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# *IN UTERO* AND PERINATAL RISK FACTORS FOR ASTHMA OR WHEEZING AND OTHER ATOPIC MANIFESTATIONS

By

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# ABSTRACT

## IN UTERO AND PERINATAL RISK FACTORS FOR ASTHMA OR WHEEZING AND OTHER ATOPIC MANIFESTATIONS

By

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A better understanding of the etiology of asthma and other atopic disorders may introduce prevention methods, thus reducing associated outcomes. We tested the hypotheses, maternal oral contraceptive (OC) use before and complications during pregnancy are risk factors for asthma or wheezing and other atopic manifestations. These tests were conducted in a follow-up study of 1,720 children who were part of the Jamaican Perinatal Morbidity and Mortality Survey (n=13, 04810). Mother-infant-pairs were interviewed at birth and babies examined. Followed-up data at six weeks and at approximately 11 years of age were also collected. All three datasets were linked using identification number and date of birth for both mother and child. After controlling for gender, smoking during pregnancy, birth weight (< 2.5 kg, 2.5kg – 4.0kg, and >=4.0 kg) and other covariates, adjusted odds ratios (AOR) and their 95% confidence interval (CI) were estimated by logistic regression analysis. Prevalence of asthma, OC use and maternal health complications during pregnancy were 16.8%, 49.9%, and 50.2% respectively. Asthma was more frequently reported for children whose mothers used OC (AOR=1.56; 95%CI 1.04–2.32), and had health complications during pregnancy, (AOR=1.75; 95%CI 1.14–2.69). Results suggest that asthma may be pre-programmed *in utero*.

## DEDICATIONS

This work is specially dedicated to the two most important women in my life; my wife Valrie and mother Patricia. Also to Jevon Brooks (nephew) for the promise he represents.

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## LIST OF ABBREVIATIONS

AD ..... Atopic Dermatitis

AOR ..... Adjusted Odds Ratios

AR ..... Allergic Rhinitis

CBMC ..... Cord Blood Mononeucleous cell

CI ..... Confidence Interval

FFUQ ..... First Follow-up Questionnaire

IFN-γ ..... Interferon Gamma

IgA ..... Immunoglobulin -A

IgE ..... Immunoglobulin –E

IgG ..... Immunoglobulin –G

IL ..... Interleukin

IUD ..... Intrauterine device

LBW ..... Low Birth Weight

MQ ..... Main Questionnaire

MRNA ..... Memory Ribonucleic Acid

OC ..... Oral Contraceptive

OR ..... Odds Ratios

SAS ..... Statistical Analysis System

SFUQ ..... Second Follow-up Questionnaire

TH ..... T-Helper Cell

VDRL ..... Venereal disease research laboratory

# INTRODUCTION

The prevalence of allergies is increasing in many parts of the world, and asthma has become the most common chronic disease in childhood. The etiology of asthma and allergic disease remains insufficiently understood, despite considerable research (1). Recent studies have expanded to include the study of novel factors such as *in utero* and perinatal exposures that may "program" the initial susceptibility to these disorders (2). Some authors have reported that maternal health complications during pregnancy and at birth and maternal estrogen levels are associated with asthma and other atopic manifestations later in life (3-5).

The current work is based on data of a follow-up study from Jamaica, which represents a geographic sub-sample of the previously conducted Jamaican Perinatal Morbidity and Mortality Survey. Offspring of mothers who participated in the Jamaican Perinatal Morbidity and Mortality Survey, conducted in September and October 1986, were re-contacted in 1998. *In utero* and perinatal factors were investigated to assess their contribution to the development of asthma and other atopic manifestations in children 11 to 12 years of age. Specifically, the association between two risk factors was tested:

(1) Maternal use of oral contraceptives (OC) before pregnancy

(2) Maternal complications during pregnancy

and their influence on the following outcomes:

(a) Asthma or wheezing,

(b) Frequent nighttime/early morning cough,

(c) Eczema, and

(d) Hay fever, sinus problems or other allergy.

## Chapter 1

# *IN UTERO* AND PERINATAL EVENTS AS RISK FACTORS FOR ASTHMA AND OTHER ATOPIC MANISFESTATIONS

### *In Utero* conditions

Although the contribution of genetics to the atopic phenotype is substantial, the penetrance of genetic traits is highly dependent on interactions with the environment. Environmental exposure begins at conception. Because the fetus contains paternal antigens, it will more likely be rejected by the mother's immune system as a transplanted allograft. In transplantation models, it is thought that Th-1 lymphocytes are responsible for acute rejection and that Th-2 cells work to maintain tolerance. During pregnancy, the maternal-fetal interface is an immunologically active site producing many cytokines. Numerous lines of evidence point to a dominance of Th-2–type cytokines in the uterine environment. Fetal cord blood lymphocytes are skewed toward the Th-2 type. Neonatal T cells produce low levels of IFN-$\gamma$ and overproduce Th-2 cytokines. Maternal lymphocytes produce IL-5 in response to normal allogenic placenta, whereas placentas from abortion-prone pregnancies cause lymphocytes to secrete IL-2 and IFN-$\gamma$ (6). At birth, the immune system of the fetus has been strongly shifted toward a Th-2 lymphocyte profile (7). In mothers with atopic disease, this effect may be exaggerated. If this skewed fetal immune response is not rebalanced by stimuli that restore the normal Th-1/Th-2 balance, the child may become predisposed to atopic manifestations (6).

Perinatal Events

Perinatal events, focuses on those pertaining to or occurring in the period shortly before, during or after birth. More specifically, those defined as beginning with completion of the twentieth to twenty eighth week of gestation and ending seven to twenty eight days after birth.

In this period of development, infants are especially vulnerable to infections, having no prior exposure to the microbes in the environment at birth. IgA antibodies are secreted in breast milk and thereby transferred to the gut of the newborn infant, where they provide protection from newly encountered bacteria until the infant can synthesize its own protective antibody.

IgA is not the only protective antibody conferred on the infant by its mother. Maternal IgG is transported across the placenta directly into the blood stream of the fetus during intrauterine life. Babies at birth have as high a level of plasma IgG as their mothers, and with the same range of specificities (8). IgG has the ability to neutralize toxins and viruses and immobilize bacteria.

T cells are also critical to the pathogenesis of allergic diseases. It has been hypothesised that atopy in children represents the persistence of prenatal and neonatal allergen specific $Th_2$ responses due to failure of immune deviation mechanisms which promote the $Th_1$ state of the normal adult immune system (9, 10). There is evidence that during pregnancy the maternal immune response is of the Th2 type, as Th1 type cell mediated immune responses are potentially harmful to the maintenance of pregnancy (10).

Early postnatal factors such as breastfeeding and sites of antigen presentation may also affect the neonate's immune response in important ways. There is evidence to suggest that exposure to maternal allogeneic cells during breastfeeding leads to donor specific hyporesponsiveness in the neonate (11).

Antibody response to environmental allergens in the perinatal period is also a concern for atopy. Immune responses to allergens early in life, perhaps even *in utero*, may be critical to the pathogenesis of atopy later in life. Children produced $IgG_1$ but not $IgG_4$ antibodies against an inhaled allergen between three and 12 months of age. Data suggest that $IgG_4$ antibodies increase with age although the majority of the studies were not performed prospectively. Inhaled allergens are known to stimulate CBMC produced IL-4, IL-5 and IL-9 (mRNA), IL-6, IL-10, and IL-13 (protein) but very little IFN-$\gamma$ (mRNA or protein). Allergen specific cytokine production changes with age. Between birth and two years IL-4 mRNA production decreased in non-atopic children but persisted in atopic children. IFN-$\gamma$ mRNA production increased significantly between birth and six months in non-atopic children but not in atopic children. Whether absolute levels of Th1 and Th2 cytokines are significantly different in atopic and non-atopic children at the age of two is less clear (10).

## Chapter 2

## ATOPIC MANIFESTATIONS/ DISORDERS

The use of the term atopy or atopic in designating an allergic reaction implies a hereditary factor expressed as susceptibility to hay fever, asthma or eczematoid dermatitis in the families of affected individuals (12). Clinically, it is an immune disorder, which is manifested as a Type 1 hypersensitivity reaction including asthma, eczema and/or rhinitis. It is characterized by a genetic predisposition for generating IgE antibodies against common environmental allergens. Atopic individuals may differ from nonatopic individuals in their ability to regulate production of IgE antibody. The production of IgE in B-lymphocytes is regulated by cytokines. IL-12 is one of the important cytokines which down-regulate IgE production (13).

### Asthma

Asthma is the most chronic disease in childhood. In the United States, it is responsible for frequent admitting diagnosis in children's hospitals than any other condition, and results nationally in 5-7 lost school days/yr/child. As many as 10-15% of boys and 7-10% of girls may have asthma at some time during childhood. There is no universally accepted definition of asthma. It may be regarded as a diffuse, obstructive lung disease with hyperreactivity of the airways to a variety of stimuli and/or a high degree of reversibility of the obstructive process, which may occur either spontaneously or as a result of treatment (12). Whilst its etiology is

still very ubiquitous, Maddox et al. suggest that it involves the interaction between genetic factors and environmental stimuli. They also postulated that the vast majority of data regarding the pathogenesis of asthma is concentrated on Th-1 and Th-2 imbalance between the phenotypes. However, asthma (reversible airflow obstruction, persistent airway hyperreactivity, and airway remodeling), may also occur through nonallergic mechanisms of inflammation. Genetics, the uterine environment, maternal and infant diet, respiratory infections, and occupational and environmental exposures all contribute to this delicate balance (6).

Occurrence of asthma in children

Asthma may have its onset at any age. Approximately 30% of patients are symptomatic by one year of age, whereas 80-90% of asthmatic children have their first symptoms before four to five year of age. The course and severity of asthma are difficult to predict. The majority of affected children have only occasional attacks of slight to moderate severity, which are managed with relative ease. A minority experience severe, intractable asthma, usually perennial rather than seasonal. It is incapacitating and interferes with school attendance, play activity, and day-to-day functioning. The relationship of age of onset to prognosis is uncertain. Most severely affected children have an onset of wheezing during the first year of life and a family history of asthma and other allergic diseases (particularly atopic dermatitis) (12).

Clinical Manifestations

The onset of an asthma exacerbation may be acute or insidious. Acute episodes are most often caused by exposure to irritants such as cold air and noxious fumes (smoke, wet paint) or exposure to allergens or simple chemicals, for example, aspirin or sulfites. Exacerbations precipitated by viral respiratory infections are slower in onset, with gradual increases in frequency and severity of cough and wheezing over a few days. Because airway patency decreases at night, many children have acute asthma at this time. The signs and symptoms of asthma include cough, which sounds tight and is nonproductive early in the course of an attack; wheezing, tachypnea, and dyspenea with prolonged expiration and use of accessory muscles of respiration; cyanosis; hyperinflation of the chest; and tachycardia and pulsus paradoxus, which may be present to varying degrees depending on the stage and severity of the attack. Cough may be present without wheezing, or wheezing may be present without cough. Tachypnea also may be present without wheezing. Manifestations will vary depending on the severity of the exacerbation (12).

Coughing

Aspiration of a laryngeal foreign body often causes a sudden onset of coughing with choking followed by wheezing. An intermittent, recurrent, dry cough or a cough productive of clear mucus is consistent with asthma, but a chronic persistent cough productive of purulent sputum suggests bronchiectasis or cystic fibrosis.

Coughing or wheezing following strenuous exercise may occur in children who have asthma. Provocation of coughing by laughter, crying, or exposure to smoke or specific odors also suggests the bronchial hyperresponsiveness characteristic of asthma (14).

Atopic dermatitis or eczema

Edward D. Perry of the University of Colombia coined the term atopy in the early 1920s (15). Wise and Sulzberg clinically characterized the term "atopic dermatitis" (AD) in 1933 (16). This term was used to describe a skin condition characterized by intense dryness of the skin, pruritus, and chronic erythematous lesions with a relapsing course.

Atopic dermatitis is clearly related to an atopic phenotype in most patients. The family history is most often positive, and elevated total IgE antibody levels, or positive specific IgE antibody to common allergens might be observed (17). There is conflicting evidence as to whether the level of IgE is related to either the severity or the extent of the dermatitis. The concentration of IgE does, however, fluctuate with the stage of the disease. The level returns to normal when the disease has been quiescent for several years. It is not established that AD is primarily an IgE-mediated allergic disorder. It is difficult to demonstrate consistently a role for allergens, whether foods or inhalants, in the pathogenesis of eczema.

Increased concentrations of IgE in atopic dermatitis may be related to a deficiency of IgE isotype-specific "suppressor" T-cell function. Impairment of cell-

mediated immunity in some patients with AD is indicated by (1) absence of the reactions of delayed hypersensitivity on intradermal skin testing with certain antigens; (2) inability to be sensitized with potent contact sensitizers (e.g., poison ivy, dinitrocholorobenzene); (3) diminished proliferative response of lymphocytes to mitogens such as phytohemagglutinin; and (4) variable phagocytic and chemotactic defects of monocytes and neutrophils.

Potential primary immune abnormalities for AD include an increased frequency of allergen-specific Th2 cells that secrete various interleukins (IL-4, IL-5, IL-13) and reduced activity of Th1 cells. Th2-type cytokines may initiate the acute inflammatory response. Allergen-reactive T cells, which express the cutaneous lymphocyte-associated antigen, may migrate to the skin and initiate disease (12).

Clinical Manifestations

Atopic dermatitis affects 2-10% of children and typically occurs in three stages with fairly distinctive features. The disease most often begins in infancy, usually during the first two to three months of life. The onset is sometimes delayed until the second or third year. Approximately 60% of patients are affected by first year of age and close to 90% by five year of age. The earliest lesions are erythematous, weepy patches on the cheeks, with subsequent extension to the remainder of the face, neck, wrists, hands, abdomen, and extensor aspects of the extremities. Involvement of flexural areas characteristically appears later, but may occur as popliteal and antecubital dermatitis in early life.

Pruritus is marked. The affected infant makes incessant efforts to scratch by rubbing the face on bedclothes and against the sides of the crib. This trauma to the skin rapidly leads to weeping and crusting. Secondary infection is common and may be extensive.

The onset of dermatitis frequently coincides with the introduction of certain foods into the infant's diet, especially cow milk, wheat, soy, peanuts, fish, or eggs. Cutaneous symptoms develop after food challenges in 50-90% of infants and children who have dermatitis and high IgE serum concentrations. Overall, about 20-30% of patients with eczema have food hypersensitivity to one or more of the six common allergens. There is an unequivocal evidence of IgE sensitivity in certain infants who have urticaria, colic, and a diffuse erythematous flush following ingestion of the offending food. The erythematous flush appears to be accompanied by intense itching, which results in scratching and then in the appearance of the skin lesions characteristic of eczema. The major role of scratching in the production of skin lesions has been demonstrated when one extremity has been encased in surgical dressings and the other left uncovered. The lesions of atopic dermatitis occur only in the uncovered extremity (12).

Hay fever, sinus problem

Allergic rhinitis (AR) or hay fever, sinus problem, is a heterogeneous disorder, which is characterized by one or more symptoms including sneezing, itching, nasal congestion, and rhinorrhea. Many causative agents have been linked to AR including pollens, molds, dust mites, and animal dander. AR affects

an estimated 20 to 40 million people in the United States alone, and the incidence is increasing; an estimated 20% of cases are seasonal allergic rhinitis (SAR); 40% of cases are perennial rhinitis; and 40% of cases are mixed (18).

Pathophysiology

Inhaled pollens, mold spores, and animal or mite antigens are deposited on the nasal mucosa. Water-soluble antigens diffuse into the epithelium and, in genetically predisposed atopic individuals, initiate the production of local IgE. IgE-stimulated release of mast cell mediators, synthesis of new mast cell mediators, and subsequent recruitment of neutrophils, eosinophils, basophils, and lymphocytes are responsible for the early- and late- phase reactions to inhalant allergens. These reactions result in mucus, edema, inflammation, pruritus, and vasodilation. Delayed inflammation may contribute to nasal hyperresponsiveness to specific allergens, a priming effect, and to nonspecific stimuli such as irritants and strong odors (12).

