



Colloque

ENVIRONNEMENT CHIMIQUE,
REPRODUCTION & DÉVELOPPEMENT DE L'ENFANT



25 novembre 2008

MINISTÈRE DE L'ÉCOLOGIE,
DE L'ÉNERGIE,
DU DÉVELOPPEMENT DURABLE
ET DE L'AMÉNAGEMENT DU TERRITOIRE
PARIS, FRANCE



Programme

Accueil et session poster
8h30 / 10h00

Introduction

Nathalie Kosciusko-Morizet, Secrétaire d'Etat chargée de l'Ecologie

Roselyne Bachelot-Narquin, Ministre de la Santé, de la Jeunesse, des Sports et de la Vie associative

Représentantes de la Présidence Française de l'Union Européenne

De l'incertitude au risque :

Etat des connaissances et du développement de la recherche (10h20/12h50).

Modérateur : **Bernard Jegou**

Président du Conseil scientifique de l'Inserm – France

- 10h20 / 10h50 « **Exposition mère/enfant aux perturbateurs endocriniens** »

Nicolas Olea - Université de Grenade – Espagne

- 10h50 / 11h20 « **Études prospectives des grossesses: des outils utiles pour la recherche étiologique de facteurs de risque environnementaux des anomalies de développement** »

Sylvaine Cordier - Inserm – France

- 11h20 / 11h50 « **Bio-monitorage des polluants persistants dans le sang du cordon et effets sur la santé du couple mère/enfant (Programme Flemish Environment & Health Survey - FLEHS 2002-2006)** »

Greet Schoeters - VITO, Flemish Institute for Technological Research – Mol – Belgique

- 11h50 / 12h20 « **Faible exposition prénatale au plomb et développement mental durant la petite enfance. Etude de la cohorte prospective de Cracovie** »

Wieslaw Jedrychowski - Jagiellonian University - Cracovie – Pologne –

- 12h20 / 12h50 « **Pollution atmosphérique, santé et développement** »

Stefan Willich - Charite University Medical Center Berlin – Allemagne –

Déjeuner en salon « **Bleu Ségur** »



14h30 « De l'éclairage scientifique à la prise de décision »

(suivi d'un débat avec la salle)

Modérateur : **Henri Poinignon**

Directeur (par intérim) de l'Agence Française de Sécurité Sanitaire de l'Environnement et du Travail

2

- **14h30 / 15h15 « Le mercure en tant que paradigme de pollution chimique : résultats de recherche, implications pour la santé publique et la prise de décisions »**

Philippe Grandjean - Université d'Odense - Danemark -

- **15h15 / 15h35 « Science et prise de décision dans la procédure REACH »**

Björn Hansen - Direction générale environnement de la Commission européenne -

« Table ronde: En quoi la santé environnementale implique-t-elle une nouvelle gestion du risque et questionne t'elle les décideurs et les politiques ? » (15h35 / 17h10)

Modérateur : **Laurent Michel**

Directeur Général de la prévention des pollutions et des risques- Ministère de l'Ecologie, de l'Energie, du Développement Durable et de l'Aménagement du Territoire

- **Didier Houssin** - Directeur général de la santé, Ministère de la Santé, de la Jeunesse et des Sports et de la Vie associative
- **Carine Giovannangeli** Ministère de l'Enseignement supérieur et de la Recherche
- **Joël Blondel** - Chef de service des relations et des conditions de travail, Ministère du travail, des Relations sociales, de la Famille et de la Solidarité
- **David Gee** - Représentant de l'Agence européenne de l'environnement
- **Gernot Klotz** - Représentant du Conseil européen des industries chimiques

Conclusions

Alfred Spira - Directeur de l'Institut de Recherche en Santé Publique - Paris, France

Pierre Jouannet - Université Paris V- Paris France

17h20 – Fin du colloque





25 novembre 2008

Colloque

ENVIRONNEMENT CHIMIQUE,
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RENSEIGNEMENTS UTILES

Ministère de l'Écologie, de l'Énergie, du Développement Durable et de
l'Aménagement du Territoire

Auditorium Serge Antoine

20, avenue de Ségur, 75007 Paris, France

Informations générales :

L'ensemble des sessions du colloque seront en traduction simultanée :

- Français
- Anglais

Des casques de traduction seront disponibles à l'accueil.

