The Environment – A Pediatric Problem

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Environment and Disease

- Making the connection between a child's disease and the environment requires a high index of suspicion
- Clinician must think like a medical detective
- Importance of asking the right questions

Learning Objectives

1. To describe a case of environmentally-related illnesses
2. To list why children are different from adults
3. To identify what pediatricians can do for prevention

Key Questions

- Who?
- What?
- When?
- Why?
- Where?

There is much at stake

If you don’t ask the right questions

- patient may not receive the right treatment
- exposure of patient and others in family and community may continue

Asking the right questions

- What you don't know can hurt you (and the patient, the patient's family & community)

- If you don't ask, they won't tell.

Case Study

Six year old girl comes to a public health clinic with severe nausea and vomiting

- Previously in good health
- No remarkable findings on physical exam

Questions in the history

- Who? (family and friends also ill)
- What? (no fever, diarrhea, or bloody stools)
- When? (started 1 day ago)
- Why? (playing with blue powder)
- Where? (at junkyard and home)

Differential Diagnosis

- *Staphylococcus aureus* (preformed toxins)
- *Bacilleus cereus* (emetic toxin)
- Heavy metals (copper, tin, cadmium, iron, zinc)
- Natural toxins (vomitoxin)

Detailed history

- Uncle was a junkyard dealer, opened a lead canister about 1 week earlier
- Luminous blue powder was in canister
- Child rubbed the blue powder on her body so that she glowed and sparkled
- She also ate a sandwich tainted with blue powder from her hands

Diagnosis

Acute radiation syndrome

from exposure to blue powder

(Cesium-137)

Acute Radiation Syndrome

- Symptom complex following whole body irradiation (> 1 Gray)

- Four clinical phases: prodrome, latent, manifest illness, and recovery

Clinical phases

- Prodrome, lasts 2 to 4 days
  - Intestinal symptoms
- Latent period
  - Lasts for approximately 1 to 2.5 weeks
- Manifest illness phase
  - Period when overt illness develops
- Recovery phase or death
  - may take weeks or months

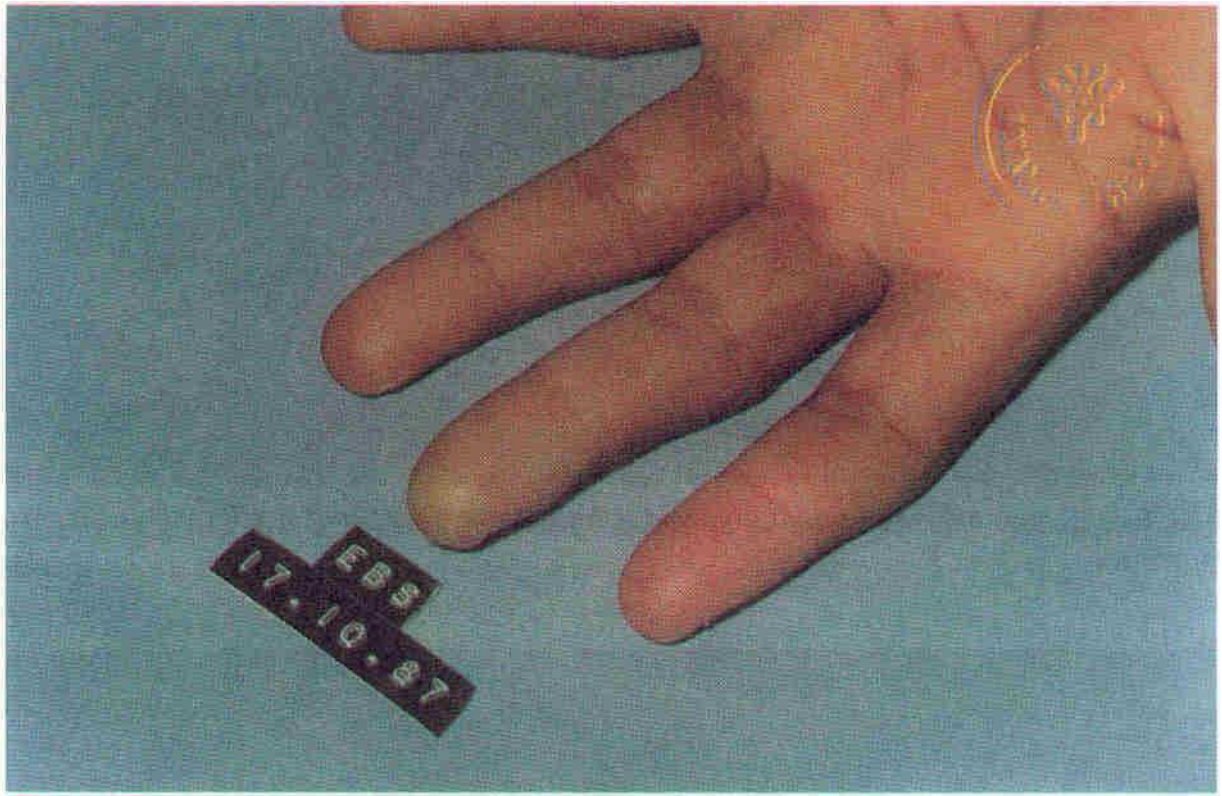


FIG. 9.1. 3 weeks after exposure. The classic aspect of a blister with its yellowish content. Residual secondary erythema can also be observed.


