Maternal blood lead level during pregnancy in South Central Los Angeles. *Arch. Environ. Health,* 54, 151-157.

Rothenberg, S.J., Poblano, A. and Schnaas, L. (2000) Brainstem auditory evoked response at five years and prenatal and postnatal blood lead. *Neurotoxicol. Teratol. ,* 22, 503-510.

Rothenberg, S.J., Schnaas, L., Cansino-Ortiz, S., Perroni-Hernandez, E., de la Torre, P., Neri-Mendez, C., Ortega, P., Hidalgo-Loperena, H. and Svendsgaard, D. (1989) Neurobehavioral deficits after low level lead exposure in neonates: the Mexico City pilot study. *Neurotoxicol. Teratol. ,* 11, 85-93.

Rothenberg, S.J., Schnaas, L., Perroni, E., Hernandez, R.M., Martinez, S. and Hernandez, C. (1999) Pre- and postnatal lead effect on head circumference: a case for critical periods. *Neurotoxicol. Teratol. ,* 21, 1-11.

Schell, L.M., Denham, M., Stark, A.D., Gomez, M., Ravenscroft, J., Parsons, P.J., Aydermir, A. and Samelson, R. (2003) Maternal blood lead concentration, diet during pregnancy, and anthropometry predict neonatal blood lead in a socioeconomically disadvantaged population. *Environ. Health Perspect. ,* 111, 195-200.

Schell, L.M., Stark, A.D., Gomez, M.I. and Grattan, W.A. (1997) Blood lead level, by year and season, among poor pregnant women. *Arch. Environ. Health,* 52, 286-291.

Schneider, J.S., Huang, F.N. and Vemuri, M.C. (2003) Effects of low-level lead exposure on cell survival and neurite length in primary mesencephalic cultures. *Neurotoxicol. Teratol. ,* 25, 555-559.

Schneider, J.S., Lee, M.H., Anderson, D.W., Zuck, L. and Lidsky, T.I. (2001) Enriched environment during development is protective against lead-induced neurotoxicity. *Brain Res.,* **896,** 48-55.

Schwartz, J. (1994) Low-level lead exposure and children's IQ: a meta-analysis and search for a threshold. *Environ. Res. ,* 65, 42-55.

Seidel, S., Kreutzer, R., Smith, D., McNeel, S. and Gilliss, D. (2001) Assessment of commercial laboratories performing hair mineral analysis. *JAMA,* 285, 67-72.

Shannon, M. (2003) Severe lead poisoning in pregnancy. *Ambul. Pediatr. ,* 3, 37-39.

Shen, X.M., Yan, C.H., Guo, D., Wu, S.M., Li, R.Q., Huang, H., Ao, L.M., Zhou, J.D., Hong, Z.Y. and Xu, J.D., et al (1998) Low-level prenatal lead exposure and neurobehavioral development of children in the first year of life: a prospective study in Shanghai. *Environ. Res. ,* 79, 1-8.

Silbergeld, E.K. (1991) Lead in bone: implications for toxicology during pregnancy and lactation. *Environ. Health Perspect. ,* 91, 63-70.

Simon, J.A. and Hudes, E.S. (1999) Relationship of ascorbic acid to blood lead levels. *JAMA,* 281, 2289-2293.

Simpson, E., Mull, J.D., Longley, E. and East, J. (2000) Pica during pregnancy in low-income women born in Mexico. *West. J. Med. ,* 173, 20-4; discussion 25.

Sowers, M., Jannausch, M., Scholl, T., Li, W., Kemp, F.W. and Bogden, J.D. (2002) Blood lead concentrations and pregnancy outcomes. *Arch. Environ. Health,* 57, 489-495.

Sule, S. and Madugu, H.N. (2001) Pica in pregnant women in Zaria, Nigeria. *Niger. J. Med. ,* 10, 25-27.

Tellez-Rojo, M.M., Hernandez-Avila, M., Gonzalez-Cossio, T., Romieu, I., Aro, A., Palazuelos, E., Schwartz, J. and Hu, H. (2002) Impact of breastfeeding on the mobilization of lead from bone. *Am. J. Epidemiol. ,* 155, 420-428.

Tong, S., McMichael, A.J. and Baghurst, P.A. (2000) Interactions between environmental lead exposure and sociodemographic factors on cognitive development. *Arch. Environ. Health,* **55,** 330-335.

Torres-Sanchez, L.E., Berkowitz, G., Lopez-Carrillo, L., Torres-Arreola, L., Rios, C. and Lopez-Cervantes, M. (1999) Intrauterine lead exposure and preterm birth. *Environ. Res. ,* 81, 297-301.

Ventura, S., Mosher, W., Curtin, S., Abma, J. and Henshaw, S. (2001) Trends in Pregnancy Rates for the United States, 1976-97: An Update. *NVSS,* 49,

Wasserman, G.A., Liu, X., Popovac, D., Factor-Litvak, P., Kline, J., Waternaux, C., LoIacono, N. and Graziano, J.H. (2000) The Yugoslavia Prospective Lead Study: contributions of prenatal and postnatal lead exposure to early intelligence. *Neurotoxicol. Teratol. ,* 22, 811-818.

West, W.L., Knight, E.M., Edwards, C.H., Manning, M., Spurlock, B., James, H., Johnson, A.A., Oyemade, U.J., Cole, O.J. and Westney, O.E. (1994) Maternal low level lead and pregnancy outcomes. *J. Nutr. ,* 124, 981S-986S.