Environmental factors and child health

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Outline

- Why children are different
- Main environmental risk factors and their effects on child health
- A closer look at neurotoxicity

- Environmental burden of disease study
- Children’s environment and health action Plan for Europe

Why children are different

Children are **uniquely susceptible** and may be **more exposed** to many environmental factors

- rapidly developing organs and systems are uniquely **susceptible** to toxicants
- specific behaviours make children **more exposed** to several environmental toxicants
- early exposure gives time enough for **long latency** agents to produce adverse health effects
- children are less aware and have **less control** over their environment than adults

Children are not little adults

Giotto, National Gallery, Washington DC

- **Until recently, childhood environmental health risks were considered as scaled down risks from adult occupational risks**

Types of risk differences between children and adults

- Differences in *susceptibility* may be *qualitative* or *quantitative*, i.e. they may regard the *nature* or the *amount* of the effect
- Differences in *exposure* are essentially quantitative

Qualitative differences in susceptibility

- During growth and development organs and systems have unique periods of high vulnerability (*critical windows).* In these periods, exposure to xenobiotics may produce adverse effects *that have no counterpart in adult life* (e.g. birth defects, neurodevelopmental disorders, etc.)
- The concept of windows of susceptibility is particularly important since it shows that the *timing* of the exposure may be critical

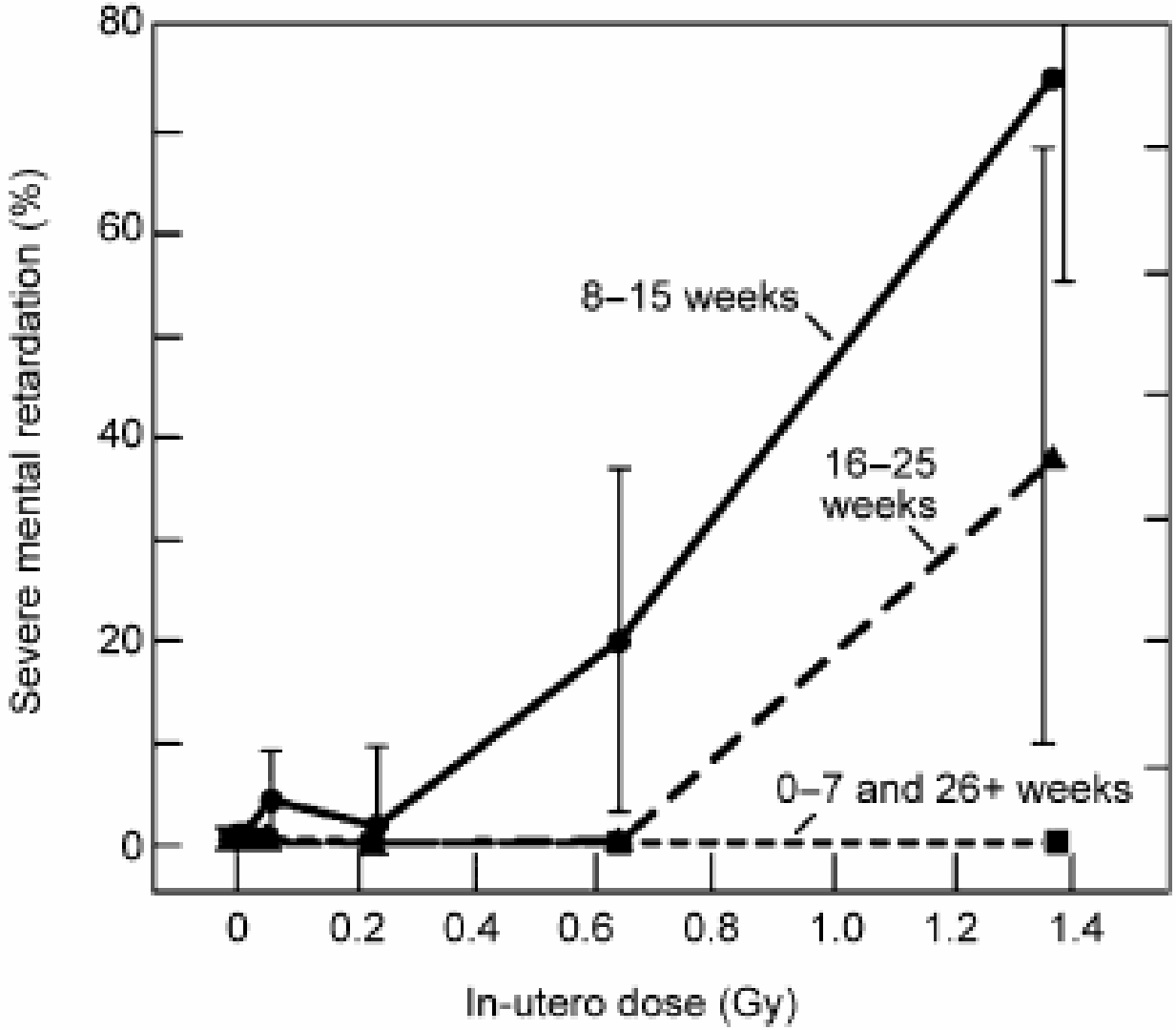


Fig. 5.1. Mental retardation in the atomic bomb in-utero study according to fetal dose and postconception age at irradiation.

Biological effects after prenatal irradiation (embryo and fetus). Ann ICRP 2003; 33: 5-206.

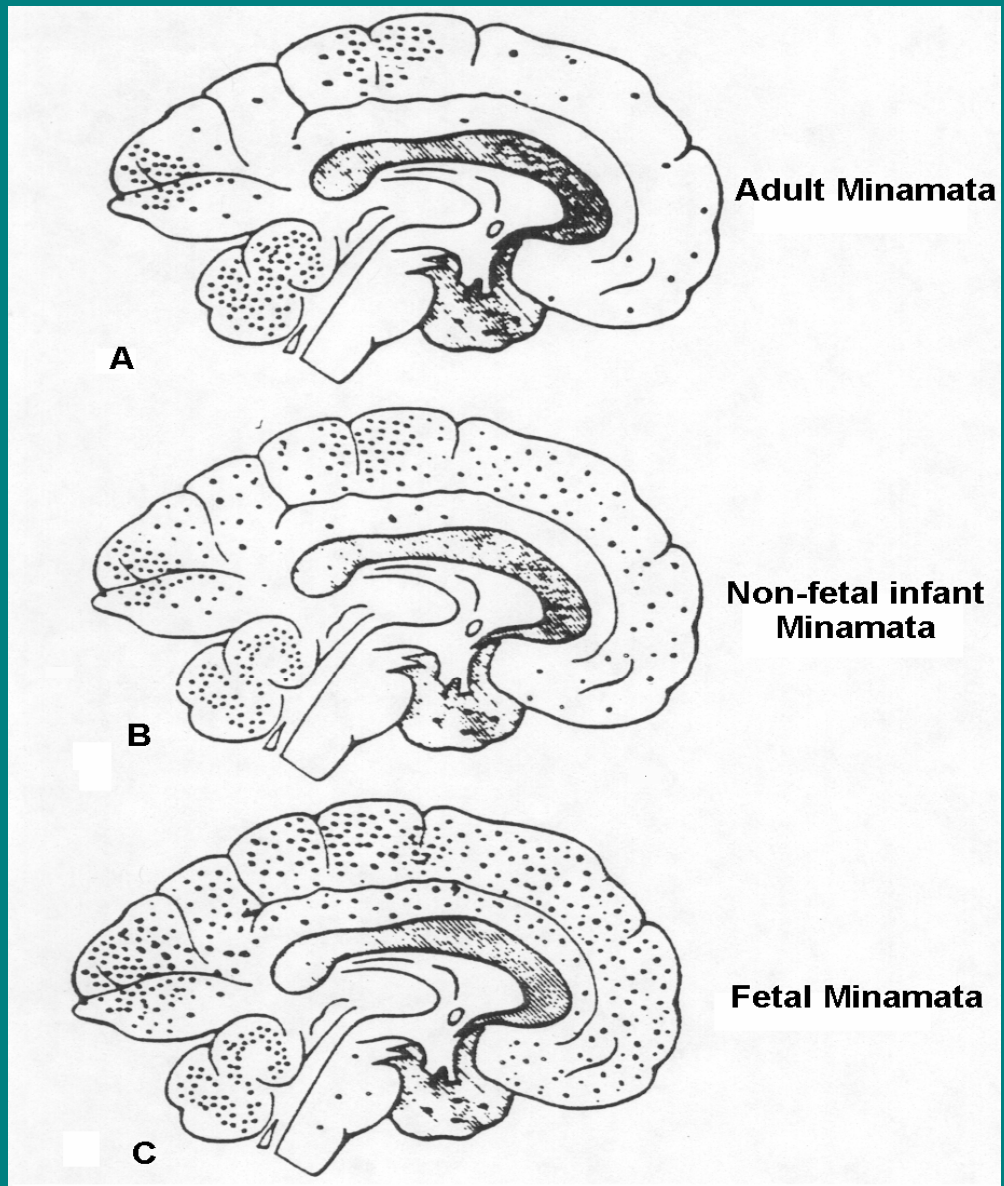


FIG 1: Comparison of the distribution of lesions among the adult (A), non-fetal infantile (B), and fetal infantile (C) Minamata disease. Takeuchi (67), with permission.

From: Choi, BH. Progress in Neurobiology, 32: 447-490, 1989.

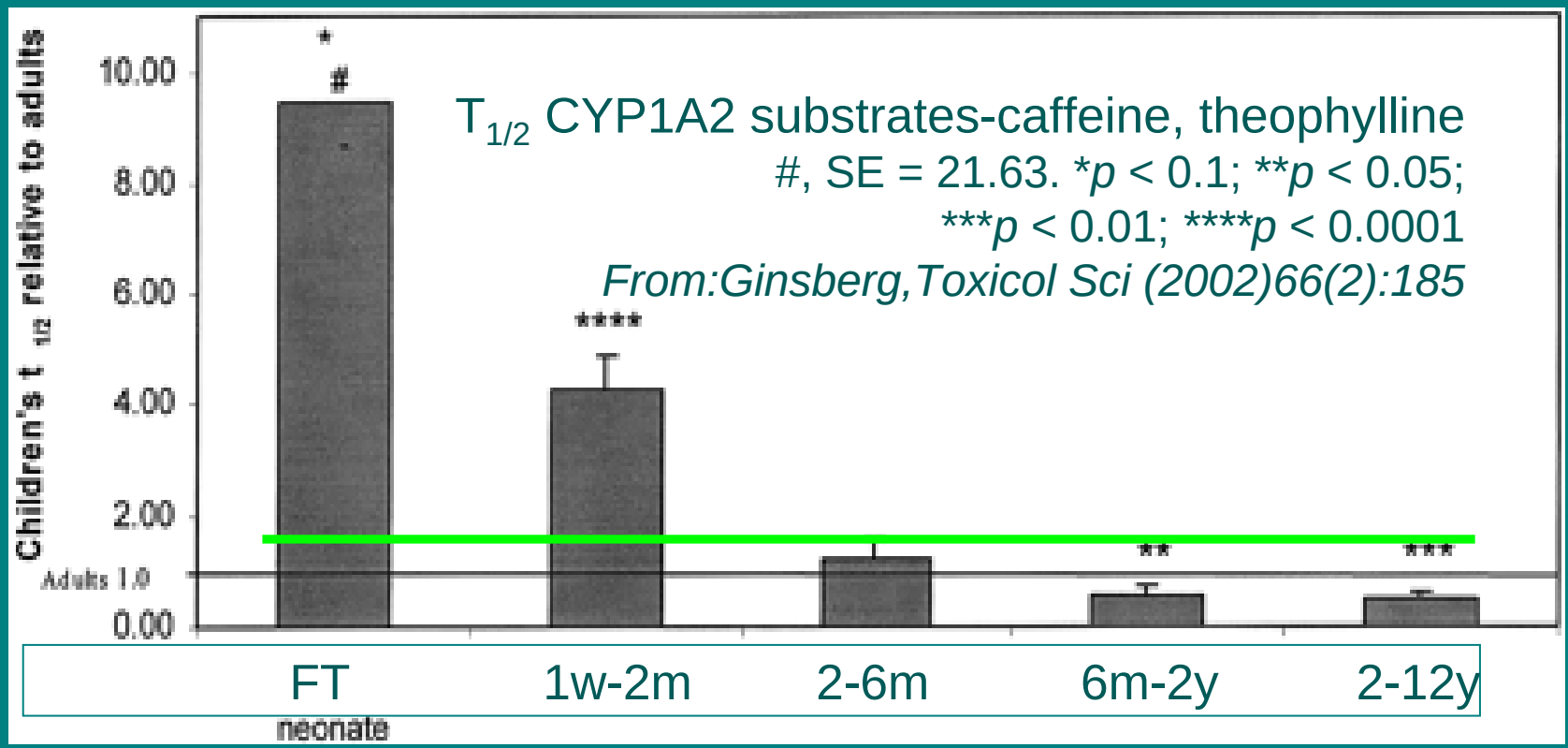
Quantitative differences in susceptibility

- **During fetal life and the first months, the ability to absorb, metabolize and eliminate xenobiotic compounds is still immature and differs from that of adults.**
- **These differences are based on complex mechanisms so that metabolic immaturity may play a role *in different ways* with respect to toxicity (e.g. increasing or decreasing it)**

Xenobiotics like Pharmaceutical Agents may be handled differently by an immature body.