Amazon River
Tapajos River
Serra do Cachimbo
BRAZIL
North Atlantic Ocean
0°
10°
20°
Salvador
Brasilia
GÔIANIA
South Atlantic Ocean
Rio De Janeiro
50°
40°

Goiania Accident

- Radiotherapy source in abandoned clinic
- Cesium-137 (30 year half-life)
- 125,000 persons screened (10% population)
- 245 contaminated
- 54 treated
  - 20 hospitalized, 4 deaths

Course of Events

13 Sept	• Canister removed from abandoned clinic
18 Sept	• Canister sold to junkyard dealer
21 Sept	• Canister opened by junkyard worker
22-23 Sept	• Blue powder given to family & friends
28 Sept	• Junkyard dealer goes to clinic
	- Nausea, vomiting
	- Flu-like symptoms
29 Sept	• Others become sick, go to clinic

Treatment

Immediate concerns in radioactive contamination:

1. Decontamination procedures
   - Remove patient's clothing
   - Wash patient with detergent and water (or have patient take a shower).
2. Measure contamination
3. Administer Prussion Blue

Extensive Consequences

Four main foci of contamination identified: 3 junkyards and 1 residence

85 residences found to have significant levels of contamination (41 of these were evacuated and a few were completely or partially demolished)

Residences about 160 km from Goiana were found with cesium contamination.

There is much at stake

- If you don’t ask the key questions
  - patient may not receive the right treatment
  - exposure of others in family and community may continue

- Could this happen in Argentina?
- Would you recognize it?

Key Message

Children are not little adults!

Depiction of children Egypt – 3300 years ago

Akhenaten and Nefertiti and their 3 daughters

CHILDREN ARE NOT LITTLE ADULTS

Giotto, National Gallery, Washington DC

Raphael, National Gallery of Art, Washington, DC

CHILDREN ARE NOT LITTLE ADULTS

Raphael, National Gallery of Art, Washington, DC

1. **Different and unique exposures**
2. **Dynamic developmental physiology**
3. **Longer life expectancy**
4. **Politically powerless**

PARADIGM SHIFT
Children are more susceptible

Nuclear weapons tests in 1954 on Bikini Island in the South Pacific

Errant fallout caused thyroid cancer

3 cancers among 35 children < 15 years

2 cancers among 46 persons ≥ 15 years

First evidence that child's thyroid gland especially vulnerable to ionizing radiation

1. DIFFERENT AND UNIQUE EXPOSURES

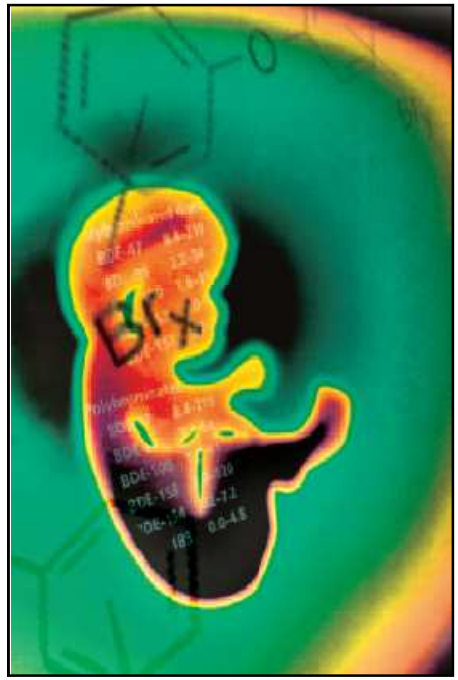
- **Unique exposure pathways**
  - Transplacental
  - Breastfeeding
- **Exploratory behaviours leading to exposures**
  - Hand-to-mouth, object-to-mouth
  - Non-nutritive ingestion
- **Stature and living zones, microenvironments**
  - Location – lower to the ground
  - High surface area to volume ratio
- **Children do not understand danger**
  - Sent by adults into risky small spaces
    - Adolescent chimney sweeps

1. DIFFERENT AND UNIQUE EXPOSURES

TRANSPLACENTAL

Lessons from pharmaceuticals:
thalidomide, diethylstilbestrol (DES)

- **Many chemicals cross the placenta**
  - Lead, mercury, PCBs…
  - Substances of abuse: alcohol
- **Some physical factors may affect the fetus directly**
  - Ionizing radiation