Contact presse : Service de presse de l'Agence française de sécurité sanitaire de l'environnement et du travail – 01 56 29 19 30.

A l'occasion de cette journée et pendant les pauses, les chercheurs financés dans le cadre du Programme National Santé-Environnement ou du Programme National de Recherche sur les Perturbateurs Endocriniens seront invités à présenter leur recherche sous forme de posters. (Mezzanine)



Programme

Registration and poster session
8.30-10.00 a.m.

4

Introduction

Nathalie Kosciusko-Morizet, French Secretary of State in charge of Ecology
Roselyne Bachelot-Narquin, French Minister for Health, Youth, Sports and Associations

French presidency of the European Union representatives

From doubt to risk: State-of-the art and research developments

Chairman: **Bernard Jegou**

Inserm – France. **Scientific Council President**

- **10.20 / 10.50 am. « Mother-child exposure to endocrine disruptors”**
Nicolas Olea - Granada University – Spain
- **10.50 / 11.20 am. « Prospective pregnancy studies: useful tools for etiological research on environmental risk factors of developmental anomalies”**
Sylvaine Cordier - Inserm – France
- **11.20 / 11.50 am. “Biomonitoring persistent pollutants in cord blood and health effects in mother-child pairs of the Flemish Environment & Health Survey (FLEHS 2002-2006)”**
Greet Schoeters - VITO - Flemish Institute for Technological Research – Mol – Belgium
- **11.50 / 12.20 pm. “Very low prenatal exposure to lead and mental development of children in infancy and early childhood. Krakow prospective cohort study”**
Wieslaw Jedrychowski - Jagiellonian University – Krakow – Poland
- **12.20 / 12.50 pm. « Atmospheric pollution, health and development”**
Stefan Willich - Charité University Medical Centre Berlin - Germany

Lunch in the salon “Bleu Ségur”





25 novembre 2008

Colloque

ENVIRONNEMENT CHIMIQUE,
REPRODUCTION & DÉVELOPPEMENT DE L'ENFANT

14.30 pm. "From scientific knowledge to decision making"

(followed by a discussion with the audience)

Chairman: **Henri Poinsignon**

AFSSET's acting Director (French Agency of Sanitary Safety of Environment and Work)

- **14.30 / 15.15 pm. "Mercury as a paradigm: Research insights, public health implications, and decision-making" – 45 min**

Philippe Grandjean - Odense University- Denmark

- **15.15 / 15.35 pm. "Science and decision making in REACH"– 20 min**

Björn Hansen - European Chemicals Agency

5

Round Table: Does environmental health imply a new risk management and addresses decision-makers?

Chairman: **Laurent Michel**

General Director, Prevention of pollutions and risks, French Ministry for Environment, Energy, Sustainable Development and Land settlement

- **Didier Houssin** - General Director, Health, French Ministry for Health, Youth, Sports and Associations
- **Carine Giovannangeli** French Ministry for Higher Education and Research
- **Joël Blondel** - Work Relationships and Conditions Department Head, Work, French Ministry for Employment, Social relationships, Family and Solidarity
- **David Gee** - European Environment Agency
- **Gernot Klotz** - European Council of chemical industries

Conclusions

Alfred Spira - Director, Public Health Research Institute – France

Pierre Jouannet - University Paris 5 - France

5.20 pm End of the conference





25 novembre 2008

Colloque

ENVIRONNEMENT CHIMIQUE,
REPRODUCTION & DÉVELOPPEMENT DE L'ENFANT

USEFUL INFORMATION

Ministère de l'Écologie, de l'Énergie, du Développement Durable et de
l'Aménagement du Territoire

Auditorium Serge Antoine

20, avenue de Ségur, 75007 Paris, France

6

General information

All congress sessions will be provided with simultaneous interpretation into:

- French
- English

Helmets of translation will be available in the reception

Press contact: News service of the French Agency of Sanitary Safety of Environment and Work- +33.01 56 29 19 30.

