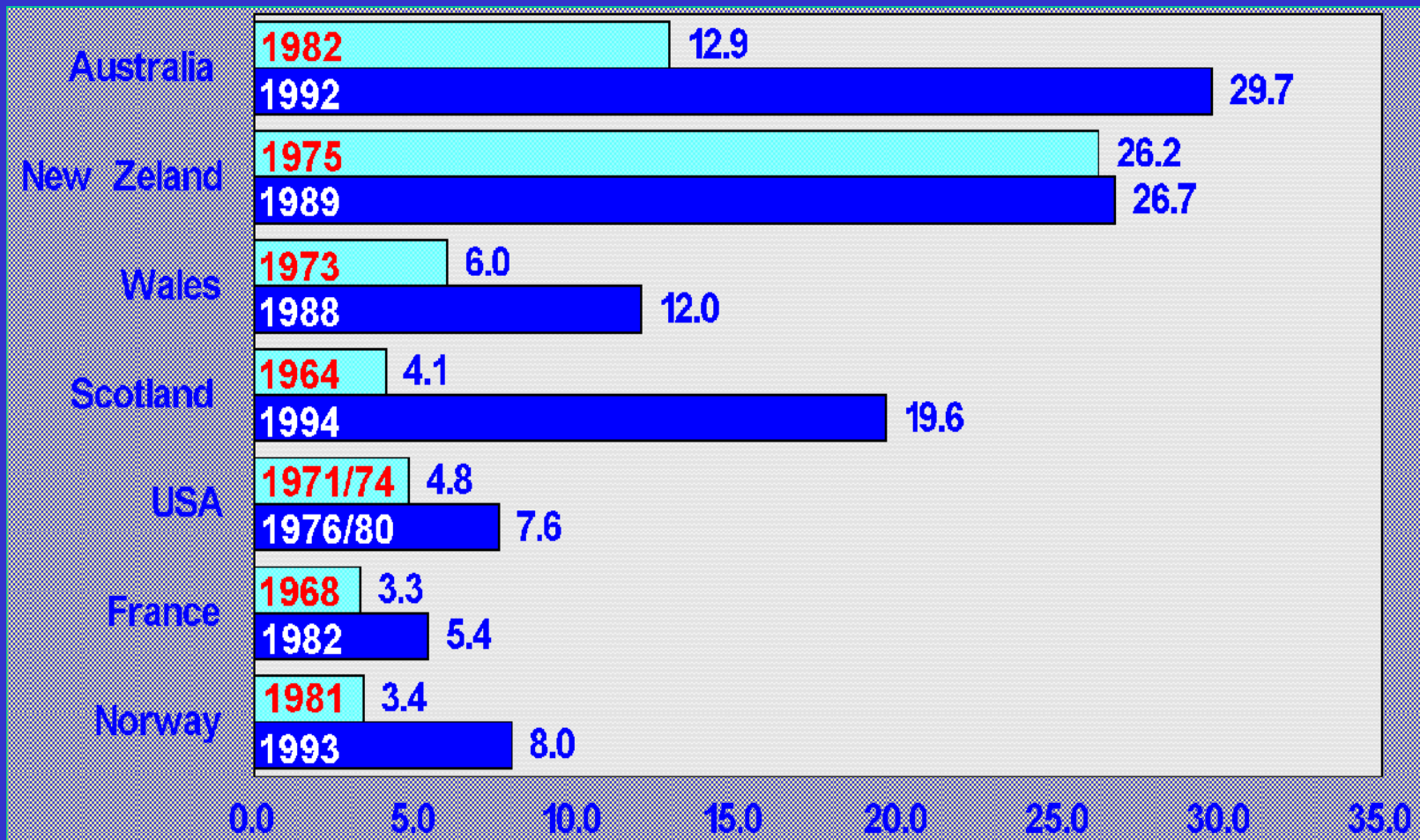


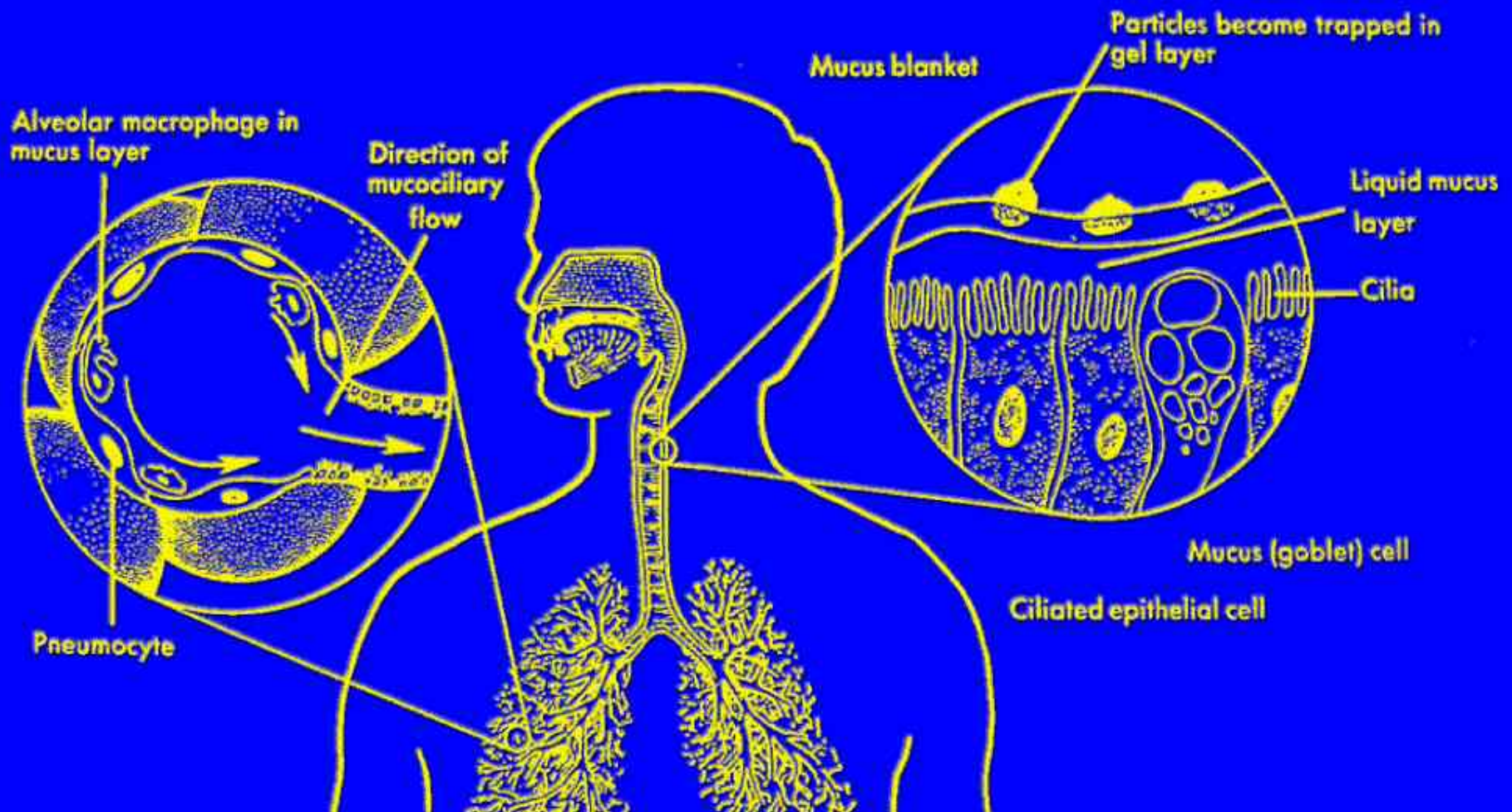
Wieslaw Jedrychowski

**Old and new environmental hazards
for respiratory health in infants
and children**

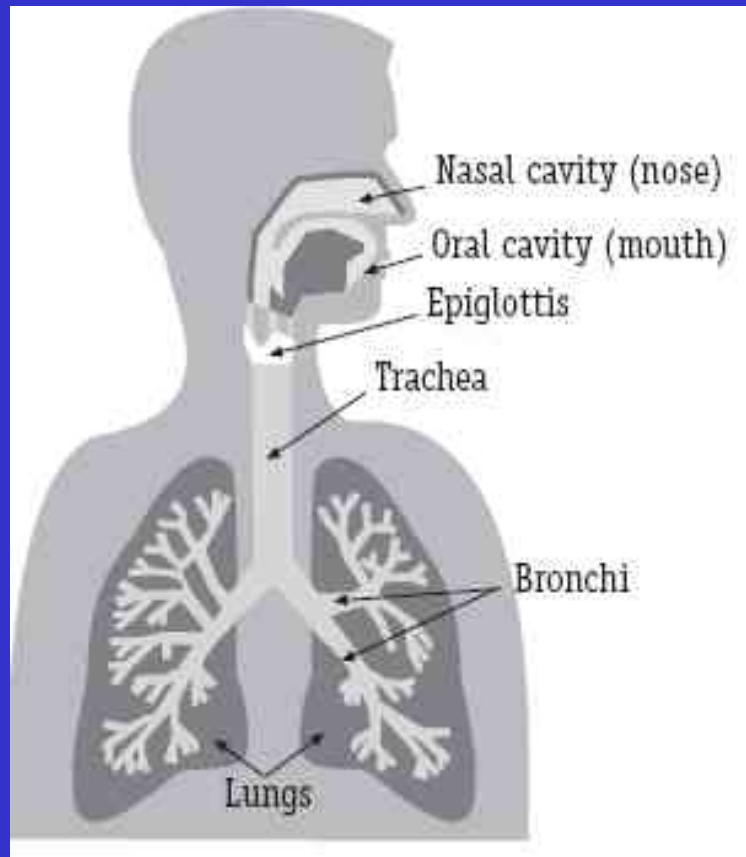
Chair of Epidemiology and Preventive Medicine,
College of Medicine