EHP

1. DIFFERENT AND UNIQUE EXPOSURES

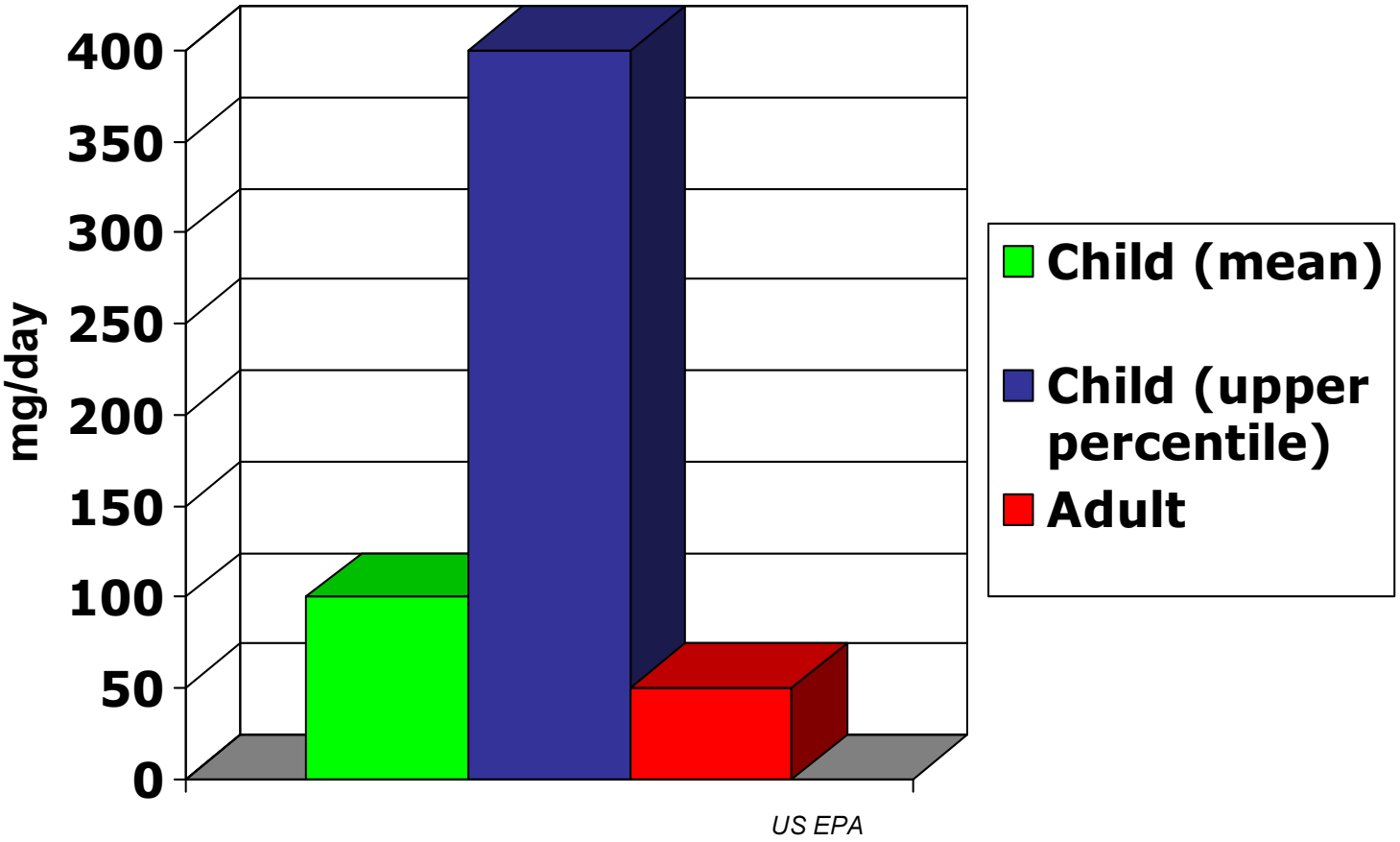
BREASTFEEDING

WHO

- **Breast milk is the safest and most complete nutrition for infants**
  - Milk (human, cow, sheep) can be a marker of environmental contamination
- **DDT, DDE, PCBs, TCDD (dioxins), nicotine, lead, methylmercury, alcohol**