During breaks, researchers supported within the framework of National Program Health/Environment or within the framework of National Program on Endocrine Disruptors will be invited to present their research on posters.



Résumés des interventions

7

From doubt to risk: State-of-the art and research developments

- Mother-child exposure to endocrine disruptors (Nicolas OLEA) [p 8](#)
- Prospective pregnancy studies: useful tools for etiological research on environmental risk factors of developmental anomalies. (Sylvaine CORDIER) [p 9](#)
- Biomonitoring persistent pollutants in cord blood and health effects in mother-child pairs of the Flemish Environment & Health Survey (FLEHS 2002-2006) (Greet SCHOETERS) [p 10](#)
- Very low prenatal exposure to lead and mental development of children in infancy and early childhood. Krakow prospective cohort study (Wieslaw JEDREYCHOWSKY) [p 11](#)
- Atmospheric pollution, health and development (Prof. Stefan N. WILLICH) [p 12](#)

« De l'éclairage scientifique à la prise de décision »

- Mercury as a paradigm: Research insights, public health implications, and decision-making (Philippe GRANDJEAN) [p 13](#)
- Science and decision making in REACH (Björn HANSEN) [p14](#)





25 novembre 2008

Colloque

ENVIRONNEMENT CHIMIQUE,
REPRODUCTION & DÉVELOPPEMENT DE L'ENFANT

Mother-child exposure to endocrine disruptors

Nicolas Olea Institution: Hospital Clínico. University of Granada, Granada, Spain

Environmental pollutants that exert adverse physiological effects by disrupting normal endocrine function are designated endocrine disruptors (ED). ED are defined as exogenous substances that alter endocrine system function(s), thereby producing adverse health effects in an intact organism or its progeny or (sub)populations. The endocrine disruption hypothesis was originally developed for chemicals that affected the oestrogen-signalling pathway. Thus, most research on endocrine disruption to date has focussed on estrogenic effects. However, it is now becoming generally accepted that several types of compounds can interact with components of cell-regulatory systems, including steroid and thyroid hormone receptor families. Endocrine disruption via nuclear receptors in cells of many organs of the body could affect brain, cardiovascular, skeletal and urogenital system development and functions. Although frequent exposure to some particular EDs has been documented in humans, the evidence of human vulnerability to EDs is weak. Our understanding of the risks that EDs pose to human health is limited by our inadequate knowledge of the effects of chronic exposure to low levels and mixtures of chemicals and of the relationship between early-life exposure and its impact in adult life. Concerns about this relationship have been heightened by indications from laboratory animal studies that early life stages may be especially sensitive to the effects of EDs and by observations of non-monotonic dose response curves. There may be a long latency period between exposure and observed response. Thus, *in utero* exposure may have developmental effects that only become manifest when the offspring reaches sexual maturity. Human maternal-infant exposure during pregnancy is of special importance as a likely window of high susceptibility associated with severe and irreversible effects during critical developmental periods. Unfortunately, to date, the conflicting results of epidemiological studies have failed to effectively test the hypothesis that endocrine disruption is associated with adverse health effects in humans. Published studies have focussed on narrowly defined groups of chemicals, without considering combined exposures, genetic polymorphisms or life style factors. Ongoing European research focuses on building up databases on male reproductive effects and exploring the mechanistic basis of male disorders, with a view to developing improved biomarkers and screening tools. Human epidemiological studies have only recently been conducted with sufficient rigour to adequately address cause-and-effect relationships between ED exposure and disease, i.e., by using well-designed biomarkers of the combined effect of oestrogenic chemicals.

8





25 novembre 2008

Colloque

ENVIRONNEMENT CHIMIQUE,
REPRODUCTION & DÉVELOPPEMENT DE L'ENFANT

Prospective pregnancy studies: useful tools for etiological research on environmental risk factors of developmental anomalies.