Jagiellonian University, Krakow, Poland



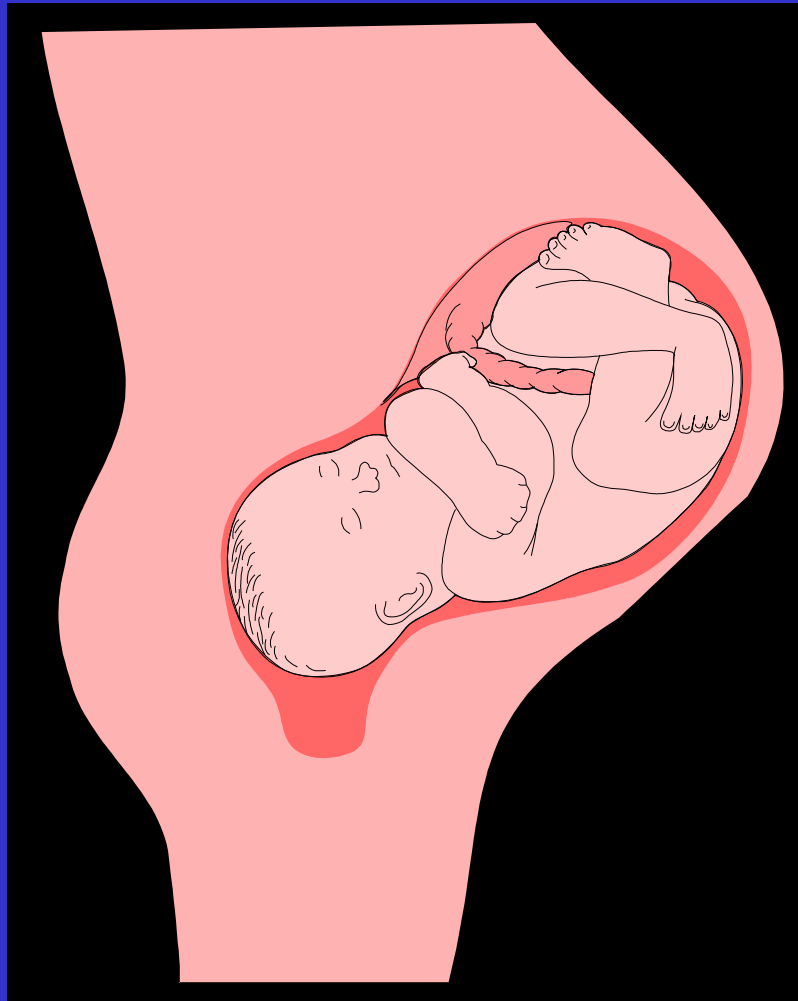
Although geographical trends of asthma in the world are clearly variable, numerous countries, have confirmed increasing prevalence of childhood asthma. It is estimated that the incidence of asthma is doubling every 10 - 15 years.



