

Epidemiologic Studies of ELF and their Contribution to Risk Assessment

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Outline

- Epidemiology and Risk Assessment
- The IARC Evaluation
- A look to the future



Uses of Epidemiologic & Toxicologic Data In Risk Assessment

- Use only epidemiology
- Use only toxicology
- Use epidemiology to model risk, toxicology to model mechanistic basis
- Use epidemiology to verify plausibility of risk and bound estimates derived from animal data
- All of the above plus mechanistic data -- weight-of-evidence approach



IARC Criteria



International Agency for
Research on Cancer (IARC)

Centre International de
Recherche sur le Cancer (CIRC)

- For each type of cancer, classify human and animal data separately as:
 - Sufficient
 - Limited
 - Inadequate
 - Lack of effect

Group 1: Is carcinogenic to humans

Group 2A: Probably is carcinogenic

Group 2B: Possibly is carcinogenic

Group 3: Not classifiable

Group 4: Is probably not carcinogenic

N.B. Greatest weight given to epidemiology



Relative Strength of Epidemiologic & Toxicologic Data

| | Human | Animal |
|--|-------|--------|
| Species Extrapolation | + | - |
| Power | + | - |
| Exposure Assessment | | |
| Control | - | + |
| Relevancy | + | - |
| Confounding/Bias | - | + |
| Effect Modification | + | - |
| High [®] Low Dose Extrapolation | +? | - |



Epidemiology Can Provide Unique Data

Relevant response in the relevant species to relevant exposure

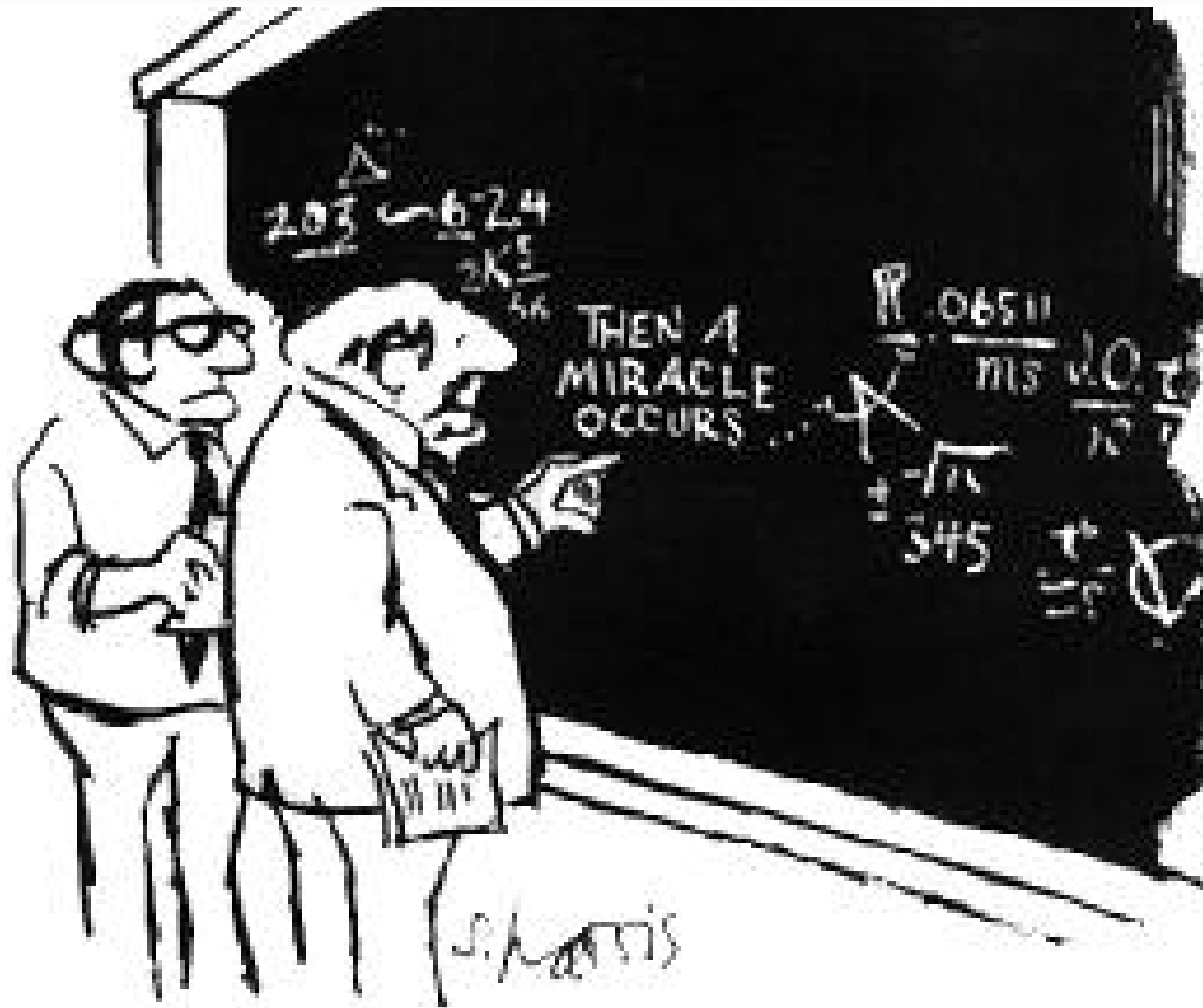
- Variability of response in genetically heterogeneous population
- Susceptible subpopulations
- Dependence of risk on age and timing of exposure
- Intermittent vs. continuous exposure
- Concomitant exposures
- Differentiation between cancer models
- Estimate of upper limit of risk