- **Biotransformation**
  - Activation/Detoxification
- **Distribution**
  - Fat/Water
  - Blood-Brain Barrier
- **Elimination**

Immature metabolism : lessons from Pharmaceuticals



$T_{1/2}$ CYP1A2 substrates-caffeine, theophylline

#, SE = 21.63. *p < 0.1; **p < 0.05; ***p < 0.01; ****p < 0.0001

From:Ginsberg,Toxicol Sci (2002)66(2):185

- **High Variability even for closely related drugs**
- **Neonate/adult difference for caffeine 13X greater than for theophylline**

Generalizations are not possible!

Differences in exposure: biological factors

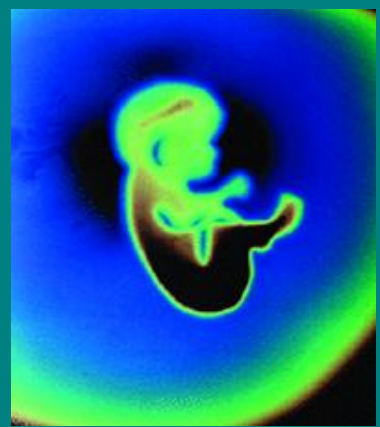
- Unique exposures (transplacental, breastfeeding, pica)
- Higher absorption (first months)
- Higher intake (per body weight) of air, water and food (first years)
- Longer time of exposure (higher risk of long term effects)

Transplacental Exposure

Lessons From Pharmaceuticals: Thalidomide, DES (diethylstilbestrol)

- **Many pollutants cross via the placenta**
  - Lead, mercury, PCBs (polychlorinated biphenyls)…
- **Some pollutants may affect the fetus directly**
  - Ionizing radiation, heat

Maternal exposures matter!



EHP

Higher intake: comparison of child to adult intake of various media

Child (< 1 year) to Adult Ratio

- **Air** **2.3**
- **Water/fluids** **4.8**
- **Food** **6.3**

Derived from data in: US Environmental Protection Agency (1997), National Research Council (1993) and Gephart et al. (1994).

Differences in exposure: social and psychosocial factors play a bigger role in children

- **greater importance of parental knowledge and attitudes**
- **greater importance of health care quality**
- **peculiar behaviour (e.g. hand-to-mouth, crawling, etc.)**
- **greater differences in risk of morbidity and mortality among children (10:1 poor to rich ratio) than among adults (2:1 ratio)**

As a consequence: greater *vulnerability to environmental hazards*

Combined and aggregate exposure

children may be exposed to the same chemical from multiple sources (*aggregate exposure*. e.g. lead, pesticides) but also be exposed simultaneously to several compounds with similar modes of action (*cumulative exposure*) with additive, or multiplicative, toxic effects (e.g. air pollutants)

Pesticides

Susceptibility

- qualitative differences: likely (immuno and neuro-toxicity)
- quantitative differences: variable (children can be more or less sensitive), usually 2-fold, up to 10-fold, limited to the first 6 - 12 months

Exposure

- can be up to 10 times higher (due to greater food intake and to combined exposures)

Lead

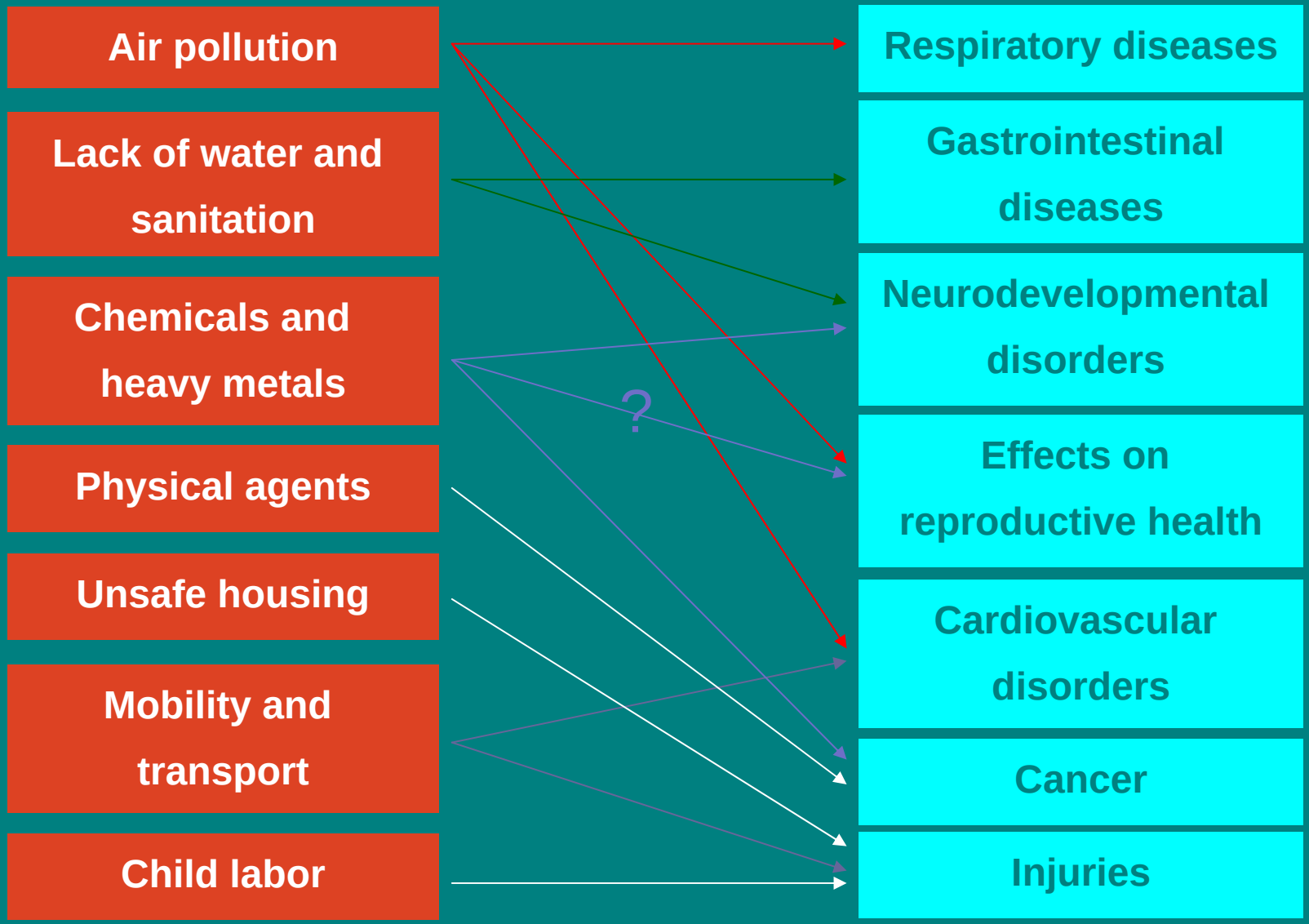
Susceptibility

- qualitative differences: yes (neurodevelopmental effects)
- quantitative differences: up to 5 times higher for acute and chronic toxic effects which are also observed in adults

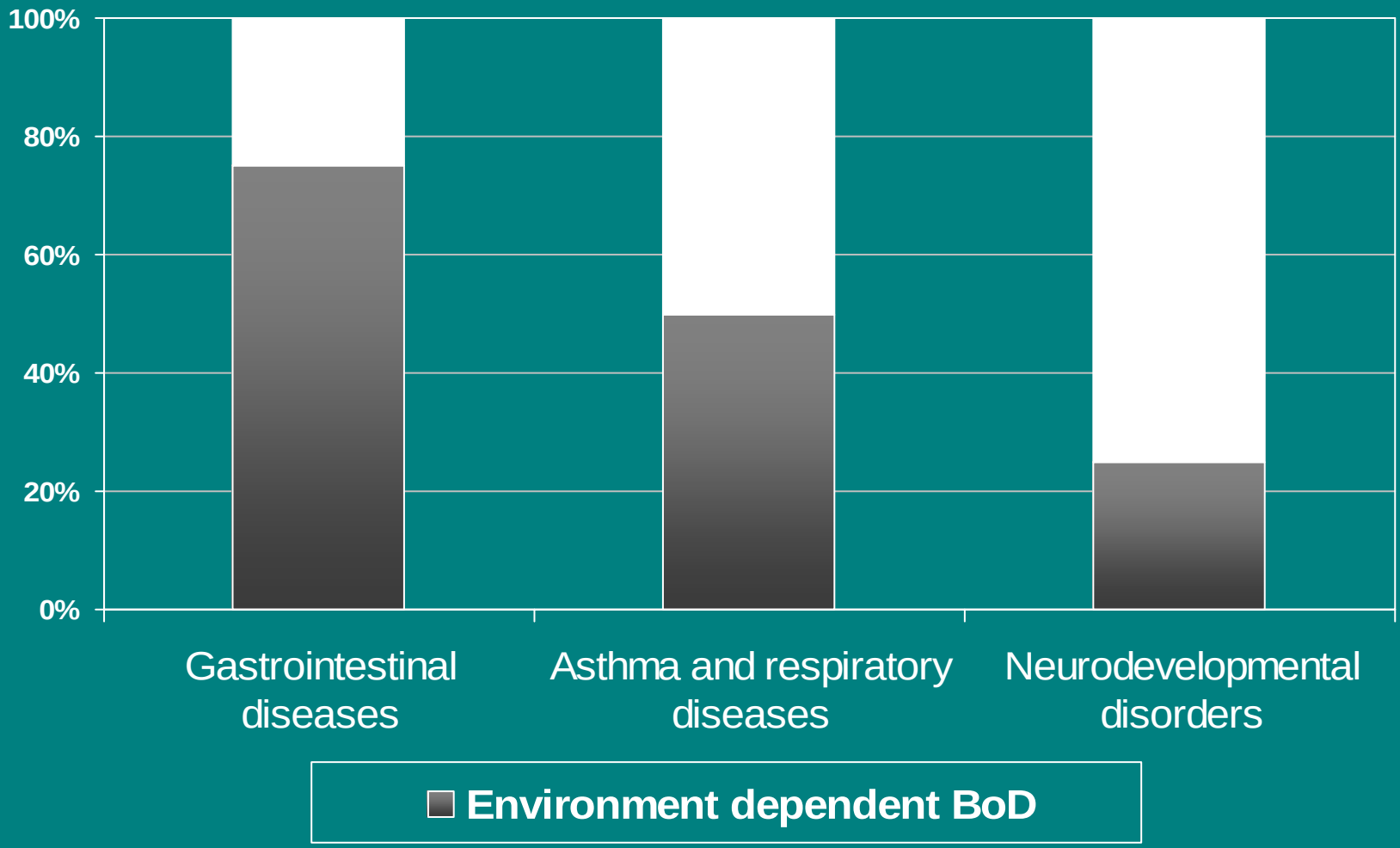
Exposure

- can be up to 10 times higher (increased absorption and accumulation, combined exposures) in exposed groups

What we know: main links between EFs and health effects



What we know: the fraction of disease which can be attributed to one (or more) environmental factors varies