The development of respiratory health effects is assumed to be attributable to air pollutants, leading to epithelium damage, edema, and bronchoconstriction



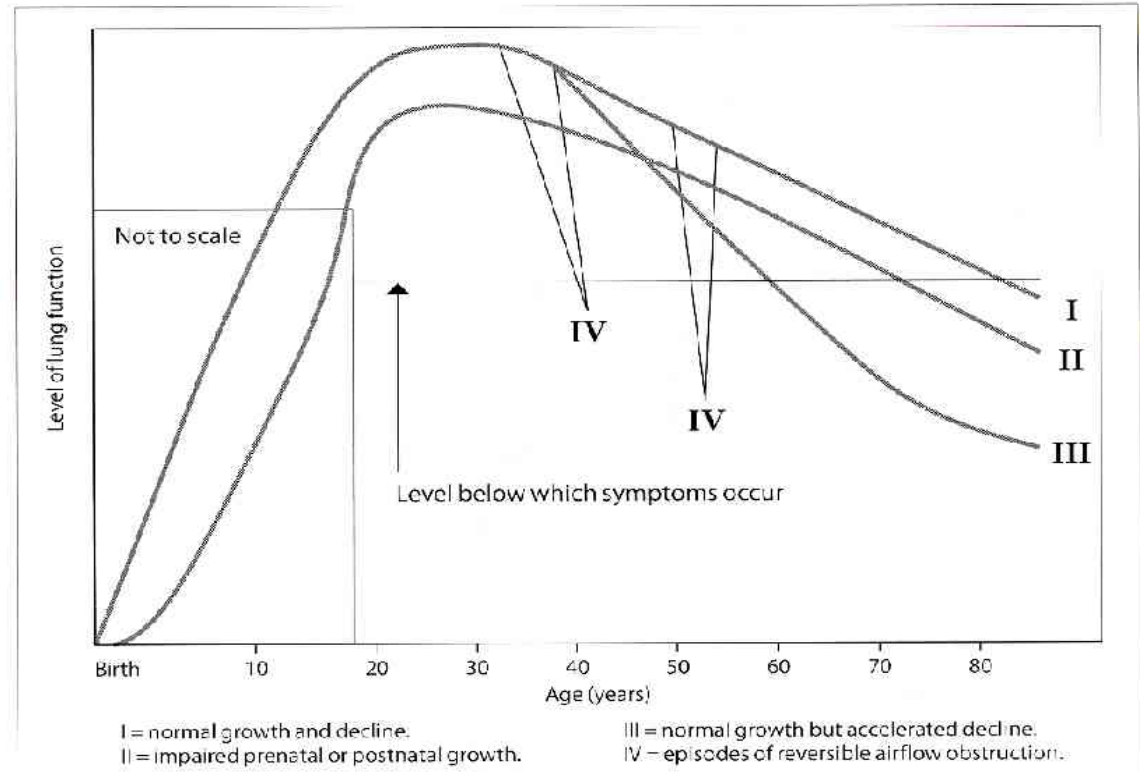
Inhalation of particles with a mass median aerodynamic diameter of $10\ \mu\text{m}$ or less is associated with increased hospitalisation for asthma, bronchiolar irritation, and lower tract infections, while exposure to particles $2.5\ \mu\text{m}$ and smaller exhibit a stronger epidemiological link with respiratory inflammatory effects.



Particles $0.1 \mu\text{m}$ or less, are thought to move beyond the respiratory system and may reach the bloodstream and cross the placenta.

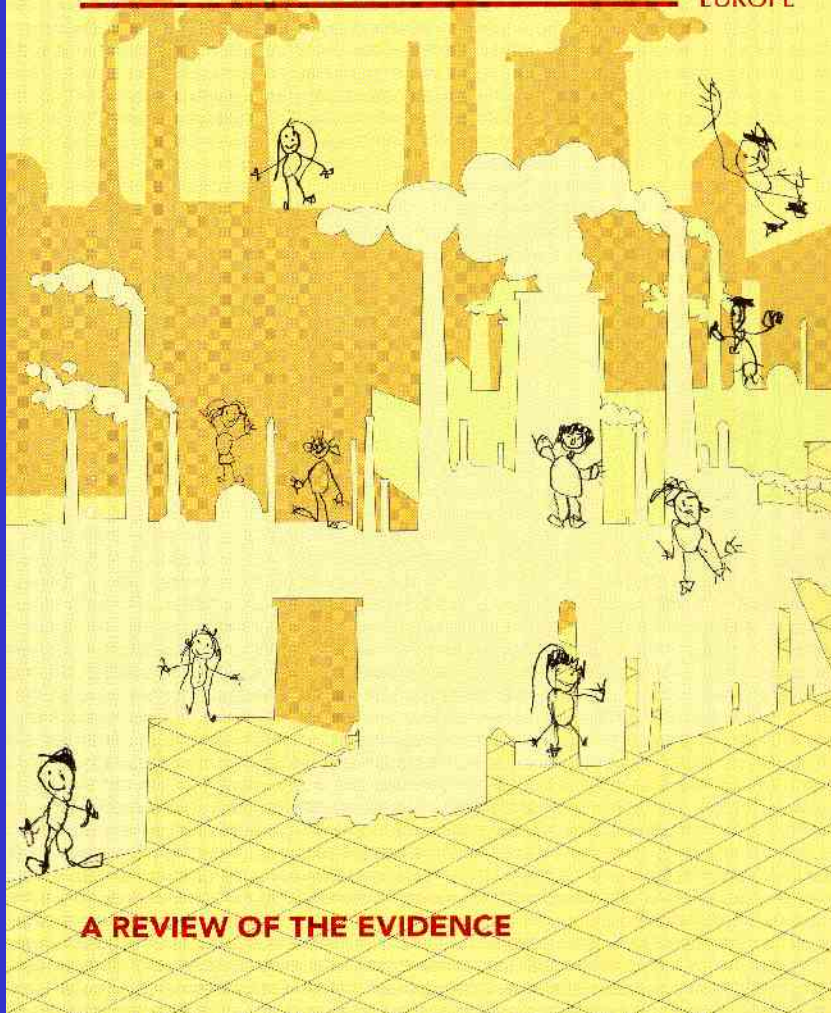
Particles $0.1 \mu\text{m}$ or less, are thought to move beyond the respiratory system and may reach the bloodstream and cross the placenta.

Fig. 1. Schematic representation of the life course of FEV_1



The $\text{PM}_{2.5}$ level should be treated as a proxy measure of a whole complex of toxic agents present in the environment.

**EFFECTS OF AIR POLLUTION ON
CHILDREN'S HEALTH AND
DEVELOPMENT**



A REVIEW OF THE EVIDENCE

An excellent review of evidence on effects of air pollution on children's health and development was published in 2005 by the WHO Working Group, Europe

Although outdoor air pollutants have been suggested as risk factors for inflammatory resp. diseases in children, but outdoor air pollutants has been declining in many countries over the last 10 years and this has not resulted in a corresponding decline in the incidence of resp. diseases in children.