Sylvaine Cordier Inserm, France

Recognition of the specific vulnerability of foetal development and its long term consequences requires careful assessment of events, both environmental exposures and induced pathological changes occurring during pregnancy and before conception. The ideal study design for a thorough investigation of etiological factors for child developmental problems should therefore include a longitudinal evaluation of environmental exposures, preferably using markers of exposure in biological samples during the appropriate windows of susceptibility. The PELAGIE cohort in Brittany includes 3421 pregnant women enrolled early in pregnancy between 2002 and 2005, and their children. Questionnaire data and urine and cord blood samples have been collected. Occupational and environmental exposures to a number of chemicals including solvents, pesticides and drinking water disinfection by-products or food contaminants are assessed using different sources. Current investigations relate these exposures to birth parameters such as duration of gestation, birth weight, head size and congenital malformations. Interactions between these exposures and some genetic determinants are also evaluated. Preliminary results concerning these various investigations will be presented and discussed.

9



Biomonitoring persistent pollutants in cord blood and health effects in mother-child pairs of the Flemish Environment & Health Survey (FLEHS 2002-2006)

Greet Schoeters¹, Elly Den Hond¹, Gudrun Koppen¹, Eva Govarts¹, Vera Nelen², Kristine Desager³, Maria Kristina Viaene^{4,5}, Griet Vermeir⁵, Stijn Verhulst³, Nicolas Van Larebeke⁶, Willy Baeyens⁷

¹Environmental Toxicology, Flemish Institute of Technological Research, Mol-Belgium

²Provincial Institute of Hygiene, Antwerp-Belgium

³Pediatrics-Respiratory Medicine, University Hospital Antwerp-Belgium,

⁴Neurotoxicity Expertise Centre, Governmental Psychiatric Hospital, Geel, Belgium

⁵Department of Occupational and Environmental Health-KULeuven, Leuven, Belgium

⁶Study Centre for Carcinogenesis and Primary Prevention of Cancer, Ghent University Hospital, Belgium

⁷Analytical and Environmental Chemistry Department, Vrije Universiteit Brussel, Brussels, Belgium

Measuring biomarkers of exposure and monitoring health effects in the same individuals of a study population is a powerful tool to increase the weight of evidence for the causal relationship between chemical exposure and adverse health effects. Moreover well documented exposure data allow bench mark dose calculations that provide valuable information for risk assessment. The early stages of life are particularly sensitive due to rapid development and maturation of tissues and organs. The concentrations of pollutants measured in breast milk or in cord blood have been associated with prenatal health effects, birth defects, neurobehavioral changes, immune parameters and puberty development.

The Flemish Centre for Environment & Health (Belgium) has organized a human biomonitoring network which included the recruitment of 1196 mothers and their newborns over a 1.5 years period (Flemish Environment and Health Survey- FLEHS (2002-2006)). Recruitment followed a stratified sampling scheme in eight Flemish geographical areas. Mothers and their newborns were contacted via 25 maternities in Flanders. There was a cooperation with two stem cell blood banks for joint use of cord blood samples in some of the regions. At birth, approximately 30 mL cord blood was collected. Persistent organochlorine compounds (PCB, p,p'-DDE, HCB, dioxin-like compounds) and heavy metals (Pb, Cd) were measured. The levels of all exposure markers were in line with those reported in other countries. Inter-regional differences in cord blood concentrations – up to a factor 2-3 – were observed. Cord blood levels of dioxin like compounds, PCBs and HCB were positively associated with increased risk for medically assisted pregnancies. These levels were also positively associated with ft3 and ft4 levels in cord blood. A cohort of 354 newborns was followed till the age of 36 months, examining, either growth, neurodevelopment or respiratory problems. Intrauterine exposure to p,p'-DDE and PCBs was associated with increased body mass index (BMI_{standard deviation score}) during early childhood (0-3 y). The neurobehavioral development of the 3-years old toddlers was negatively influenced by intrauterine concentrations of PCBs and Pb (all <10µg/dL). The effects seen in the behavioral tests were sex-linked.

