**Subcommittee on Children's Health**
**Committee on Environment and Public Works**
**United States Senate**
**Hearing on Children's Environmental Health**
**September 29, 2009**

**Statement of**
**Linda S. Birnbaum, Ph.D., DABT, ATS**
**Director**
**National Institute of Environmental Health Sciences**
**National Institutes of Health**
**and**
**Director, National Toxicology Program**
**U.S. Department of Health and Human Services**

Madam Chairwoman and distinguished members of the Subcommittee, I am pleased to appear before you today to present testimony on research supported by the Department of Health and Human Services (HHS) on effects of the environment on children's health. My name is Linda Birnbaum; I am the Director of the National Institute of Environmental Health Sciences (NIEHS) within HHS's National Institutes of Health (NIH), and Director of the National Toxicology Program (NTP).

As a public servant, a scientist, a mother, and a grandmother, I am convinced that a healthy environment is vitally important to the healthy development of a child. We know that young children are especially vulnerable to adverse health consequences of a wide variety of environmental exposures. They receive a proportionately greater exposure compared to their size than adults do; their behaviors can result in excess exposures; the active growth of children's organs and tissues enhances their susceptibility to environmental damage; and the body's mechanisms for reducing toxicity or excreting toxic substances may not be not fully operational in young children.

We also know much more about the linkages between environmental exposures and specific diseases and dysfunctions – not just childhood diseases, but effects of prenatal and childhood exposures that can show up years later, for example, as reproductive problems or cancer. In some cases, environmentally linked diseases such as asthma can affect an individual's entire life, with potentially large impacts on both quality of life and health care costs. In other cases, we are only starting to unravel the connection between the fetal and/or childhood environment to other diseases or conditions. These are some of the new areas of research which are benefiting from our cutting-edge scientific tools and uncovering the scientific information we need to make our children and our entire population healthier.

Since NIEHS was established in 1966, it has recognized the critically important need for research on children's environmental health and has made a major investment in this area. Other Institutes at NIH also support research in this area, including the Eunice Kennedy Shriver National Institute of Child Health and Human Development, the National Institute of Allergy and Infectious Diseases (NIAID), and the National Cancer Institute (NCI). In FY 2008, NIEHS spent more than $106 million on children's environmental health research. Today our program is more vibrant than ever. I would like to share with you some recent scientific findings from NIEHS-funded research.

For instance, asthma is a disease of children, as well as adults, and is of huge public health concern. Allergens found in the environment clearly trigger asthmatic attacks, but we are still learning about how the environment exerts its effects either as a cause of primary asthma or as a trigger of symptoms in an asthmatic child. A new NIEHS-funded study by researchers at the University of Southern California (USC) has found that maternal smoking during pregnancy can

cause lifelong effects in the child through specific pattern modifications in DNA molecules. *In utero* exposure to tobacco smoke can lead to changes in the way genes work without changing the genes themselves.[1] This kind of research will give us important insights into understanding how what happens in the womb is tied to health outcomes later in life. For example, prenatal exposure to smoke is associated with a number of health problems later in life, including childhood obesity[2], respiratory disease, and cancer.[3]

An important report on a link between asthma and air pollution, specifically ozone, came out of collaboration between the NIEHS and the USC. Researchers found that the incidence of new cases of asthma was associated with high exercise levels outdoors in communities with high levels of ozone. Exercise in areas of low ozone did not increase asthma risk.[4]

The same NIEHS researcher published a report a few years ago from a study in Mexico City (an area with high ozone exposure) showing that asthmatic children having a specific gene variant are more susceptible than those with a normal gene to a decline in lung function from ozone exposure – but that the children with the gene variant also derived greater benefit from supplementation with vitamins C and E in reversing some of the observed decline in lung function.[5]

The neurological and cognitive development of children is especially vulnerable to some environmental effects. This past summer, a study from the NIEHS/Environmental Protection Agency (EPA)-funded Children's Environmental Health Center at Columbia University reported that a mother's exposure to urban air pollutants known as polycyclic aromatic hydrocarbons (PAHs) can adversely affect a child's IQ. PAHs are chemicals released into the air from the

burning of coal, diesel, oil and gas, or other organic substances such as tobacco. In urban areas, motor vehicles are a major source of PAHs. The study found that children exposed to high levels of PAHs in New York City had full scale and verbal IQ scores that were 4.3 and 4.7 points lower than those of less exposed children, a statistically significant difference. A difference of more than four points, the average seen in this study, is educationally meaningful in terms of decreased success in school.[6]