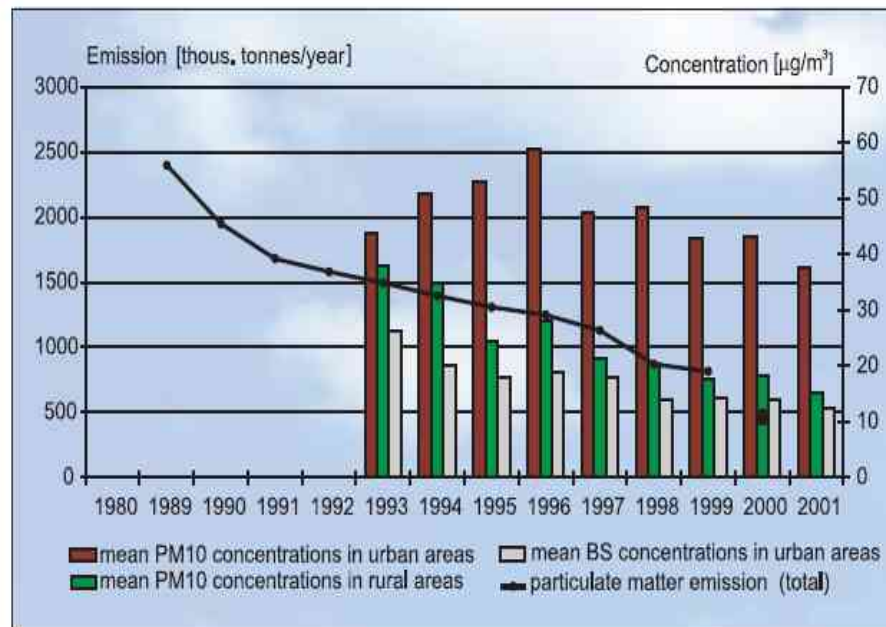


Figure 3.3.15. Changes in mean annual particulate matter concentrations in Poland, averaged for the entire country (according to data from the basic network) against the background of changes in total national emission (emission in 2000 was calculated using new estimation method). Source: SEMS, MoE.

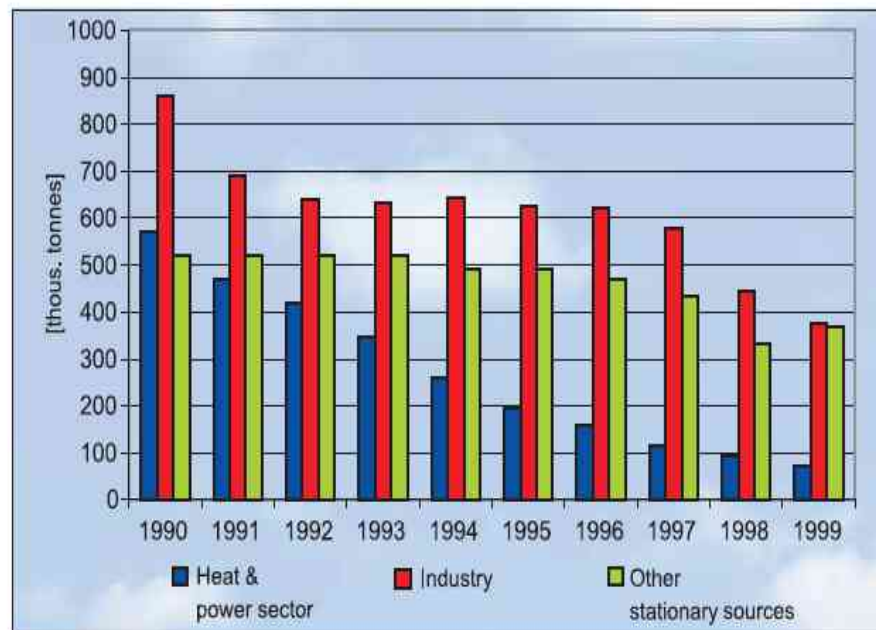


Figure 3.2.8. Trends in particulate matter emission from major types of sources distinguished by the Central Statistical Office. Source: MoE, CSO.

Sources of indoor air pollutants:

- Heating/cooking (particulate matter, SO₂, NO₂, PAHs)
- Cleaners (particulates, VOCs, formaldehyde)
-
- Paints (particulates, VOCs, PAHs, ketones etc)
- Furnishings and clothing (PAHs, vinyl chlorides, phthalates)
- Tobacco smoke (over 3000 compounds, particulates, VOCs, PAHs, metals etc)
- Allergens (mites, moulds, cockroaches, pets)

The ALSPAC study measured the frequency of use of 11 chemical domestic products from questionnaires completed by women during pregnancy and the total chemical burden score was derived. Four mutually exclusive wheezing patterns were defined for the period from birth to 42 months, based on parental questionnaire responses.

Multinomial logistic regression models were used to assess the relationship between these wheezing outcomes and exposure score while accounting for numerous potential confounding variables. The authors found that an increased use of domestic chemical products was associated with persistent wheezing during early childhood (OR=1.06; 95%CI: 1.03 - 1.09) but not with transient early wheeze or late wheeze.

Phthalate esters have recently been suggested to act as either allergens or adjuvants.

(Oie et al. 1997, Jakkola et al. 1999)

The association between asthma and allergic symptoms in children and phthalates in house dust was confirmed in a Swedish Study.

(Bornehag et al. 2004)

Phthalates are a class of chemicals with high production volume. They are commonly used in the home environment.

Phthalates are used as:

- Plasticizers (PVC, vinyl chloride resins)
- Emollients (skin softeners)
- Humectans (skin moisturizers)
- Antifoaming agents in aerosols
- Agents to prevent brittleness and cracking in nail polishes
- Sealants
- Cosmetics, desodorants, fragrance, hair spray,
- Enamels
- Insect repellants
- Building products (roofing, vinyl wall covering, carpeting, flooring, upholstery, clothing, packaging, toys plastic, containers)

Soft PVC can consist of up to 40% of DEHP (diethylhexyl phthalate). As the plasticizers are not chemically bound to the polymer, they leach, migrate or gas out into atmosphere, into foodstuff or directly into body fluids.

DEHP is a known reproductive and development toxicant in animals exerting its toxicity in utero and is suspected endocrine disruptor/modulator.