Agents classified by IARC (834)

| IARC Classification | Examples of Agents |
|---|---|
| Carcinogenic to humans (75) (usually based on strong evidence of carcinogenicity in humans) | Asbestos Alcoholic beverages Benzene Mustard gas Radon gas Solar radiation Tobacco (smoked and smokeless) X-rays and Gamma |
| Probably carcinogenic to humans (59) (usually based on strong evidence of carcinogenicity in animals) | Creosotes Diesel engine exhaust Formaldehyde Polychlorinated biphenyls (PCBs) |
| Possibly carcinogenic to humans (225) (usually based on evidence in humans which is considered credible, but for which other explanations could not be ruled out) | Coffee ELF magnetic fields Gasoline engine exhaust Glass wool Pickled vegetables Styrene |



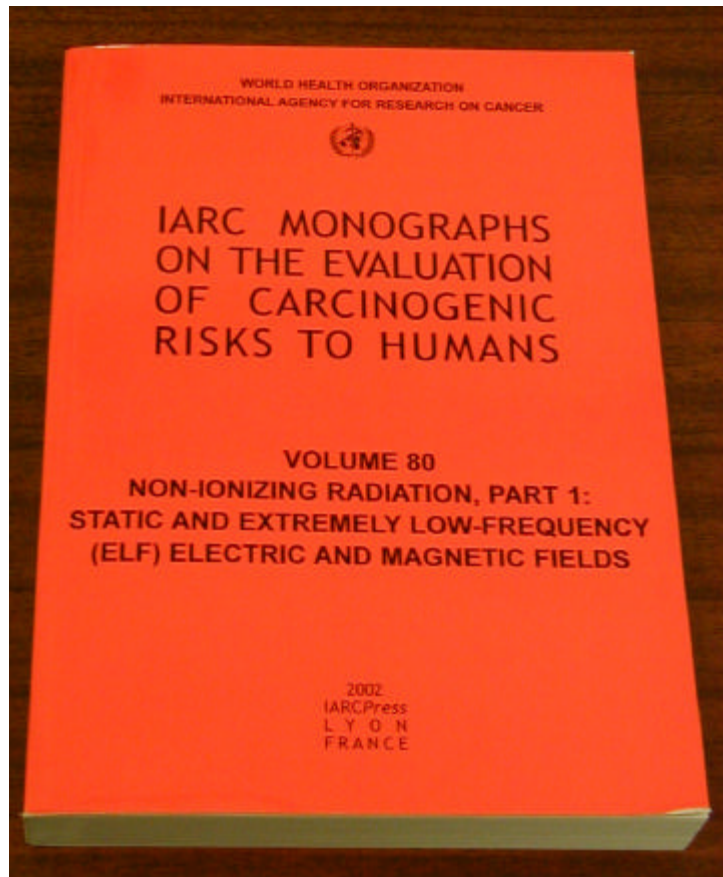


"I think you should be more explicit here in step two."