Atopic Disorders Closing Notes

In closing, it is important to note that there is a noticeable proportion of combined occurrence of eczema, hay fever and allergic asthma in childhood. Kuehr et al. support this in a study in a cross-sectional study of 1376 eight-year-old pupils (19).

## Chapter 3

### A REVIEW OF THE ASSOCIATION BETWEEN *IN UTERO* AND PERINATAL EXPOSURES AND ATOPIC MANIFESTATIONS.

Aretaeus, Greek physician of Cappadocia, is believed to be the first to attempt to associate a cause for asthma. In the 2nd or 3rd century AD, he described the cause to be a coldness and humidity of the spirit (20). Ever since, researchers have been conducting studies in this area, identifying a plethora of potential factors involved in the pathogenesis of asthma and other atopic manifestations. These factors span three general time-windows; namely, *in utero* or prenatal, peripartum or perinatal, and neonatal or postnatal periods.

In the *in utero* or prenatally time window, maternal smoking, estrogen levels and infection during pregnancy, are some factors, which may increase the risk for asthma and atopy. Mode of delivery, neonatal or early childhood illness, and breast-feeding are all suspected factors during the peripartum or perinatal period. Postnatally, neonatal or early childhood illness and breast-feeding are under increasing scrutiny as to their possible role in the development of asthma (20).

In an attempt to sort out the complex interrelationships of some of these potential influences on the development of atopy, this paper will focus on two of the three above-mentioned time-windows, namely the *in utero* and perinatal.

## Factors associated with the *in utero* time-window

### Maternal smoking

Studies investigating the hazardous effects of contact with tobacco on the health of the infant can be traced back to as early as 1931. Mgalobeli compared women who worked in different industries and found that workers in tobacco factories had a greater infant mortality rate in the age range 1 –3 years (21). Sontag and Wallace in 1935 found a direct impact on the fetus when they observed that cigarette smoking during pregnancy increases the human fetal heart rate (22).

There has been a renewed interest in the association between *in utero* cigarette smoke and childhood health outcomes. Oliveti et al. assessed the relation between *in utero* risk factors and asthma using a case-control study of 262 African-American children aged 4-9 years, both asthmatic and nonasthmatic, all of whom resided in a poor urban area and received health care at a local hospital-based clinic. Risk factors were ascertained through review of obstetric, perinatal, and pediatric records. They found mothers of asthmatic children were more likely to have smoked during pregnancy (50% vs. 27%), than mothers of nonasthmatic children. Multiple logistic regression showed maternal smoking during pregnancy (OR = 2.8) to be one of the strongest independent predictors of asthma (23).

Though not a universal finding, maternal smoking during pregnancy has been reported to increase cord blood IgE and IgD levels and to increase substantially the risk for atopic disease (eg, dermatitis, asthma, or food allergy or

intolerance) before 18 months of age. These effects were most pronounced in infants of mothers who had no history of atopic disease. The mechanisms by which maternal smoking may exert its effects are unknown. However, active smoking has been shown to increase the inducibility of peripheral blood mononuclear cells to secrete IL-4, an effect that wanes fairly rapidly upon smoking cessation. It is conceivable that this effect extends beyond maternal circulating immune cells to placental or fetal cells (20).

Estrogen levels during pregnancy

In an aggregative study, Wjst et al. performed an assessment of women using OC from the Great Britain Population Report of 1997, and of children aged 5-14 years who were discharged from the Welsh hospital after being diagnosed with asthma. They found a geographic trend, which showed asthma prevalence in children running parallel to that of maternal OC use. This similarity was most notable during 1970 when and sharp decrease in the rate of increase of OC use was followed by a similar decrease in rate of hospital discharge with a diagnosis of asthma. Results of an aggregative (ecological) study, Wjst et al. deduced that mother's oral contraceptive use fits well into the geographic and temporal background of this increase in asthma prevalence (3).

Many studies have presented evidence, which suggest that early age of menarche is associated with higher levels of estrogen in adulthood (24-26). A geographically defined cohort of 5188 subjects born in northern Finland was used to evaluate whether maternal age at menarche is associated with atopy among offspring at age 31 years. Logistic regression models were used to adjust

for maternal age, parity, smoking, season of birth, parental allergy, and measures of adiposity and socioeconomic status. Results showed the prevalence of atopy at 31 years of age, was lower in children whose mothers reached menarche at a later age, especially after age 15. Table 1 shows the adjusted odds ratio for children whose mothers started menarche younger than or at age12, 13, 14 and

**Table 1. Association between maternal age at menarche and occurrence of atopy in children at 31 years (4).**

| Maternal age at menarche (years) | Total no. (atopic) | % | Crude OR (95% CI) | Adjusted OR* (95% CI) |
|---|---|---|---|---|
| ≤12 | 694 | 34.9 | 1.49 | 1.43 |
| | (242) | | (1.19 to 1.87) | (1.12 to 1.83) |
| 13 | 1181 | 32.8 | 1.36 | 1.29 |
| | (387) | | (1.11 to 1.66) | (1.03 to 1.60) |
| 14 | 1406 | 30.2 | 1.21 | 1.15 |
| | (424) | | (0.99 to 1.47) | (0.93 to 1.42) |
| 15 | 1145 | 30.0 | 1.20 | 1.19 |
| | (344) | | (0.98 to 1.47) | (0.95 to 1.48) |
| ≥16 | 762 | 26.4 | 1.00 | 1.00 |
| | (201) | | | |
| p for trend | | | 0.000 | 0.005 |

*** Adjusted variables were defined in the following ways: maternal age ≤20, 21-25, 26-30, 31-35, and ≥36 years; maternal social classes I + II (professionals with the highest education and other white collar workers), III (skilled workers), IV (unskilled workers) and farmers; maternal smoking in pregnancy yes or no; parity 0, 1, 2-3 and ≥4; seasons at birth March-May, June-August, September-November and December-February; parental allergy yes if either the father or mother had allergic disorders, otherwise no; current vocational training in five categories; maternal BMI, ponderal index and current BMI in quintiles (4).**

15 years of age compared to those who started menarche 16 years or over (4).

These results suggest that the intrauterine environment might be important in later life in terms of development of adult atopy, at least for the mechanism

underlying the association observed (4). This finding supports previous hypotheses that high maternal estrogen level is a risk factor for atopy.

Maternal infection during pregnancy

It has been shown that transplacental sensitization of the fetus can be accomplished by maternal immunization during pregnancy. A study of children, nine to 16 years of age, born to mothers infected with *Onchocerca volvulus* during pregnancy found higher levels of skin microfilariae than in children of uninfected mothers. This correlated with higher production of $Th_2$-type cytokines in response to onchocercal antigens by peripheral blood mononuclear cells from these children compared with controls. This Th2-like response is similar to that observed in models of neonatal sensitization (20).

Results from a prospective study of 8088 children of the northern Finland birth cohort 1985-1986, showed that children had a higher risk of asthma if their mothers experienced vaginitis and febrile infections during pregnancy, OR = 1.41, (95% CI: 1.08-1.84) and 1.65 (95% CI: 1.25-2.18) respectively. A clear time trend in risk of childhood asthma corresponding to the timing of maternal febrile infections in pregnancy was also seen. Adjusted OR for the first, second, and third trimesters were 2.08, (95% CI: 1.13-3.82), 1.73 (95% CI: 1.09-2.75) and 1.44 (95% CI: 0.97-2.15) respectively (27).

Maternal complications during pregnancy

There is a paucity of studies on the relationship between maternal complications during pregnancy and the risk of having asthma or any atopic

disorders. Nafstad et al. conducted a population-based, four-year, cohort study involving 2531 children (28). Information was collected on maternally- (hyperemesis, hypertension, and preeclampsia) and uterus- (antepartum hemorrhage, preterm contractions, insufficient placenta, and restricted growth of the uterus) related complications in pregnancy. Asthma was assessed at age four years. After controlling for potential confounders, they found that uterus-related complication increased the risk of having asthma (AOR, 3.0; 95% CI, 1.8-5.4) and allergic rhinitis (AOR, 2.9; 95% CI, 1.6-5.2).

Complications, which occur in the perinatal period and their relation to asthma, was also addressed by Annesi-Maesano et al. (5). Using a large British birth cohort of 4065 natural children of 2583 mothers, from the National Child Development Study. Maternal complications during pregnancy was defined as any complication which had needed medical supervision apart from routine checks and hospital admissions at any time during pregnancy before labor began. After adjusting for relevant confounders, they found maternal complications during pregnancy to be a risk factor of asthma (OR, 2.01; 95% CI, 1.52-2.67) in the offspring. To assess the possibility that this association was not purely due to a specific complication, independent analyses were conducted to test the association between each specific complication and asthma. Only early or threatened labor and malposition and malpresentation of the fetus at birth (namely, breech, transverse lie, and face presentation) was found to have significantly increased the risk of asthma for the child.

Factors associated with the perinatal time-window

Mode of delivery

The relation between factors associated with parturition, and their influence on the pathogenesis of atopy is uncertain. In a prospective birth cohort born in northern Finland in 1966, Xu et al. evaluated the relationship of caesarean section to the risk of asthma in adulthood. Information on current doctor-diagnosed asthma and other allergic disorders was obtained from 1953 subjects by a self-administered questionnaire and skin prick test. Results showed that caesarean section had a strong effect on current doctor-diagnosed asthma in adulthood with an adjusted odds ratio (OR) of 3.23 (95% CI 1.53, 6.80). However, no substantial effects were observed for atopy, hay fever, and atopic eczema (29).

Annesi-Maesano et al. challenged this finding using the afore mentioned cohort from the National Child Development Study. Analyses were adjusted for potential confounders. It was found that delivery by emergency caesarean was not significantly related to childhood asthma. Adjusted OR =0.92; 95% CI 0.44, 1.86) (5).

Later, McKeever et al. supported findings of Xu et al. In a birth cohort of 24 690 children who contributed to the West Midlands General Practice Research Database they assessed whether the way in which babies were born has an impact on their subsequent risk of allergic disease. After controlling for potential confounders (sex, prematurity, consulting behavior of the child, parental atopy, year of birth, general practice, maternal age, and parental smoking) they found that being born by forceps or vacuum extractor delivery was associated

with an increased risk of developing eczema, incidence rate ratio [(IRR) 1.21; 95% CI, 1.11-1.31]. Similarly, there was an increased risk of asthma with a caesarean birth (IRR 1.09; 95% CI, 1.01-1.18). They concluded that this did not provide an association strong enough to suggest that babies born by caesarean, forceps, or breech delivery had an increased risk of developing allergic disease (30).

Neonatal and early childhood illness

Whilst there are numerous studies addressing the specific association between childhood infection and atopy, there is but one to my knowledge that assesses the non-specific childhood illness atopy relationship. This area was one examined in the previously mentioned study by Annesi-Maesano et al. The exposure "childhood illness" was based on whether the child had any illness or complication during the first week of life. They found child illness or health complications during the first week of life to be a risk factor for asthma at age 33 years (AOR =1.35; 95% CI 1.01–1.82) (5).

Breast-feeding

Since Grulee and Sanford in 1936 (11), first reported that breastfeeding protects against infantile eczema, the relation between breastfeeding and childhood atopic disorders have been conflicting.

The relation between breastfeeding and the prevalence of asthma among a childhood population was tested in a population-based case-control study. The study population included 2,315 students with asthma and 21,513 controls all from public elementary and junior high schools in Tokorozawa, Japan (age

range, 6–15 years). After adjusting for age, gender, parental smoking status, and parental history of asthma, a significantly higher prevalence of asthma was noted among children who had been breastfed (adjusted OR = 1.198; 95% CI: 1.05, 1.36). Results from this study suggest that breastfeeding in infancy may be related to a higher prevalence of asthma during preadolescence (11).

After conducting a systematic review of prospective studies that evaluated the association between exclusive breast-feeding during the first 3-months after birth and asthma, Gdalevich et al. found the opposite to be true. They found summary odds ratio (OR) for the protective effect of breast-feeding to be 0.70 (95% CI 0.60, 0.81). Their conclusion was that exclusive breast feeding during the first months after birth is associated with lower asthma rates during childhood (31).

## Chapter 4

# THE JAMAICAN PERINATAL MORBIDITY AND MORTALITY SURVEY

For this project, preexisting datasets from the Jamaican Perinatal Morbidity and Mortality Survey were used. These datasets provided the exposure variables whilst the outcome variables came from the follow-up study conducted when the children were approximately 11 years old.

## Background and Rationale

The motivating factors, which lead to the development of the Jamaican Perinatal Morbidity and Mortality Survey is based on the results of the Child Mortality Study of 1972 that clearly demonstrated the extent of under-reporting of early infant deaths. Following these results, the research team submitted a project proposal with draft questionnaires in December 1984 and funding approved in June 1985. It was agreed that the study would be implemented through the University of the West Indies' Child Health Department, although the principal investigators were full time employees of the Ministry of Health. Preparatory work for implementation of the study was initiated in December 1985.

## Aims and Objectives

The overall aim of this study was to provide information that will help improve the maternal and childcare services and reduce perinatal morbidity and mortality in Jamaica.

## Objectives specific to this study

### Morbidity

1. To identify the infants who get ill in the neonatal period and determine the causes of neonatal morbidity.
2. To identify maternal, environmental and clinical characteristics predictive of serious neonatal morbidity.
3. To determine whether criteria used to identify pregnancies at high risk of mortality also adequately identify those at high risk of major morbidity.

### Low birth weight

1. To identify the birthweight distribution and birthweight-specific mortality and morbidity rates.
2. To determine maternal, environmental and clinical factors associated with: (a) low birthweight associated with short gestation; (b) low birthweight associated with growth retardation.

## Methodology

In order to achieve the objectives of the study, observation periods of different lengths were required in order to attain adequate sample sizes. The survey was divided into four components: (a) main cohort study (2 months), (b)

neonatal morbidity (6 months), (c) perinatal mortality (12 months) and (d) service evaluation to run concurrent with the cohort study.

Organization and administration of the study

A 15 member Steering Committee was established in January 1986 to act as an advisory body, providing the necessary input advice and critique in the organization and implementation of the study. This included obstetricians, pediatricians, pathologists and midwives.

Staffing

There were two full-time professional members of staff employed on the study - the Study Administrator and the Pediatric Research Officer.

At the field level, each parish had a coordinator with responsibility for managing study activities and supervising the team of interviewers. The eight larger parishes also had an assistant coordinator. Full-time interviewers were assigned to the hospitals and a core of district midwives (field interviewers) were selected to interview mothers delivering at home. A nominal cash incentive of two Jamaican dollars, equivalent to $US0.36, was offered to other members of the primary health care team who brought the occurrence of a delivery to the attention of the field interviewers.

The main cohort

In this phase, all pregnant women were included who had a live birth, or stillbirth of 500 g or more, during the two-month period September 1, 1986 to October 31, 1986, regardless of the place of delivery. These women were interviewed and their babies examined, usually within the first 48 hours after delivery. Between

six weeks and three months after delivery mothers and their infants were again interviewed and examined at postnatal clinics. Those persons who went to private doctors or who failed to show up for their clinic appointments were visited at home to facilitate completion of the follow-up questionnaire.

Morbidity component

All babies with major illnesses admitted to any of the neonatal care units in any of the eight hospitals with pediatric consultants were included in the morbidity study. Each case had a neonatal admission questionnaire completed by the attending pediatrician and the mother was interviewed. The survivors were followed up at six weeks.

Service evaluation

In order to measure the potential impact of services on outcome, an evaluation of institutional and domiciliary services was undertaken.

(i) Institutions (public hospitals and maternity centers) were assessed by direct observation of the practice of obstetrical care on randomly selected days during the two months of the main cohort study. An inventory of basic equipment and supplies used for obstetric and newborn care and the staff complement were also included.

(ii) For the field domiciliary evaluation, a 25% sample of district midwives was interviewed to assess the knowledge and practice of domiciliary midwifery and the availability of basic supplies and equipment.