Other recent studies looking at the effects on IQ of various environmental agents show similar results. For example, researchers at Columbia University working with a cohort of children in Bangladesh found that both arsenic[7] and manganese[8] levels in drinking water were associated in a dose-dependent fashion with decreases in intelligence. The same levels of arsenic studied in this research are found in well water in some areas of the U.S.[7] (This work was supported by the NIEHS Environmental Health Center Program and the NIEHS Superfund Research Program.) In addition, a researcher at NIEHS led an important study[9] to test the efficacy of chelation treatment of mild to moderate lead poisoning with respect to effects on IQ (the Treatment of Lead in Children, or TLC study). This study established that once lead is elevated in the blood, subsequent treatment with chelators cannot restore the "lost" IQ, affirming the importance of primary prevention of lead exposure.

The Superfund Amendments and Reauthorization Act of 1986 ("SARA") authorized NIH to fund university-based research ($49.6 million in FY 2009) to conduct the science needed for human health risk assessment and decision-making for remediation of hazardous waste sites. Based on population numbers from the US 2000 Census, it is estimated that almost 1 million children under the age of five are living within one mile of a Superfund site in the United States and Puerto Rico; within a four-mile buffer, the number of children under the age of five increases to

over 5 million. Almost 14 million children between the ages of five and 17 live within four miles of a Superfund site.

Researchers at Brown University's Superfund Research Program have been using a science-based approach to advise communities on the site location of schools. Siting schools on former industrial properties is a practice that may put children at risk of exposure to toxicants previously assumed to be contained below ground. Vapor intrusion is a complex process that is difficult to predict and has been the cause of many misguided school development projects throughout the Northeast, particularly in environmental justice communities. The researchers at Brown have developed models[10] that provide a science-based assessment of the fate and transport of these hazardous substances in the subsurface. These investigators are working with the Rhode Island Department of Environmental Management, translating their research findings into improved sampling and modeling techniques to inform city planners about vapor intrusion risks prior to building on a site. In addition, the Brown University Superfund Community Outreach Project is working to develop alternative models for school siting through an Environmental Equity Stakeholder Workgroup. Through their work, the researchers have empowered regulators and community groups with tools to prevent exposure among vulnerable youth.

Another NIEHS-funded Superfund researcher at the University of California at Berkeley is exploring the causes of the DNA mutations that produce childhood leukemia by asking parents about their exposures to household chemicals, such as paints and solvents. The researcher found that the risk of acute lymphoblastic leukemia (ALL) is significantly associated with paint exposure, with a higher risk observed when paint was used postnatally by a person other than the mother. No significant association was found between petroleum-based solvent (i.e., toluene and

xylene) use and ALL risk overall. However, a second rarer form of childhood leukemia, acute myeloid leukemia, was associated with petroleum-based solvents, but not with paint exposure.[11]

NIEHS funding of research projects in the Tar Creek Superfund site (Tar Creek, OK) assisted the local Board of Health in monitoring blood lead levels among children and pregnant mothers, allowing them to direct limited public health resources to prevent lead exposure, educating the community about methods to limit exposure, and assessing the movement and toxicity of metals in the local environment. A birth cohort at Tar Creek, the MATCH study (Metals Assessment Targeting Community Health), was founded in 2002 from funding obtained from the Superfund Research Program. The project was a collaboration between Harvard University, Integris Baptist Regional Health Center, L.E.A.D Agency, and the Ottawa County Health Department.

MATCH is unique because it partnered with both community groups and local health care providers to combine research on both human health effects work in children with environmental ecological research on metal chemistry and movement in the environment. While individually such studies may be common, they are typically done by separate teams that do not plan integrated work or share data. Doing them together under a single umbrella is a unique aspect of the NIEHS Superfund program. This collaboration drove the research toward questions that were directly relevant to the Tar Creek community, such as how metal waste undergoes chemical changes in the environment--making exposure more or less likely, and whether children who are exposed are impacted by these metals. MATCH investigators have given presentations to participants in the study, local community groups, and regulatory agencies such as EPA, HHS's Agency for Toxic Substances and Disease Registry (ATSDR), and the Oklahoma Department of

Environmental Quality, helping those agencies responsible for the remediation of the site and educating study participants in ways to reduce exposure.