- **A closer look at neurotoxicity**

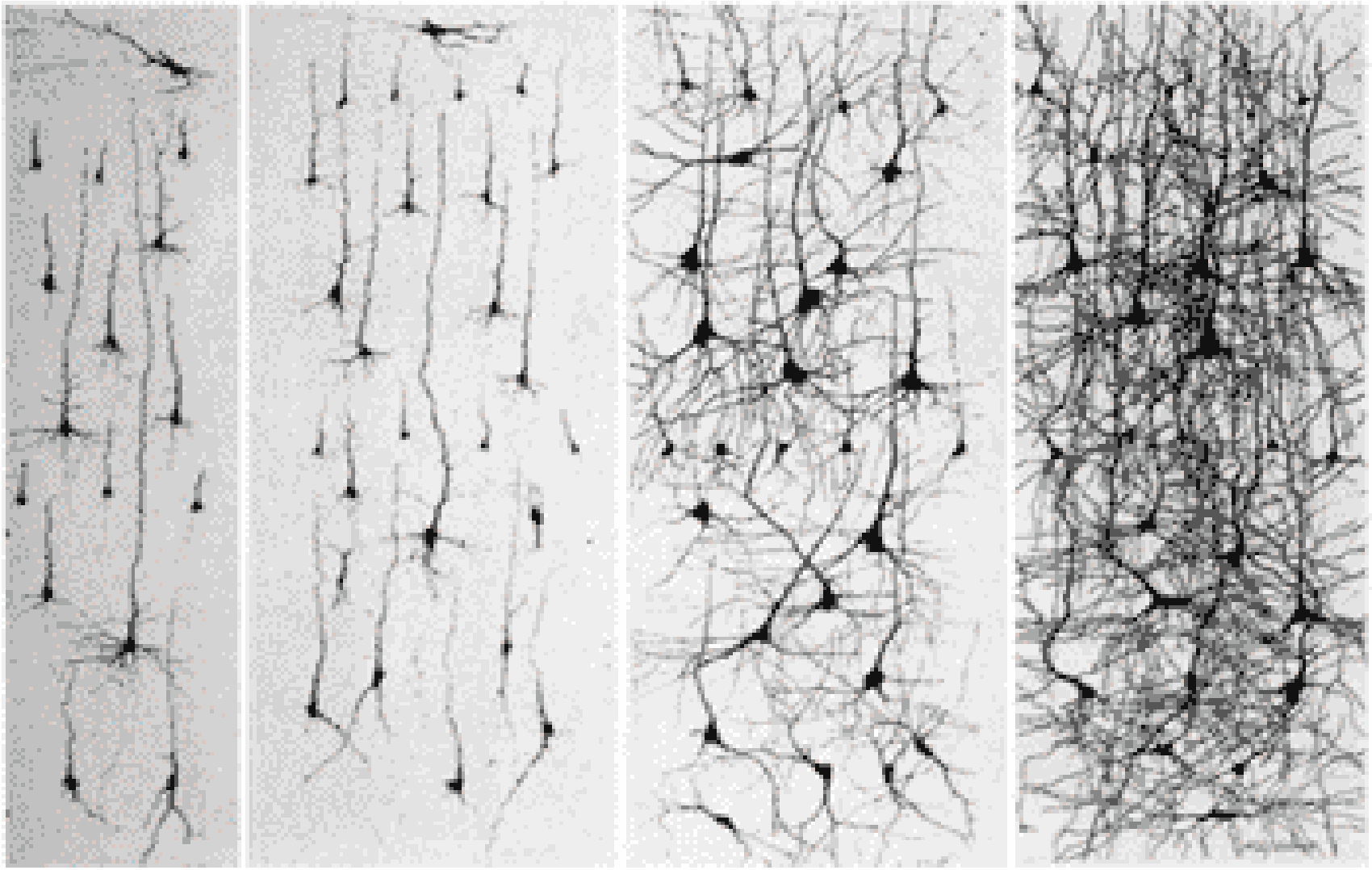
Known Environmental Causes of Neurodevelopmental Disorders

- Lead
- Methyl Mercury
- Polychlorinated Biphenyls (PCBs)
- Certain Pesticides (Probably)

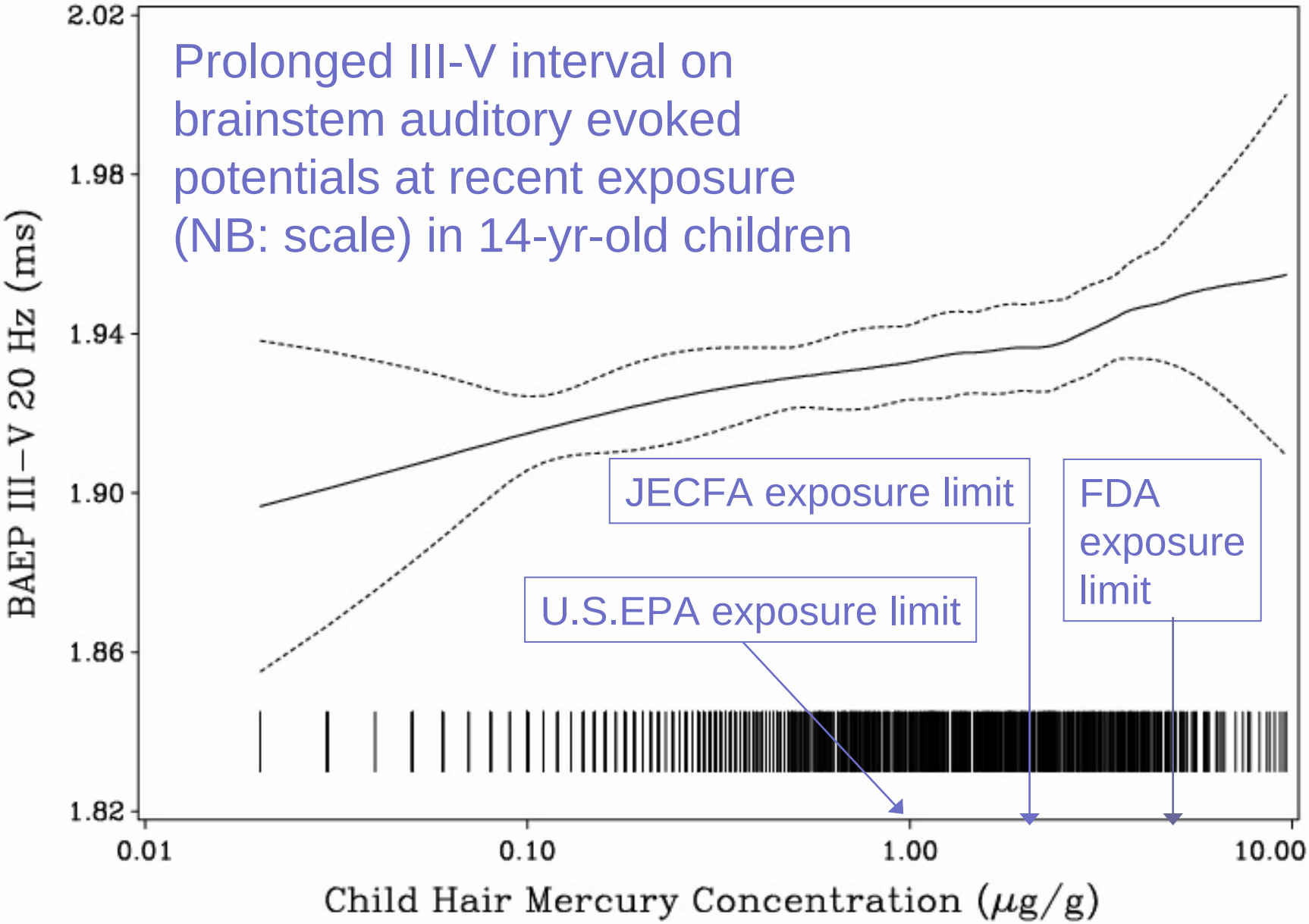
causes of vulnerability of young children to neurotoxicants

- Brain development is maximal in the first 2 years
- Exposure to maternal accumulated toxicant burdens during gestation
- After birth exposure to toxicants may continue via human milk and/or food (higher metabolic rate, water intake, oxygen uptake, energy requirment)
- Synergic effects with other causes of impaired development (parental neglect, malnutrition etc.)

A Child's Brain Development Over Time



Newborn 1 month 6 months 2 years



Murata et al., Journal of Pediatrics, February 2004

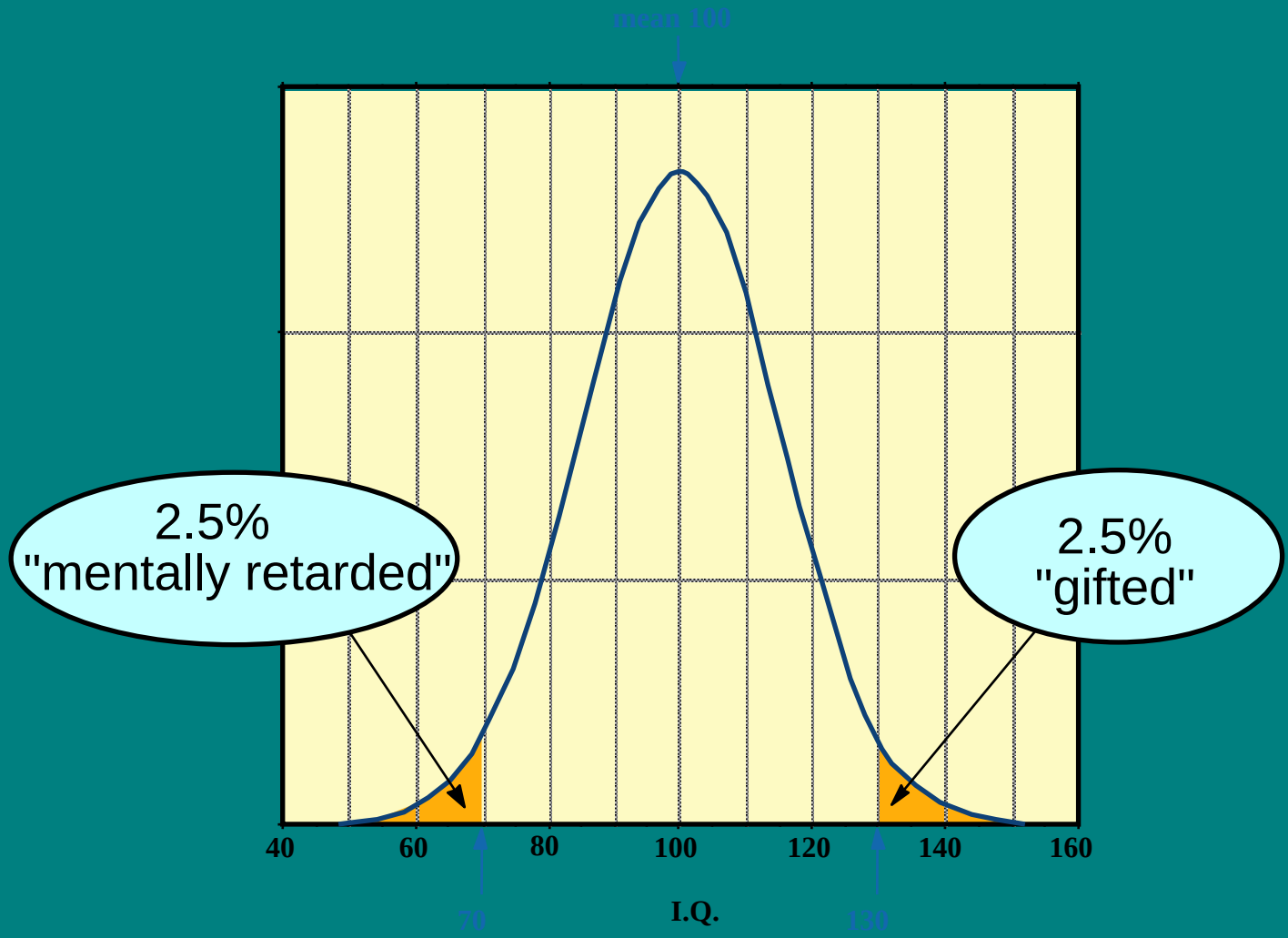
The Spectrum of Neurotoxicity

Neurodevelopmental disability is not limited to clinically obvious conditions.