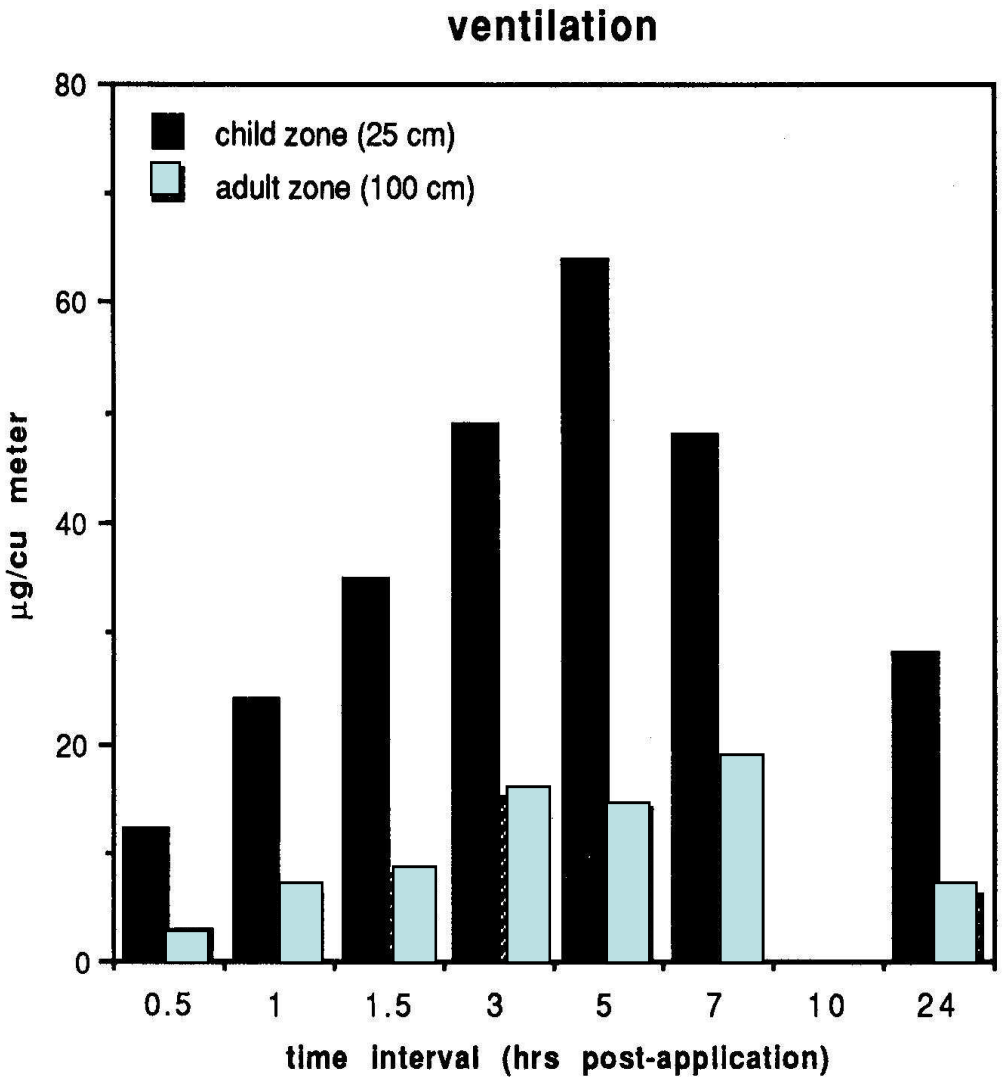
1. DIFFERENT AND UNIQUE EXPOSURES

BEHAVIOUR AND SOIL CONSUMPTION



1. DIFFERENT AND UNIQUE EXPOSURES

STATURE AND BREATHING ZONES



Guzelian, ILSI,1992

Adjusted* Odds Ratios and 95% Confidence Intervals for Childhood Acute Lymphoblastic Leukemia in Relation with Maternal Frequency of Use† of Pesticides in the Garden, the Yard, and on Interior Plants

Type of Pesticides	Controls (N)	Cases (N)	OR	95% CI
Herbicides				
No exposure	417	369	1.00	
1–5 times	66	112	1.83	1.31–2.57
>5 times	2	6	3.72	0.72–19.06
Plant insecticides				
No exposure	444	412	1.00	
1–5 times	34	60	1.89	1.20–2.97
>5 times	3	12	4.01	1.12–14.32
Products against trees				
No exposure	451	425	1.00	
1–5 times	36	56	1.65	1.07–2.54
>5 times	2	6	3.27	0.64–16.69
Repellents and sprays against outdoor insects				
No exposure	427	443	1.00	
1–5 times	24	16	0.47	0.21–1.05
>5 times	15	17	1.06	0.52–2.13

*Adjusted for maternal age and maternal level of schooling; Cases and controls are matched for age, sex, and geographical region.
†Exposure of the mother from 1 month before pregnancy to the end of pregnancy.

1. DIFFERENT AND UNIQUE EXPOSURES

CHILDREN / ADOLESCENTS DO NOT RECOGNIZE DANGER

- **Pre-ambulatory children are unable to remove themselves from danger**
- **Pre-reading children cannot read warning signs & labels**
- **Pre-adolescent / adolescent children put at risk because of small size (chimney sweeps)**