IARC Evaluation

Extremely Low Frequencies (ELF)



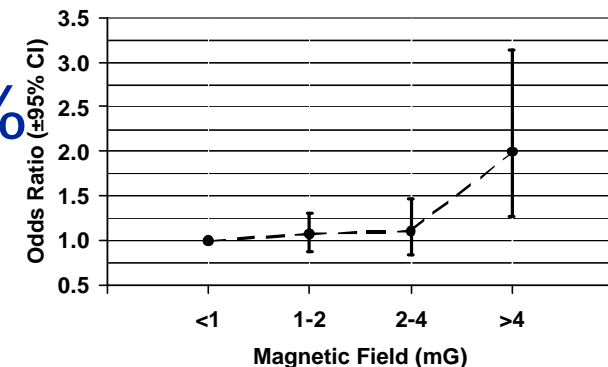
- IARC evaluation completed in June 2001, monograph published 2002
- ELF magnetic fields classified as *Group 2B “Possible Carcinogenic”*
 - based on epidemiologic studies of childhood leukemia
 - animal data inadequate
- Other exposures and outcomes considered “inadequate to classify”



Pooled Analysis

Ahlbom et al 2000; Greenland et al 2000

- \approx 2-fold increase in risk above 0.3 - 0.4 μT
- Association more consistent with measured fields than with wire codes
- Attributable fraction estimate + 3%
- No confounding evident
- Selection bias may be a partial explanation
- Unlikely to be due to random variability



What can new epidemiologic studies of childhood leukemia contribute?

- Unlikely to substantially change the observed association
- Need to be designed to test specific hypotheses:
 - **other aspects of exposure**
 - **selection bias**
 - **susceptible subgroups**



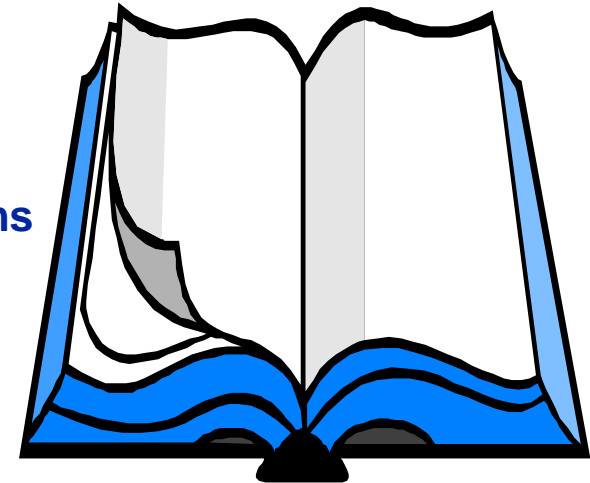
WHO Environmental Health Criteria

- In depth **weight-of-evidence** critical review and evaluation of the EMF research world wide
- A two-step process:
 - **IARC hazard identification and classification of possible carcinogens using cancer studies** (*Monographs*)
 - **EMF Project assessment of all studies** (*Environmental Health Criteria*)



Table of Contents

- Summary
- Introduction
- Sources of exposure and Measurement
- Environmental levels and human exposure
- Internal Dosimetry
- Effects on laboratory mammals and in vitro test systems
- Effects on humans
 - ⇒ Cancer
 - ⇒ Reproduction
 - ⇒ Cardiovascular
 - ⇒ Neurodegenerative
 - ⇒ Behavioural
 - ⇒ Hypersensitivity
- Methodological Issues in ELF Health Risk Assessment
- Evaluation of Dose-Response
- Evaluation of human health risks
- Protective measures (including Precautionary Approach)
- Conclusions & recommendations for protection of the human health and the environment
- Further research



Scientific Issues in ELF Risk Assessment

- Relevance and weight of biophysical arguments
- Reconciling epidemiologic and toxicologic data