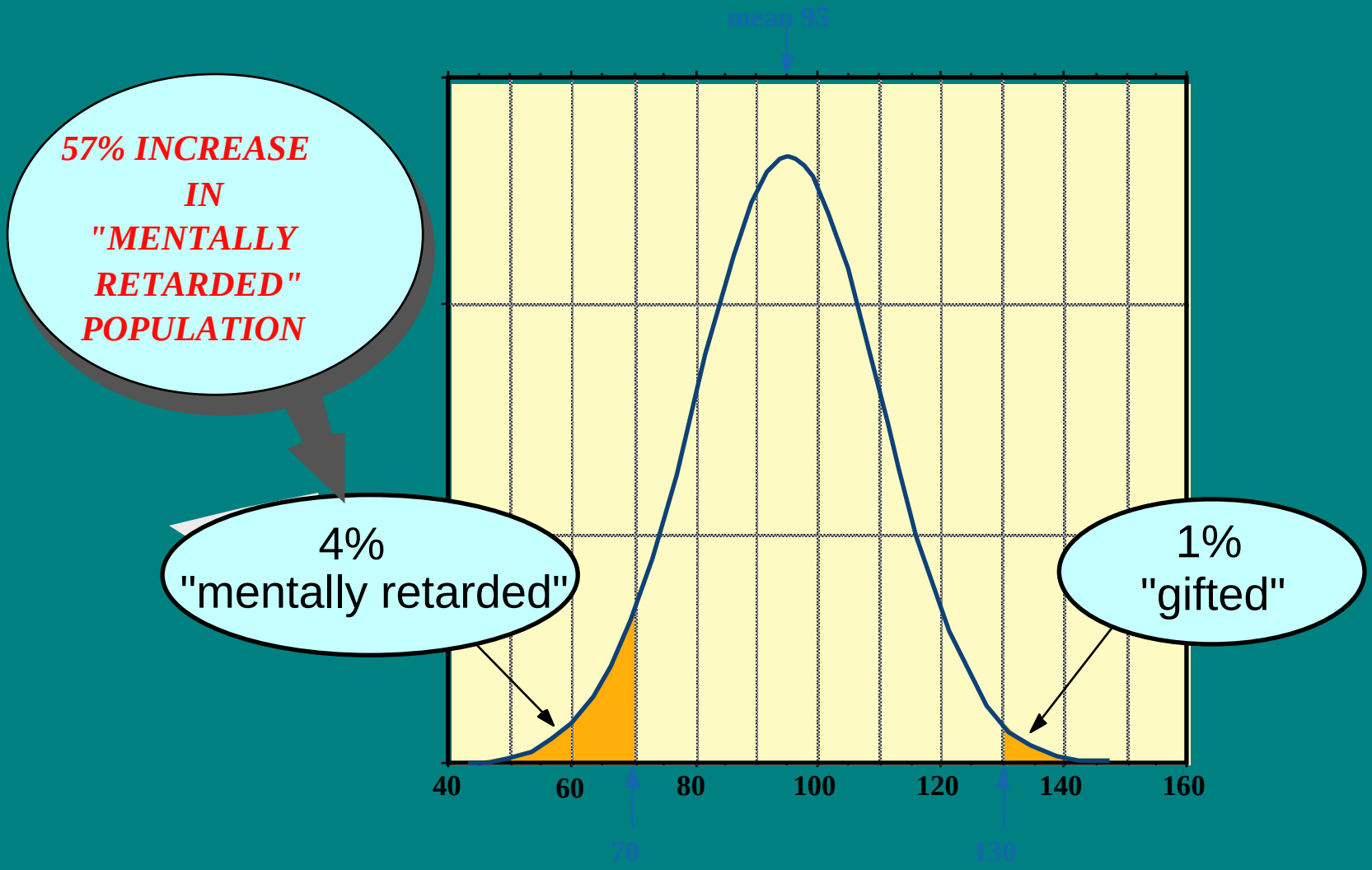
It also includes an entire spectrum of diminished function, termed *subclinical toxicity*.

Widespread subclinical neurotoxicity can affect the health, well-being, intelligence and even the security of an entire nation

The “normal” IQ distribution

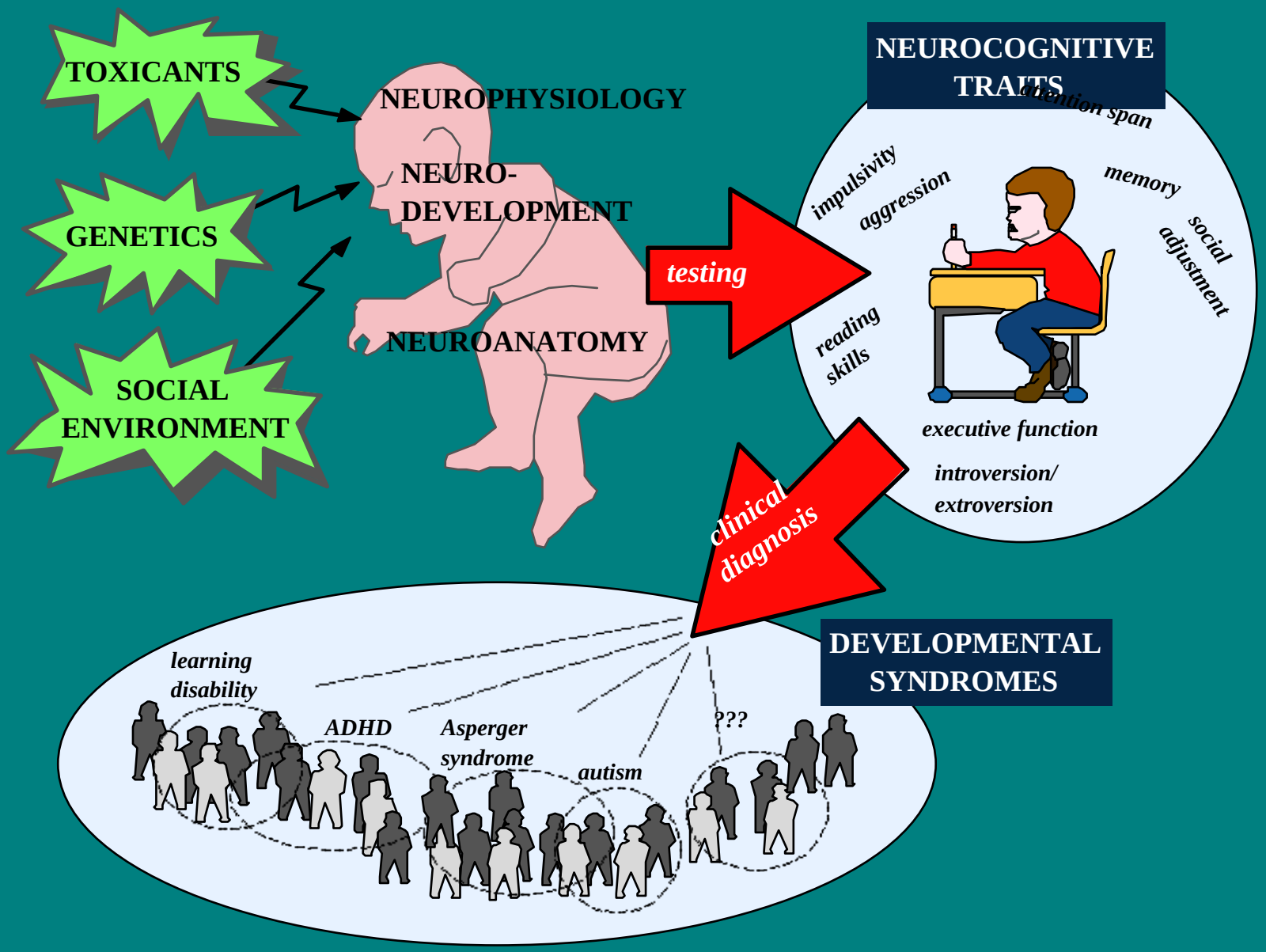


Effects on IQ distribution of < 5 point decrease in mean IQ (i.e. the effects of blood lead levels > 10 ug/dl in young children

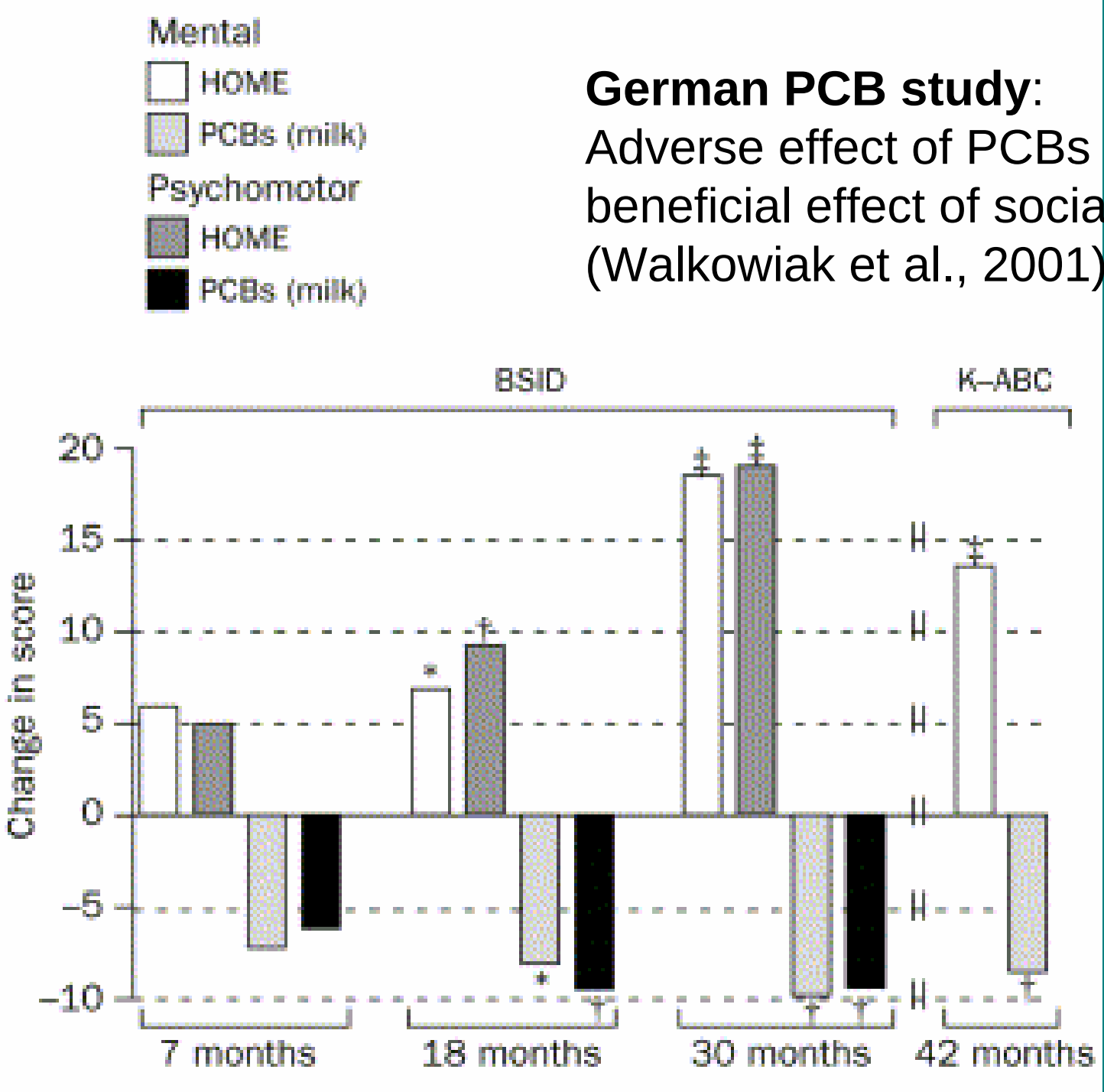


(IHW.A.04a.c)