Training and sensitization

The project manager received training in perinatal epidemiology, two of the pathologists spent one and two weeks undergoing instruction in perinatal pathology. Parish coordinators, their assistants and interviewers were trained in the two months prior to implementation of the study.

A series of briefing meetings were held between the study team and members of staff of each parish Health Department (primary care), obstetric and pediatric units and other relevant staff at all hospitals (private and government), members of the Association of general practitioners, Pediatric Association of Jamaica, Medical Association of Jamaica and the Association of Obstetricians and Gynecologists. The Heads of the Departments of Pathology and Microbiology at the University of the West Indies were also briefed and their help and cooperation solicited.

Management

The island (Figure 1) was divided into four regions along the major migratory routes of patients in search of medical care. Coordinators could therefore come in contact with persons in adjacent parishes where a mother may have had antenatal care or been delivered.

Coordinators would visit hospitals daily in the first phase (September and October 1986) and at least twice weekly in the second phase (November 1986 to August 1987) to keep track of deliveries, neonatal admissions and deaths, collect completed questionnaires and ensure their submission to the national office. The mail service was not to be used, as this can sometimes be unreliable with long

delivery delays. All material was to be transferred by messenger or by the coordinators themselves.

Each parish coordinator was provided with a supervisor's manual setting out guidelines for completion and preliminary processing of the questionnaires as well as administrative procedures and the maintenance of a register of all deliveries and deaths in the parish during the study period.

Interviewers were also provided with manuals, which outlined basic interviewing techniques and took them through each question on the relevant questionnaires. Administrative procedures were also outlined.

Hospitals participating in the morbidity survey were provided with neonatal admission forms and newborn nursery charts to guarantee the collection of uniform basic information on the neonate. The neonatal admission questionnaires were for completion on discharge (or death) of the infant.

Each mother who attended between six weeks and three months post-delivery was presented with a certificate on which was included her child's study number. At one year of age the infants were sent birthday cards. These were used in the hope that they will facilitate subsequent follow-up studies of the cohort.

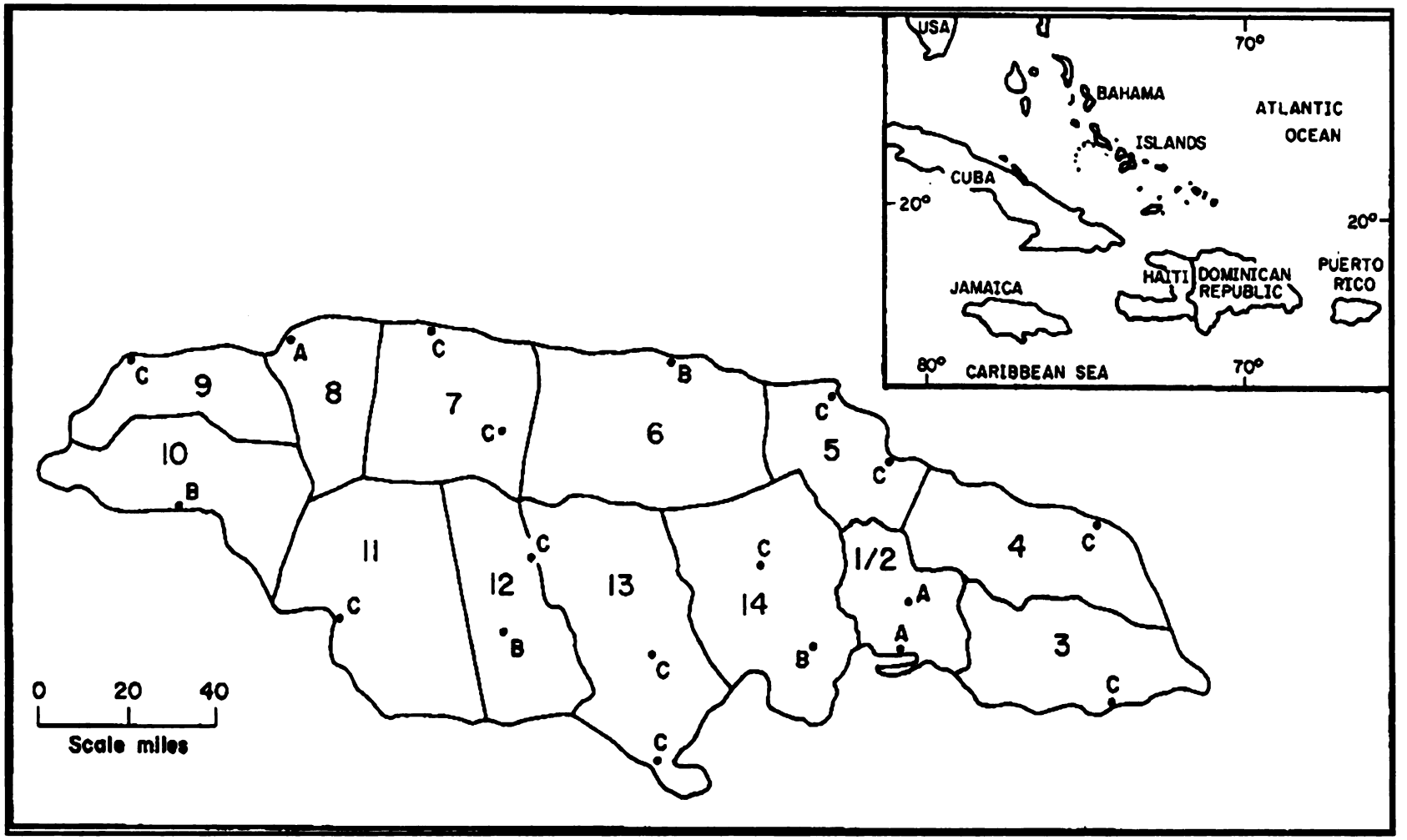


**Figure 1. Jamaica: parishes, regional administrative areas and distribution of hospitals. West: 10=Westmoreland; 9=Hanover; 8=St James; 7=Trelawny. South: 11=St Elizabeth; 12=Manchester; 13=Clarendon. North East: 6=St. Ann; 5=St Mary; 4=Portland. South East: 14=St Catherine; 1 / 2=Kingston and St Andrew; 3=St Thomas.**

Questionnaires relevant to this study

Three questionnaires were developed, pre-tested and finally used in the study; all but the pathology questionnaire were pre-coded.

1. The main questionnaire contained information on past obstetric history, social and environmental factors, the antenatal period, labor and delivery. Infants were examined and supplementary information from institutional record included. Antenatal, intrapartum and postpartum data were supplemented by other hospital, clinic or doctor's records as necessary. Often this entailed collaboration between parish coordinators, especially where antenatal records were required.
2. The follow-up questionnaire contained sections relating to the postnatal status of the mother and the infant. The questionnaire was completed by interviewing the mother, and examining both mother and infant.
3. The neonatal admission form was completed by the attending pediatrician or study research pediatrician for each newborn admitted to newborn nurseries before the age of 28 days.

Prior to the implementation of the study a standardized newborn nursery chart was introduced in all nurseries to facilitate completion of the neonatal admissions questionnaire.

Data Processing

Questionnaires were checked by the clerical staff and reviewed by the Study Administrator, the pediatrician and a small team of reviewers. These questionnaires were then microfilmed prior to being coded and the data were put on transcription sheets. These sheets were then transferred to a private data

processing company for data entry and computer editing (range and logic tests). This was supervised by the statistician at the Health Information Unit of the Ministry of Health.

Preliminary results

There were 10,310 births during the main cohort study, 8,956 (87%) of these were followed up in the postnatal period. A total of 393 deaths were identified in the main cohort giving a perinatal mortality rate of 38.1 per 1000 total births.

There were 1,405 neonatal admissions to specialist units during the 6-month study period.

A total of 1,855 fetal and early neonatal and 73 late neonatal deaths were identified during the 1-year study. Postmortem examinations were undertaken on 1,021 of the 1,855 perinatal deaths yielding an overall postmortem rate of 55%.

A total of 78 midwives were interviewed for the domiciliary service evaluation. Observations were done at all public hospitals and maternity centers. Information for this section (The Jamaica Perinatal Morbidity Mortality Survey) to this point was taken from the publication on the preliminary work of this survey (32).

Follow-up of 11 to 12 year old children.

Subsequent to the completion of the first follow-up at six weeks of age, the 11 to 12 year old children follow-up was initiated. This aspect of the study was conducted chiefly in the parish of Kingston and St. Andrew in the island of Jamaica. These parishes are the two most highly urbanized of the fourteen and

function as a single political unit. Approximately 27% of the island's population lives in Kingston and St. Andrew. It is only in this sub-population that the health questionnaire was administered. This instrument was used to obtain information on early childhood development, past medical illnesses, and current medical concerns (33). The current work is responsible for merging datasets from the Jamaica Perinatal Morbidity and Mortality Survey and the follow-up study for the first time.

# Chapter 5

## METHODS

### Study Population and Design

The Jamaican Perinatal Morbidity and Mortality Survey was aimed at all pregnant women who had a live birth or stillbirth during the two-month period from September 1, 1986 to October 31, 1986. A face-to-face interview was conducted with these women and their babies examined, usually within the first 48 hours after delivery. A standardized questionnaire was used to get at data during the antenatal, labor and delivery, and perinatal periods. This questionnaire is referred to as the main questionnaire (MQ). Overall, 10,310 (94 %) of the births in the two-month period were identified and included in the study (main cohort study) (34).

At the first follow-up, at six weeks of age, information on breastfeeding and the infant's health were ascertained using another standardized questionnaire during a face-to-face interview. For the benefit of this project this questionnaire will be referred to as the first follow-up questionnaire (FFUQ).

A geographic sub-sample of 1,720 eleven to twelve year old children, representing those born in Kingston and St. Andrew, was selected for a second follow-up. In a cross-sectional survey of these children, data on health outcomes were collected from the parent or guardian and recorded using the second follow-up questionnaire (SFUQ).

All three datasets were carefully linked using a unique identification number and date of birth for both mother and child for the analysis proposed in this project.

Questionnaires and definition of variables

*- Copies of questionnaires are provided in the appendix.*

The primary goals of the Jamaica Perinatal Morbidity and Mortality Survey was to assess a more precise estimate of perinatal mortality, to identify causes of death and to determine the maternal, social and environmental factors predictive of fetal and early infant deaths in Jamaica. To this end standardized questionnaires adapted in part from the First British Perinatal Mortality Survey (34) were developed. Questions enabling us to determine *in utero* and perinatal exposures were included. Using the MQ, the gender of the child was recorded. This questionnaire was also use to get at information on past obstetric history was obtained by asking mothers:

1. Have you ever been pregnant at any time *before* this pregnancy?
2. Total number of pregnancies____
3. Have you ever used a contraceptive? If yes, which methods have you used? I will go through a list: a). Intrauterine device (IUD) or coil, b). Depo provera or injection, c). Contraceptive pill, d), Spermicidal cream, e). Diaphragm, f). Vaginal foam, g). Condom, h). Rhythm method, i). Withdrawal, j). Other if yes please describe_____

Questions pertaining to the mother during pregnancy were:

1. Did you smoke tobacco regularly at any time during this pregnancy?

2. Did you have vaginal bleeding in the *first* 28 weeks of pregnancy?
3. Did you have vaginal bleeding *after* 28 weeks (7 months)?
4. Have there been any other complications, disorder or serious illness during this pregnancy?
5. After starting antenatal care, were you referred during pregnancy for any reason?
6. Were you admitted to hospital or rural maternity center during this pregnancy but before labor?

Additional information from the antenatal records were used to answer the following questions for this section:

1. Was the mother referred to the medical officer during pregnancy for any reason?
2. Did the mother have vaginal bleeding in the *first* 28 weeks of pregnancy?
3. Did the mother have vaginal bleeding *after* 28 weeks of pregnancy?
4. Did she have a vaginal discharge or infection during this pregnancy?
5. Did the mother have any of the following during this pregnancy: a). Urinary tract infection, b). Tuberculosis, c). Rubella (German measles), d). Gonorrhea, e). Syphilis, f) Genital sores or blisters during pregnancy?
6. Indicate results and dates of venereal disease research laboratory (VDRL) test.
7. Was the mother diagnosed as having hypertension, pre-eclampsia or eclampsia during this pregnancy?

8. Did the mother have any of the following during this pregnancy; epilepsy, eclamptic fits or heart disease and lastly, any other complications, disorder or serious illness during this pregnancy?

Responses from these questions allowed the creation of the "maternal complications during pregnancy" and "maternal infections during pregnancy" variables. Whether delivery was induced or by any other method was ascertained by asking: How did labor start? [1] spontaneously [2] after induction [3] no labor (elective CS) or [4] in other way. Information relating to whether analgesic or anesthetic was given during labor was extracted from hospital delivery notes. Additionally, the midwife was interviewed where necessary.

The variable "Maternal health complications during labor and delivery" was defined as a positive answer to any of the following questions from the labor, delivery and post partum section of the MQ:

1. Did the mother have eclamptic fits?
2. Did she haemorrhage?
3. Was labor obstructed?
4. Did the uterus rupture?
5. Was mother transferred during labor?
6. Did the cord prolapse?
7. Was there meconium in the liquor?
8. Were there any other complications?

Child's birth weight was also recorded in the labor, delivery and post partum section of the MQ. To facilitate analyses in this study, this variable was categorized into <2.5kg, 2.5-4.0 kg and >4.0 kg.

At the first follow-up, when the child was four to six weeks of age, the following questions were asked from the first follow-up questionnaire (FFUQ):

1. Was the baby referred to a medical officer?
2. Was the baby admitted to hospital or special care baby unit?
3. Were any abnormal symptoms noted in the baby?

A positive response to the abovementioned, in addition to hospital notes at birth and questions from the SFUQ were used to create the variable "child's illness or health problems in first week of life".

1. Current status of baby – [1] Alive, healthy [2] Alive, ill [3] dead [4] NK.
2. Since birth until 28 days old, did the baby have any of the following:
    a. Jaundice
    b. Convulsions / twitching
    c. Persistent vomiting
    d. Diarrhea (3 or more loose stools)
    e. Sticky or discharging eyes
    f. Cord infection
    g. Other infection
    h. Other problems

3. Had the baby been admitted to hospital in the first 28 days of life

At the 11 to 12 year follow-up, parents were asked, "Has your child ever had...:

1. Asthma or wheezing?
2. Frequent night time or early morning cough?
3. Eczema?
4. Hay fever, sinus problem or some other allergy?"

Children were defined as experiencing any of the above if their parents gave a positive response to the respective outcome.

The dependent variables of interest (asthma/wheezing, coughs, eczema and hay fever) were captured as binary variables.

Statistical analysis

Prevalence of the four atopic manifestations for the different ante- and perinatal exposures were tabulated. Adjusted odds ratios (AOR) and their 95% confidence intervals (95% CI) were estimated by logistic regression analysis. All calculations were carried out using SAS software, release 8.2 (35).

Logistic Regression

Logistic regression is an adaptation to dichotomous outcomes of the classical linear regression model for continuous outcomes. It is primarily used to describe the relationship to the outcome of a primary exposure after adjusting for the effects of other (independent) variables that may influence both the outcome and exposure.

Formally, in formulating a logistic model let Y (0 or 1) denoting the dichotomous outcome of interest with Y =1 labeling the presence of the condition under study. Then the logistic model for $P[ Y=1 \mid X_1, X_2 \ldots X_k ]$ is written simply as $P(\mathbf{X})$ where **X** is a shortcut for $X_1$ through $X_k$. The model formula is given by

$$P(\underline{X}) = \frac{1}{1 + e^{-(\alpha + \Sigma \beta_i X_i)}}$$ in which $\alpha$ and $\beta_i$ is representing unknown parameters to be estimated based on the observed exposure variables $X_1$ through $X_k$ and the outcome variable Y. The coefficients $\beta_1$ through $\beta_k$ can be interpreted as adjusted log-odds ratios. For example, if $X_1$ is the primary exposure, coded $X_1 = 1$ for "exposed" and $X_1 = 0$ for "not exposed", then assuming the variables $X_2$ through $X_k$ do not include $X_1$, the AOR is given by $\exp(\beta_1)$.