P,p'-DDE levels in cord blood were associated with increased risk of wheezing at age of 2 years, and to a minor extend, with the average risk on wheezing in the first 3 years of life. For each child, exposure to outdoor air pollutants in the period of pregnancy and in the first year of life, was calculated. Measured concentrations of NO₂, benzene and ozone, were interpolated in geographical 4x4 km grids covering the child's residence. Wheezing at 1 year and skin prick allergy tests at 3 years of age were associated with average air pollutant levels over the period of pregnancy or during the first year of life.

The data from the Flemish cohort support the idea that exposure to environmental factors early in life, affect the young child's (0-3 y) biometry, behavior and respiratory health.



Very low prenatal exposure to lead and mental development of children in infancy and early childhood. Krakow prospective cohort study

Wieslaw Jedreychowsky Chair of Epidemiology and Preventive Medicine, Medical College, Jagiellonian University in Krakow, Poland

11

Background Humans begin to accumulate lead in their bodies during prenatal development. Because the fetal and infant brains are in a state of rapid growth, impairment of later cognitive function may result from even minor environmental toxic exposure. Since the placenta is not an effective biological barrier, pregnant women represent the group at increased risk because of maternal exposure of the fetus to lead.

Aim of the study Primary purpose of the study was to establish possible association between very low-level of prenatal exposure to lead and mental development of children at 12, 24 and 36 months of age.

Material and methods The study sample consisted of 444 children born to mothers, who attended ambulatory prenatal clinics in Krakow inner city in the first and second trimesters of pregnancy. We assessed exposure to lead by the cord blood lead measurements and mental development in infancy and early childhood using the Bayley Mental Development Index (MDI). The relationship between prenatal lead exposure and MDI scores at each follow-up period was evaluated with linear multivariate regression. To assess the overall effect of maternal exposure to lead during pregnancy on the Bayley test scores at 12, 24 and 36 months of age we used the Generalized Estimating Equations (GEE) longitudinal panel model as well. The median lead level in cord blood was 1.23 $\mu\text{g}/\text{dL}$ in the range of 0.44 to 6.90 $\mu\text{g}/\text{dL}$.

Results Although the infants in our study were exposed prenatally to a very low lead concentrations we observed inverse associations between cord blood lead level deficits in cognitive functioning of children already at lead levels below 5.0 $\mu\text{g}/\text{dL}$. An adverse effect of prenatal lead exposure (log transformed lead concentrations) on MDI score at 12 months of age was of border significance (beta coeff. = -5.42, 95%CI: -11.19 to 0.35). Subsequent testing of children at 24 months of age showed the significant inverse association of mental function and lead exposure (beta coeff. = -7.65, 95%CI: -14.68 to -0.62). Significant deficit in cognitive function due to prenatal lead exposure has also been confirmed at 36 months of age (beta coeff. = -6.72; 95%CI: -12.55 to -0.89). The GEE panel model showed that the average deficit in the cognitive development attributable to lead exposure over three years was also significant (beta coefficient = -6.62, 95%CI: -11.52 to -0.172). Mental function scores of girls were better than in boys, and the effect of maternal education remained strongly significant in relation to mental function of three olds. **Conclusions** The results of the presented analysis argue for a reduction in blood lead levels that are below the level of 5 $\mu\text{g}/\text{dL}$ and show the need for re-defining the primary prevention standards of childhood lead exposure. Current definition of an elevated blood lead level > 10 $\mu\text{g}/\text{dL}$ recommended by the CDC and the World Health Organization should be revised since neurotoxic impact of very low-level prenatal lead exposure below 5 $\mu\text{g}/\text{dL}$ occur in infants and very young children.





25 novembre 2008

Colloque

ENVIRONNEMENT CHIMIQUE,
REPRODUCTION & DÉVELOPPEMENT DE L'ENFANT

Atmospheric pollution, health and development

Prof. Stefan N. Willich Institute for Social Medicine, Epidemiology and Health Economics
Charité University Medical Center, Berlin, Germany

Development of chronic and acute diseases are influenced by biological and environmental factors, the latter consisting of climate, air pollution, traffic exposure, noise burden, and stress. We will present recent evidence of the impact of noise and pollution on coronary heart disease.