The aim of the preliminary study in Krakow was to examine the effect of prenatal exposure to fine particles and phthalates (di-cyclo-hexal phthalate, DCHP) on the occurrence and duration of wheeze during the first two years in children, who were taking part in the ongoing cohort study on the environmental determinants of respiratory health of children.

Acknowledgement

The project is the part of the collaborative study on the vulnerability of fetus and child to environmental factors carried out by the Chair of Epidemiology and Preventive Medicine, Coll. Med. Jagiellonian University in Krakow, Poland, and the Columbia Center for Children's Environmental Health, Mailman School Public Health, Columbia University, New York, NY, US
(principal investigator: Prof.F. Perera)

Prenatal studies on developmental toxicity are very important since:

1. the mother's chemical body burden is shared with her fetus or neonate, and the child is then likely to be exposed to larger doses relative to the body weight.
2. susceptibility to adverse effects is increased during development, from preconception through adolescence.
3. developmental exposures to toxicants can lead to life-long functional deficits and manifestations of increased disease risks.

Exposure



Health outcome



Prenatal exposure (FP and DCHP)



B

C

D

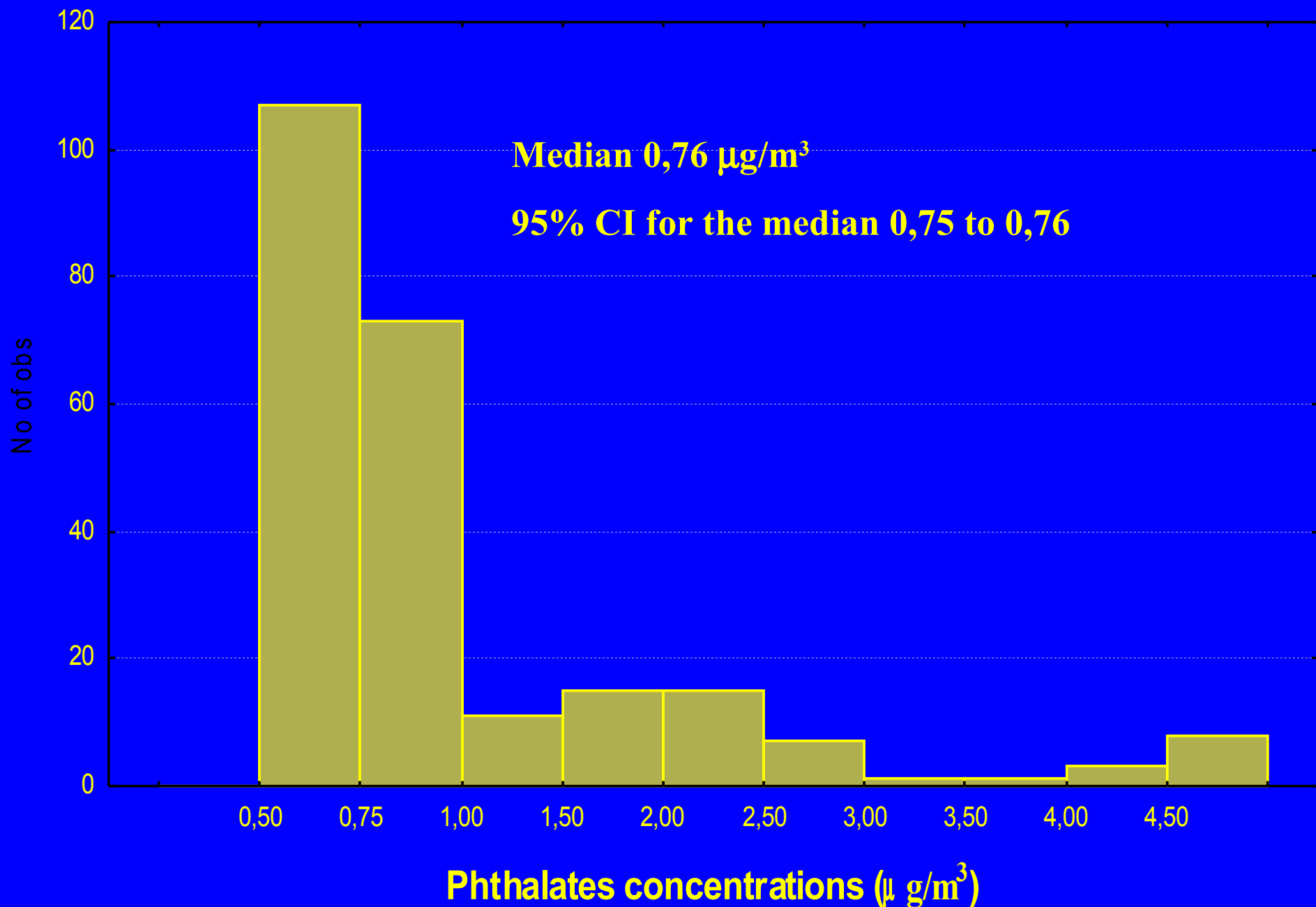
Interviews on prenatal and perinatal exposure and nutrition