The proposed hypotheses were tested in a model with gender, maternal infection during pregnancy, maternal hospital admission during pregnancy, induced labor, analgesic or anesthetic given during labor, maternal health complications during labor or delivery, smoking during pregnancy, feeding (breast only, breast and formulae, formulae only), birth weight (<2.5kg, 2.5 – 4.0kg and >4.0kg), and child's illness or health problems in first week of life as covariates.

## Chapter 6

## RESULTS

From the three data sets, we were able to successfully link 1040 (60.4%) of the 1720 mother-child pairs from the Kingston or St. Andrew sub-cohort. One child was deceased. Table 2 shows the prevalence of the outcome variables from the total subpopulation compared to those from the linked data set. Approximately 17% of the children at approximately 11 years suffered from asthma or wheezing while 20% experienced hay fever sinus problem or some other allergy. Frequent nighttime or early morning cough was found in approximately 5% of the children while approximately 6% had eczema.

**Table 2. Comparison characteristics of outcome variables in sub-population and linked data set.**

| | Sub-population data (%) | Linked maternal child pairs (%) |
|---|---|---|
| **N** | **1163** | **1040** |
| Factors | | |
| Asthma or Wheezing | 17.0 | 17.3 |
| Frequent night time or early morning cough | 4.8 | 5.3 |
| Eczema | 6.5 | 6.7 |
| Hay fever sinus problem or some other allergy | 19.6 | 20.0 |

Prevalence for each exposure variable is prevented in Table 3. Male gender accounted for 47% of the cohort. There was a 50% prevalence of both maternal OC use, and complication during pregnancy. The proportion of mothers who had

infection during pregnancy, and who were admitted to hospital during pregnancy was approximately 25.7% and 12.3 % respectively. Labor was induced for approximately 7% of the mothers while approximately 23% were given analgesic or anesthetic during labor. There were 14.5% of mothers who experienced health complications during labor or delivery while 7.5% smoked during pregnancy. Report on breastfeeding showed 35% of the children were breastfed exclusively, 59% had both breast and formulae feed while 6.4% were exposed to formulae only. The proportion of children born low birth weight (<2.5 kg) was 12.2%, normal birth weight (2.5 kg – 4.0 kg) was 83.4% while 4.4% were born weighing over four kilogram. Of the children in the study, 20.3% were ill or had health complications in the first four weeks of life.

**Table 3. Comparison characteristics of exposure variables in main and linked datasets.**

| | Main Cohort (%) | Linked Data (%) |
|---|---|---|
| **N** | **13048** | **1040** |
| **Factors** | | |
| Maternal oral contraceptive use | 45.2 | 49.9 |
| Maternal complications during pregnancy | 43.3 | 50.2 |
| Maternal infections during pregnancy | 24.0 | 25.7 |
| Maternal hospital admission during pregnancy | 14.6 | 12.3 |
| Induced labor | 6.0 | 6.7 |
| Analgesic or anesthetic given during labor | 14.6 | 22.6 |
| Maternal health complications during labor or delivery | 15.5 | 14.5 |
| Smoking during pregnancy | 7.0 | 7.5 |
| Feeding – Breast only | 45 | 34.9 |
| Breast and formulae | 49 | 59.0 |
| Formulae only | 5.2 | 6.4 |
| Birth weight - <2.5 kg | 18.2 | 12.2 |
| 2.5 kg - 4.0 kg | 77.5 | 83.4 |
| >4.0 kg | 4.3 | 4.4 |
| Child's illness or health problems in first week of life | 20.3 | 20.3 |

The proportion of atopic disorders in relation to their *in utero* potential risk factors is presented in Table 4. There was no difference in the proportion of asthma in females *vs.* male gender. The prevalence for asthma or wheezing, frequent nighttime or early morning cough, eczema, and hay fever, sinus problem or some other allergy for children of female gender *vs.* those of male gender did not present significant variation. Children of mothers, who used, compared to those who did not use OC before pregnancy, had a higher prevalence of asthma (20% *vs.* 13.4%), frequent nighttime or early morning cough (7.4% *vs.* 3.6%) and eczema (7.4% *vs.* 5.5%). Asthma (19.3% *vs.* 14.3%), frequent nighttime or early morning cough (6% *vs.* 4.6%), eczema (7.4% *vs.* 5.3%), and hay fever, sinus problem or some other allergy (22.2% *vs.* 18%) were more common in those children whose mothers had complications during pregnancy than in those who did not. Reports of asthma or wheezing, frequent nighttime or early morning cough, and hay fever sinus problem or some other allergy for children of mothers who had infections during pregnancy were to those who did not. The proportion asthma or wheezing, frequent nighttime or early morning cough, and eczema were not significantly different for children born to mothers who were and those who were not admitted to hospital during pregnancy. When compared to children whose mothers did not smoke during pregnancy, the proportion of mothers who smoked during pregnancy were similar.

**Table 4. Proportion of atopic disorders in relation to their *in utero* risk factors.**

| | Gender | | Maternal oral contraceptive use | | Maternal complications during pregnancy. | | Maternal infections during pregnancy | | Maternal hospital admissions during pregnancy | | Smoking during pregnancy | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **N** | 488 | 547 | 511 | 509 | 522 | 518 | 267 | 773 | 127 | 907 | 78 | 962 |
| **Outcome %** | Male | Female | Yes | No | Yes | No | Yes | No | Yes | No | Yes | No |
| Asthma or Wheezing | 16.7 | 16.9 | 20.0 | 13.4 | 19.3 | 14.3 | 18.9 | 16.1 | 18.1 | 16.7 | 11.5 | 17.2 |
| Frequent night time or early morning cough | 4.5 | 6.0 | 7.4 | 3.6 | 6.0 | 4.6 | 5.9 | 5.1 | 7.1 | 5.1 | 5.3 | 5.3 |
| Eczema | 6.0 | 6.7 | 7.4 | 5.5 | 7.4 | 5.3 | 5.7 | 6.5 | 10.2 | 5.8 | 6.4 | 6.3 |
| Hay fever sinus problem or some other allergy | 19.1 | 21.1 | 20.3 | 20.0 | 22.2 | 18.0 | 21.0 | 19.8 | 15.9 | 20.8 | 11.7 | 20.8 |

Table 5 shows perinatal risk factors and the proportion of their related atopic disorders. Children who were delivered by induced labor reported having a higher prevalence of asthma or wheezing (18.6% *vs.* 16.7%), eczema (11.4% *vs.* 6%), and hay fever sinus problem or some other allergy (20.3% *vs.* 20.1%) when compared to those who were delivered otherwise. Mothers who received, when compared to those who did not receive analgesic or anesthetic during labor, reported having children with a higher prevalence of asthma or wheezing (18.3% *vs.* 16.6%), eczema (12.2% *vs.* 4.7%), and hay fever sinus problem or some other allergy (28.8% *vs.* 17.2%). Children of mothers who had complications during labor or delivery had a greater proportion of asthma or wheezing (18% *vs.* 16.6%), frequent nighttime or early morning cough (8.1% *vs.* 4.8%), eczema (7.3% *vs.* 6.2%), and hay fever sinus problem or some other allergy (21.5% *vs.* 19.9%). Of the feeding groups "breast only", "breast and formulae", and "formulae only", asthma or wheeze (14.8%, 18.7% and 17.4%), and frequent nighttime or early morning cough (5.9%, 6% and 4.6%) were more frequently reported for those who were fed breast and formulae. There was a higher proportion of hay fever sinus problem or some other allergy for those who were fed formulae only, (16.5%, 20.6% and 24.4%) whilst frequent nighttime or early morning cough was more frequently reported for the "breast only" group (5.9%, 6% and 4.6%). Children who were born with LBW (<2.5kg) compared to those born 2.5kg – 4 kg, and >4 kg had more frequent nighttime or early morning cough (8.1%, 5.1%, and 4.4%) respectively. Asthma or wheezing (17.7% *vs.* 16.6%), frequent nighttime or early morning cough (5.8% *vs.* 5.2%), eczema

(10.5% *vs.* 5.3%) and hay fever sinus problem or some other allergy (27.4% *vs.* 18.3%) were more common for children who had illness or health problems in their first week of life.

**Table 5. Proportion of atopic disorders in relation to their perinatal potential risk factors.**

| | Induced labor | | Analgesic or anesthetic given during labor | | Maternal complications during labor or delivery | |
|---|---|---|---|---|---|---|
| **N** | 70 | 970 | 232 | 794 | 522 | 518 |
| **Outcome** | Yes | No | Yes | No | Yes | No |
| Asthma or Wheezing | 18.6 | 16.7 | 18.3 | 16.6 | 18.0 | 16.6 |
| Frequent night time or early morning cough | 4.4 | 5.4 | 5.0 | 6.6 | 8.1 | 4.8 |
| Eczema | 11.4 | 6.0 | 12.2 | 4.7 | 7.3 | 6.2 |
| Hay fever sinus problem or some other allergy | 20.3 | 20.1 | 28.8 | 17.2 | 21.5 | 19.9 |

**Table 5. (continue) Proportion of atopic disorders in relation to their perinatal potential risk factors.**

| | Feeding | | | Birth weight | | | Child's illness or health problems in first 4 weeks of life | |
|---|---|---|---|---|---|---|---|---|
| N | 266 | 715 | 761 | 125 | 852 | 45 | 211 | 829 |
| **Outcome** | Breast only | Breast & Formulae | Formulae only | < 2.5 kg | 2.5 kg 4.0 kg | > 4.0 kg | Yes | No |
| Asthma or Wheezing | 14.8 | 18.7 | 17.4 | 12.8 | 17.6 | 17.8 | 17.7 | 16.6 |
| Frequent night time or early morning cough | 5.9 | 6.0 | 4.6 | 8.1 | 5.1 | 4.4 | 5.8 | 5.2 |
| Eczema | 6.8 | 6.1 | 6.5 | 3.2 | 6.7 | 8.9 | 10.5 | 5.3 |
| Hay fever sinus problem or some other allergy | 16.5 | 20.6 | 24.4 | 15.5 | 21.1 | 15.6 | 27.4 | 18.3 |

Adjusted odds ratios for asthma or wheeze, and frequent nighttime or early morning cough are reported in Table 6. Maternal OC use before pregnancy and maternal complications during pregnancy were significantly associated with asthma in the offspring, (AOR: 1.56 [95% CI 1.04 – 2.32]) and (AOR: 1.75 [95% CI 1.14 – 2.69]) respectively. Additionally, maternal OC use before pregnancy was also significantly associated with frequent nighttime or early morning cough (AOR: 2.28 [95% CI 1.17 – 4.46]), while maternal complications during pregnancy was significantly associated with hay fever sinus problem or some other allergy (AOR: 1.77 [95% CI 1.17 – 2.70]).

Table 7 shows odds ratios for eczema and hay fever, sinus problem or some other allergy. Surprisingly, analgesic or anesthetic given during labor and child's illness or health problems in first week of life were both significantly associated with eczema, (AOR: 2.27 [95% CI 1.17 – 4.42]) and (AOR: 2.30 [95% CI 1.11 – 4.72]) respectively. Analgesic or anesthetic given during labor was also significantly associated with hay fever, sinus problem or some other allergy (AOR: 1.73 [95% CI 1.10 – 2.71]). The effect of maternal OC use before pregnancy was stronger for girls (AOR: 1.98 [95% CI 1.13 – 3.45]) than the effect for boys (AOR: 1.18 [95% CI 0.65 – 2.14]) in the association with asthma. Smoking during pregnancy (*in utero* smoking) was not significantly associated to childhood asthma (5.2% in asthmatic *vs.* 8.1% in others; NS).

**Table 6. Relationships of antenatal and perinatal risk factors to asthma or wheezing, and frequent nighttime or early morning cough.**

| Factors | Asthma or Wheezing | | Frequent night time or early morning cough | |
|---|---|---|---|---|
| | Crude OR (95%CI) | Adjusted OR (95%CI) | Crude OR (95%CI) | Adjusted OR (95%CI) |
| **Antenatal outcomes** | | | | |
| Gender – Male | 1.01(0.73, 1.40) | 0.96 (0.65, 1.43) | 1.36 (0.77, 2.40) | 1.34 (0.69, 2.56) |
| Maternal oral contraceptive use | 1.62 (1.15, 2.26) | 1.56 (1.04, 2.32) | 2.17 (1.21, 3.89) | 2.28 (1.17, 4.46) |
| Maternal complications during pregnancy | 1.43 (1.03, 1.99) | 1.75 (1.14, 2.69) | 1.30 (0.75, 2.28) | 1.04 (0.51, 2.12) |
| Maternal infections during pregnancy | 1.21 (0.84, 1.74) | 0.93 (0.59, 1.46) | 1.15 (0.62, 2.14) | 0.84 (0.39, 1.77) |
| Maternal hospital admission during Pregnancy. | 1.10 (0.68, 1.79) | 0.92 (0.49, 1.69) | 1.43 (0.68, 3.01) | 1.39 (0.54, 3.55) |
| Smoking during pregnancy | 0.63 (0.31, 1.28) | 0.42 (0.16, 1.09) | 0.99(0.35, 2.82) | 0.92 (0.27, 3.15) |
| **Perinatal outcomes** | | | | |
| Induced labor | 1.14 (0.61, 2.13) | 0.93 (0.44, 1.95) | 0.81 (0.25, 2.67) | 0.77 (0.22, 2.67) |
| Analgesic or anesthetic given during labor | 1.11 (0.76, 1.64) | 1.17 (0.73, 1.89) | 1.34 (0.72, 2.48) | 1.24 (0.59, 2.57) |
| Maternal complications during delivery | 1.10 (0.70, 1.74) | 0.84 (0.46, 1.53) | 1.74 (0.89, 3.39) | 1.52 (0.67, 3.42) |
| Child illness or health problems in first week of life | 1.08 (0.73, 1.62) | 0.93 (0.54, 1.60) | 1.13 (0.58, 2.19) | 1.07 (0.48, 2.35) |
| Feeding - Breast only (reference) | 1 | 1 | 1 | 1 |
| Breast and formulae | 1.32 (0.87, 2.00) | 1.28 (0.83, 1.97) | 1.01(0.53, 1.94) | 0.91 (0.47, 1.79) |
| Formulae only | 1.32 (0.59, 2.95) | 1.15 (0.49, 2.72) | 0.73 (0.16, 3.29) | 0.61 (0.13, 2.85) |
| Birth weight <2.5kg | 0.69 (0.39, 1.20) | 0.77 (0.40, 1.49) | 1.66 (0.81, 3.41) | 1.85 (0.80, 4.27) |
| Reference 2.5 kg – 4.0 kg. | 1 | 1 | 1 | 1 |
| >4.0 kg | 1.01 (0.46, 2.22) | 0.78 (0.29, 2.14) | 0.87 (0.20, 3.73) | 1.27 (0.28, 5.83) |

**Table 7. Relationships of antenatal and perinatal risk factors to eczema, and hay fever or sinus problem or some other allergy.**

| Factors | Eczema | | Hay fever or sinus problem or some other allergy | |
|---|---|---|---|---|
| | Crude OR (95%CI) | Adjusted OR (95%CI) | Crude OR (95%CI) | Adjusted OR (95%CI) |
| **Antenatal outcomes** | | | | |
| Gender – Male | 1.12 (0.68, 1.86) | 1.06 (0.57, 1.97) | 1.14 (0.84, 1.55) | 1.27 (0.86, 1.88) |
| Maternal oral contraceptive use | 1.35 (0.81, 2.24) | 1.01 (0.55, 1.86) | 0.98 (0.72, 1.33) | 0.96 (0.65, 1.41) |
| Maternal complications during pregnancy | 1.43 (0.86, 2.37) | 2.02 (1.01, 4.06) | 1.29 (0.95, 1.76) | 1.77 (1.17, 2.70) |
| Maternal infections during pregnancy | 0.87 (0.48, 1.57) | 0.78 (0.39, 1.58) | 1.07 (0.76, 1.52) | 0.82 (0.52, 1.28) |
| Maternal hospital admission during Pregnancy. | 1.85 (0.98, 3.50) | 1.44 (0.63, 3.33) | 0.72 (0.43, 1.19) | 0.53 (0.27, 1.04) |
| Smoking during pregnancy | 1.01 (0.39, 2.60) | 0.92 (0.26, 3.21) | 0.50 (0.25, 1.03) | 0.64 (0.27, 1.48) |
| **Perinatal outcomes** | | | | |
| Induced labor | 2.04 (0.93, 4.46) | 1.40 (0.56, 3.52) | 1.01 (0.55, 1.86) | 0.61 (0.28, 1.37) |
| Analgesic or anesthetic given during labor | 2.81 (1.68, 4.71) | 2.27 (1.17, 4.42) | 1.96 (1.39, 2.75) | 1.73 (1.10, 2.71) |
| Maternal complications during delivery | 1.19 (0.61, 2.34) | 0.53 (0.22, 1.30) | 1.10 (0.72, 1.68) | 0.86 (0.49, 1.51) |
| Child illness or health problems in first week of life. | 2.12 (1.24, 3.63) | 2.30 (1.11, 4.72) | 1.69 (1.19, 2.40) | 1.40 (0.84, 2.31) |
| Feeding - Breast only | 1 | 1 | 1 | 1 |
| Breast and formulae | 0.89 (0.48, 1.65) | 0.70 (0.37, 1.34) | 1.31 (0.88, 1.96) | 1.27 (0.83, 1.94) |
| Formulae only | 1.24 (0.42, 3.85) | 0.88 (0.27, 2.87) | 1.56 (0.73, 3.28) | 1.21 (0.53, 2.79) |
| Birth weight <2.5kg | 0.47 (0.17, 1.31) | 0.36 (0.10, 1.23) | 0.68 (0.41, 1.14) | 0.55 (0.28, 1.10) |
| Reference 2.5 kg – 4.0 kg. | 1 | 1 | 1 | 1 |
| >4.0 kg | 1.37 (0.47, 3.96) | 1.17 (0.32, 4.33) | 0.69 (0.30, 1.57) | 0.72 (0.26, 1.98) |

Further analysis was conducted on the specific complications used to define the "maternal complications during pregnancy covariate". A parsimonious model was produced by allowing only variables which had $p<0.10$ to remain in the model. After adjusting for potential confounders, only "have there been any other complications, disorder or serious illness during this pregnancy?" conferred a significantly increased risk for asthma in the child.