12

Chronic noise exposure has been shown to be associated with increased catecholamine levels and adverse effects on blood pressure and plasma lipids, and may thus contribute to the progression of coronary artery disease. The large German NaRoMI Study (Noise and Risk of Myocardial Infarction) demonstrated, that annoyance by environmental noise (including street, air and railway traffic, industrial and construction noise) was associated with increased risk of MI in women but not in men. The noise exposure level at work tended to be associated with increased risk of MI in men but not in women.

A case-crossover study using data from the Cooperative Health Research in the Region of Augsburg Myocardial Infarction Registry found an association between exposure to traffic and the onset of a myocardial infarction. The time which subjects spent in cars, on public transportation, or on motorcycles or bicycles was consistently linked with an increase in the risk of myocardial infarction.

Due to migration from rural to metropolitan areas the exposure to environmental factors which influence health and quality of life is continuously growing for the individual. Public health strategies in the future should include the prevention of exposure to pollution and noise.



Mercury as a paradigm: Research insights, public health implications, and decision-making

Philippe Grandjean, University of Southern Denmark, Odense, Denmark; and Harvard School of Public Health, Boston, MA, USA

13

The foetus and the child are particularly vulnerable to pollution. The foetus shares the mother's exposure and accumulated body burdens of pollutants, and many chemicals are transferred to the infant via human milk. In relation to the body weight, the newborn or small child needs much more water, energy and oxygen than does the adult, and contaminant exposures can therefore be comparatively larger. In addition, during early life, cell differentiation and organ development must happen in a particular sequence and at certain times to create optimal functions of the mature organism. Research conducted by nutritionists and epidemiologists shows that predisposition to serious diseases, such as coronary heart disease, diabetes, and obesity, may be generated during early development. In regard to functional deficits, this vulnerability is particularly important for the nervous system. Because there is only one chance to develop a brain, developmental exposure to toxic substances like lead can cause losses of IQ – the social impact of which can be calculated in terms of billions of Euros per year. Although the sensitivity of the brain is well documented, the effect of individual pollutants is poorly documented. In a recent review (Lancet 2006; 368: 2167-78), we identified over 200 industrial chemicals known to cause brain toxicity in humans. All of them are also suspected to harm the developing brain, and about half of these chemicals are produced in high volumes. However, only a small number of industrial chemicals – lead, methylmercury, polychlorinated biphenyls, arsenic, and toluene – are recognised causes of developmental brain dysfunction.

Methylmercury serves as a key example that certain chemical exposures during early development can cause brain injury at dose levels much lower than those that affect adult brain function. However, recognition of such risks is cumbersome and may take decades, because the full impact of neurotoxicity may not be apparent before school age. In addition, systematic testing of chemical substances for neurotoxicity is lacking, although over one thousand chemicals have been reported to be neurotoxic in laboratory models. Because their toxicity to the developing human brain is not known, current regulations do not aim to protect children's brain development. Even mercury pollution is only slowly getting regulated. Among major impediments to preventing developmental toxicity are the great gaps in testing chemicals and the high level of proof required for regulation. New, precautionary approaches are required for chemical testing and control that recognise the unique vulnerability of the developing organism, in particular the brain. As indicated by the Faroes statement (www.pptox.dk), it is not only the dose that makes the poison – the timing of the dose is also important, although frequently overlooked. Prevention should therefore not await definitive evidence of causality, and risk management procedures must address the need to protect the most vulnerable life stages through greater use of precautionary approaches to exposure reduction.





25 novembre 2008

Colloque

ENVIRONNEMENT CHIMIQUE,
REPRODUCTION & DÉVELOPPEMENT DE L'ENFANT

Science and decision making in REACH

Björn Hansen - European Chemicals Agency

Texte à venir

14



