The Spanish Environment and Childhood Research Network (INMA study)

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Abstract

Prenatal and early life exposure to environmental agents, including dietary exposure, is associated with child health and human development and predisposes to late adult effects. Children are more vulnerable than adults to chemical, physical and biological hazards in air, water and soil, because they are still growing and their immune system and detoxification mechanisms are not fully developed. The physical, social and intellectual development of children from conception to the end of adolescence requires a protected environment that is also protective of their health. Following WHO and European Union recommendations, the Cooperative Environment and Childhood Research Network was funded by the Spanish Ministry of Health to study effects of environment and diet on foetal and early childhood development in different geographical areas of Spain. This network integrates different multidisciplinary research groups and is comprised of six cohorts – three pre-existing and three de novo – which will prospectively follow up 3600 pregnant women from start of pregnancy until the children are 4–6-year old.

Keywords: Biological samples; Childhood growth; Child development; Cohort study; Diet; Endocrine disruptors; Prenatal exposures

Introduction

In 2003, in accordance with WHO and European Union recommendations, the Cooperative Environment and Childhood Research Network was supported by the Spanish Ministry of Health to study effects of environment and diet on foetal and early childhood development in different geographical areas of Spain. This network brings together different multidisciplinary research groups and is comprised of six cohorts – three pre-existing and three de novo – for the prospective
follow-up of 3600 pregnant women from start of pregnancy until their children are 4-6-year old. The general objectives of the network are:

1. To transfer knowledge and methodology among different Spanish groups studying the environment and health.
2. To prepare a common research protocol.
3. To describe the degree of individual contamination to persistent organic pollutants and metals and the burden of exposure during pregnancy and early childhood.
4. To evaluate the impact of exposure to different contaminants and both protective and negative factors of diet on the growth, health and development of children.
5. To evaluate the interaction among toxic, nutritional and genetic factors in foetal health and early childhood development.
6. To compare hypotheses generated from other ongoing cohorts.

Nutritional factors and biological, environmental and psychosocial exposures in prenatal and postnatal periods will be evaluated. Outcomes include prenatal and birth health events, neurodevelopment, behavioural functioning, immunity and hormonal disruption. The results of these studies will become available within the next few years and will help to determine levels of childhood exposure in several areas of Spain and their impact on public health.

Methods: design and participants

The INMA Study is a prospective population-based cohort study on the effects of pre- and postnatal environmental exposure on growth, development and health from early foetal life to young adulthood. Extensive assessments are carried out in pregnant women and children.

The follow-up is performed every three months during gestation and at birth and at the age of 1 and 4 years and will continue for at least two decades. The information is gathered from a variety of sources: questionnaires ad hoc administered in face-to-face interviews by trained interviewers, clinical data, physical examinations, ultrasound scans, biological samples (plasma, serum samples, placenta, urine, saliva, mothers’ milk, hair and nails) biomarkers, diet determinants and environmental measurements (air pollution, water pollution and persistent and semi-persistent pollutants).

Studies of prevalent environmental exposure require protocols with detailed personal information, complete environmental data and collaboration between epidemiologists and exposure assessment experts. Interaction with other studies is also important.

INMA is based on the experience acquired by groups studying the following cohorts: a cohort in Ribera d’Ebre (n = 102), in which the relationship between organochlorine or methyl-mercury exposure and neurological development is evaluated; a cohort in Menorca (n = 482), in which the relationship between air pollution and allergies or asthma is studied; and a cohort in Granada (n = 668), in which the incidence of infant reproductive health disorders is related to potential environmental exposures. New cohorts have been created to evaluate the impact of environmental exposure and diet on children’s health in Valencia (n = 1000), Sabadell (n = 800), Asturias (n = 500), Madrid (n = 500) and the Basque Country (n = 500).

Inclusion criteria for mothers are (a) residence in study area (specific in each cohort), (b) age of ≥16 years, (c) singleton pregnancy, (d) first prenatal visit (at 10–13 weeks of gestation) in main public hospital or health centre of area, (e) non-participation in an assisted reproduction programme, (f) willingness to deliver in reference hospital and (g) no communications handicap.

INMA field staff has been specifically trained for the project. All measurements have been tested for inter- and intra-reproducibility. An electronic database has been prepared to monitor the cohort in order to facilitate follow-up and minimise losses to the study. INMA staff members collect information on maternal identification, inclusion number, information required for follow-up (e.g., inclusion date, date of last menstrual period or expected date of delivery), and calendar for visits and sampling procedures. Minimum information is also gathered for mothers refusing participation in order to compare basic socio-demographic characteristics with those of participants.

The study has been approved by the Ethics Committee of the hospitals involved in the study. Pregnant women receive written and oral information about the study. Participants are asked for their written informed consent twice, first for their participation in prenatal visits and then for inclusion of their child in the follow-up study.

Exposure assessment

The air pollutant exposure protocol consists of:

- **Questionnaire:** assessment of exposure to traffic and environmental tobacco smoke by questionnaire during pregnancy (28–32 weeks) and at ages of 1 and 4 years.
- **Biological samples:** measurement of hydroxypyrene in urine in a subsample of pregnant women (at 10–12 weeks of gestation) and 4-year-old children.
• **Measurement of environment**: measurement of volatile organic compounds (VOCs), and NO$_2$ in outdoor and indoor samples. Measurement of particulates, polycyclic aromatic hydrocarbons, ozone and other pollutants in outdoor samples. Measurement of particulates, VOCs, NO$_2$ and ozone in air quality registries. Measurement of personal exposure to particulates in children aged 1 year.

• **Personal exposure modelling**: prediction of individual exposure using the geographic information system (GIS).

The water pollution exposure protocol consists of:

• **Questionnaires**: water consumption during pregnancy and childhood by questionnaire at 28–32 weeks of gestation and at 1 and 4 years. Measurement of environment: trihalomethanes and other disinfection by-products in water from a subsample of residences.

The persistent and semi-persistent pollutant exposure protocol consists of:

• **Questionnaires**: exposure during pregnancy and childhood by questionnaire at 28–32 weeks of gestation and at the ages of 1 and 4 years.

• **Biological samples**: measurement of organochlorine compounds, polybrominated diphenyl ethers, phthalates and phenols in maternal serum at 12 weeks of gestation, in cord serum and in children’s serum at age of 4 years.

• Arsenic in mothers’ and children’s nails at age of 4 years. Lead (in children’s serum) and methyl-mercury (in children’s hair) at birth and at age of 4 years.

• Measurement of different endocrine disrupters with oestrogenic activity in placentas.

The dietary protocol consists of:

• **Questionnaires**: maternal diet assessment by food frequency questionnaires at 10–13 and 28–32 weeks of gestation. Infant and child diet assessment by breast-feeding questionnaire at age of 1 year and food frequency questionnaire at age of 4 years.

• **Biological samples**: measurement of fatty acids, vitamins C and E and folate in maternal serum, fatty acids in cord blood, vitamins E and C in breast milk and fatty acids and vitamins at age of 4 years.

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Further reading