A study in a population of pregnant women with relatively low arsenic exposures in the same Tar Creek, OK, locality showed that arsenic was associated with impaired glucose tolerance during pregnancy and therefore may be associated with increased risk of gestational diabetes.[12] Gestational diabetes poses significant risks to the developing child, as well as an increased risk of Type 2 Diabetes in the mother later in her life; gestational diabetes is associated with increased risk of stillbirths, major congenital malformations, and complications during delivery and the perinatal period. Infants born to mothers with impaired glucose tolerance or full-blown gestational diabetes are at increased risk of subsequent impaired glucose tolerance and obesity.[13]

Researchers from the Duke University Superfund Research Program recently learned that exposure to fipronil, a new pesticide being introduced to replace organophosphates for both household and agricultural use, results in the same adverse effects on neurodevelopment as the organophosphates. They also showed that the metabolic alterations evoked by early-life exposure to compounds often classified as "developmental neurotoxicants" support the idea of the potential involvement of environmental contaminants in the dramatic increase in childhood obesity and diabetes.[14,15]

NIEHS partners with EPA in funding the Children's Environmental Health Centers program. The Centers form a national network of university-based programs that fosters communication, innovation, and research excellence with the ultimate goal of reducing the burden of morbidity among children as a result of exposure to harmful environmental agents. The Centers: (1)

capitalize on the research findings and resources from ongoing epidemiology and clinical studies of pregnant women and children; (2) enhance the application of novel findings and approaches in areas of basic or mechanistic research to human studies; (3) develop and apply new or improved biomarkers to best characterize exposure effects on human biology and to predict long-term clinical consequences; (4) train new investigators who can address emerging issues in children's environmental health; and (5) ensure active participation of stakeholders and communities in the research process and translation of research findings in order to enhance effectiveness of the research and facilitate translation of research into policy and practice. The Children's Environmental Health Center Research Program not only continues to support the multi-project, multi-disciplinary research project grants that have been its mainstay over the past ten years, but is adding new "Formative Centers" to foster new research ideas in children's environmental health that are in the early phase of scientific inquiry and where the preliminary data or partnerships may be limited. The total investment by NIEHS and EPA for these two programs will be $12 million, with $9 million annually to support six comprehensive Research Programs and an additional $3 million to support approximately four Formative Centers beginning in FY 2010.

The Children's Centers Program is expanding into new areas of research including birth defects, childhood cancer (leukemia), diabetes, pubertal development, and the fetal basis of adult disease. It is enhancing the basic sciences directed towards additional children's environmental health issues such as epigenetics, trans-generational effects, diet, oxidative stress, and epithelial cell sensitivity. Its investigators and NIEHS staff are exploring possible collaborations with the National Children's Study, the Pediatric Environmental Health Specialty Units (a national network of regional centers of excellence funded jointly by ATSDR and EPA), and national and

regional birth defect surveillance programs. The Children's Center program continues its mentoring and support of new investigators and also actively supports the engagement of new community groups involved in children's environmental health issues.

The NIEHS Breast Cancer and Environment Research Program, co-funded with NCI, is investigating whether periods of susceptibility exist in the development of the mammary gland, when exposures to environmental agents may impact the breast and endocrine systems that can influence breast cancer risk in adulthood. It is examining the determinants of puberty in girls and integrating environmental, genetic, biologic, lifestyle, and socioeconomic factors, in recognition of the studies linking breast cancer risk to pubertal maturation. A major area of study is the role of chemicals in the environment, with a primary focus on hormonally active agents (endocrine disruptors) and the use of personal care or household products that are sources of these agents. A major accomplishment across Centers is the measurement of 51 environmental agents and their metabolites in biospecimens from approximately 1,190 girls who were enrolled in the study before breast development began. The types of chemicals measured include phenols and phthalates found in many personal care products and plastics; phytoestrogens found in foods; persistent pesticides (such as DDT); flame retardants used in hard plastic and foam furniture; polychlorinated biphenyls (PCBs); perfluorinated compounds used in a variety of materials, most notably Teflon; and cotinine, a tobacco smoke metabolite. The data include the first report in children of extraordinary levels of a number of hormonally active chemicals such as enterolactone, benzophenone-3, and monoethyl-phthalate. This investigation confirms that significant levels of such chemicals are found in the girls, and the data provide important additional information to the National Health and Nutrition Examination Survey (NHANES) data for U.S. citizens.