Additionally, it is well established that "All that wheezes is not asthma" (36) therefore, the variables asthma or wheezing and frequent night time or early morning cough were combined to create one outcome variable. The association between maternal OC use before pregnancy and this variable was then assessed in a full model. This did not change the association significantly (AOR: 2.7, 95% CI 1.1 – 6.9).

## Chapter 7

# DISCUSSION AND CONCLUSION

## Discussion

Findings for this study support the hypothesis that children whose mothers used OC before pregnancy, may be predispose to a higher risk for developing asthma or wheezing at age 11 to 12 year of age. Results also support the hypothesis that maternal complication during pregnancy is a risk factor for asthma and wheezing in the offspring, as well as for eczema, 'hay fever, sinus problem, or some other allergies'. These associations persisted after adjusting for known confounders.

Surprisingly, we found analgesic or anesthetic given during labor to be statistically significantly associated with eczema, and 'hay fever, sinus problem, or some other allergies'. Additionally, child illness or health problems in the first week of life were statistically significantly associated with eczema.

The study showed that children whose mothers used OC before pregnancy were 1.5 times, more likely to have asthma (AOR: 1.56 [95% CI 1.04 – 2.32]) than those whose mothers did not use OC before pregnancy. This finding is in concordance with those of Wjst who, based on aggregative data on OC sales and hospital discharge data, was the first to hypothesize that maternal use of OC is a risk factor for asthma in the offspring. (3) To the best of my knowledge, this is the first study to assess the association between, maternal OC use and asthma or wheeze in offspring, using individual data.

The most popularly OC in Jamaica during the study period was the Pearl. Active components were Ethinyloestradiol (30 μg) and Levonorgestrel (150 μg), an estrogen and progesterone respectively. Wjst suggested, that estrogen might alter the activity of $Th_2$ type cytokines (3) predisposing the fetus to atopic disorders later in live. In agreement with this assumption, Xu et al. reported that atopy in adults was more common among those whose mothers experienced an early age of menarche (4). A likely explanation for the atopy – age at menarche association are findings that early age of menarche is associated with higher levels of estrogen in adult women (24-26, 37). Hence, the fetus of women with an early age at menarche may experience a higher exposure to estrogens.

Regarding OC use, it has been suggested that women who used OC have higher estrogens levels after discontinuing its use (38), however, the evidence is less convincing (26). Michel et al. reported that IgE levels in the cord blood were significantly increased among neonates whose mothers had taken progesterone during pregnancy (39). Furthermore, it is assumed that progesterone can also function as a potent inducer of the production of the $Th_2$ type cytokines (40).

These endocrine effects during pregnancy may play a role in immunologic development as progesterone seems to promote the preferential development of $Th_2$-type cells (41, 42). The proposed mechanism may explain the OC – atopy association, as T-helper (Th) cells are thought to be important in the development of allergy. Th cells of the $Th_2$ type produces large quantities of interleukin (IL)-4, IL-5, and IL-13 which promote the production of IgE and eosinophil infiltration in the airways and ultimately orchestrate the development of allergy and asthma (43-45).

To our knowledge, there is no data whether use of OC is associated with a different progesterone response in the luteal phase after discontinuing OC use.

The effect of OC use, however, may be independent of estrogen or progesterone level after stopping. There are two other possible scenarios, which may explain this association. Either maternal exposure to estrogen via OC use may trigger a programmed change in the $Th_1$ / $Th_2$ activity. A persistent change in $Th_2$ activity during pregnancy thus predisposes the fetus to a higher risk of developing atopy later in life, a Th2-mediated disorder (46) (44, 47). Alternatively, women who used OC continuously, discontinuing before becoming pregnant, may have created an environment of higher estrogen or progesterone levels. This higher level, in turn, may result in an increased $Th_2$ activity impacting the fetus transplacentally.

Children born to mothers who had complications during pregnancy were at a 1.7-fold increased risk of having asthma compared to their counterpart (AOR: 1.75 [95% CI 1.14 – 2.69]). It might be that complications during pregnancy is reflective of other underlying factor such as a threatened pregnancy which will alter the $Th_1$ / $Th_2$ balance. Hence, we speculate that not specific diseases but a general threat of miscarriage may be responsible for the association. For instance, data from this study showed that not specific complications but among the variables comprising the "maternal complications during pregnancy" variable, only "have you had any other complication or disorder during this pregnancy" was found to be significantly associated with asthma in the offspring.

Child's illness or health problem in the first week of life was found to be significantly associated with eczema (AOR: 2.30 [95% CI 1.11 – 4.72]). Since

the present analysis adjusted for birth weight, which can be used as an indicator of prematurity, it would be prudent to suggest that child's illness or health problem in the first week of life might be a risk factor for asthma. The actual role of child illness or health problems in the first week of life is a topic worth investigating further.

A number of studies have suggested that some analgesics and anesthetics may be associated with an increased risk and severity of asthma (48-51). However, to-date, there has not been any studies addressing the effect of analgesics administered during delivery and allergies in offspring. A succinct explanation of the mechanistic explanations of the analgesics or anesthetic – eczema, and "hay fever or sinus problems or some other allergy" association found in this study is not readily clear. It is beyond the scope of the present study to address the independent association between anesthetic and asthma. However, the thought that a single exposure to anesthetic during delivery is associated to asthma would be rejected on the grounds of weak biological plausibility. The logical supposition then is that the association is purely due to analgesics. In an effort to explain the association between analgesics and asthma, one would first postulate that analgesics given during delivery might be an indication of a low pain threshold in the mother. It is prudent to assume that if there is a low maternal threshold for pain, then the mother may also have been exposed to analgesics during and before pregnancy. It has been shown that allergens, in this case analgesic (52, 53) (54), may cross the fetal membranes where the maternal (decidua) and fetal tissues are in intimate contact (47). There is evidence to suggest that immune response to allergen may begin *in*

*utero* (46). It is clear to see how fetal T cell responses may be initiated before birth via the transplacental transfer of low levels of analgesics to which the mother is exposed during pregnancy.

Following along the trend of thought that "analgesics given during delivery might be an indication of a low pain threshold in the mother", another possible explanation may be that analgesic, acting as an allergen, may have activated an existing dormant allergic disorder in the mother. This then triggers a chain of immunologic reaction, which includes the modification of IFN-$\gamma$ activity. IFN-$\gamma$ production in neonates with a family history of atopic disease is noticeably decreased when compared to normal neonates (55, 56). This reduction has been shown to be a risk factor for allergic diseases (47, 57, 58). Lastly, one cannot ignore the fact that if the mother has the tendency of using more analgesics than is usually expected, due to a low pain threshold, this would suggest that her offspring would also have greater access and thus be more exposed. This may lead to higher analgesic use in the offspring, resulting in atopic disorders independent of allergen transfer via the placenta. Information on analgesic use in the offspring is not available in this study thus testing this latter supposition is not possible.

Given that Xu (29) found a positive association between mode of delivery and asthma while both Annesi-Maesano et al. (5) and McKeever et al. (30) were unable to support this finding, it is well advised that further studies be conducted. The primary purpose of these suggested studies would be to assess the possible role anesthetic and or analgesics may play in the mode of delivery – asthma

association since it is practical to suppose that anesthetic and analgesics given during delivery are both highly correlated with mode of delivery.

The strengths of the current investigation are in its prospective design, being derived from a large population based cohort, with all the exposure information collected during pregnancy, at birth and four weeks after. This presents a clear time-order, as outcomes were not assessed until approximately 11 years after. This also reduces the effect of recall bias. Additionally, controlling for a broad range of confounders reduced the possibility of these findings occurring purely by chance.

The findings should be interpreted with some caution as they may be influenced by selection bias, as follow-up rate was 60.4%. However as shown in tables 3 and 4 no significant difference were found between the characteristics of the variables from the main and sub-cohort when compared with those of the linked dataset. Another limitation is that information on how long before pregnancy OC was used and if it was the last method of birth control used. This may impact the serum levels of maternal estrogen during pregnancy and hence significantly alter our association.

The definition or measurement of asthma or wheezing may also be of concern as wheezing is a heterogeneous disorder (59) and not all that wheezes is asthma (36). The impact this misclassification may have was assessed by combining the variables asthma or wheezing and frequent night time or early morning cough to create one outcome variable.

The association between this new variable and maternal OC use before pregnancy was assessed and results showed did not reflect a significant change

the positive association previously found (AOR: 2.7 [95% CI 1.1 – 6.9]). Also since all the children in the cohort would have had equal chance of been misdiagnosed, this would result in non-differential misclassification and thus would not alter our findings significantly.

## Conclusion

The present work provides results of a follow-up study of 11 to 12 year old children. These results are in support of previous findings that maternal OC use, and complications during pregnancy are important in the development of asthma. Further studies are hereby encouraged to corroborate with these results. This will not only provide a better understanding of these reported findings, but more effective preventive strategies could also be developed.

# APPENDICES

# APPENDIX - A
# Main Questionnaire
# Perinatal Survey - Jamaica

PERINATAL SURVEY – JAMAICA
MAIN QUESTIONNAIRE

A1. To be completed on all women who (1) deliver in September and October 1986, *or* who give birth to an infant who is hospitalized prior to 28 days of life (Sept. 1986–May 1987) *or* whose infant is stillborn or dies in the first 28 days of life (September 1986–September 1987).

A2. Mother's name _____ _____ _____ _____
surname first middle pet name

A3. Mother's date of birth _____ / _____ /19____

A4. Mother's home address (usual residence) _____

_____ parish _____

A5. Landmark (if not an exact address) _____

A6. Next of kin (name) _____

A7. Next of kin (address) _____

A8. Surname of child _____

A9. Place of delivery: [1] hospital, specify _____

[2] rural maternity centre, specify _____

[3] health centre, specify _____

[4] private nursing home, specify _____

[5] other home, specify relationship _____

[6] own home [9] not known

[7] other, specify _____

A10. Date of delivery _____ / _____ /198____

A11. Sex of baby [1] male [2] female [3] intersex [4] undetermined
[9] not known

A12. Current status of mother [1] alive, healthy [2] alive, ill
[3] dead* [9] not known

A13. Current status of baby [1] alive, healthy [2] alive, ill
[3] dead** [9] not known

A14. *If* infant ill, [1] ill at home, diagnosis _____

[2] ill, being treated at health centre, diagnosis _____

[3] ill, being treated at hospital outpatients, diagnosis _____

[4] ill, admitted to _____ hospital, diagnosis _____

_____

If admitted or transferred to VJH Nursery, Bustamante, UHWI, CRH, Spanish Town, Mandeville, St. Ann's Bay, complete NEONATAL ADMISSION QUESTIONNAIRE

[1] completed [2] not completed [9] NK

* Complete MATERNAL DEATH QUESTIONNAIRE [1] completed [2] not completed

** Complete STILLBIRTH/INFANT DEATH QUESTIONNAIRE

[1] completed [2] not completed

The information in the following sections is to be collected by interviewing the mother (or next of kin if a maternal death has occurred).

B. THE PARENTS. This section gathers background information on the parents and should not be considered as being asked for any other reasons.

B1. What is the name of the community in which you live?

_____

Are any of the following services available within 1–2 miles walking distance of where you live.

| | | | | |
|---|---|---|---|---|
| Public transportation | [1] yes | [2] no | [9] NK | |
| Bank | [1] yes | [2] no | [9] NK | |
| Market | [1] yes | [2] no | [9] NK | |
| Primary School | [1] yes | [2] no | [9] NK | |
| Post Office | [1] yes | [2] no | [9] NK | |
| Health Centre | [1] yes | [2] no | [9] NK | |
| Police Station | [1] yes | [2] no | [9] NK | |
| Total Score | (no, yes) _____ | | | |

B2. How would you describe the relationship you have with your child's father/partner (union status).

[1] married [2] common law [3] visiting
[4] not living with husband [9] not stated
[5] not living with common law partner
[6] other, specify _____

B3. How long have you been associated with the father of your child _____ yrs.

B4. What was the highest education level completed.

[0] no formal education [1] primary
[2] junior secondary [3] secondary/high
[4] technical [5] university
[6] other tertiary [7] H.E.A.R.T.
[8] other education, please describe

_____

[9] not stated

B5. How many adults and children, including yourself, compose your household and eat together?

_____ adults
_____ children 0–10 years
_____ children 11–18 years

B6. Are you the major wage earner?

[1] yes [2] no

B7. What is the actual job of the major wage earner?

_____

If yes to B6, go on to B9.

B8a. If you are not the major wage earner, are you usually employed?

[1] yes [2] no, housewife [3] no, unemployed

b. If yes what do you do _____

c. Please describe the relationship between yourself and the major wage earner:

[1] partner [2] parents [3] non-relative
[4] other relative, please specify _____
_____ [9] not stated

B9. How much is spent *weekly* for food $ _____

B10. Do you or your family own or rent the home in which you live?

[1] own [2] rent [9] not known
[3] other, please describe _____

B11a. What type of toilet facilities are available to the household?

[1] water closet (flush type)
[2] pit latrine [3] none [9] NK
[4] other, please describe _____

b. Are the toilet facilities used exclusively by the family?

[1] yes [2] no [9] NK

B12. What is the source of water used by the household?

[1] public, piped into dwelling
[2] public piped into yard
[3] private, piped into dwelling
[4] private catchment, not piped
[5] public standpipe [9] NK
[6] other, please describe _____

B13. How many rooms in the house are used for sleeping?

_____

This next section contains questions on past pregnancies, if any, and use of family planning.

C. PAST OBSTETRIC HISTORY

C1. Have you ever been pregnant at any time *before* this pregnancy?

[1] yes [2] no [9] NK

If *no*, go to question C8.

