



QLK4-CT-2000-00279
March 2001 – February 2006

Margaret Saunders
University of Bristol, Bristol, UK

Plutocracy

'government by wealth or wealthy'

Placental Uptake and Transfer of Environmental Chemicals Relating to Allergy in Childhood Years

Plutocracy - Purpose

- To determine whether there is a link between *in utero* fetal exposure to environmental chemical pollutants (xenobiotics) and the development of allergy during early childhood

Background

- Unborn child more sensitive to environmental exposure effects
- Mechanism, effects, long-term health outcomes unclear
- Is there a link between in utero exposure to environmental chemical pollutants and adverse health outcomes?
- Identification of risk factors: allergies

Background II

- Allergy or hypersensitivity – deviation from the normal state; inappropriate immune response to innocuous foreign substance
- Atopy – “strange disease” – familial syndrome of asthma and hayfever and eczema or atopic dermatitis – IgE dominated
- Allergies – immune reaction to common inhaled or ingested proteins – allergens
- Reaction occurs after re-exposure of sensitised individual to same allergen
- Symptoms range from hayfever to anaphylaxis

Epidemic

- Asthma – 155 million individuals worldwide
- Eczema – affects 10-20% of children in western populations
- Epidemic of the 21st Century – developed countries

Pollution

- ↑ air pollution (ozone & particulates) thought to be associated with asthma but pollution ↓ as asthma ↑ in westernised countries
- German reunification – Leipzig: high pollution, low AD; Munich low pollution, higher AD, atopy less common in E Germany
- E Germany more westernised, ↑ prevalence of atopy
- Factors associated with “western lifestyle”
- Other environmental factors

Plutocracy hypotheses

- Driver: association between organochlorines and elevated total IgE levels in newborns, ↑ atopic eczema in industrial region (Reichrtova et al 1999)
- Not genetics alone – environmental factors
- Exposure to environmental chemicals (xenobiotics) during pregnancy
- Placental transfer may lead to fetal exposure
- Placental accumulation may affect placental function (enzymatic, hormonal, immunological)
- Skewing of *in utero* cytokine balance may result in development of allergy in early childhood

List of selected persistent organochlorine compounds

	1,4+1,3-DCB	1,4+1,3-dichlorobenzene	
	1,2-DCB	1,2-dichlorobenzene	¹⁴ C-labelled version available
	1,3,5-TCB	1,3,5-trichlorobenzene	
A	1,2,4-TCB	1,2,4-trichlorobenzene	¹⁴ C-labelled version available
	1,2,3-TCB	1,2,3-trichlorobenzene	
	TeCB	Σ(1,2,3,5+1,2,4,5)tetrachlorobenzene	
	PCB	pentachlorobenzene	
	HCB	hexachlorobenzene	¹⁴ C-labelled version available
	alpha-HCH	alpha-hexachlorocyclohexane	
	beta-HCH	beta-hexachlorocyclohexane	
B	gamma-HCH	gamma-hexachlorocyclohexane	
	delta-HCH	delta-hexachlorocyclohexane	
	p,p'-DDT	1,1,1-trichloro-2,2-bis(p-chlorophenyl)ethane	¹⁴ C-labelled version available
	p,p'-DDE	1',1'-dichloro-2,2-bis(p-chlorophenyl)ethylene	¹⁴ C-labelled version available
	PCB - 28	(2,4,4'-trichlorobiphenyl)	
	PCB - 52	(2,2',5,5'-tetrachlorobiphenyl)	¹⁴ C-labelled version available
	PCB - 101	(2,2',4,5,5'-pentachlorobiphenyl)	
C	PCB - 118	(2,3',4,4',5'-pentachlorobiphenyl)	
	PCB - 138	(2,2',3,4,4',5'-hexachlorobiphenyl)	
	PCB - 153	(2,2',4,4',5,5'-hexachlorobiphenyl)	¹⁴ C-labelled version available
	PCB - 180	(2,2',3,4,4',5,5'-heptachlorobiphenyl)	

A - chlorinated benzenes, B - organochlorine insecticides, C - polychlorinated biphenyls (indicator congeners)

WP1 – assessment of *in utero* exposures of the birth cohort

- WP1.1 (WPL: P2 – Luba Palkovicova, SR)
 - Recruitment of up to 200 pregnant women and evaluation of atopic status (total and specific IgE, q^s status) x 5 regions; selection for follow-up (100 per region)
- WP1.2 (WPL: P2 – Luba Palkovicova, SR)
 - Measurement of maternal environmental exposure to selected organochlorines and heavy metals (Cd, Pb)
 - Placental tissue, peripheral blood, breast milk samples
 - 100 sets per region
- WP1.3 (WPL: P5 – Scott McNabb, USA)
 - Epidemiological assessment of exposure
 - Questionnaires developed to obtain information on gestation period, pregnancy outcome and placenta

WP2 – modulation of placental function and fetal sensitisation (WPL: Rosette Van den Heuvel, Be)

- Oxidative enzyme analysis of placenta and erythrocyte lysate from cord and maternal peripheral blood
- Proliferative and cytokine responses of mononuclear cells from maternal peripheral blood and cord blood in response to food and inhalant allergens
- Cytokine balance of culture placental trophoblast cells
- Low level total IgE levels in cord blood serum

WP3 – transfer of organochlorines across perfused placenta (WPL: Margaret Saunders, UK)

- Determine uptake and transfer of selected radiolabeled organochlorines across human placenta *ex vivo*
- Aim to correlate likely fetal uptake with known maternal exposure

**WP4 – Fetal biodistribution and
placental transfer of organochlorines
(WPL: Margaret Saunders, UK)**

- Determine *in vivo* uptake and placental transfer of selected radiolabeled organochlorines in suitable model
- Determine extent of fetal exposure
- Identify fetal organs potentially at risk

**WP5 – Postnatal exposure and risk
assessment
(WPL: Luba Palkovicova, SR)**

- Postnatal follow-up of children from cohort at age of 18 months
- Postnatal questionnaire
- Clinical assessment
- Peripheral blood sample
 - sIgE determination
 - Cytokine profile

**WP6 – Environmental exposure data
(WPL: Scott McNabb, USA)**

- Group exposure of children
- Seasonal measurement of outdoor air
 - PM2.5, PM10 at selected sites related to location of children
- Environmental monitoring

**WP7 – Data analysis (WPL: Scott
McNabb, USA)**

- Standardised data collection and entry
- Clean data, manage database
- Develop final dataset for questionnaire and laboratory data
- Perform analyses in order to determine risk factors for development of allergic disease within the cohort

**WP8 – Coordination & management
(WPL: Margaret Saunders, UK)**

- Communication
- Preparation of reports
- Packaging of deliverables
- Finances
- Meetings
- Project amendments
- Ethical issues
- Final Conference

Partners

- P1 University of Bristol, Bristol, UK
- P2 Slovak Medical University, Research Base of the SMU – Institute of Preventive and Clinical Medicine, Bratislava, Slovak Republic
- P3 University of Medicine and Pharmacy “Carol Davila”, Bucharest, Romania
- P4 Vito, Vlaamse Instelling voor Technologisch Onderzoek NV, Mol, Belgium
- P5 Emory University, Atlanta, USA
- P6 University of Antwerp, Wilrijk, Belgium
- AP2.1 Comenius University, Bratislava, Slovak Republic
- AP3.1 National Research and Development Institute for Environmental Protection, Bucharest, Romania