2. DYNAMIC DEVELOPMENTAL PHYSIOLOGY

Xenobiotics may be handled differently by an immature body

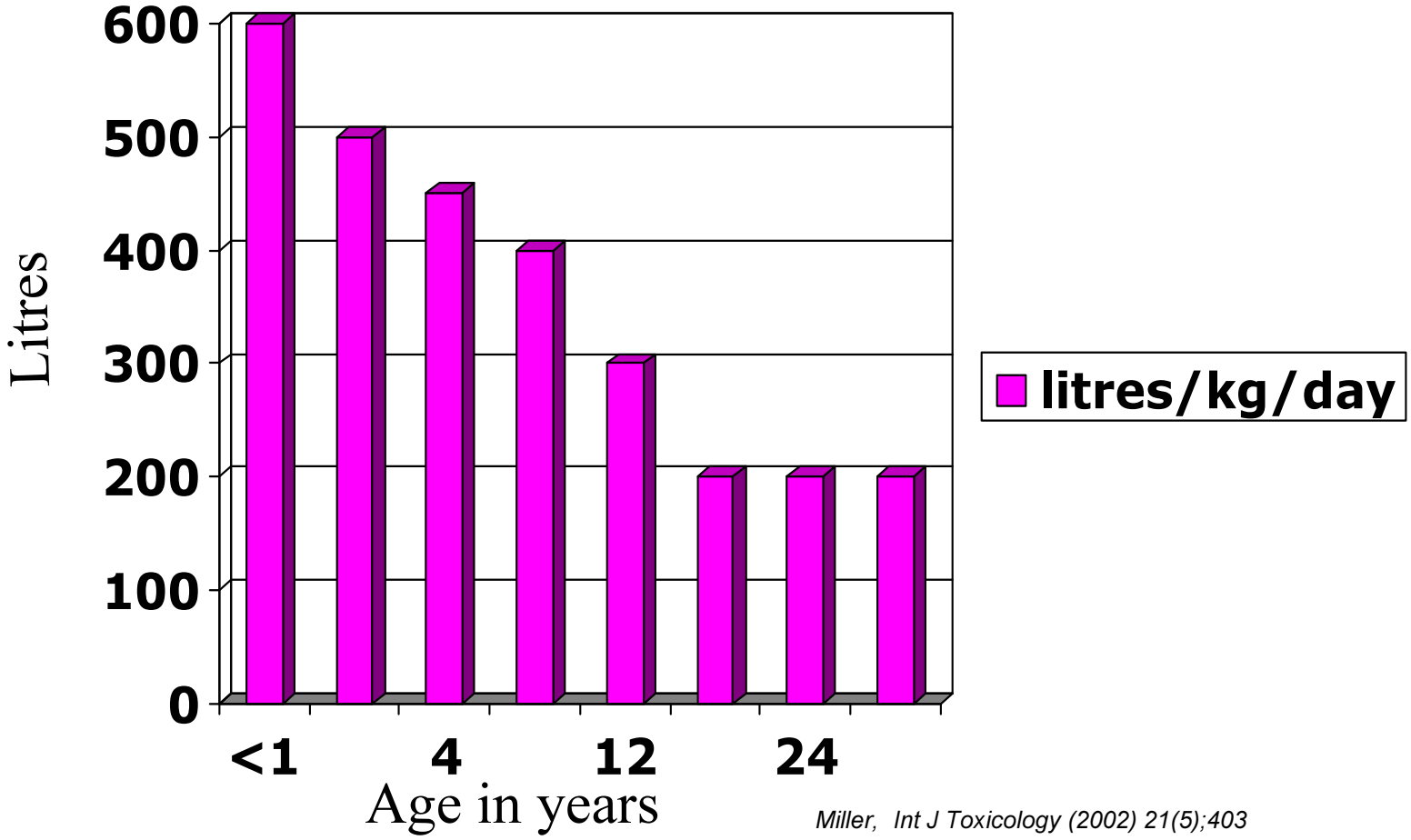
- Increased energy, water and oxygen consumption of anabolic state
- Absorption
- Biotransformation
- Distribution
- Elimination
- Critical windows of development