C2. Please help us list these previous pregnancies in order, including miscarriages, terminations and stillbirths, starting with the first one, giving outcome of each and the date. Please include pregnancies which may not have resulted in a livebirth.

1st _____ date ____ / ____ /19
outcome, sex or name

2nd _____ date ____ / ____ /19

3rd _____ date ____ / ____ /19

4th _____ date ____ / ____ /19

5th _____ date ____ / ____ /19

6th _____ date ____ / ____ /19

7th _____ date ____ / ____ /19

8th _____ date ____ / ____ /19

9th _____ date ____ / ____ /19

10th _____ date ____ / ____ /19

11th _____ date ____ / ____ /19

12th _____ date ____ / ____ /19

13th _____ date ____ / ____ /19

14th _____ date ____ / ____ /19

15th _____ date ____ / ____ /19

C3a. Total number of pregnancies _____

b. How many of the previous pregnancies resulted in a miscarriage _____

c. How many were terminated _____

d. How many of these were twins or triplets _____

e. How may stillbirths were there _____

f. How many infants born alive, died in the first week?

g. How many infants born alive, died later and at what age _____

h. How many are alive now _____

i. How many children, excluding this new baby, do you have for your current partner? _____

C4. How many other partners have you had

_____

C5. How old were you when you became pregnant for the first time _____

C6. In any previous pregnancy, did you have any of the following

| | | | |
|---|---|---|---|
| a. Caesarean section | [1] yes | [2] no | [9] NK |
| b. Eclamptic fits | [1] yes | [2] no | [9] NK |
| c. Forceps delivery | [1] yes | [2] no | [9] NK |
| d. Antepartum haemorrhage | [1] yes | [2] no | [9] NK |
| e. Postpartum haemorrhage | [1] yes | [2] no | [9] NK |
| f. Puerperal depression | [1] yes | [2] no | [9] NK |
| g. Pre-eclampsia or hypertension | [1] yes | [2] no | [9] NK |
| h. Syphilis | [1] yes | [2] no | [9] NK |
| i. Other complications | [1] yes | [2] no | [9] NK |

Please specify _____

_____

C7a. What was the outcome of the pregnancy immediately before this one

[1] full term live birth
[2] premature live birth
[3] stillbirth
[4] miscarriage
[5] termination

b. What was the date of delivery of the last pregnancy before this pregnancy

_____ / _____ /19

c. If your last pregnancy was a livebirth, did you breastfeed?

[1] yes [2] no [9] NK

d. If yes, for how long did breastfeeding continue?

_____ months

C8. At the time you became pregnant, were you trying to get pregnant?

[1] yes [2] no [3] indifferent [9] NK

C9. At what age did you start having sexual relations _____ yrs.

C10. Have you ever used contraception?

[1] yes [2] no [9] NK

If *no*, go to section D.

C11. If *yes*, which methods have you used?

I will go through a list

a. IUD or coil [1] yes [2] no [9] NK

b. Depo provera or injection [1] yes [2] no [9] NK

c. Contraceptive pill [1] yes [2] no [9] NK

d. Spermicidal cream [1] yes [2] no [9] NK

e. Diaphragm [1] yes [2] no [9] NK

f. Vaginal foam [1] yes [2] no [9] NK

g. Condom [1] yes [2] no [9] NK

h. Rhythm method [1] yes [2] no [9] NK

i. Withdrawal [1] yes [2] no [9] NK

j. Other [1] yes [2] no [9] NK

Please describe _____

C12a. On the occasion you became pregnant, were you using a contraceptive method?

[1] yes [8] no [9] NK

b. If *yes*, please give method involved

_____

This next section asks questions on activities and health status during this current pregnancy.

D. THE MOTHER DURING PREGNANCY

D1a. Do you know the date of the first day of your last menstrual period?

[1] yes, with certainty

[2] yes, but doubtful

[3] no period immediately before pregnancy

[4] no

b. If *yes*, what was the date of the first day of your last menstrual period?

_____ / _____ /19_____

D2a. Did you smoke tobacco regularly at any time during this pregnancy. And if *yes*, what did you smoke?

[1] no [2] yes, cigarettes [9] NK

[3] yes, cigars [4] yes, pipe

[5] yes, other, please describe

_____

b. If *yes*, how many (or how often) per day did you smoke?

_____

D3a. Did you smoke ganja at any time during this pregnancy?

[1] no [2] yes, specify method

_____ [9] NK

b. If *yes*, how often per week did you smoke? ____

D4a. Did you drink any alcoholic drinks during pregnancy?

[1] no [2] yes [9] NK

b. If *yes*, how many drinks per week did you have ___

D5a. How were you spending your days at around the time of quickening (when the baby started to move, approximately 5 months)

[1] in full-time paid job [9] NK

[2] in part-time paid job

[3] helping with family business

[4] looking after own family, housewife

[5] other, please describe _____

_____

b. What were you actually doing _____

_____

D6. If in a job, at what week of pregnancy did you stop working? _____

D7. What was your weight at the start of pregnancy _____ [9] NK

D8a. Did you have any vaginal bleeding in the *first* 28 weeks of pregnancy?

[1] yes [2] no [9] NK

If *yes*, please describe _____

_____ _____

b. Did you have any vaginal bleeding *after* 28 weeks (7 months)

[1] yes [2] no [9] NK

If *yes*, please describe _____

_____

D9. Have there been any other complications, disorders or serious illness during this pregnancy?

[1] yes [2] no [9] NK

If *yes*, please describe _____

_____

D10a. Did you attend antenatal clinic?

[1] yes [2] no [9] NK

b. If *yes*, where did you attend?

[1] health centre, specify _____

[2] hospital, specify _____

[3] private doctor, specify _____

[4] other, specify _____

D11. How many weeks pregnant were you at your first visit? _____

D12. How many antenatal visits did you make?

a. first trimester (less than 12 wks) _____

b. second trimester (12–28 wks) _____

c. third trimester (29 wks & over) _____

D13. How many of these visits were

a. at the health centre _____

b. hospital _____

c. private doctor _____

D14. Did you have antenatal care anywhere else?

[1] yes [2] no [9] NK

If yes, where? _____

D15a. After starting antenatal care, were you referred during pregnancy for any reason?

[1] yes [2] no [9] NK

If *yes*, please give

b. Reason for referral _____

c. Diagnosis made _____

d. Treatment given _____

e. Where saw Medical Officer _____

_____

D16a. Were you given a Maternal Record Card?

[1] yes [2] no [9] NK

b. *If* in hospital. Did you bring it to hospital?

[1] yes [2] no [9] NK

c. May I see it? Is the card completed and up to date?

[1] yes [2] no [3] not seen

D17. Were any traditional medications or home remedies (e.g. bush teas) taken during this pregnancy?

[1] yes [2] no [9] NK

If *yes*, please describe what was taken and reasons why taken.

_____

_____

_____

D18. Were any of the following medications taken during this pregnancy?

a. aspirin [1] yes [2] no [9] NK

b. antibiotics, [1] yes [2] no [9] NK

specify _____

c. Other prescribed [1] yes [2] no [9] NK

medications, specify _____

_____

d. Other over-the-counter [1] yes [2] no [9] NK

medications, specify _____

_____

e. Folic acid [1] yes [2] no [9] NK

f. Iron [1] yes [2] no [9] NK

g. If *yes*, how many times per day was the iron treatment taken _____

h. For how many months of the pregnancy did you take the iron treatment? _____

D19a. Were you admitted to hospital or rural maternity centre during this pregnancy but before going into labour?

[1] yes [2] no [9] NK

b. If *yes*, please give:

| | Date of Adm. | No. of days | Hosp. or RMC | Reasons for Admission |
|---|---|---|---|---|
| 1st | _____ | _____ | _____ | _____ |
| 2nd | _____ | _____ | _____ | _____ |
| 3rd | _____ | _____ | _____ | _____ |

D20a. Did you feel sad at any time during your pregnancy?

[1] yes [2] no

b. If *yes*, when? [1] beginning [2] middle [3] end

c. With whom did you share these feelings?

[1] partner [2] doctor [3] nurse/midwife [4] other, specify _____

D21. Has anyone been particularly helpful to you during your pregnancy?

[1] yes [2] no

If yes, who?

[1] mother [2] partner/child's father [3] neighbour [4] friend [5] other

D22. How often per week were you having sexual intercourse?

a. around the time of quickening (5 months) _____

b. in the last week before delivery _____

---

This final section of the interview has a few questions relating to the time you went into labour, your delivery and the immediate post-partum period.

---

E. LABOUR, DELIVERY AND POST PARTUM

E1. Do you know what time your membranes (bag of waters) ruptured or broke?

_____ hr _____ min [ ] a.m. [ ] p.m.

Date _____ / _____ /19_____

E2. How did the membranes rupture?

[1] spontaneously before labour [9] NK
[2] spontaneously during labour
[3] artifically
[4] at Caesarian section

E3. How did labour start?

[1] spontaneously [2] after induction
[3] no labour (elective CS) [9] NK
[4] in other way, please describe _____

E4. If baby was a livebirth, were you given your baby to hold immediately after delivery?

[1] yes [2] no [9] NK
[8] not applicable (Caesarian section)

E5. Was baby put to breast immediately after delivery?

[1] yes [2] no [9] NK
[8] not applicable (Caesarian section)

E6. What have you learnt from staff concerning care of your baby?

| | Spontaneous | Prompted | Not at all |
|---|---|---|---|
| a. Breastfeeding | [1] | [2] | [3] |
| b. Cord care | [1] | [2] | [3] |
| c. Jaundice | [1] | [2] | [3] |
| d. Infection | [1] | [2] | [3] |
| e. BCG vaccine | [1] | [2] | [3] |
| f. Other vaccination | [1] | [2] | [3] |
| g. Family planning | [1] | [2] | [3] |
| h. Other, specify | [1] | [2] | [3] |

E7. Where do you plan to go for your 6-week post natal visit?

[1] health centre, specify _____

[2] hospital, specify _____

[3] private doctor, specify (a) paediatrician _____ (b) obstetrician _____

[4] other, specify _____

[8] had not planned to go [9] NK

E8. Height of mother: ft. _____ ins. _____

E9. Weight of mother after delivery (please weigh) _____ lbs/kg

---

Encourage mother to attend post natal clinic at nearest health centre and give her a pamphlet "JUST HAD A BABY".

Ask mother's permission to briefly examine her infant(s) and complete section G – THE BABY IN THE FIRST 48 HOURS. Complete a separate sheet for each infant in the case of multiple births. ALSO borrow the Maternal Record Card and complete as much of Section H – Supplementary Antenatal Questionnaire – as is possible.

---

END OF INTERVIEW

---

This section is to be completed by consulting hospital delivery notes and if necessary interviewing the midwife who did the actual delivery.

F1a. How did the membrane rupture?

[1] spontaneously before labour

[2] spontaneously during labour

[3] artificially

[4] at Caesarian section [9] NK

b. Time of delivery.

☐ a.m. ☐ p.m. _____ hrs _____ mins

c. Was there an abnormal amount of liquor?

[1] yes, excessive (hydramnios)

[2] yes, very little (oligohydrammios)

[3] no, normal amount [9] NK

F2a. How did labour start?

[1] spontaneously [2] after induction

[3] no labour (elective CS) [9] NK

[4] in other way, please describe _____

_____

If induced, please give:

b. reasons _____

c. method _____

F3. What was the presentation?

[1] vertex anterior (OA) [3] breech

[2] vertex posterior (OP) [9] NK

[4] vertex, A or P unknown

[5] other, please describe _____

_____

F4a. What was the method of delivery?

[1] spontaneous [2] assisted breech

[3] breech extraction [4] vacuum extraction

[5] forceps, please describe whether low, mid or high _____

[6] Caesarian section, elective

[7] Caesarian section, emergency

[8] other, please describe _____

_____

b. If delivered by Caesarian section please give reasons

_____

_____

F5. How long did labour last

a. 1st stage _____ 2nd stage _____

F6. Was an oxytocic given during labour?

[1] yes, please give drug _____

[2] no [9] NK

F7. Was an analgesic/anaesthetic given during labour?

[1] yes, please give type(s) _____

_____ [2] no [9] NK

F8. Were any other drugs given?

[1] yes, specify and give reasons _____

_____ [2] no [9] NK

DURING LABOUR AND DELIVERY

F9a. Did the mother have eclamptic fits?

[1] yes [2] no [9] NK

b. Did she vomit?

[1] yes [2] no [9] NK

c. Did she haemorrhage?

[1] yes [2] no [9] NK

If yes, please describe:

type _____

when _____

extent _____ mls

d. Was labour obstructed?

[1] yes [2] no [9] NK

If yes, please describe _____

_____

e. Did the uterus rupture?

[1] yes [2] no [9] NK

f. Were there any abnormalities in foetal heart rate?

[1] yes, please describe _____

_____ [2] no [9] NK

g. Was mother transferred during labour?

[1] yes, give reason _____

_____ [2] no [9] NK

Where was patient transferred from?

_____

h. Did the cord prolapse?

[1] yes [2] no [9] NK

i. Was there meconium in the liquor?

[1] yes [2] no [9] NK

j. Was an episiotomy given?

[1] yes [2] no [9] NK

k. Were there perineal tears?

[1] yes [2] no [9] NK

l. Were there any other complications?

[1] yes [2] no [9] NK

If yes, please list _____

_____

_____

F10a. Was an oxytocic given to mother after delivery?

[1] yes, please specify drug _____

[2] no [9] NK

b. Were any other drugs given to the mother after delivery?

[1] yes, specify drug _____

reason _____ [2] no [9] NK

F11. Who actually did the delivery?

[1] doctor [2] midwife [3] other health personnel specify _____

[4] unattended (in hospital)

[5] Nana [6] self-delivery (not in hospital)

[7] other, specify _____

F12. Was the mother's blood pressure taken in labour?

[1] yes [2] no [9] NK

If yes, specify the blood pressure reading with the highest diastolic.

_____ / _____

F13a. Was the mother's urine tested for protein in labour?

[1] yes [2] no [9] NK

b. If yes, give result _____

F14. Was oedema present in labour? [1] yes, give sites _____ [2] no [9] NK

F15a. Was haemoglobin measured in the 48 hours after delivery?

[1] yes [2] no [9] NK

If yes, please give:

b. result _____

c. method _____

POSTPARTUM

F16a. In the first 48 hours after delivery did the mother have eclamptic fits?

[1] yes [2] no [9] NK

b. Did the mother have a postpartum haemorrhage?

[1] yes, if yes, give extent _____ mls

[2] no [9] NK

c. Was any transfusion given?

[1] yes, if *yes*, how much _____ mls

[2] no [9] NK blood group _____

d. Did the mother have any other complications?

[1] yes [2] no [9] NK

If *yes*, please list _____

_____

_____

e. Was mother transferred to hospital or to another hospital after delivery?

[1] yes, please give reason _____

_____

name of hospital _____

[2] no [9] NK

END OF MATERNAL QUESTIONNAIRE

---

Please complete the top of the first page of the SUPPLEMENTARY ANTENATAL QUESTIONNAIRE making sure to record the facility/facilities which provide antenatal care to the mother.

Go on to examine the infant(s) and complete the schedule for THE BABY IN THE FIRST 48 HOURS. In the case of multiple births, a separate sheet must be completed for each infant.

---

## THE BABY IN THE FIRST 48 HOURS

### TO BE COMPLETED ON ALL LIVEBIRTHS, STILLBIRTHS & NEONATAL DEATHS

Name of Mother _____ Date of Delivery _____ / _____ / 19_____

Surname of Baby _____ Baby [1] Baby [2] Baby [3] Parish of Delivery _____

---

Completion of this section requires a brief examination of the baby as well as consultation of the notes. For multiple births, a separate sheet must be completed for each baby and attached to the maternal interview.

---

G1a. Is this baby a single, twin or triplet?

[1] single [2] twin, 1st born, [9] NK
[3] twin, 2nd born [4] triplet, 1st born
[5] triplet, 2nd born, [6] triplet, 3rd born
[7] twin, order unknown [8] triplet, o/u

G2. What was the time of birth of this baby.