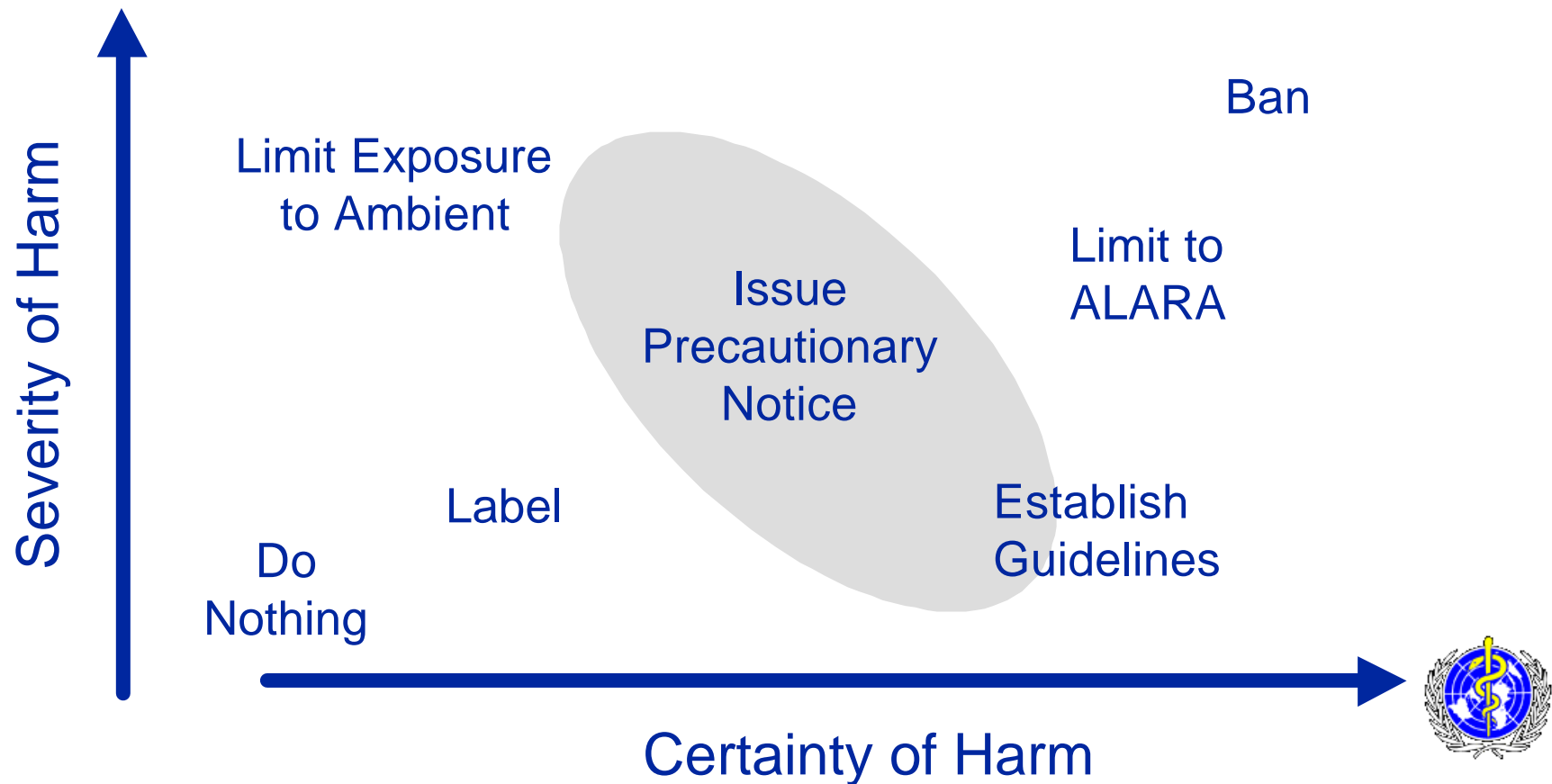
| | | | |
|-------|---|--------|----|
| | | Animal | |
| | | + | - |
| Human | + | ✓ | ?? |
| | - | ? | ✓ |

- Uncertainty and misclassification in epidemiologic studies
- Exposure distribution, risk function and if and how to combine them
- Refutation of alternative hypotheses



Developing Policy in the face of uncertainty

- Implication of 2B classification
- Developing Precautionary Principle framework
- Evaluation of Policy Options



WHICH IS WORSE ?

Concluding

Scientist

Public

There is an effect when none exists (false positive)

As low as possible

Type I Error

There is no effect when one exists (false negative)

As low as possible

Type II Error



Specifics of Application of PP to EMF

- Benchmark using existing exposure levels
- Distinguish new and existing facilities
- Distinguish voluntary and involuntary sources of exposure
- Distinguish exposure to children and adults
- Choice of arbitrary or achievable levels



Policy Options should:

- **Include scientific evaluations**
- **Evaluate ALL credible scenarios with rigor**
- **Provide for means to reduce uncertainty (research)**
- **Provide for ways to monitor, refine and revise actions (surveillance)**
- **Use good judgement**



EHC Monograph on ELF and Static Fields

- Not just another review
- Blueprint for future EHC on RF

| Static and ELF | | RF | |
|---|-----------|--|------|
| IARC | 2001-2002 | IARC | 2005 |
| EHC | 2002-2003 | EHC | 2006 |
|  | |  | |