Framework For Understanding



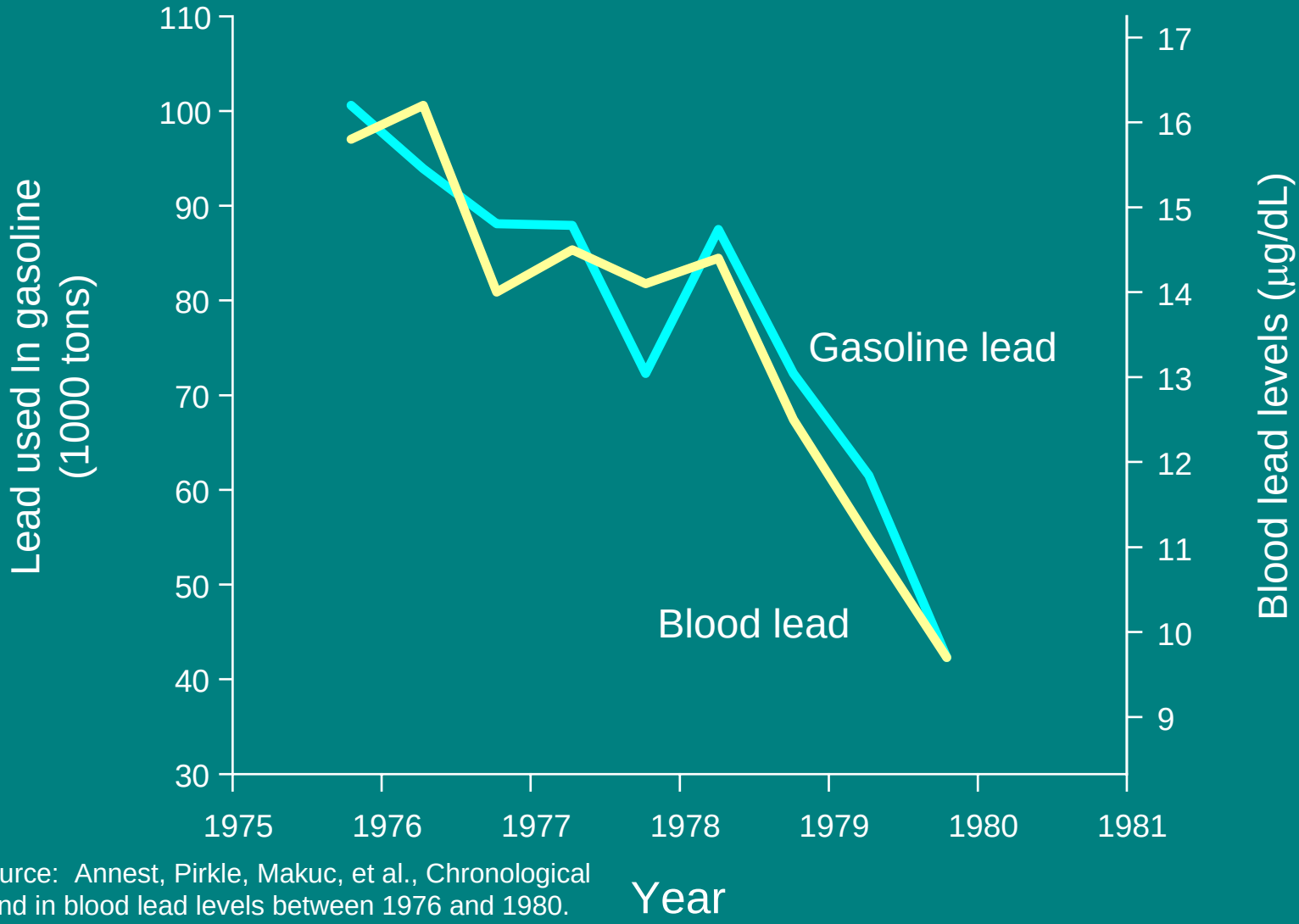
German PCB study:
Adverse effect of PCBs similar to beneficial effect of social environment (Walkowiak et al., 2001)



K-ABC was significantly affected by postnatal exposure

Lead in gasoline and lead in blood

NHANES II, 1976-1980



Source: Annest, Pirkle, Makuc, et al., Chronological trend in blood lead levels between 1976 and 1980. NEJM 1983; 308;1373-7.

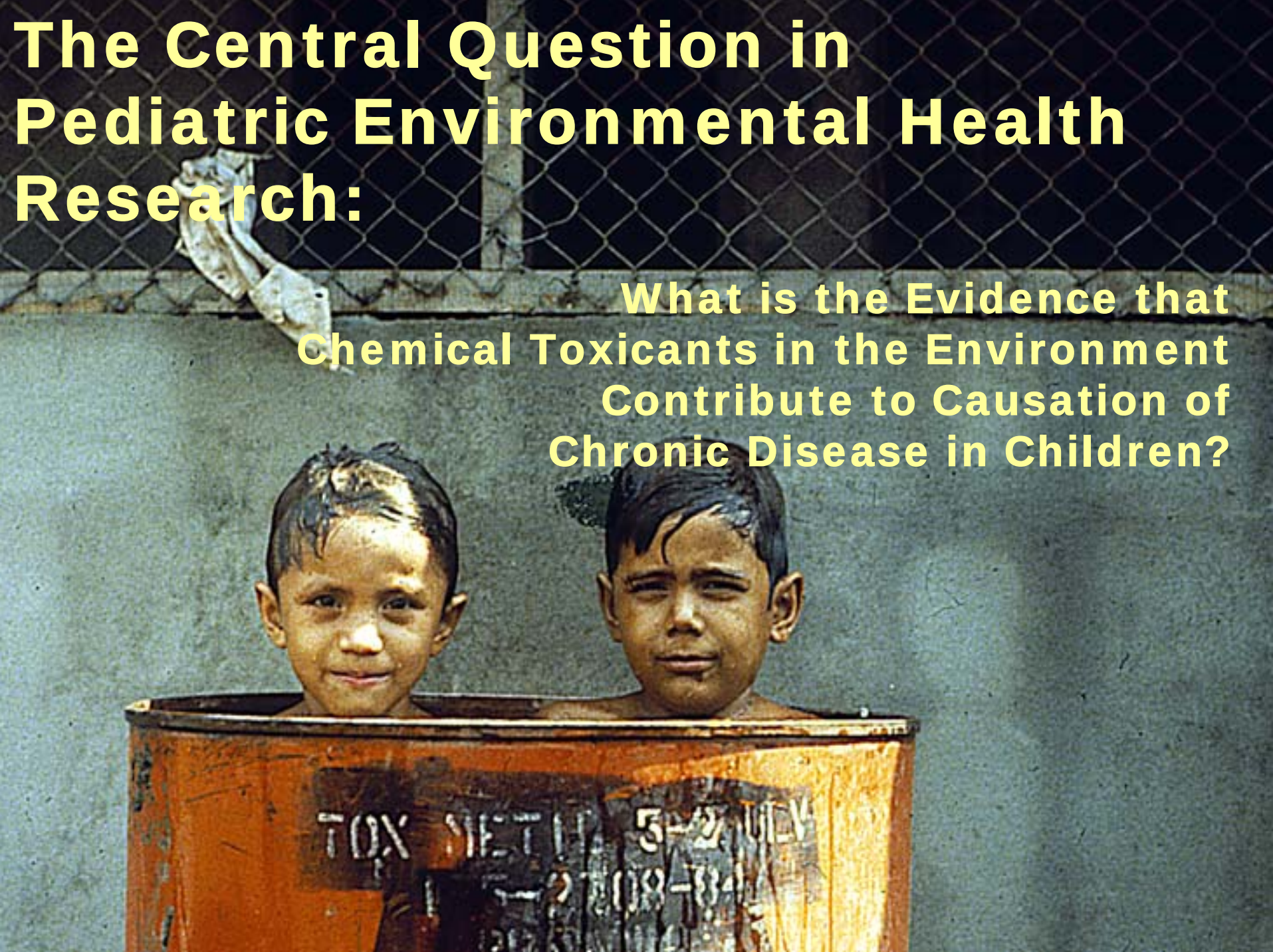
Early Exposure to Neurotoxins May Increase Risk of Degenerative Disease in Later Life

- Alzheimer's disease
- Parkinson's disease

An emerging area of research

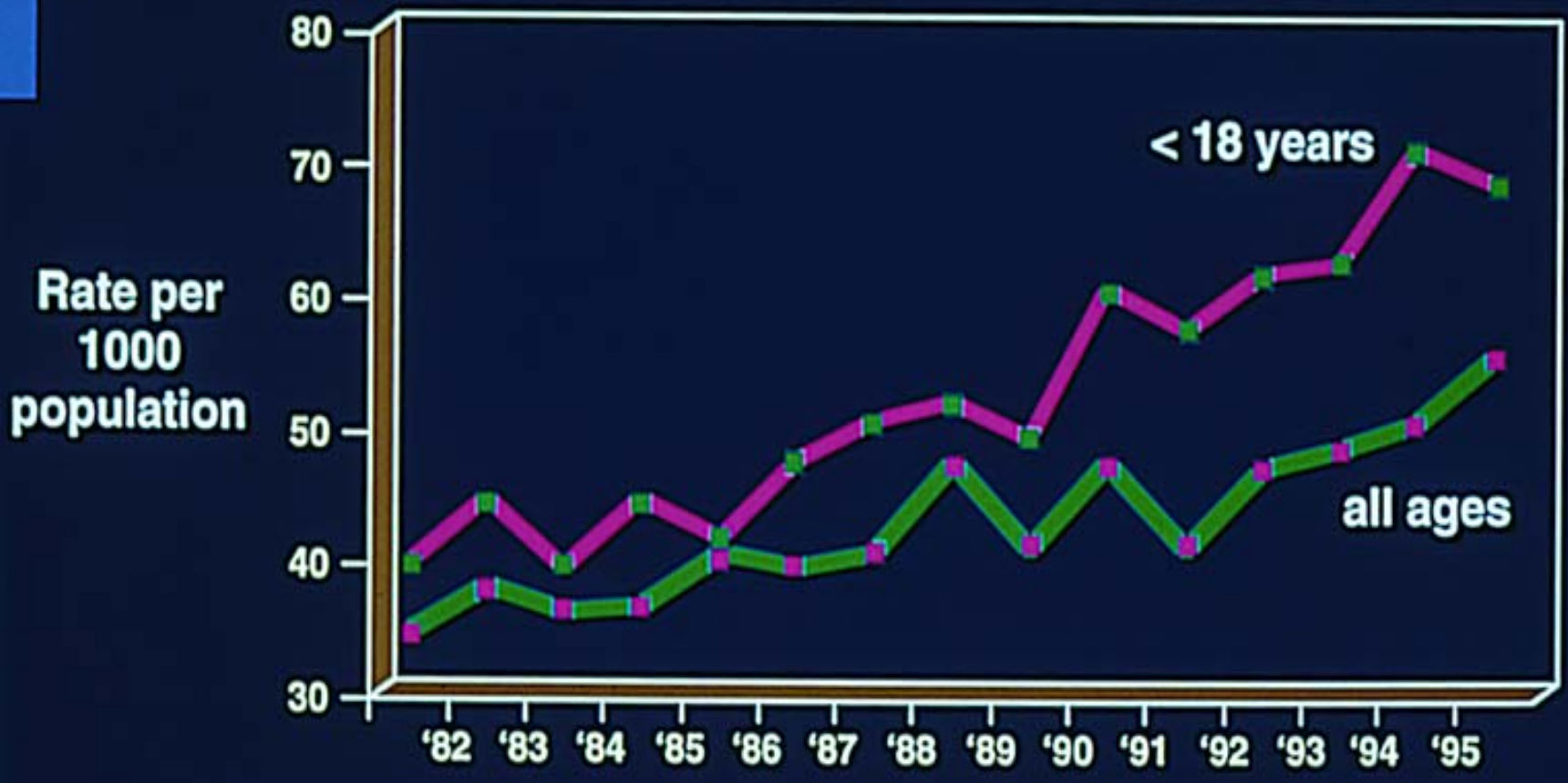
The Central Question in Pediatric Environmental Health Research:

What is the Evidence that Chemical Toxicants in the Environment Contribute to Causation of Chronic Disease in Children?