_____ hr _____ mins ☐ a.m. ☐ p.m.

G3. How old was the baby when examined for this questionnaire?

_____ hrs

G4. What was the outcome of this delivery?

[1] spontaneous abortion (miscarriage)
[2] induced abortion [3] stillbirth
[4] died after delivery, age at death
_____ hrs [5] alive now, healthy
[9] NK [6] alive now, admitted to hospital [7] other, please describe
_____

G5. What is the sex of this baby?

[1] male [2] female [3] intersex
[4] undertermined [9] NK

G6. Give the birthweight of this baby

_____ lbs _____ ozs (_____ gms)

G7. What is the crown-heel length of the baby

_____ inches/cms

G8. What is the head circumference _____ ins/cms

G9a. Please measure size of baby's breasts

right _____ mm left _____ mm

b. Please describe nipples:

[1] barely visible [2] flat areola
[3] raised areola [9] NK

G10. Please describe sole creases

[1] none present [2] one-third [9] NK
[3] two-thirds [4] heel creases present

G11. Please describe ears

[1] no return [2] slow return
[3] springy and firm [9] NK

G12. Please describe testes

[0] not applicable (girl)
[1] undescended [2] in groin
[3] in neck [4] in scrotum [9] NK

G13. Please describe labia

[0] not applicable (boy) [9] NK
[1] minora > majora [2] minora = majora [3] majora > minora
[4] majora covers minora

G14. Did the baby cry immediately after birth

[1] yes [2] no [9] NK

G15. What was the apgar score

a. at 1 min _____ b. at 5 min _____

G16a. Please describe the first feed the baby was given:

[1] breast-fed [2] glucose water-bottle fed
[3] formula bottle fed [4] other, please describe _____
[7] not applicable (baby died) [9] NK

b. At what age did baby have the first feed _____ hrs

G17. Did the baby have any convulsions?

[1] yes [2] no [9] NK

G18a. Was the baby jaundiced?

[1] yes [2] no [9] NK

*If yes, please give*

b. age at onset _____ hrs

c. bilirubin level (highest) _____

d. probable cause _____

e. treatment, if any _____

_____

G19a. Was the baby's haemoglobin measured?

[1] yes [2] no [9] NK

*If yes, please give*

b. result _____ date _____ / _____ / _____

c. method used _____

G20. Were the following given:

a. silver nitrate [1] yes [2] no [9] NK

b. Vitamin $K_1$ [1] yes [2] no [9] NK
(Konakion)

c. BCG vaccine [1] yes [2] no [9] NK

G21. Examine the infant system by system and record whether any of the following systems show signs of abnormality or congenital malformation.

*If yes, please describe.*

a. SKIN [1] no [2] yes _____ [9] NK

b. EYES [1] no [2] yes _____ [9] NK

c. EARS [1] no [2] yes _____ [9] NK

d. NOSE [1] no [2] yes _____ [9] NK

e. MOUTH [1] no [2] yes _____ [9] NK

f. PALATE [1] no [2] yes _____ [9] NK

g. FONTANELLE & SUTURES [1] no [2] yes _____ [9] NK

h. SKULL SHAPE [1] no [2] yes _____ [9] NK

i. NUTRITIONAL STATUS [1] no [2] yes _____ [9] NK

j. RESPIRATORY [1] no [2] yes _____ [9] NK

k. HEART [1] no [2] yes _____ [9] NK

l. ABDOMEN [1] no [2] yes _____ [9] NK

m. UMBILICUS [1] no [2] yes _____ [9] NK

n. ANUS [1] no [2] yes _____ [9] NK

o. GENITALIA [1] no [2] yes _____ [9] NK

p. NEUROLOGICAL [1] no [2] yes _____ [9] NK

q. SKELETAL

r. – clavicle [1] no [2] yes _____ [9] NK

s. – hips [1] no [2] yes _____ [9] NK

t. – feet [1] no [2] yes _____ [9] NK

u. OTHER [1] no [2] yes _____ [9] NK

Please describe any of the above further if necessary.

_____

_____

_____

G22. Were any other illnesses or abnormal symptoms noted in the baby?

[1] yes [2] no [9] NK

*If yes, please list* _____

_____

_____

G23. Was the baby referred to a medical officer?

[1] yes [2] no [9] NK

*If yes, give reason for referral*

_____

_____

_____

G24a. Was the baby admitted to hospital or special care baby unit?

[1] yes [2] no [9] NK

b. If transferred, give name of hospital

_____

c. Reason for transfer _____

_____

COMPLETION OF QUESTIONNAIRE

PLEASE CHECK THAT EVERY QUESTION HAS BEEN ANSWERED.

COMPLETE IDENTIFICATION INFORMATION ON SUPPLEMENTARY ANTENATAL QUESTIONNAIRE.

IF BABY HAS DIED, PLEASE ALSO FILL IN A *STILLBIRTH/INFANT DEATH QUESTIONNAIRE.*

IF THE MOTHER DIED, PLEASE ALSO FILL IN A *MATERNAL DEATH QUESTIONNAIRE.*

IF THE BABY HAS BEEN ADMITTED TO VJH NURSERY, BUSTAMANTE, UHWI, CRH, MANDEVILLE, SPANISH TOWN, ST. ANN'S BAY, PLEASE ALSO GET A *NEONATAL ADMISSION QUESTIONNAIRE* COMPLETED BY THE PAEDIATRICIAN OR PAEDIATRIC HOUSE OFFICER.

THIS QUESTIONNAIRE WAS COMPLETED BY

Name: _____

Position: _____

Date: _____

CHECKED BY:

Name: _____

Date: _____

N.B. The Supplementary Questionnaire that follows is to be completed from all antenatal records.

**Identifying information, including the study number, should be entered by the interviewer. Information available on the MATERNAL RECORD CARD should be transcribed at this time.**

Name of Mother _____

Health Centre/Hospital providing antenatal care in 3rd trimester _____

Parish antenatal care received _____

Date of Delivery _____

Parish of Delivery _____

Place of Delivery _____

Study Number: ☐☐☐ ☐☐☐☐ ☐

---

**This section is to be completed from the ANTENATAL RECORDS of the institution providing these services. The MATERNAL RECORD CARD is part of these records and should be consulted first, if available.**

H1a. Blood group and Rh of mother

[1] A positive [2] A negative
[3] B positive [4] B negative
[5] AB positive [6] AB negative
[7] O positive [8] O negative [9] NK

b. Results of Coombs test (for blood group antibodies)

[1] positive [2] negative [8] not done
[9] NK

H2. Did the mother have any blood disorder during this pregnancy?

[1] yes, sickle cell disease (SS) [6] no
[2] yes, sickle cell trait (AS) [9] NK
[3] yes, sickler, AS or SS unknown
[4] yes, anaemic
[5] yes, other, please describe _____

H3a. Was the haemoglobin measured during any antenatal visit?

[1] yes [2] no [9] NK

If *yes*, please give:

b. Number of readings _____

c. Lowest reading _ date ____ / ____ /19____

d. Method _____

e. Was any treatment given for anaemia?

[1] no, none [2] yes, oral iron
[3] yes, oral iron and folic acid
[4] yes, IM iron [9] NK
[5] yes, blood transfusion
[6] yes, other, please describe _____

_____

f. Hb results after treatment

_____ date ____ / ____ /19____

H4a. How many times was the VDRL done during this pregnancy _____

b. Indicate results and dates

[1] neg [2] pos ____ / ____ /19____
[1] neg [2] pos ____ / ____ /19____
[1] neg [2] pos ____ / ____ /19____

H5. Was the mother fully immunized against tetanus

[1] yes, before this pregnancy
[2] yes, during this pregnancy
[3] no, not fully immunized [9] NK

H6a. How many times was the mother's blood pressure taken during pregnancy?

_____ [88] not at all

b. What was the first reading recorded

____ / ____ date ____ / ____ / ____

c. What was the reading with the highest diastolic?

____ / ____ date ____ / ____ / ____

d. What was the reading with the highest systolic?

____ / ____ date ____ / ____ / ____

H7. Did the mother have diabetes during this pregnancy?

[1] yes please describe _____

[2] no [9] NK

H8a. How many times was urine tested for protein during this pregnancy?

_____ [88] not at all

b. If non-infective proteinuria was found, what was the highest level

_____ date _____ / _____ /19_____

H9a. What was the mother's weight at the start of pregnancy _____ lbs/kgs

b. What was the mother's weight at the first antenatal visit _____ lbs/kgs

c. How many weeks gestation was this _____

H10. What was the mother's maximum weight during this pregnancy

_____lbs/kgs date _____ / _____ /_____

H11. Was oedema noted during any antenatal visit?

[1] yes, please give sites _____

_____

describe _____

_____ [2] no [9] NK

H12a. Was the mother diagnosed as having hypertension, pre-eclampsia or eclampsia during this pregnancy

[1] yes [2] no [9] NK

b. If yes, what treatment was given _____

_____

c. At how many weeks gestation was this first diagnosed _____

H13a. Was the mother referred to the medical officer during pregnancy for any reason?

[1] yes [2] no [9] NK

b. Reason for referral _____

c. Diagnosis made _____

d. Treatment given _____

END OF MATERNAL RECORD CARD INFORMATION

H14. Did the mother have any vaginal bleeding in the *first* 28 weeks of pregnancy

[1] yes, please describe _____

_____

at _____ wks gestation [2] no

[9] NK

H15. Did she have any vaginal bleeding *after* 28 weeks of pregnancy

[1] yes, please describe _____

_____

at _____ weeks gestation [2] no

[9] NK

H16. Did she have a vaginal discharge or infection during this pregnancy

[1] yes, please describe treatment given _____

and type of infection (if known)

_____

[2] no [9] NK

H17. During this pregnancy did the mother suffer from:

a. abnormal weight loss [1] yes

[2] no [9] NK

b. excessive weight gain [1] yes

[2] no [9] NK

H18. Was the mother thought to be either malnourished or obese

[1] yes, undernourished

[2] yes, obese

[3] no, neither [9] NK

H19. Was the mother put on a special diet during this pregnancy

[1] yes, high caloric, high protein

[2] yes, weight controlling [6] no

[3] yes, salt restriction [9] NK

[7] other, please describe _____

_____

H20. Did she have any worm infestation during this pregnancy

[1] yes, please describe _____

_____

[2] no [9] NK

H21. Did the mother have any of the following during this pregnancy

a. Urinary tract infection [1] yes [2] no [9] NK

b. Tuberculosis [1] yes [2] no [9] NK

c. Rubella (German measles) [1] yes [2] no [9] NK

d. Gonorrhoea [1] yes [2] no [9] NK

e. Syphilis [1] yes [2] no [9] NK

f. Genital sores or blisters [1] yes [2] no [9] NK

g. Epilepsy [1] yes [2] no [9] NK

h. Eclamptic fits [1] yes [2] no [9] NK

i. Heart disease [1] yes [2] no [9] NK

If yes, please describe _____

_____

H22. Have there been any other complications, disorders or serious illness during this pregnancy

[1] yes, please list _____

_____

_____

[2] no [9] NK

H23. Medications prescribed by the health care team. Please list.

_____

_____

_____

_____

_____

_____

Completed by: _____

Position: _____

Date _____

Checked by: _____

Date: _____

# APPENDIX - B
# Follow-up Questionnaire – Six Week
# Perinatal Survey - Jamaica

PERINATL SURVEY – JAMAICA

NK – not known FOLOW-UP QUESTIONNAIRE

DATE OF DELIVERY _____

PARISH OF DELIVERY _____

FOR OFFICE USE ONLY

A1. Study No.: ☐☐☐☐☐☐ ☐

To be completed between 6 weeks and 3 months after delivery. Data to be collected by interviewing the mother and checking the notes at post-partnum clinic visit, if made. Otherwise, attempts must be made to locate mother and baby before 3 months of age.

A2. Name of mother _____ ☐☐☐☐☐
Surname first middle pet name

A3. Mother's date of birth _____

A4. Mother's home address: _____ Parish _____ ☐☐☐

A5. Date of delivery _____ ☐☐☐☐☐

A6. Place of delivery: _____

A7. Full name of child: _____ ☐☐☐☐
Surname first middle

A8. Sex of baby ☐ male ☐ female ☐ intersex ☐
☐ undetermined ☐ NK

A9. Is this baby ☐ a single ☐ 1st twin ☐ 2nd twin ☐
☐ 1st triplet ☐ 2nd triplet ☐ 3rd triplet

A10. Names of hospital to which bay admitted (if at all) ☐☐☐☐
_____ Date _____/19____ ☐☐☐☐☐
_____ Date _____/19____ ☐☐☐☐

A11. Mother seen ☐ yes ☐ no ☐ NK ☐☐☐☐☐
Baby seen ☐ yes ☐ no ☐ NK

A12. Mother interviewed at 6 wk clinic ☐ yes ☐ no ☐ NK ☐☐
Mother interviewed at home after 6 weeks ☐ yes ☐ no ☐ NK ☐☐

A13. Date of interview _____/19_____ ☐☐☐☐☐

A14. Current status of mother
☐ alive, healthy ☐ alive, ill ☐ dead* ☐ NK ☐
Current status of baby
☐ alive, healthy ☐ alive, ill ☐ dead** ☐ NK ☐

A15. If infant ill, ☐ ill at home, diagnosis _____ ☐☐☐☐

☐ ill, being treated at health center, diagnosis_____ ☐☐☐
☐ ill, being treated at hospital outpatient, diagnosis_____
☐ ill, admitted to hospital, specify_____
diagnosis_____ ☐☐

If admitted or transferred to VJH Nursery, UHWI, Bustamante, CRH, Spanish Town, Mandeville, St. Ann's Bay, complete NEONATAL ADMISSION QUESTIONNAIRE ☐

☐ completed ☐ not completed

---

* If death after discharge from hospital, a MATERNAL DEATH QUESTIONNAIRE must be completed☐ completed ☐ not completed ☐ NA ☐

** If death after discharge, an INFANT DEATH QUESTIONNAIRE must be completed and if possible, a post mortem arranged. ☐

☐ questionnaire completed ☐ not completed ☐ NA

Post mortem arranged ☐ yes ☐ no ☐ infant already buried ☐ NA ☐

NK – not known

FOLOW-UP QUESTIONNAIRE, CONTINUED
MATERNAL HISTORY

DATE OF DELIVERY _____
PARISH OF DELIVERY _____
FOR OFFICE USE ONLY
Study No.: ☐☐☐☐☐☐

I1. Since delivery of the baby has the mother had any of the following

| | | | | |
|---|---|---|---|---|
| a. | postpartum hemorrhage | yes | no | NK |
| b. | Anemia | yes | no | NK |
| c. | Mastitis | yes | no | NK |
| d. | Breast engorgement | yes | no | NK |
| e. | Puerperal depression | yes | no | NK |
| f. | Infected lochia | yes | no | NK |
| g. | High blood pressure | yes | no | NK |
| h. | Other disorder | yes | no | NK |

specify _____

If yes to any of the above, please describe_____

I2. Was the mother admitted to hospital at all during the period since the birth of the baby? yes no NK

If yes, give dates of and reason for admission and treatment given:

| | Date admitted | No. days in hospital | Reason | Treatment given |
|---|---|---|---|---|
| i | __/___/19___ | _____ | _____ | _____ |
| ii | __/___/19___ | _____ | _____ | _____ |

I3 Has menstruation returned? yes no NK
if yes, date returned ___/_____/19_____

I4a. Have you felt sad since your delivery? yes no NK

I4b. If yes, with whom have you shared these feelings
partner doctor other, specify_____
relative midwife NK

I5a. Has anyone been particularly helpful o kind to you since you have had your baby?
yes no NK

b. If yes, whom: mother partner neighbor
friend other, specify_____
NK

FOLLOW-UP QUESTIONNAIRE, CONTINUED
EXAMINATION OF THE MOTHER

NK – not known

DATE OF DELIVERY _____
PARISH OF DELIVERY _____
FOR OFFICE USE ONLY
Study No.: ☐☐☐☐☐

J1. Date of examination _____/19____
J2. Hb. level_____Method
J3. Blood pressure_____
J4. Weight _____kg/lb
J5a. Is the mother using a contraceptive method at the moment?
yes no NK
b. If yes, which method? Pill injection (Depo Provera)
IUD diaphragm condom Spermicidals Sterilization
other, specify NK
c. When did she start using this method after delivery
___/____19____.
d. If no, is she planning to do so in the future? yes no
NK
e. If yes, please give proposed method
_____
(if infant was stillborn, interview ends here).