In the National Toxicology Program (NTP), which I also direct, additional work is underway in animal studies to look at the effects of some of these compounds. The NTP is an interagency program that coordinates toxicity testing across the federal government, providing toxicological evaluations on substances of public health concern through its testing and scientific analysis activities. The NTP has carried out studies[16,17] in animals exploring the fetal basis for adult disease. We are learning of more ways in which exposure to specific types of chemicals, even at very low levels, can disrupt our endocrine systems and affect children's development. NTP scientists have examined numerous substances that affect endocrine signaling processes for their influence on development. Studies have been performed or are underway on estrogenic compounds including genistein, found in soy products, and bisphenol A (BPA). A wide variety of herbal supplements, chemicals used in everyday products such as plastics or fabrics, and even radiofrequency radiation emissions from cellular telephones are being studied in multiple generations of laboratory animals. These studies are critical to understanding any potential linkages between environmental exposures during pregnancy and in early-life stages with a variety of effects, sometimes subtle, not only on growth and development, but on late-life chronic degenerative and proliferative diseases such as Parkinson's disease or cancer.

The NTP established the Center for the Evaluation of Risks to Human Reproduction (CERHR) to enhance its scientific evaluations. Following comprehensive reviews of the scientific literature, this Center issues monographs that carefully assess all the available evidence, including what is known about current human exposures, about how a given environmental chemical, physical substance, or mixture may cause adverse effects on human reproduction and/or development. To our knowledge, CERHR is the only program of its kind. Its monographs are recognized as

authoritative evaluations by many regulatory agencies.[18] For example, CERHR evaluations were cited as the basis for the listing of five different phthalates: 1-bromopropane, 2-bromopropane, and methanol, as reproductive or developmental toxicants in California.

The impact of CERHR analysis activities was most evident during the significant public attention given to the recent evaluation of BPA. Bisphenol A is a chemical produced in large quantities, primarily for use in the production of polycarbonate plastics and epoxy resins. People, including children, are exposed to BPA in food and beverages when it leaches from the protective internal epoxy resin coatings of canned foods and also from consumer products such as polycarbonate tableware, food storage containers, water bottles, and baby bottles. The CERHR report concluded that current human exposure is of "some concern" for effects on the development of the prostate gland and brain and for behavioral effects in fetuses, infants and children. Based on these findings, NTP has included BPA in its testing program; in addition, NTP is partnering with U.S. Food and Drug Administration's National Center for Toxicological Research to obtain data for constructing models of BPA kinetics to understand the effects of different exposure levels. NIEHS gave a high priority to BPA research in the grants program undertaken with stimulus funds from the American Recovery and Reinvestment Act of 2009 (ARRA). NIEHS is spending $14.9 million in ARRA funds on ten projects focusing on BPA. Our total investment in BPA research is more than $31 million.

CERHR is currently conducting an evaluation of soy infant formula, which exposes infants to high levels of naturally occurring estrogenic compounds at a stage of development when circulating estrogens are usually very low. Soy formula use is common, and there is public health concern about its effects on infants and young children.[19] Other NIEHS programs are also

looking at soy formula. Soy-fed infants have much higher exposure to endocrine-active compounds in their diets than do cow milk- or breast milk-fed infants. Soy-fed infants may be the group with the highest exposure to any environmental estrogen.[20] It is not known, though, whether these soy exposures are high enough to act as hormones in children. Researchers at NIEHS have begun an observational study with infants and toddlers to see whether feeding with soy formula can result in hormonal effects; this work will advance the field of endocrine disruptor science and provide better information for the use of policymakers and parents.

The NIEHS is supporting research that examines both the developmental origins of obesity and the possibility that environmental exposures during development play an important role in the current epidemic of obesity, diabetes, and metabolic syndrome. Most of the current data are from animal studies; there are data showing weight gain in rats and mice after developmental exposure to a number of different substances. This new hypothesis broadens the focus on obesity from solely genetics and lifestyle to include environmental exposures. It also poses questions about time of susceptibility to obesity from being an adult onset problem to being an early life exposure/developmental problem. This is an emerging area of research that NIEHS is exploring.