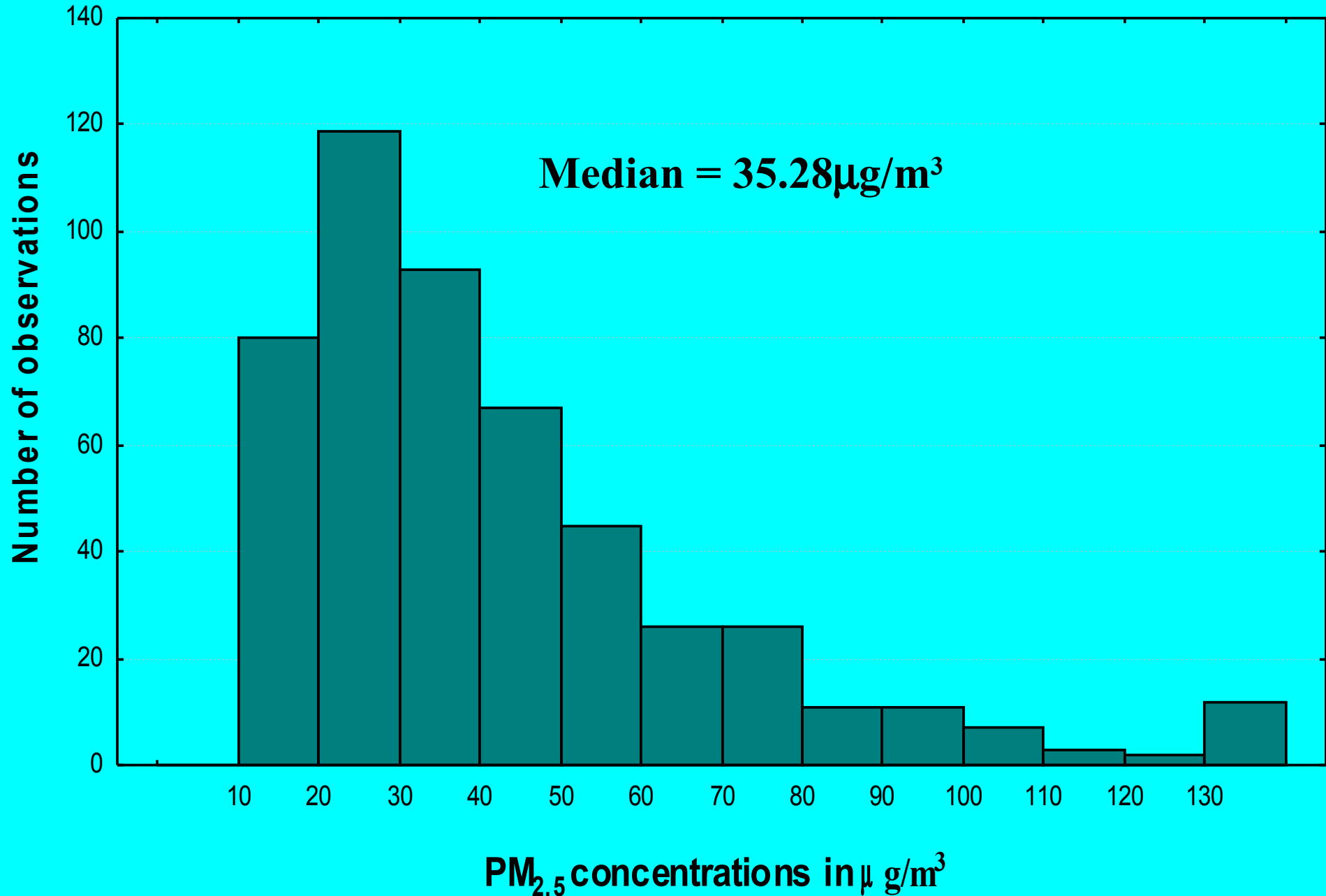
Pumps operated continuously at 2 L/min collecting particles $\leq 2.5 \mu\text{m}$ in diameter on precleaned quartz microfiber filter, and semivolatile vapours and aerosols on a polyurethane foam (PUF) cartridge backup.

The PUF and filters were once a month shipped to Southwest Research Institute, Texas, USA, where they were analysed for the di-cyclo-hexal phthalate (DCHP).

Personal exposure to phthalates measured in the second trimester of pregnancy



Personal exposure to PM_{2.5} measured in the second trimester of pregnancy

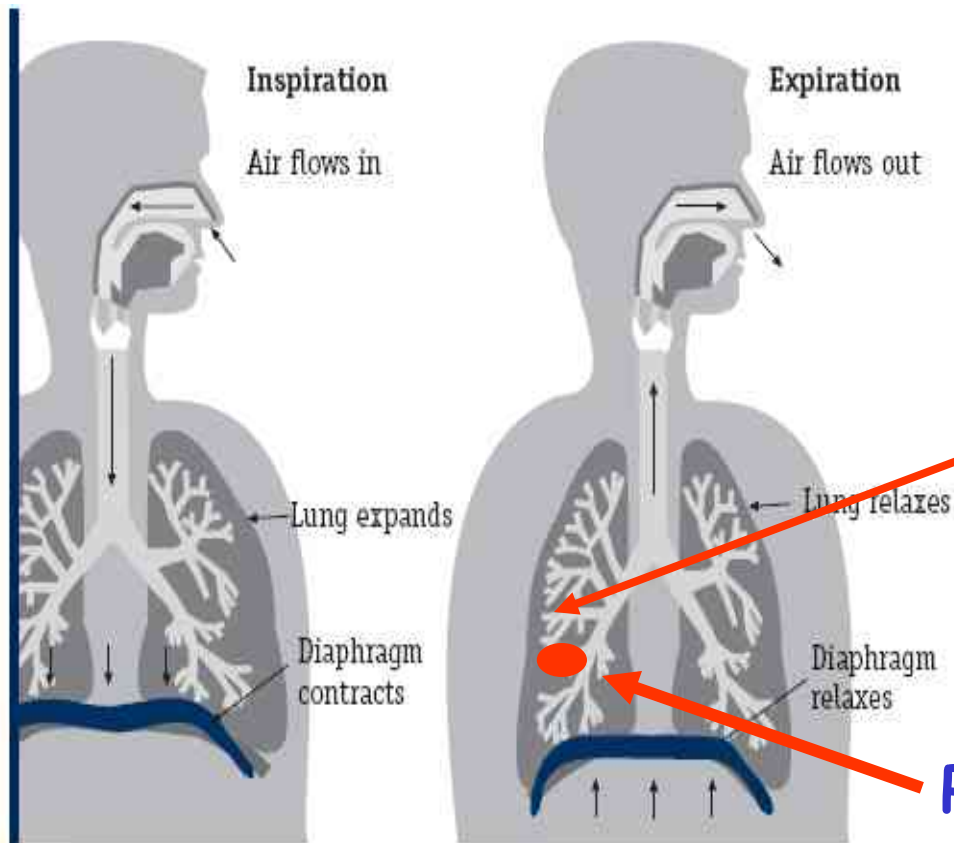


Adjusted odds ratios and 95% confidence intervals (CIs) for incidence of wheezing for phthalate exposure (log-transformed) estimated from the multivariate logistic regression model.