WHO

2. DYNAMIC DEVELOPMENTAL PHYSIOLOGY

OXYGEN DEMAND

Minute ventilation per kg body weight/day



Miller, Int J Toxicology (2002) 21(5);403

Childhood leukemia and traffic.
Crosignani et al., Int J Cancer 108: 596: 2004

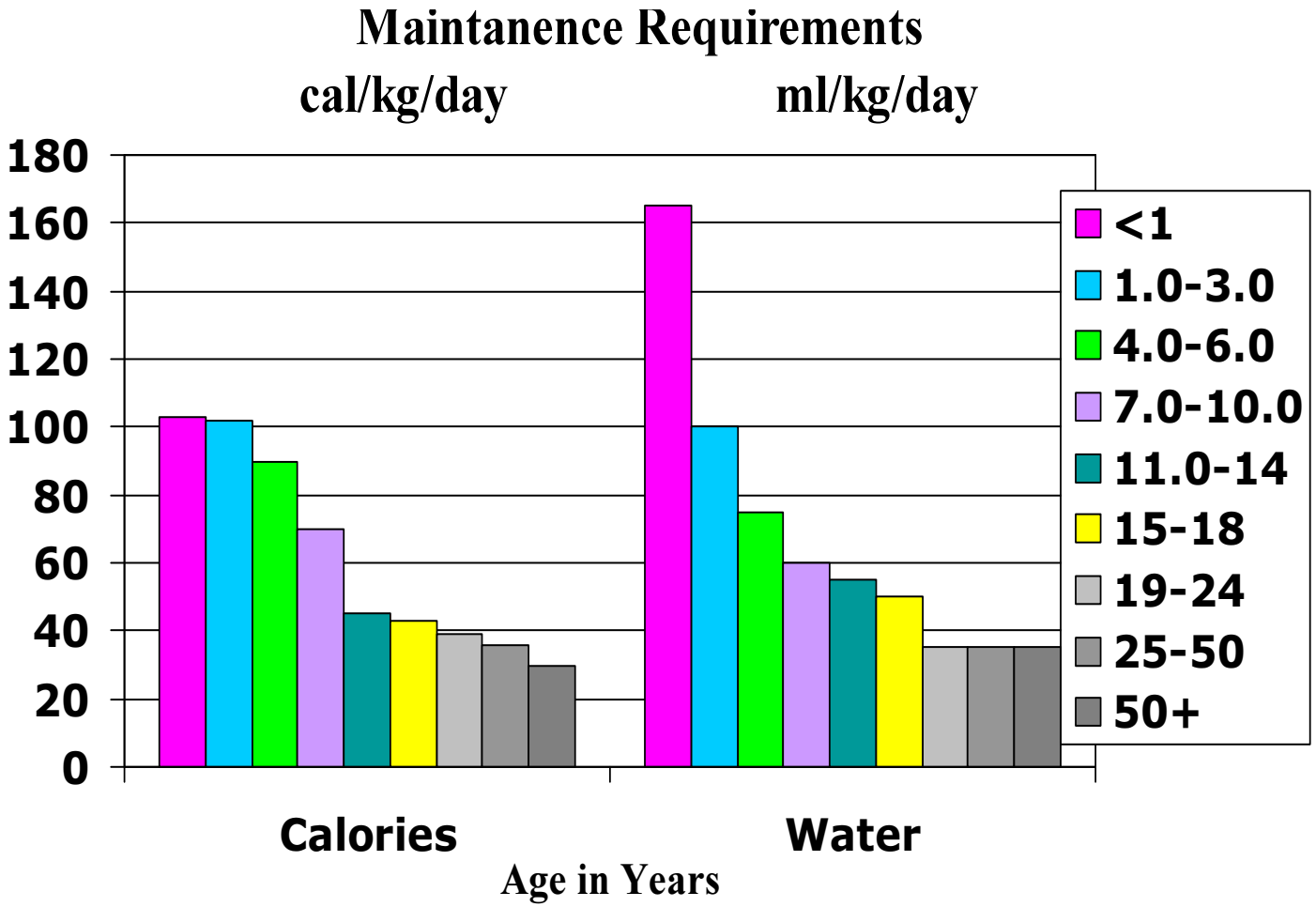
TABLE II – RATE RATIOS FOR ESTIMATED EXPOSURE TO BENZENE

Benzene ($\mu g/m^3$)	Cases	Controls	RR[1] (95% CI)
<0.1	88	399	1[2]
0.1–10	25	73	1.51 (0.91–2.51)
>10	7	8	3.91 (1.36–11.27)
Totals	120	480	
p-value for trend			0.005

[1]Evaluated by conditional logistic regression.–[2]Reference category.