Epidemiology studies support the findings in animals and show a link between exposure to chemical such as PCBs, DDT, and some persistent organic pollutants and the development of obesity. In addition, the use of soy-based infant formula containing genistein has been positively associated with obesity later in life.[21]

A number of studies point to a relationship between obesity in children and asthma. Scientists in Australia showed an association between asthma symptoms and obesity in a cohort of 4- to 5-year-old children.[22] A meta-analysis of the effect of high body weight, either at birth or later in childhood, showed that these children are at an increased risk for future asthma. Potential biological mechanisms include diet, gastro-esophageal reflux, mechanical effects of obesity, allergy, and hormonal influences.[23]

I also want to mention the NIEHS involvement in the National Children's Study (NCS). This research project has been designed to study the effects of environmental influences on the health and development of 100,000 children across the U.S., following them from before birth until age 21. NIEHS is one of the four lead agencies on the study, and our scientists have been part of the discussion and planning since its inception. Enrollment in pilot studies is underway at seven locations. The NCS has the potential to give us an unprecedented opportunity to answer some of the difficult questions about many of the diseases and exposures that I have mentioned in this statement.

As well as NIEHS, HHS's Centers for Disease Control and Prevention (CDC) emphasizes the necessity of effective prevention programs to alleviate children's exposure to harmful environmental elements. CDC's National Center for Environmental Health (NCEH) has several programs in this area. One such program is Built Environment- Healthy Places, which focuses on healthy community design to prevent health effects such as asthma, obesity, diabetes, and attention deficit disorder. Additionally, the Lead Poisoning Prevention Program has had great success in its efforts to eliminate elevated blood lead levels in children. Also, the CDC Asthma National Control Program and its many partners make up the public health response to asthma

control. Its goals are to reduce the number of deaths, hospitalizations, emergency department visits, school days or workdays missed, and limitations on activity due to asthma.

These are but a few examples of critically important environmental health research and programs at HHS and the immediate and tangible impact they will have on the health of our nation's children. I am happy to answer any questions that you have.

## ENDNOTES

[1]CV Breton, HM Byun, M Wenten, F Pan, A Yang, FD Gilliland. Prenatal tobacco smoke exposure affects global and gene-specific DNA methylation. Am J Respir Crit Care Med. 2009 Sep 1: 180(5):462-7.

[2] Aimin Chen, Michael L Pennell, Mark A Klebanoff, Walter J Rogan and Matthew P Longnecker IJE Advance Access originally published online on October 31, 2005, Maternal smoking during pregnancy in relation to child overweight: follow-up to age 8 years, International Journal of Epidemiology 2006 35(1):121-130; doi:10.1093/ije/dyi218

[3] Smith, A.H., G. Marshall, Y. Yuan, C. Ferreccio, J. Liaw, O.S von Ehrenstein, C. Steinmaus, M.N. Bates, and S. Selvin. August 2006. Increased Mortality from Lung Cancer and Bronchiectasis in Young Adults Following Exposure to Arsenic *In Utero* and Early Childhood. *Environmental Health Perspectives* 114(8):1293-1296.

[4]R McConnell, K Berhane, F Gilliland, SJ London, T Islan, WJ Gauderman, E Avol, HG Margolis, JM Peters. Asthma in exercising children exposed to ozone: a cohort study. Lancet. 2002 Feb 2: 359(9304):386-91. Erratum in: Lancet 2002 Mar 9; 359(9309):896.

[5]I Romieu, JJ Sienra-Monge, M Ramirez-Aguilar, H Moreno-Macias, NI Reyes-Ruiz, B Estela del Rio-Navarro, M Hernandez-Avila, SJ London. Genetic Polymorphism of GSTM1 and antioxidant supplementation influence lung function in relation to ozone exposure in asthmatic children in Mexico City. Thorax. 2004 Jan; 59(1):8-10.

[6]FP Perera, Z Li, R Whyatt, L Hoepner, S Wang, D Camann, V Rauh. Prenatal airborne polycyclic aromatic hydrocarbon exposure and child IQ at age 5 years. Pediatrics. 2009 Aug;124(2): e195-202.

[7] Wasserman, G.A., X. Liu, F. Parves, H. Ahsan, P. Factor-Litvak, A. van Geen, V. Slavkovich, N.J. LoIacono, Z. Cheng, I. Hussain, H. Momataj, and J.H. Graziano. September 2004. Water Arsenic Exposure and Children's Intellectual Function in Araihazar, Bangladesh. *Environmental Health Perspectives* 112(13):1329-1333.