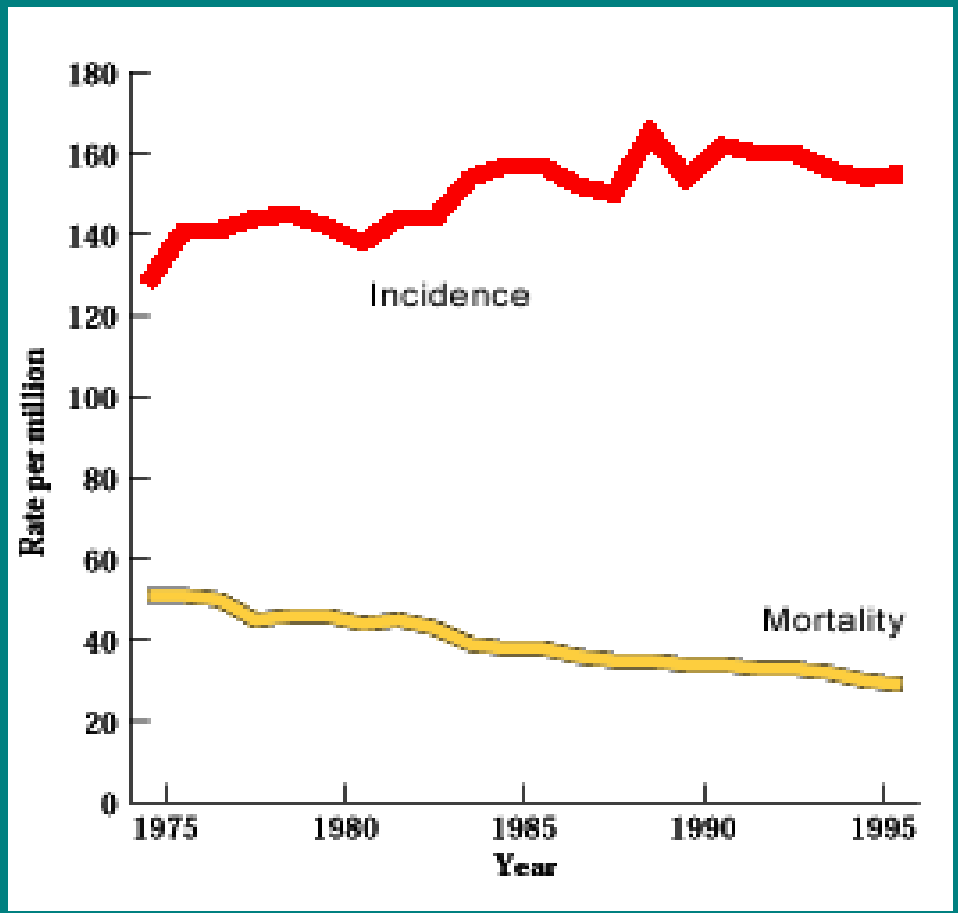
Office of Children's Health Protection

Prevalence Rates for Asthma by Age and Year, United States, 1984-1994



Source: Centers for Disease Control & Prevention

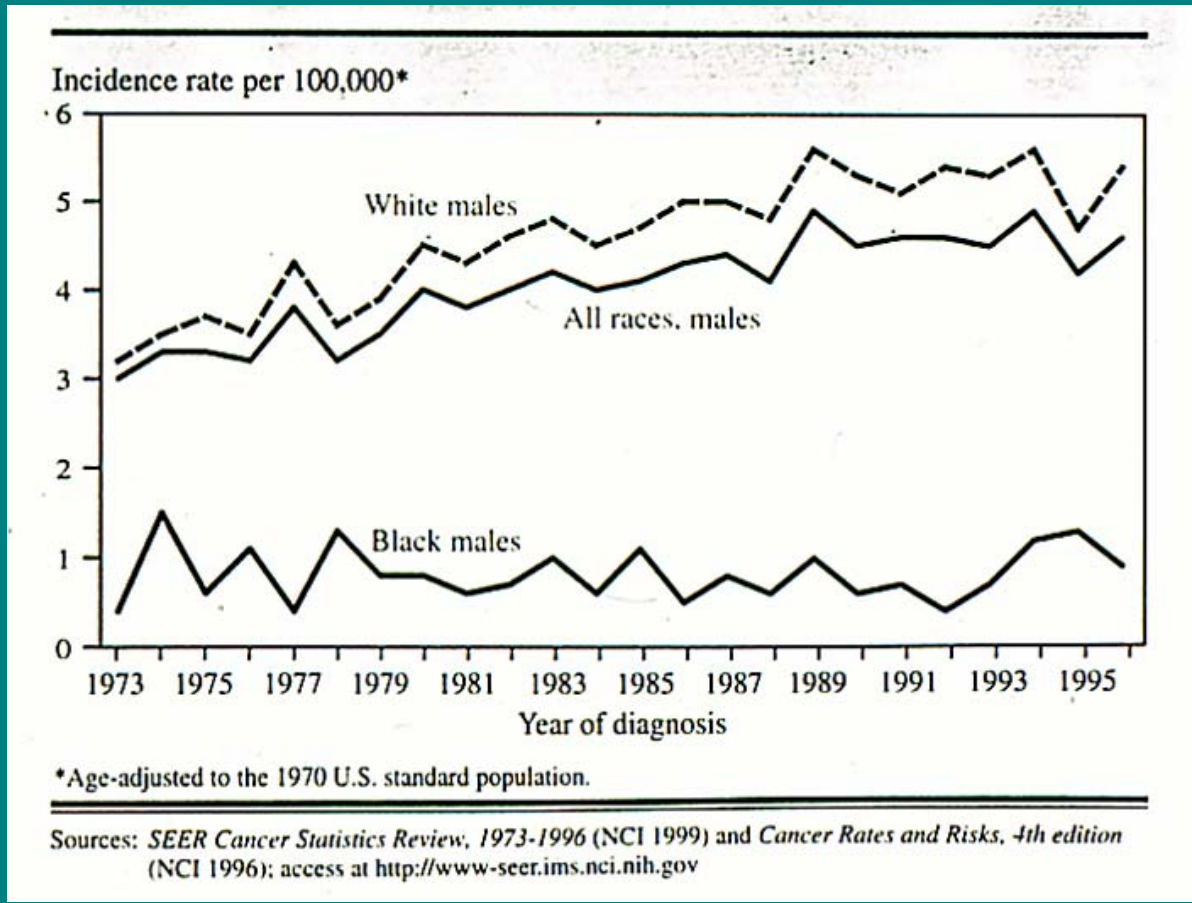
Childhood Cancer Incidence and Death Rates, 1975-1996



Source: Pediatric Monograph 1999, Surveillance, Epidemiology, and End Results Program Division of Cancer Control and Population Sciences, National Cancer Institute.
American Cancer Society, Surveillance Research

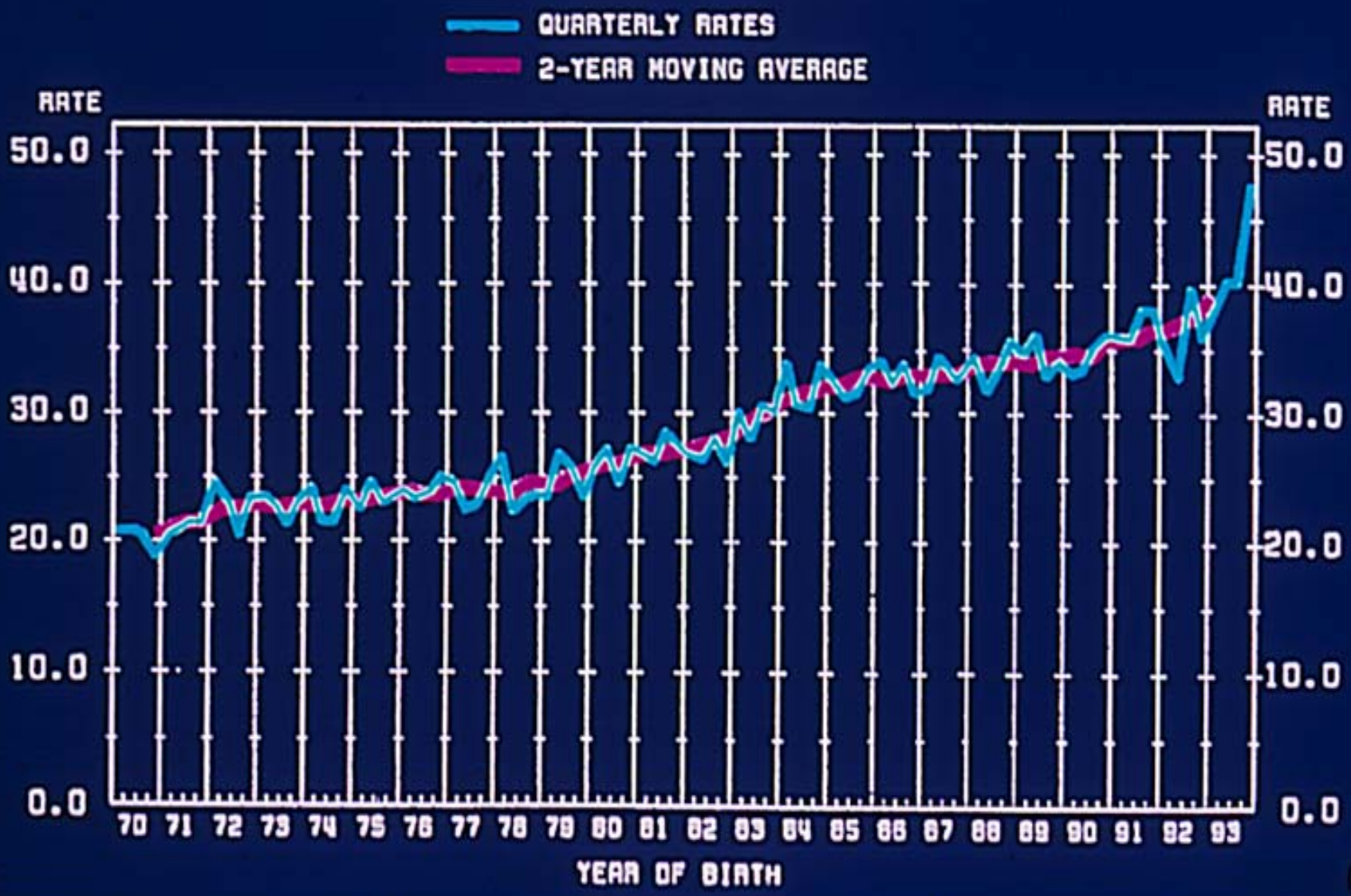
Incidence of Testicular Cancer

The overall incidence of testicular cancer rose substantially in the United States from 1973 to 1996. Specifically rates in white males increased 51.2% over that period, while rates for black males rose only 17.3% (the latter increase was not statistically significant). While undescended testes, inguinal hernia, and prenatal factors have been implicated as possible risk factors, the cause of the trend in unknown.