2. DYNAMIC DEVELOPMENTAL PHYSIOLOGY

CALORIE AND WATER NEEDS



2. DYNAMIC DEVELOPMENTAL PHYSIOLOGY

ABSORPTION

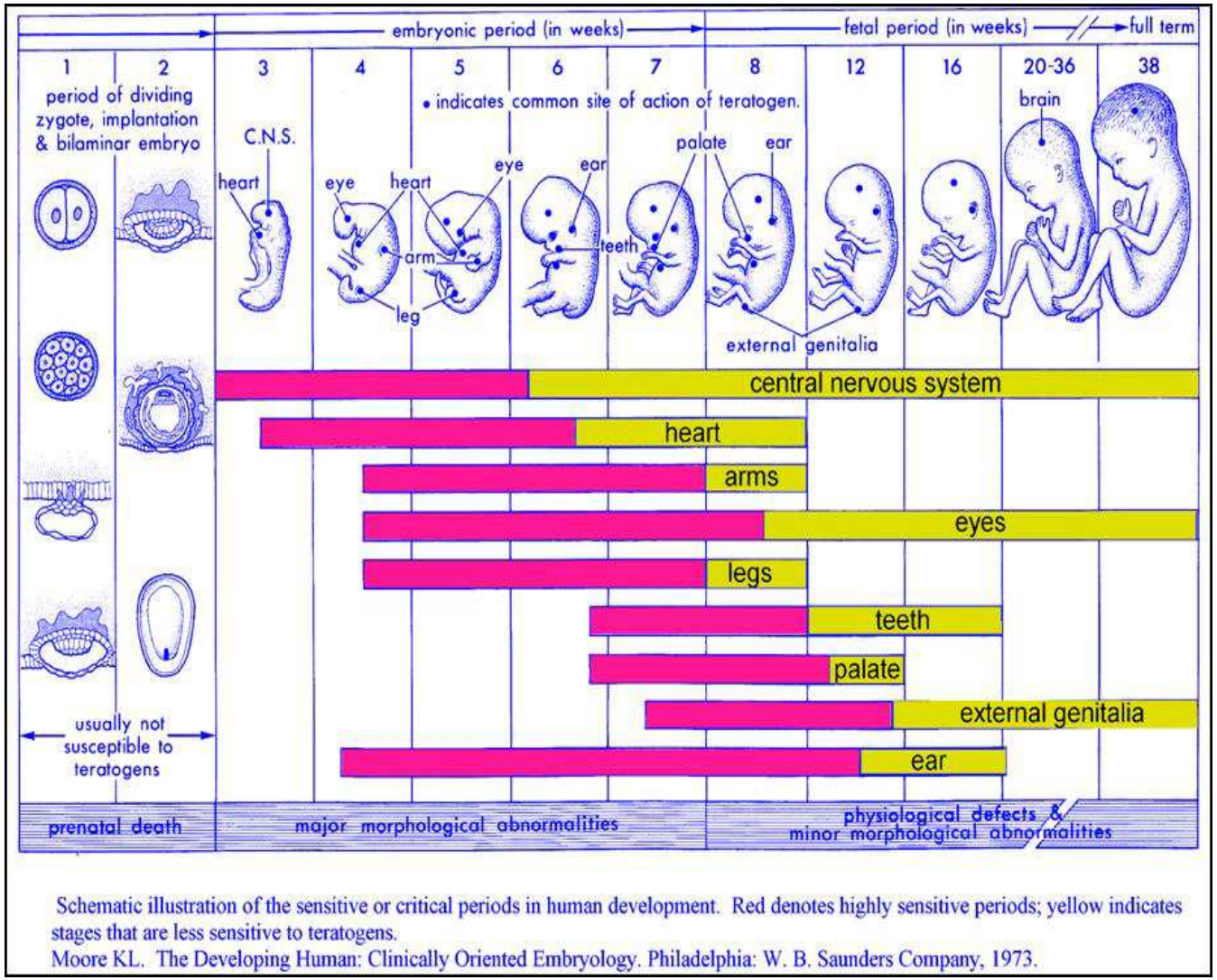
- **A child is building a "body for a lifetime"**

- **The demands of rapid growth and development**
  - Require higher breathing rate, caloric and water intakes
  - Satisfied by enhanced absorption and retention of nutrients

For example:

GI absorption of lead in toddler: 40–70% of oral dose (1/3 retention)
GI absorption of lead in non-pregnant adult: 5–20% (1% retention)

WINDOWS OF DEVELOPMENT



Schematic illustration of the sensitive or critical periods in human development. Red denotes highly sensitive periods; yellow indicates stages that are less sensitive to teratogens.
Moore KL. The Developing Human: Clinically Oriented Embryology. Philadelphia: W. B. Saunders Company, 1973.