[8] Wasserman, G.A., X. Liu, F. Parvez, H. Ahsan, D. Levy, P. Factor-Litvak, J. Kline, A. van Geen, V. Slavkovich, N.J. LoIacono, Z. Cheng, Y. Zheng, J.H. Graziano. 2005. Water Manganese Exposure and Children's Intellectual Function in Araihazar, Bangladesh. *Environmental Health Perspectives*. 114(1):124-129.

[9] Rogan, W. J., Dietrich, K. N., Ware, J. H., Dockery, D. W., Salganik, M., Radcliffe, J., Jones, R. L., Ragan, N. B., Chisolm, J. J., and Rhoads, G. G. The effect of chelation therapy with succimer on neuropsychological development in children exposed to lead. *New England Journal of Medicine,* 344 (19): 1421-1426, 2001.

[10] Pennell, K. G., Bozkurt, O., Suuberg, E. M. [3]Development and Application of a 3-D Model For Evaluating Site-Specific Features on Vapor Intrusion Rates in Homogenous Geologies Journal of Air and Waste Management Association. 59: 447-460. 2009.

[11] Scelo, Ghislaine, Catherine Metayer, L. Zhang, Joseph L. Wiemels, Melinda C. Aldrich, Steve Selvin, Stacy Month, M.T. Smith, and Patricia A. Buffler. 2009. Household exposure to paint and petroleum solvents, chromosomal translocations, and the risk of childhood leukemia. *Environmental Health Perspectives*. **117(1):**133-9.

[12] Adrienne S. Ettinger, Ami R. Zota, Chitra J. Amarasiriwardena, Marianne R. Hopkins, Joel Schwartz, Howard Hu, and Robert O. Wright. 2009. Maternal Arsenic Exposure and Impaired Glucose Tolerance during Pregnancy. *Environmental Health Perspectives* 117(7): 1059-1064.

[13] http://diabetes.niddk.nih.gov/dm/pubs/gestational/

[14] Slotkin, Theodore A. and Fredric J. Seidler. 2009. Protein kinase C is a target for diverse developmental neurotoxicants: transcriptional responses to chlorpyrifos, diazinon, dieldrin and divalent nickel in PC12 cells. *Brain Research* **1263:**23-32.

[15] Slotkin, Theodore A., Bethany E. Bodwell, Edward D. Levin, and Fredric J. Seidler. 2008. Neonatal exposure to low doses of diazinon: long-term effects on neural cell development and acetylcholine systems. *Environmental Health Perspectives* **116(3):**340-8.

[16] National Toxicology Program. NTP Technical Report on the Multigenerational Reproductive Toxicology Study of Genistein (CAS No. 446-72-0) in Sprague-Dawley Rats (Feed Study). Technical Report Series No. 539. NIH Publication No. 07-4477. National Institutes of Health, Public Health Service, U.S. Department of Health and Human Services, Research Triangle Park, NC.

[17] National Toxicology Program. NTP Technical Report on the Multigenerational Reproductive Toxicology Study of Ethinyl Estradiol (multigenerational) (CAS No. 57-63-6) in Sprague-Dawley Rats (Feed Studies). Technical Report Series No. 547. (DRAFT) National Institutes of Health, Public Health Service, U.S. Department of Health and Human Services Research Triangle Park, NC.

[18] http://cerhr.niehs.nih.gov/reports/index.html

[19] Barrett JR. The Science of Soy: What Do We Really Know. 2006 *Environ Health Perspect* 114(6):A352.

[20] Bernbaum JC, Umbach DM, Ragan NB, Ballard JL, Archer JI, Schmidt-Davis H, Rogan WJ. Pilot Studies of estrogen-related physical findings in infants. 2008 *Environ Health Perspect* 116:416–420.

[21] RR Newbold, E Padilla-Banks, WN Jefferson. Environmental estrogens and obesity. Molecular and Cellular Endocrinology 304 (2009) 84–89

[22]A Tai, A Burton, R Volkmer. Association between asthma symptoms and obesity in preschool children. Asthma. 2009 May; 46(4)362-5

[23]V Flaherman, GW Rutherford. A meta-analysis of the effect of high weight on asthma. Arch Dis Child. 2006 Apr; 91(4):334-9