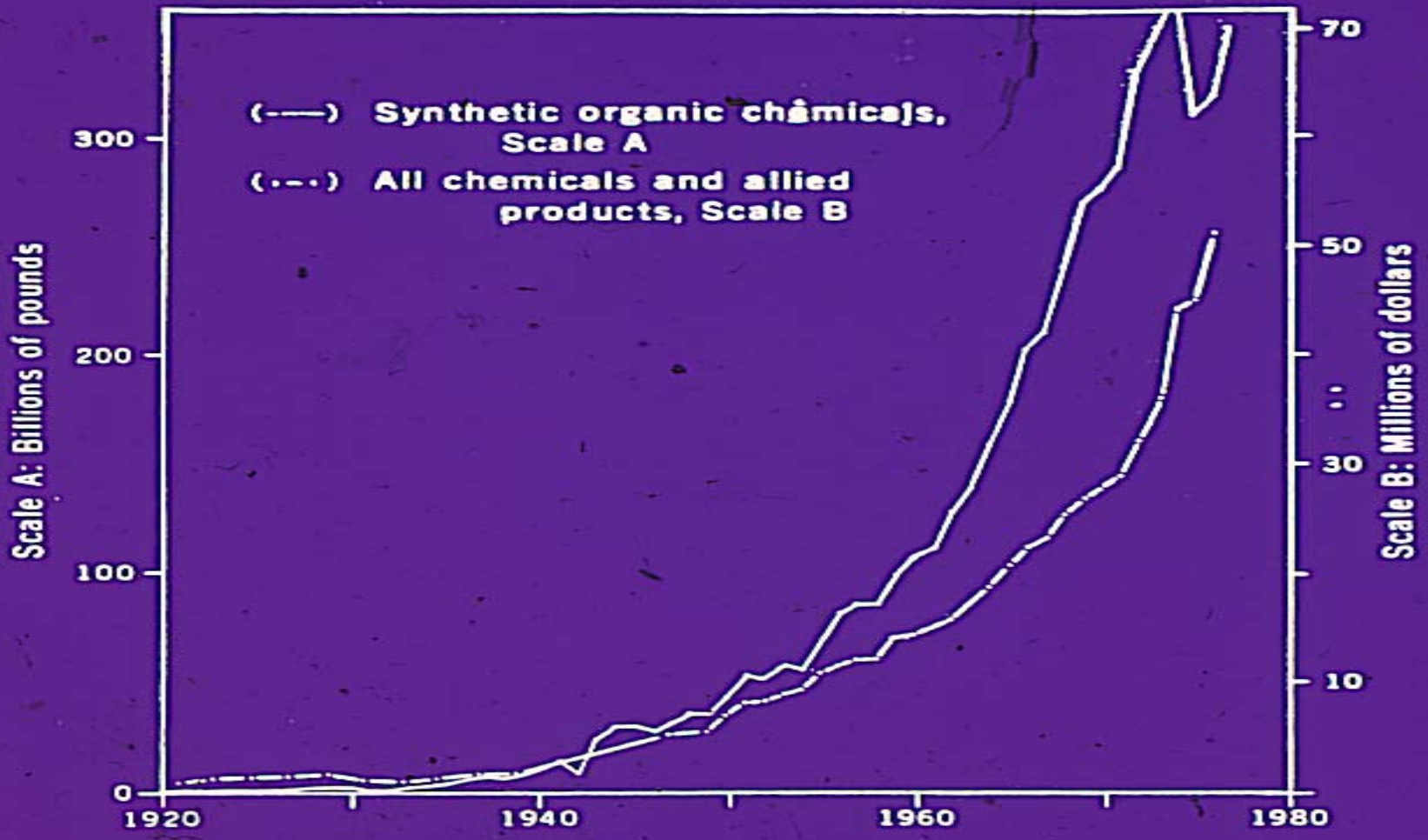
HYPOSPADIAS/EPISPADIAS

TRENDS IN REPORTED INCIDENCE, BY QUARTER OF BIRTH,
BIRTH DEFECTS MONITORING PROGRAM / CPHA
JAN 1970 - DEC 1993
(RATES PER 10,000 TOTAL BIRTHS)



CDC

Synthetic Organic Chemical Production



. Total synthetic organic chemicals production (excluding tar, tar crudes, and primary products from petroleum and natural gas). Total chemicals and allied products, annual value added.

Most chemicals to which children are exposed have not been adequately tested for toxicity

- 80,000 + chemicals in commerce
- 2,863 produced or imported in quantities of 1 million pounds or more per year (high production volume [HPV] chemicals)
- No basic toxicity information is publicly available for about half of HPV chemicals
- Information on developmental toxicity is publicly available for fewer than 20% of HPV chemicals

--EPA: Chemical Hazard Data Availability Study, 1998

Existing areas of uncertainty: a. causality links

- **Effects which may arise only for exposure during very narrow susceptibility windows, particularly *in utero,* may be missed by toxicology testing due, for example, to differences in sensitivity and to different (i.e. more closely spaced) susceptibility windows between animals and humans.**
- **Effects that have a very long (i.e. several decades) latency period, that are prolonged into adult life or that can be observed only in the offspring (intergenerational effects) may also be missed.**

Existing areas of uncertainty: b. susceptibility

- **Existence of great variability in susceptibility to different toxicants among children of different age groups due to rapid changes in metabolism, distribution, excretion etc.**
- **Existence of genetic variability in susceptibility. Existence of biological factors (ex. nutritional status) that can modify susceptibility**

Existing areas of uncertainty: c. exposure

- **Variability in exposure among children of different age groups due to both biological factors (i.e. increased absorption, usually limited to the first 6 months, but possibly extending to later ages in particularly susceptible children) and behavioural patterns**
- **Wide variability in exposure among children with different socio-economic and cultural background**

Existing areas of uncertainty: d. risk characterisation

- **When exposure to an hazardous agent is sufficient to produce toxicity, the ultimate health effect can be *magnified* by factors that, in children to a much greater extent than in adults, can increase susceptibility (i.e. concomitant disease or malnutrition) and/or overall vulnerability (i.e. lack of adequate care seeking and/or access to quality health care) and/or modify the ultimate effect (e.g. quality of parenting).**
- **This is particularly important because it introduces further factors of variability with respect to socio-economic and cultural factors (exposure scenarios).**

The Environmental Burden of Disease (EBD) study

- **While there is a fair – but still insufficient - amount of knowledge on causal links between environmental factors and effects on child health, we do not know enough to which extent children are exposed to the various environmental factors and what is the magnitude of the health effects**

- **This information is of utmost importance since it is on this knowledge base that priorities can be set and appropriate policies identified**

The EBD study (Lancet, 2004)

ARTICLES

Burden of disease attributable to selected environmental factors and injury among children and adolescents in Europe

Francesca Valent, D'Anna Little, Roberto Bertollini, Leda E Nemer, Fabio Barbone, Giorgio Tamburlini

The study was aimed at estimating

- the burden of disease (deaths and DALYs) for **ARI, diarrhoea, mild mental retardation**
- attributable to selected major environmental risk factors (**outdoor air pollution, indoor air pollution, lack of water, sanitation and hygiene, lead**)
- and the burden of **injury**
- in the European region (**EurA, EurB, and EurC**)

The EBD study. Limitations and methodological challenges (1)

- The EBD study focused on a **limited number of disease outcomes and on specific age groups**, those for which strong evidence exists of an association and for which available data (on exposure and dose - response) are sufficient for large scale estimates

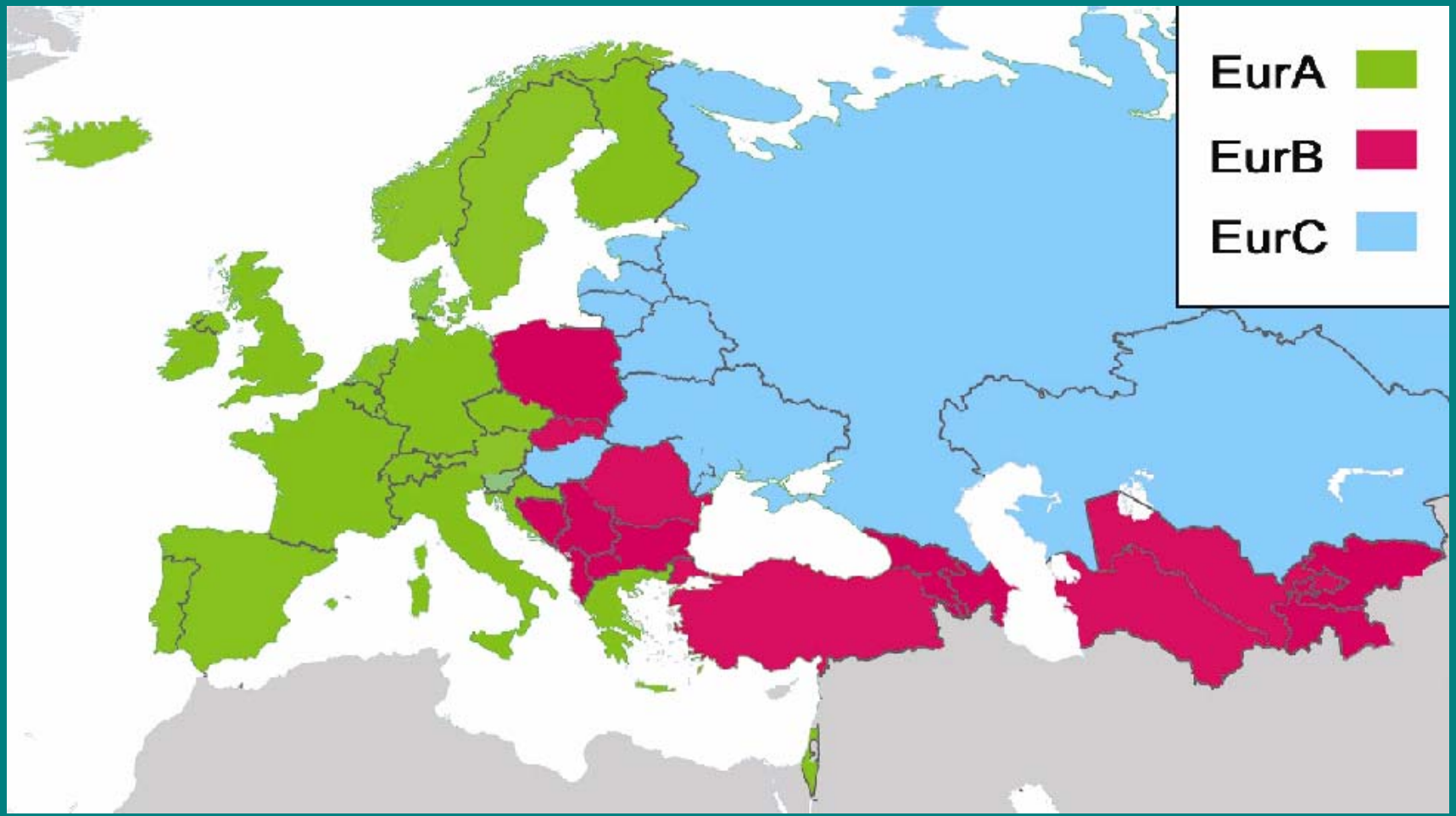
The EBD study. Limitations and methodological challenges (2)

- **GBD 2001 estimates were reported directly only for injuries. To estimate the BoD attributable to the other EFs we used indirect and direct methods, depending on the type of EFs and on data availability**

- **In the direct method (W&S-DD, lead-MMR) the BoD was calculated directly starting from the exposure distribution, the incidence rate of disease, age at onset, duration and disability weight**

- **In the indirect method we used the distribution of risk factor exposure, the dose-response relation and the DALYs lost for the disease to estimate the impact fraction. To describe the dose-response relation, we used an exposure-based approach when we were able to specify a continuos numerical relation between cause and outcomes (eg. OAP-ARI) and a scenario-based approach for W&S-DD and IAP-ARI)**

Analyses were performed separately for **3 European subregions**, according to the classification used by WHO



Estimates of child exposure to the 4 risk factors

Table 2. Estimates of child exposure to 4 environmental risk factors in the European subregions.

Risk factor	Type of exposure measure	EurA	EurB	EurC
Outdoor air pollution	PM10 outdoor concentration ($\mu g/m^3$)	24·84 * 35·96 †	67·01 * 53·86 †	55·67 * 61·00 †
Indoor air pollution	Prevalence of exposure to smoke form indoor solid fuel use (% of households using solid fuels x ventilation factor)	0%	20·5%	6·4%
Water, sanitation, and hygiene	% of population in scenarios I-VI (as defined in text)	100% in II	12% in VI 1% in Vb 8% in Va 79% in IV	1% in VI 5% in Va 94% in IV
Lead	Blood lead level (µg/dl)	2·8 ‡ 4·5 §	3·9 ‡ 14·9 ‖	6·2 ‡ 5·5 §

*Average PM10 concentration calculated from the World Bank estimates [19]
†Average PM10 concentration calculated from epidemiological studies [Lancet website]
‡Mean blood lead level in urban areas [Lancet website]
§Mean blood lead level in rural areas [Lancet website]

The EBD study. An overview of the findings

Environmental risk factor	Deaths			DALYs		
	Deaths	% of deaths from all causes	Deaths per 10 000 children	DALYs	% of DALYs from all causes	DALYs per 10 000 children
Outdoor air pollution (0–4 years)	3 861 13 796[a]	1.8 6.4[a]	0.7 2.7[a]			
Indoor air pollution (0–4 years)	9 845	4.6	1.9	340 818	3.1	66.1
Water, sanitation and hygiene (0–14 years)	13 548	5.3	0.8	549 940	3.5	31.53
Lead (0–4 years)				156 619	1.4	3.0
Injuries (0–4 years)	75 159	22.6	3.1	4 793 557	19.0	200.4

[a] Lower and upper estimates.

Huge variation of BoD across subregions : the example of diarrheal diseases.