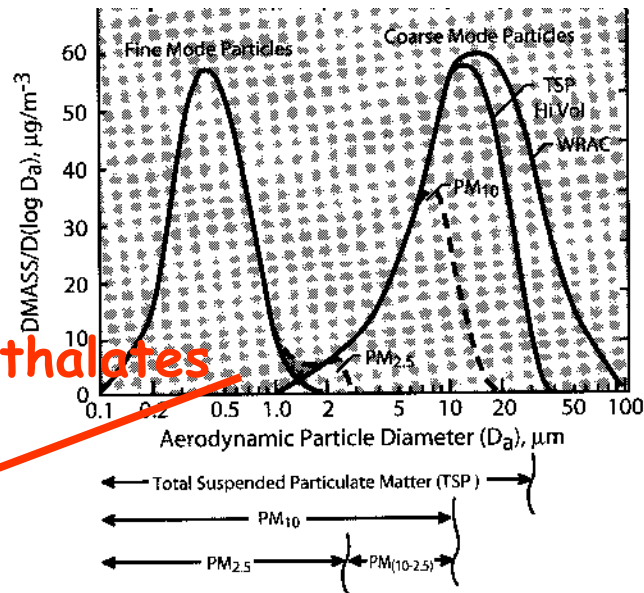
Predictor variables	Coefficient	St. Error	OR	95% CI
Maternal education (years)	0.0519	0.062	1.05	0.93 – 1.19
Gender of child (Girls)	0.0728	0.318	1.08	0.58 – 2.01
Maternal atopy	-0.1653	0.380	0.85	0.40 – 1.79
ETS	0.8543	0.373	2.35	1.13 – 4.91
Moulds at home	1.9480	0.686	7.01	1.81 – 27.1
Log (PM2.5)	-0.5062	0.645	0.60	0.17 – 2.15
Log (Phthalates)	1.4920	0.606	4.45	1.35 – 14.7

Adjusted incidence risk ratios (IRR) and 95% confidence intervals (CIs) for duration of wheezing in the follow-up period due to phthalate exposure (log-transformed) estimated from the multivariate Poisson regression model (with inclusion in the model of wheezing in the first three months of age)

Predictor variables	IRR	Std. Err.	z	P>z	[95% Conf. Interval]	
Wheezing in the first 3 months of life	1.05	0.001	35.17	0.000	1.05	1.05
Moulds	4.48	0.448	14.98	0.000	3.68	5.45
ETS	1.21	0.134	1.73	0.084	0.97	1.50
Maternal education	1.02	0.028	0.90	0.368	0.97	1.08
Parity	1.19	0.053	4.02	0.000	1.09	1.30
Gender of child	0.86	0.060	-2.35	0.019	0.73	0.97
Gestational age	1.01	0.024	0.41	0.685	0.96	1.06
Maternal atopy	1.64	0.125	6.46	0.000	1.41	1.90
PM2.5 (log)	1.67	0.206	4.14	0.000	1.31	2.13
Phthalate (log)	2.28	0.078	24.22	0.000	2.13	2.44