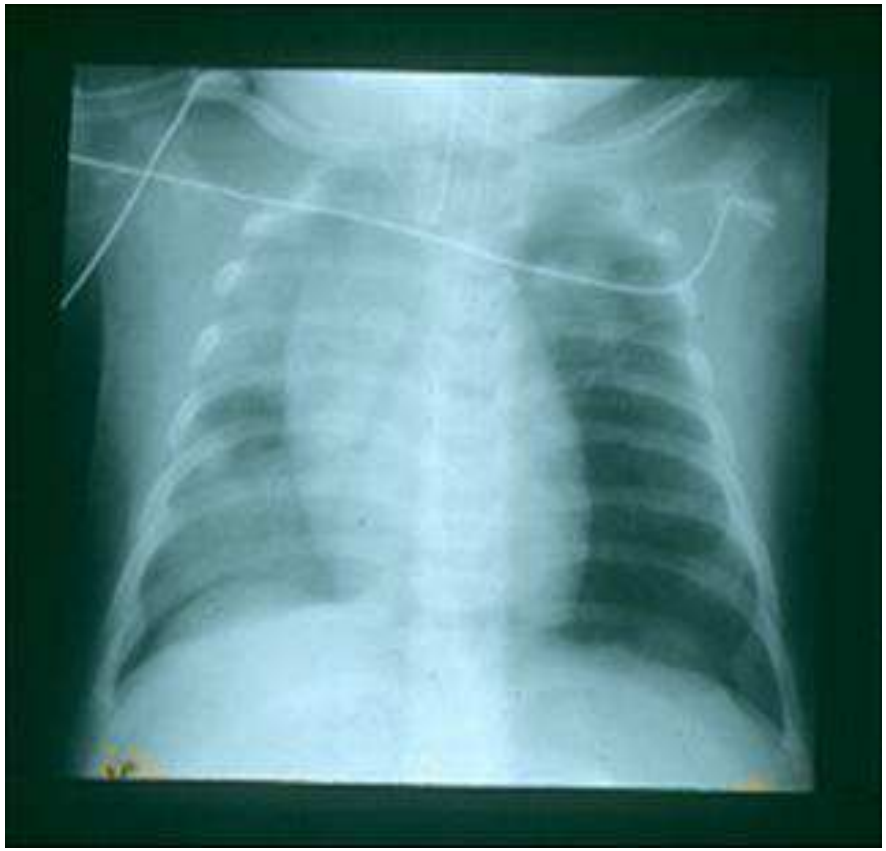
Moore, Elsevier Inc, 1973

Table 8 Variations with age of radiation risk (RR) for thyroid cancer (after exposure to 1 Gy) (thyroid weights: birth 1 g, 6 months 2 g, 4 years 4 g, 10 years 20 g, 18 years 20 g; *NS* not significant)

Patients [21]		Survivors of Hiroshima and Nagasaki [101]	
Age	RR	Age	RR
0–4 years	40	0–9 years	9.5
5–9 years	20	10–19 years	3
10–14 years	10	20–39 years	0.3 NS
20–30 years	1	>40 years	0.2
>30 years	0		

Tubiana M (2000) Radiat Environ Biophys 39: 3-16.

INFANT ACUTE PULMONARY HEMORRHAGE



- Lungs continue growing rapidly in 1st year of life
- Exposures to molds in homes is association with acute lung bleeding
- Mycotoxins on surface of mold spores lead to capillary fragility
- 10% fatal

Etzel RA et al. *Arch Pediatr Adolesc Med* 1998,152(8):757-62.

BLEEDING FROM TRICHOTHECHENE MYCOTOXINS: EVIDENCE FROM ANIMALS

Alimentary Toxic Aleukia (ATA)

- First appeared in 1913 in far eastern Siberia
- Responsible for the death of at least 100,000 Russian people between 1942 and 1948
- Necrotic ulcers in the mouth, throat, nose, stomach and intestines
- Bleeding from the nose, mouth, GI tract, and kidneys
- Associated with eating grains (wheat and corn) which had been under snow the previous winter
- Grains contaminated with *Fusarium* and *Stachybotrys*

Fathers and their Offspring

Occupational exposures – suggestive evidence

- Paint, solvents
  - germ cell tumors
  - hepatic tumors
  - brain and CNS tumors
  - acute lymphoblastic leukaemia
- Welder
  - renal tumors
  - retinoblastoma

Fathers and their Offspring

Occupational exposures – suggestive evidence

- Petroleum
  - acute lymphoblastic leukaemia
  - brain and CNS tumors
  - hepatic tumors
- Paper or pulp mill
  - brain tumors

Paternal Smoking and Childhood Cancer

Cancer	Relative Risk	CI, p-value
Rhabdomyosarcoma	3.9	p=0.003
Brain	2.0	1.0-4.1
Infant leukemia	1.56	1.03-2.36
All types (1953-55)	1.89 highest tertiile	0.84-4.24, p=.001
All types (1971-76)	1.63 highest quintile	1.23-2.15, p=.001
All types	1.7 highest tertile	1.2-2.5, p=.006
ALL	3.8 highest tertile	1.3-12.3, p=.01
Lymphoma	4.5 highest tertile	1.2-16.8, p=.07
Brain	2.7 highest tertile	0.8-9.99, p=.14
All types	1.77 highest quintile	0.94-3.34, p=.02
Astroglial	1.4	1.1-1.9

DYNAMIC DEVELOPMENTAL PHYSIOLOGY

WINDOWS OF DEVELOPMENT: MOTHERS AND THEIR OFFSPRING

		→	
In utero	**Thalidomide**	→	**phocomelia**
	DES	→	**vaginal cancer**
	X-rays		**leukemia**

3. LONGER LIFE EXPECTANCY

WHO

- **Exposures early in life permit manifestation of environmental illnesses with long latency periods**
  - **More disease**
  - **Longer morbidity**

EARLY CHILDHOOD EXPOSURES

predisposing to adult cancer

1. Ionizing radiation
   → breast cancer, ALL, thyroid cancer
2. Radiotherapy for Hodgkin's disease
   → osteosarcoma, leukaemia, skin cancer,
   breast cancer, soft tissue sarcoma
3. UV sunlight
   → melanoma, basal and squamous cell carcinomas
4. Tobacco
5. Asbestos
6. Diet - fats and aflatoxins
   → Cancer of colon, breast, and liver

4. POLITICALLY POWERLESS

- **No political voice**
- **Advocacy by health sector**
- **Environmental laws and regulations**
  - Local
  - National
  - International

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“green behind the ears”

“green between the ears”