Table 3. Indirect estimates of the burden of diarrhoeal disease attributable to water, sanitation and hygiene in the European Region, children 0–14 years of age, in 2001

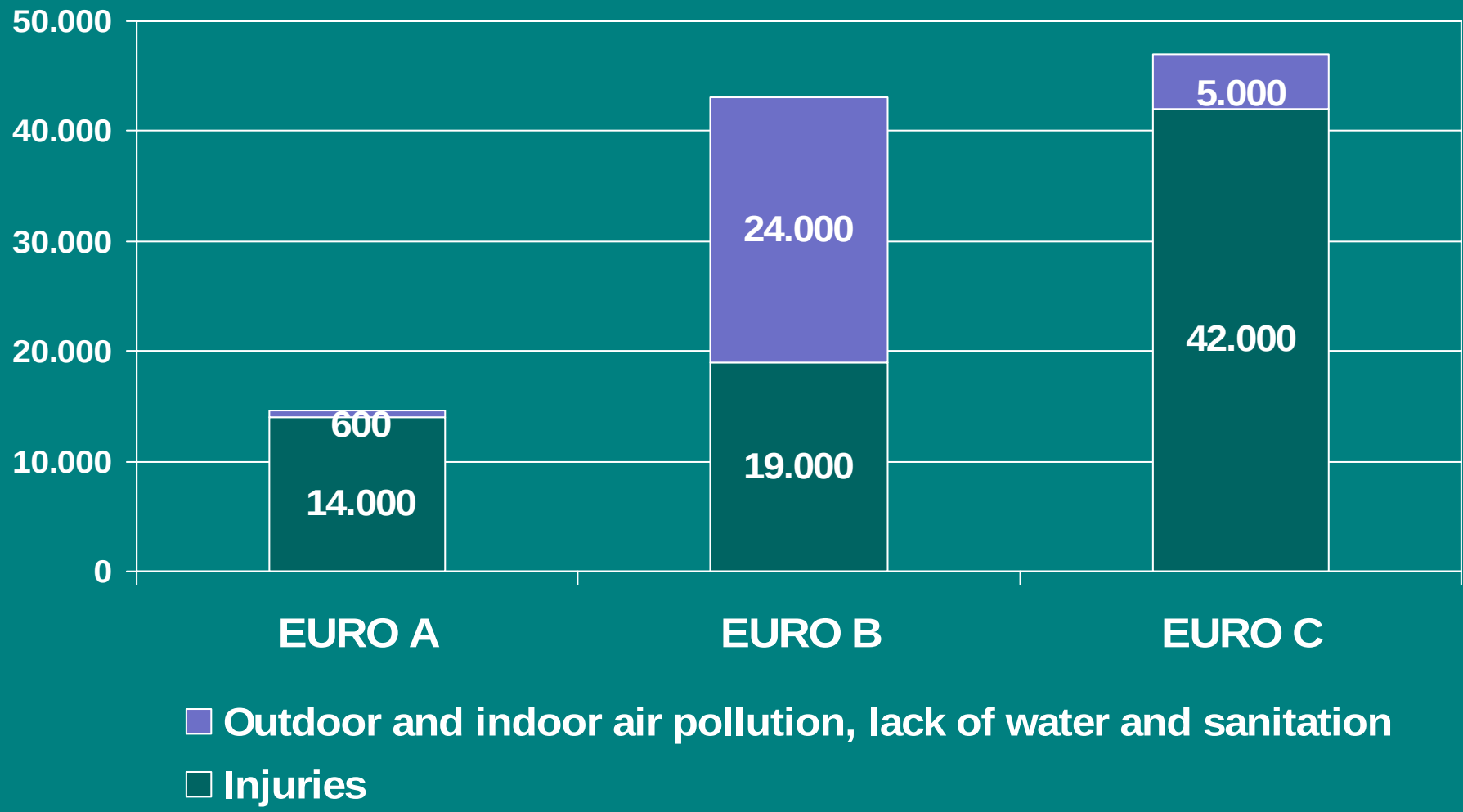
Subregion	Deaths			DALYs		
	Deaths	% of deaths from all causes	Deaths per 10 000 children	DALYs	% of DALYs from all causes	DALYs per 10 000 children
EURO A	63	0.2	0.01	25 946	0.8	3.71
EURO B	11 876	7.5	2.01	446 763	5.2	75.75
EURO C	1 609	2.4	0.36	77 231	1.6	17.04
Total	13 548	5.3	0.77	549 940	3.5	31.53

. . . much less variation for injuries

Table 5. Burden of injuries in the European Region, children 0–19 years of age, in 2001

Subregion	Deaths			DALYs		
	Deaths	% of deaths from all causes	Deaths per 10 000 children	DALYs	% of DALYs from all causes	DALYs per 10 000 children
EURO A	13 450	30.2	1.4	894 947	14.9	94.2
EURO B	18 933	10.7	2.4	1 528 037	13.8	192.5
EURO C	42 776	38.8	6.6	2 370 573	29.1	365.6
Total	75 159	22.6	3.1	4 793 557	19.0	200.4

The magnitude and the composition of the EBD differ substantially across the three subregions



The EBD study: summary of the findings (1)

- **Children in EurB and C are much more exposed** to outdoor and indoor air pollution, unsafe water and sanitation, and lead than children in EurA
- In the age group 0-4, **mortality rates per 10,000 children were highest in EurB for all factors** except for injuries which were more frequent in EurC
- **In EurA and C, the highest number of deaths and DALYs/10,000 children was found in the age group 15-19 and was entirely due to injuries**.
- **In EurB, the highest rates were found in the age group 0-4**, and outdoor and indoor air pollution and unsafe water conditions accounted for more deaths, as well as for a greater number of DALYs, than injuries.

The EBD study: summary of the findings (2)

- In the European region as a whole, the 5 outcomes considered in the present study accounted for **26·5% (21.9%) of deaths from all causes and 22·7% of all DALYs among children 0-4 years of age.**

- Among children 5-14, **injuries alone accounted for 41·2% of all deaths and 29·8% of all DALYs**. In the age group 15-19, the proportion of all deaths caused by injuries was even higher (59·9%).

- Assuming that the EBD was negligible at ages other than the ones we considered, it contributed to **31.6-36% of all cause deaths and 26% of all cause DALYs in the overall 0 to19 years age group.**

- Results of sensitivity analyses show that there was a **substantial uncertainty** around the estimates of deaths due to OAP (upper estimate 8 fold the lower). For indoor air pollution, the upper estimate of the burden of ALRI was approximately twice the lower estimate. For diarrhoeal disease and lead uncertainty was less.

Conclusions. 1: Targetted action is needed to protect children's health

- **The estimated EBD differed markedly across the European region and among age groups. The findings indicate the urgent need for a plan of action specifically addressing a few priority areas - with different priorities in different regions - and targeted to specific population groups.**
- **Interventions aimed at reducing children's exposure to environmental risk factors and at preventing injuries can result in substantial public health gains.**
- **The complex nature of exposure indicates the need for multi-sectorial action (beyond the health and environment sectors)**
- **The existing evidence on higher/much higher environmental exposure and related health effects in vulnerable groups of the population also points to the need for emphasis on the poorest segments of the population.**

Conclusions. 2 : Efforts are needed to fill our knowledge gaps

- **In the EBD study only a few health effects could be considered for a limited number of factors: we do not know enough (lack of data on exposure and health effects, uncertainties on dose-response relations) to complete the picture**
- **The goal is a more comprehensive EBD at intraregional level**
- **Governments and the relevant International Agencies need to make a collaborative effort to to develop comprehensive environment and health information systems (including biomonitoring) and research programs**

Children's environmental health lies at the very heart of sustainable development

L'uomo bianco non capisce. Per lui un pezzo di terra non si distingue da un altro pezzo di terra, dato che lui è un estraneo che arriva di notte e strappa la terra a chi ne ha bisogno. La Terra non è sua sorella ma sua nemica e, dopo averla assoggettata, egli se ne va alla ricerca di un altro luogo. Tratta sua madre, la Terra, e suo fratello, il Cielo, come cose da comprare e da rubare, come se fossero pelli di capretto o perline senza valore. La sua bramosia esaurirà la terra, lasciando dietro di se solamente dei deserti **(Capo Indiano Seattle , 1865)**

Fourth Ministerial Conference
on Environment and Health

Budapest, Hungary, 23–25 June 2004

Children's Environment and Health Action Plan for Europe

<u>Regional Priority Goal I.</u> We aim to prevent and significantly reduce the morbidity and mortality arising from gastrointestinal disorders and other health effects, by ensuring that adequate measures are taken to improve access to safe and affordable water and adequate sanitation for all children.

- We aim to achieve this goal in accordance with the commitments made in the Millennium Development Goals and the WSSD Plan of Implementation by:
- ensuring that all child care institutions and schools are provided with adequate safe water and basic sanitation, ensuring safe and affordable water and adequate sanitation infrastructure and service development and better implementation of the Protocol on Water and Health;
- implementing national plans to increase the proportion of households with access to safe and affordable water and adequate sanitation, thereby ensuring that all children have access to clean water and sanitation by 2015;
- raising awareness among the population, particularly caregivers, and ensuring the provision of education on basic hygiene.

<u>Regional Priority Goal II.</u> We aim to prevent and substantially reduce health consequences from accidents and injuries and pursue a decrease in morbidity from lack of adequate physical activity by promoting safe, secure and supportive human settlements for all children.

- We will address the overall mortality and morbidity due to external causes in children and adolescents by:
- developing, implementing and enforcing strict child-specific measures that will better protect children and adolescents from injuries at and around their homes, playgrounds, schools and workplaces;
- advocating the strengthened implementation of road safety measures, including adequate speed limits as well as education for drivers and children, and enforcement of the corresponding legislation
- advocating, supporting and implementing child-friendly urban planning and development as well as sustainable transport planning and mobility management, by promoting cycling, walking and public transport
- providing and advocating for safe and accessible facilities (including green areas, nature and playgrounds) for social interaction, play and sports for children and adolescents.

<u>Regional Priority Goal III.</u> We aim to prevent and reduce respiratory disease due to outdoor and indoor air pollution, and to ensure the right of all European that children can to live in an environment with clean air.

by:

- implementing the Framework Convention on Tobacco Control, by the enforcement of the necessary regulations and by …health promotion programmes that will reduce smoking and the exposure of pregnant women and children to ETS;
- improving access of households to healthier and safer heating and cooking systems as well as cleaner fuel;
- applying and enforcing building regulations to improve indoor air quality, especially in housing, child care centres and schools, with particular reference to construction and furnishing materials;
- reducing emissions of outdoor air pollutants from transport-related, industrial and other sources through appropriate legislation and regulatory measures which ensure that air quality standards such as those developed under EU legislation. In particular we call upon car manufacturers to equip new diesel motor vehicles with …appropriate technologies in order to drastically reduce emissions, and to that effect … develop regulatory measures as well as economic incentives.

<u>Regional Priority Goal IV.</u> We commit ourselves to reducing the risk of disease and disability arising from exposure to hazardous chemicals (such as heavy metals), physical agents (e.g. excessive noise) and biological agents and to hazardous working environments during pregnancy, childhood and adolescence.

- We will aim at reducing the proportion of children with birth defects, mental retardation and developmental disorders, and decrease the incidence of skin cancer in later life by passing and enforcing regulations and implementing national and international conventions and programmes to:
- reduce exposure of children and pregnant women to hazardous chemical, physical and biological agents to levels that do not produce harmful effects on children's health
- protect children from exposure to harmful noise at home and at school
- ensure appropriate testing for effects on developing organisms of chemicals, products and technologies before their marketing and release into the environment
- ensure the safe collection, storage, transportation and destruction of non-hazardous and hazardous waste, with particular attention to toxic waste

Regional Priority Goal IV (cont.)

- monitor in a harmonized way the exposure of children, as well as women of reproductive age, to hazardous chemical, physical and biological agents;
- ensure that the Stockholm Convention on POPs, …..are applied;
- implementing policies to raise awareness and endeavour to ensure reduction of exposure to UV radiation, particularly in children and adolescents;
- promoting programmes, including those for the adequate dissemination of information to the public, that will prevent and minimize the consequences of natural disasters and major industrial and nuclear accidents such as Chernobyl and that take into consideration the needs of children and people of reproductive age.
- We commit ourselves to advocating the elimination of the worst forms of child labour by applying International Labour Organization (ILO) Convention 182.

The EC European Environment and Health Strategy

13 actions with focus on :

- Improving the information (EH indicators, biomonitoring)
- Fill the knowledge gap (strengthening research)
- Response: review policies and improve communication (public health, training)