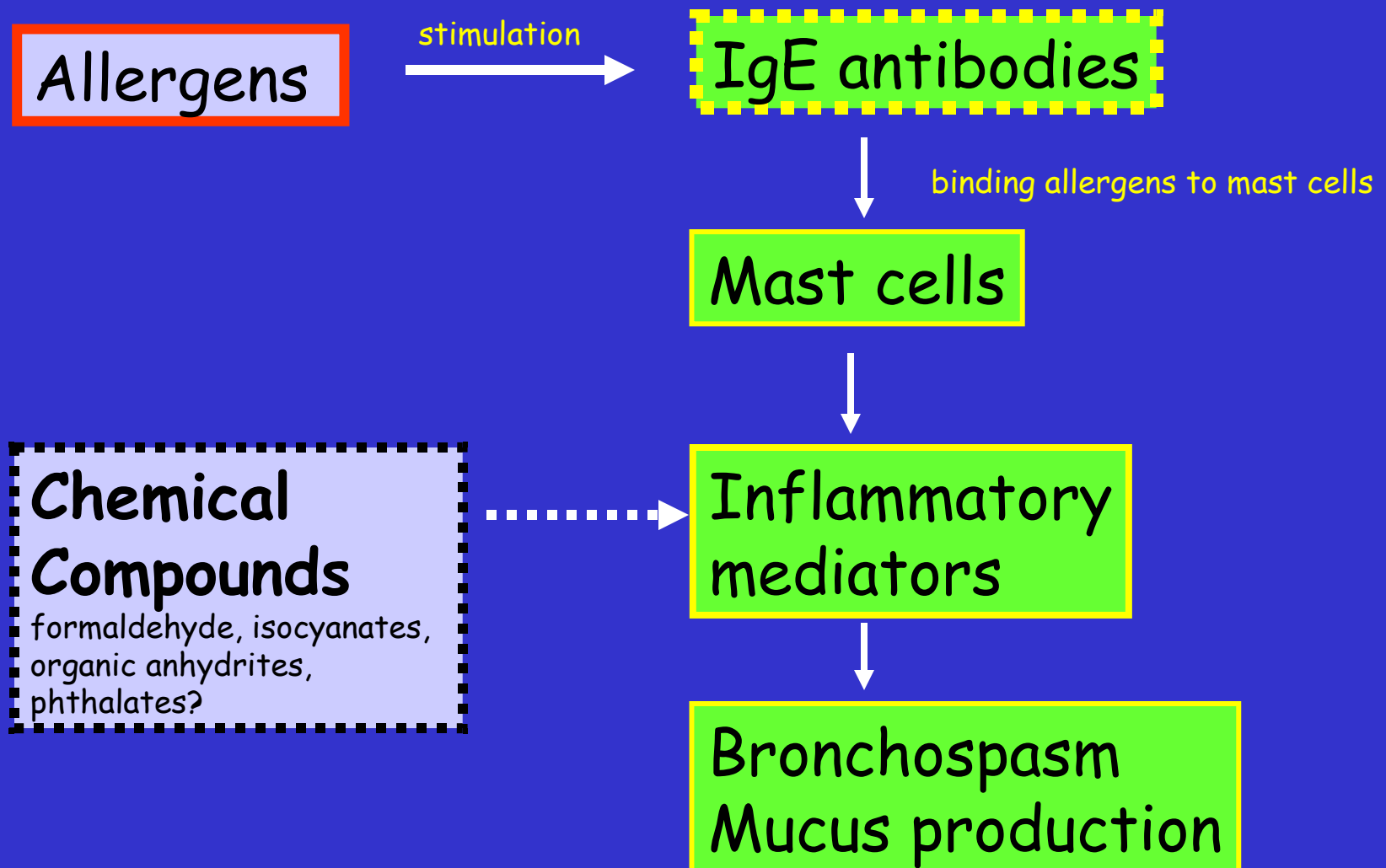
phthalates

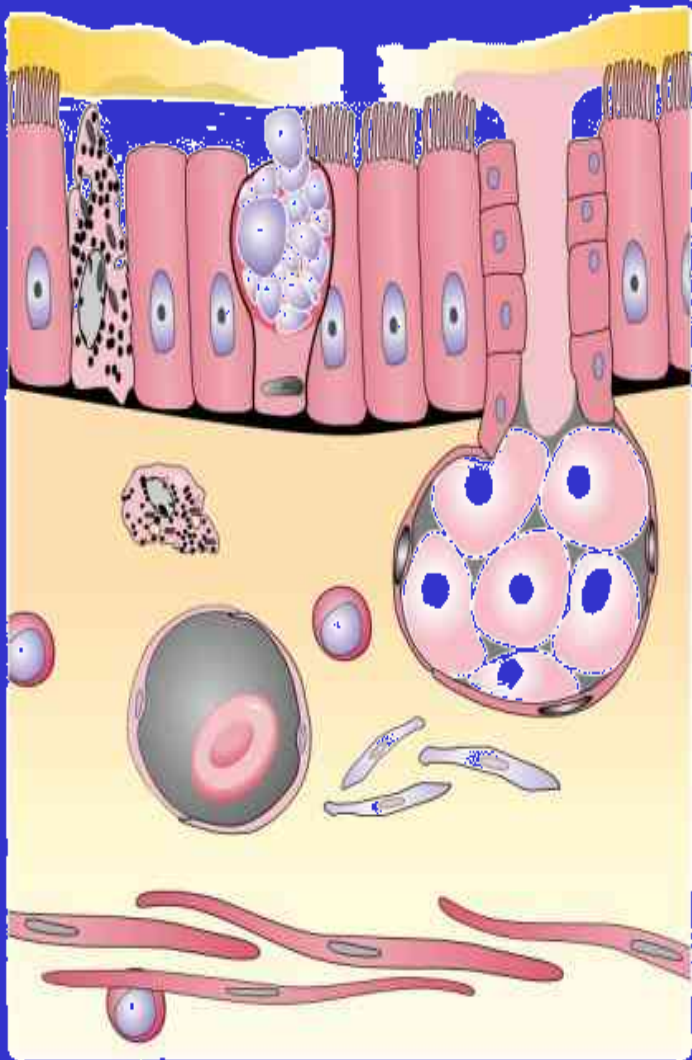


Average child breathes over 5 cubic metres of air every day. DEHP exposure would be in the range 0.4 - 5.5 $\mu\text{g}/\text{day}$ (mean 1.85 $\mu\text{g}/\text{day}$).

Phthalates penetrate deeply in the bronchial tree and alveoli and are very slowly removed from the lungs.

Inflammation of airways is an important part of the mechanism of asthma and other respiratory health outcomes





Hydrolysis products of DEHP mimics inducing prostaglandins (PG) and thromboxanes in the lungs, thereby increasing inflammation in the airways, which is characteristic of asthma.

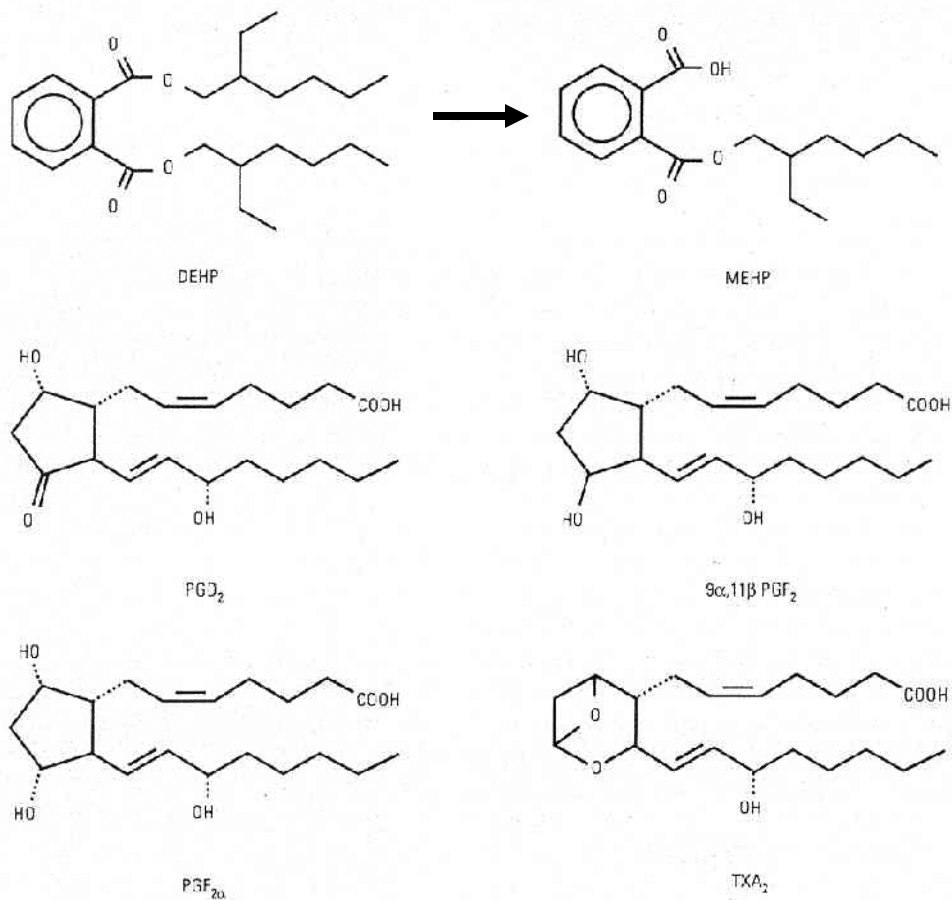


Figure 3. Structural similarities between proposed xenobiotics (DEHP and MEHP) and inflammation prominent mediators as prostaglandins and thromboxanes. Abbreviations: DEHP, di(2-ethylhexyl) phthalate; MEHP, mono(2-ethylhexyl) phthalate; PGD₂, prostaglandin D₂; 9 α ,11 β PGF₂, 9 α ,11 β prostaglandin F₂; PGF_{2 α} , prostaglandin F_{2 α} ; TXA₂, thromboxane A₂.

Conclusions:

1. The results of the Krakow study highlight the importance of prenatal exposure to phthalates and to $PM_{2.5}$ in the occurrence of respiratory inflammatory symptoms during early infancy and show that this effect is independent of the postnatal air indoor quality (environmental tobacco smoke and/or moulds in the households)

2. Since the phthalate exposure of children is worldwide, the results of the study have global implications and may better explain the increasing worldwide trends in the occurrence of respiratory problems in children than classical air pollutants, which has been declining over the last 10 years.

The old paradigm, developed over four centuries ago by Paracelsus, was that "the dose makes the poison". However, for exposures sustained during early development, the most important issue is that "the timing makes the poison". This extended paradigm deserves wide attention to protect the fetus and child against preventable hazards.

(Faroe PPTOX Conference , May, 2007)

That's all, thanks