EXAMINATION OF THE BABY

K1. Hb. level _____
Method_____
K2. Weight _____kg/lbs
K3. Crown-heel length _____cm.

K4. Head circumference _____cm.
K5. What is baby currently being fed? Breast breast & formula formula only other, please describe _____NK

K6. If not breast fed how is feed given bottle cup & spoon
other, specify _____

K7a. If the babay is presently receiving breast milk, how often per 24 hr period? _____feeds per 24 hrs.
b. If the baby is not currently receiving breast milk, at what age did the baby stop receiving breast milk _____days.
c. If receiving bottle, at what age was it introduce _days/weeks
d. If being fed by cup and spoon, at what age were they introduce ___days/weeks

FOLLOW-UP QUESTIONNAIRE, CONTINUED

DATE OF DELIVERY _____
PARISH OF DELIVERY _____
FOR OFFICE USE ONLY
Study No.: ☐☐☐☐☐

NK – not known

K8. What drinks and foods were given to the baby in the first 28 days?

| | | | | |
|---|---|---|---|---|
| a. | Glucose water | yes | no | NK |
| b. | Bush tea, specify _____ | yes | no | NK |
| c. | Cow's milk | yes | no | NK |
| d. | Formula | yes | no | NK |
| e. | Fruit Juice | yes | no | NK |
| f. | Porridge | yes | no | NK |
| g. | Other, please describe | yes | no | NK |

K9. Please describe below, in detail, what the baby was given to eat and drink in the past 24 hours ending at midnight last night.

| Time (24 Hr clock) | Quantity (if breast Milk, state length of time on breast) | Food/drink given |
|---|---|---|
| _____ | _____ | _____ |
| _____ | _____ | _____ |
| _____ | _____ | _____ |
| _____ | _____ | _____ |
| _____ | _____ | _____ |

K10. Since birth until 28 days old, did the baby have any of the following?

| | | | | |
|---|---|---|---|---|
| a. | Jaundice | yes | no | NK |
| b. | Convulsions/twitching | yes | no | NK |
| c. | Persistent vomiting | yes | no | NK |
| d. | Diarrhea (3 or more Loose stool) | yes | no | NK |
| e. | Sticky or discharging eyes | yes | no | NK |
| f. | Cord infection | yes | no | NK |
| g. | Other infection If yes, please describe | yes | no | NK |
| h. | Other problems Please describe _____ | yes | no | NK |

K11. Examine the anterior fontanelle. Check all that apply. Is it

Open Closed Depressed

Bulging Normal NK

FOLLOW-UP QUESTIONNAIRE, CONTINUED

DATE OF DELIVERY _____

PARISH OF DELIVERY _____

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K12. On examination of the infant, were any of the following systems found to be abnormal or show congenital malformation.

| | | | | |
|---|---|---|---|---|
| a. | Skin | no | yes | NK |
| b. | Eyes | no | yes | NK |
| c. | Ears | no | yes | NK |
| d. | Nose | no | yes | NK |
| e. | Mouth | no | yes | NK |
| f. | Palate | no | yes | NK |
| g. | Fontanelle & sutures | no | yes | NK |
| h. | Skull shape | no | yes | NK |
| i. | Nutritional status | no | yes | NK |
| j. | Respiratory system | no | yes | NK |
| k. | Heart | no | yes | NK |
| l. | Abdomen | no | yes | NK |
| m. | Umbilicus | no | yes | NK |
| n. | Anus | no | yes | NK |
| o. | Genitalia | no | yes | NK |
| p. | Neurological | no | yes | NK |
| | Skeletal | | | |
| q. | – clavicle | no | yes | NK |
| r. | – hips | no | yes | NK |
| s. | – feet | no | yes | NK |
| t. | Other | no | yes | NK |

K13. Had the family been admitted to hospital in the first 28 days of life

no yes NK

if yes, give details below

| Name of hospital | Date admitted | Reason | Treatment |
|---|---|---|---|
| _____ | __/__/19__ | _____ | _____ |
| _____ | __/__/19__ | _____ | _____ |
| _____ | __/__/19__ | _____ | _____ |
| _____ | __/__/19__ | _____ | _____ |

K14a. Is the baby living with the mother no yes NK

b. If no, who is caring for the child

Other relative, describe

Non-relative, describe

Foster care or adoption

K15. Is father supporting the child no yes not applicable NK

This questionnaire was filled in by _____

Position _____ Date _____/19_____

# APPENDIX - C
# Child Health Questionnaire
# The Jamaica Cohort Study

Child's ID No. [__][__][__][__] [__][__][__][__]

Mother's ID No. [__][__][__] [__][__][__][__] [__]
*(As recorded in Perinatal Survey)*

Interviewer ID [__][__]

Date of interview [__][__] [__][__] [1][9][9][__]
(day) (month) (year)

## THE JAMAICAN COHORT STUDY

## CHILD HEALTH QUESTIONNAIRE

(To be administered to the study child's **mother/mother figure** or **father/father figure)**

**A. IDENTIFICATION**

1 Child's Surname_____ Forenames_____

2. Sex: [1] M ale [2] Female

3. Child's Date of birth [__][__] [__][__] [1][9][9][__]
(day) (month) (year)

**B. DEVELOPMENTAL MILESTONES**

4. Before your child was 3 years old, were you ever concerned that he/ she

   a. Began to walk later than other children? [1] Yes [2] No [3] Don't remember [9] N K
   b. Began-to talk later than other children? [1 ] Yes [2] No [3] Don't remember [9] N K

5. At what age did your child first take a few steps without any help? [_][_] mths.
*(Probe: If you-had to take a guess, what would you say?)*

6. At what age did your child first say his/her first word? [_][_] mths
(e.g."ma-ma", "da-da" to call you)

7. At what age did your child first put two or three, words together? [_][_] mths

8. At what age was your child toilet trained? [_][_] mths
*(Exclude night-time bed-wetting.)*

9. At what age did your child stop bed wetting at night? [_][_] mths

10. As a baby under the age of <u>six months</u> did your child have any of the following difficulties?

   a) Excessive crying [1] Yes [2] No [9] Not know
   b) Frequent feeding problems. [1] Yes [2] No [9] Not know
   c) Frequent sleeping difficulty at night [1] Yes [2] No [9] Not know

## C. GENERAL HEALTH

11. At present, how would you rate your child's health?

[1] Excellent [2] Good [3] Fair [4] Poor

12. a) Has your child ever been so sick that you thought that he/she might die?
[1] Yes [2] No [3] Not known

b) If yes, how old was your child when this happened? [_][_]yrs [_][_]mths.

c) What was his/her diagnosis?

13. a) Has your child ever been admitted to hospital overnight or longer or had an operation as a day case? *(Remember to enquire about circumcision, grommets, hernia, squint op.)* [1 ]Yes [2] No [3] Don't know

b) If *yes,* please give details below of each admission:

| Admission | 1 | 2 | 3 | 4 | 5 |
|---|---|---|---|---|---|
| Age at admission | | | | | |
| No. of nights | | | | | |
| Reason for admission | | | | | |
| Operations or procedures | | | | | |
| Hospital name | | | | | |

*(If child has had more than 5 admissions, please continue on back page)*

14. Has this child attended a hospital outpatient or specialist clinic or attended a specialist privately for any condition?

[I] Yes [2] No [3] Don't know

b) If yes, please give details below of **each** condition or illness resulting in attendance?

| Condition/Illness | 1 | 2 | 3 | 4 | 5 |
|---|---|---|---|---|---|
| Age (first visit) | | | | | |
| Total no. visits | | | | | |
| Diagnosis | | | | | |
| Treatment | | | | | |

*(If child has'h6d more than 5 conditions, please continue on back page)*

15. Has this child ever suffered any of the following?***

a) Accidental swallowing of medicines or poisons* [1] Yes [2] No [3] Not know
b) Burns or scalds [1] Yes [2] No [3] Not know
c) Involvement in a motor-vehicle accident [1] Yes [2] No [3] Not know
*(Include pedestrian, cycle or vehicle accidents)*
d) Injury to the head, other than in c) above [1] Yes [2] No [3] Not know
e) Broken bones or fractures** [1] Yes [2] No [3] Not know
f) Any other accident [1] Yes [2] No [3] Not know

Please give tails of each accident below:

| Accident | 1 | 2 | 3 | 4 | 5 |
|---|---|---|---|---|---|
| Age (yrs.) | | | | | |
| Place (home, school, road) | | | | | |
| What happened? | | | | | |
| Injuries received (burn, fracture, cut, LOC) | | | | | |
| Treatment facility (hosp., clinic, pvt. doctor, home) | | | | | |
| Treatment | | | | | |

*(If more than 5 accidents, please continue on back page)*
* *If ingestion, please give name of substance* ** *Indicate site of fracture*
****Please check that all accidents resulting in admission or outpatient attendance are also documented at q. 13 and 14.*

16. During the past 6 months, do you think that your child has had any emotional or behavioral problems?
[1] Yes [2] No [3]Not known

17. During the past 6 months, do you think that your child has had any difficulty learning or remembering things?
[I]Yes [2]No [3]Not known

18. Has your child ever received care from any of the following?
a) Speech therapist [1] Yes [2] No [3]Not known
b) Occupational therapist [1] Yes [2] No [3]Not known
c) Physiotherapist [1] Yes [2] No [3]Not known
d) Family counselor [1] Yes [2] No [3]Not known
e) Child psychiatrist/psychologist [1] Yes [2] No [3]Not known

If yes, give details below: Age, Reason, Where treated:

19. I am going to read to you a list of sicknesses or conditions that some children have. For each one can you tell me whether or not your child has ever had it? Has your child ever had:

a. Frequent sore throats [] Yes []No []Don't known
b. Frequent ear infections (Number = ) [] Yes [] No []Don't known
c. Hay fever sinus problem or some other allergy [] Yes [] No []Don't known
d. Asthma or wheezing [] Yes [] No []Don't known
e. Rheumatic fever [] Yes [] No []Don't known
f. Other heart condition [] Yes [] No []Don't known
g. Arthritis or rheumatism (other than rheumatic fever)[]Yes[]No []Don't known
h. Fits with fever [] Yes [] No []Don't known
i. Fits without fever/Epilepsy [] Yes [] No []Don't known
j. Cerebral palsy/Stiff limbs [] Yes [] No []Don't known
k. Slow development in any area [] Yes [] No []Don't known
l. Mental retardation [] Yes [] No []Don't known
m. Muscular dystrophy or other muscle disease) [] Yes [] No []Don't known
n. Abnormality of spine (e.g.Spina bifida, scoliosis) [] Yes [] No []Don't known
o. Missing fingers, hands, arms, toes, feet or legs [] Yes [] No []Don't known
p. Any stiffness or deformity of the foot, leg, fingers arms or back [] Yes [] No []Don't known
q. A condition since birth such as club foot or cleft palate [] Yes [] No []Don't known
r. Paralysis or weakness of any kind [] Yes [] No []Don't known
s. Regular severe headaches [] Yes [] No []Don't known
t. Any difficulty with coordination or clumsiness [] Yes [] No []Don't known
u. Sickle cell disease or trait [] Yes [] No []Don't known
v. Diabetes [] Yes [] No []Don't known
w. Eczema [] Yes [] No []Don't known
x. Frequent night, time or early morning cough [] Yes []No []Don't known
y. Urinary tract infection (infection in urine/kidney) [] Yes [] No []Don't known
z. Other condition, please specify [] Yes [] No []Don't known

If yes to any of the above, and condition not already documented above, please give details below (Age at illness, Diagnosis, Where treated, Treatment, Outcome)

20. Has your child had any of the following childhood illnesses?

a) Measles [] Yes [] No []Don't known If yes, age [_][_]yrs.
b) Mumps [] Yes [] No []Don't known If yes, age [_][_]yrs.
c) Chicken Pox [] Yes [] No []Don't known If yes, age [_][_]yrs.
d) Whooping cough [] Yes [] No []Don't known If yes, age [_][_]yrs.
e) German measles [] Yes [] No []Don't known If yes, age [_][_]yrs.

21. Please list all medication taken by your child in the last seven ays.

Name Reason taken

_____ _____
_____ _____
_____ _____

22. What immunizations has this child received to date? (Verify from immunization record.)

| | | | | | |
|---|---|---|---|---|---|
| a) BCG | [1] [2] | e)Measles | [1] [2] [3] | h) HepatitisB | [1] [2][3] |
| b)DPT | [1] [2] [3][4] | f) MMR | [1] [2] [3] | 1) HIB | [1] [2][3] |
| c) DT | [1] [2] [3][4] | g)Tetanus | [1] [2] [3] | j) Other, specify_____ | |
| d) OPV | [1] [2] [3] [4] | | | _____ | |

Immunization record not seen [9]

23. Where does your child usually receive medical care?

[1] Hospital [3] Family/ general doctor [5] Other, specify_____
[2] Clinic [4] Pediatrician

24. How often does your child visit the dentist?

[1] Never [3] Occasional check-ups [5]Other, specify_____
[2] Only when tooth trouble [4] Regular check ups 6-12 mths. [9] Not known

**D. FUNCTIONAL ABILITY**

I WILL NOW ASK YOU A FEW QUESTIONS ABOUT YOUR CHILD'S VISION, HEARING, SPEECH AND MOVEMENT.

**Vision:**

25. a) Is your child unable to see from one or both eyes?

[1] Yes, one eye only
[2]. Yes, both eyes
[3]. No

b) If yes, how long has he/she had this problem? [_][_] yrs. [_][_] mths

26. a) Does your child wear prescribed glasses or contact lenses?

[1] Yes [2] No

b) If yes, how long has he/she been wearing these? [_][_] yrs. [_][_] mths

27. a) Does your child have any difficulty reading regular printed words?

[1] Yes [2] No [9] Not known

b) If yes, how long has he/she had difficulty seeing words? [_][_] yrs. [_][_] mths

**Hearing**

28. a) Is your child unable to hear from one or both ears?
    [1 ]. Yes, one year only
    [2]. Yes, both ears
    [3]. No
    b) If yes, how long has he/she had this problem? [_][_] yrs. [_][_] mths

29. a) Does your child wear a hearing aid ?
    [1] Yes [2] No

    b) If yes, how long has he/she been wearing this? [_][_] yrs. [_][_] mths

30. a) Does your child have any difficulty hearing regular conversation?
    [1] Yes [2] No [9] Not known

    b) If yes, how long has he/she had difficulty hearing? [_][_] yrs. [_][_] mths

**Speech**

31. a) Is your child unable to communicate at all using words or speech?
    [1] Yes [2] No

    b) If yes, how long has he/she had this problem? [_][_] yrs. [_][_] mths

32. a) Does your child stammer, lisp or have difficulty being understood by others?
    [1] Yes [2] No [9] Not known

    b) If yes, how long has he/she had difficulty speaking? [_][_] yrs. [_][_] mths

**Movement**

33. a) Does your child need any assistance to move around (e.g. a person or artificial aid)? [1] Yes [2] No

    b) If yes, what does he/she use to get around?
    [1]. A wheelchair [1] Yes [2] No
    [2]. Artificial limbs or braces [1] Yes [2] No
    [3]. Cane or crutches [1] Yes [2] No
    [4]. Other, specify _____

    c) If yes, how long has he/she had this problem? [_][_] yrs. [_][_] mths

34. a) Does your child need any assistance using his hands and fingers, e.g., eating, dressing, using the toilet?
    [1] Yes [2] No
    b) If yes, how long has he/she had this problem? [_][_] yrs. [_][_] mths

*THANK RESPONDENT FOR PARTICIPATING IN THE SURVEY AND REMIND HER THAT THE INFORMATION WILL BE KEPT CONFIDENTIAL.*

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