

Emerging E & H Issues: Implications for Prevention and Research

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Summary

- What is an Emerging issue and an Early Warning
- Emerging Scientific Issues in E&H
- From Knowledge to Evidence
- From Evidence to Action
- Some Research Options

What is an “Emerging E&H Issue”?

“Some evidence of new aspects of socio-economic and scientific realities, arising from new knowledge or perceptions, and which presents potential threats to health and/or environments”.

(EEA, 2007)

What is an “Early Warning”?

- ***“An initial assessment of an emerging issue which suggests that potential threats are plausible”.***

(EEA, 2007)

Asbestos: the Early Warning, 1898

“the evil effects of asbestos have also instigated a microscopic examination of the mineral dust ..clearly revealed was the sharp glass-like jagged nature of the particles, and when they are allowed to rise and to remain suspended in the air of the room in any quantity **the effects have been found to be injurious as might have been expected**” (Lucy Deane, Factory Inspector ,1898, EEA “Late Lessons from Early Warnings”,p11)

Antimicrobial Feed Additives (AFA): An “Early Warning” 1969

‘Despite the gaps in our knowledge .. We believe ... on the basis of evidence presented to us, that this assessment is a **sufficiently sound basis for action** .. The cry for more research should not be allowed to hold up our recommendations’

UK Medical Research Council’s Swann Committee, HMSO, UK, Nov. 1969)

Some emerging issues from the Ecology/biology interface..

- **Infectious diseases (R.May,1991; IOM,US,03)**
- **Pharmaceuticals in the Environment
Pesticides & Growth Hormones and
Endocrine mediated diseases**
- **Climate Change: disease vectors and
chemicals re-mobilisation**
- **Nano-medicines**
- **Foetal origins of lifetime diseases
(cancer,neurodevelopmental,obesogenic),**
- **Increased Well being from Nature**

The Active Recognition of an Early Warning...

..depends, inter alia, on **overcoming vested interests** in both current knowledge and paradigms...and in current economic and political activities.

The Power of the Paradigm...

A “surprise” arises not so much from an absence of knowledge as by the presence of **flawed assumptions or paradigms...**

...and from **scattered, not integrated information.**

(See Late Lessons case studies; and the 9/11;Columbia;Katrina;Pearl Harbour reports; and Hurricane analyses by Swiss Re)

As scientific knowledge expands,
the **inter-connections** between
ecological and biological systems,
and the **complexity** of the systems
science 'become' greater.

Complex systems ... a number of attributes

- Multiplicity of legitimate perspectives
- Non-linearity; tipping points; low dose effects
- Emergence: “the whole is more than the sum of its parts”
- Cancer: from “the” cell to “societies of cells”
- Irreducible uncertainties

Complex Biological Systems

- Such systems feature “**emergent properties** ...the properties at one level of biological complexity (e.g. tissues) cannot be ascribed directly to their component parts (cells, etc)...**a new integrated, conceptual framework is needed...**
- Prof Ana Soto, BPTOX, 2008

From “simple” genes to complex biological systems.....

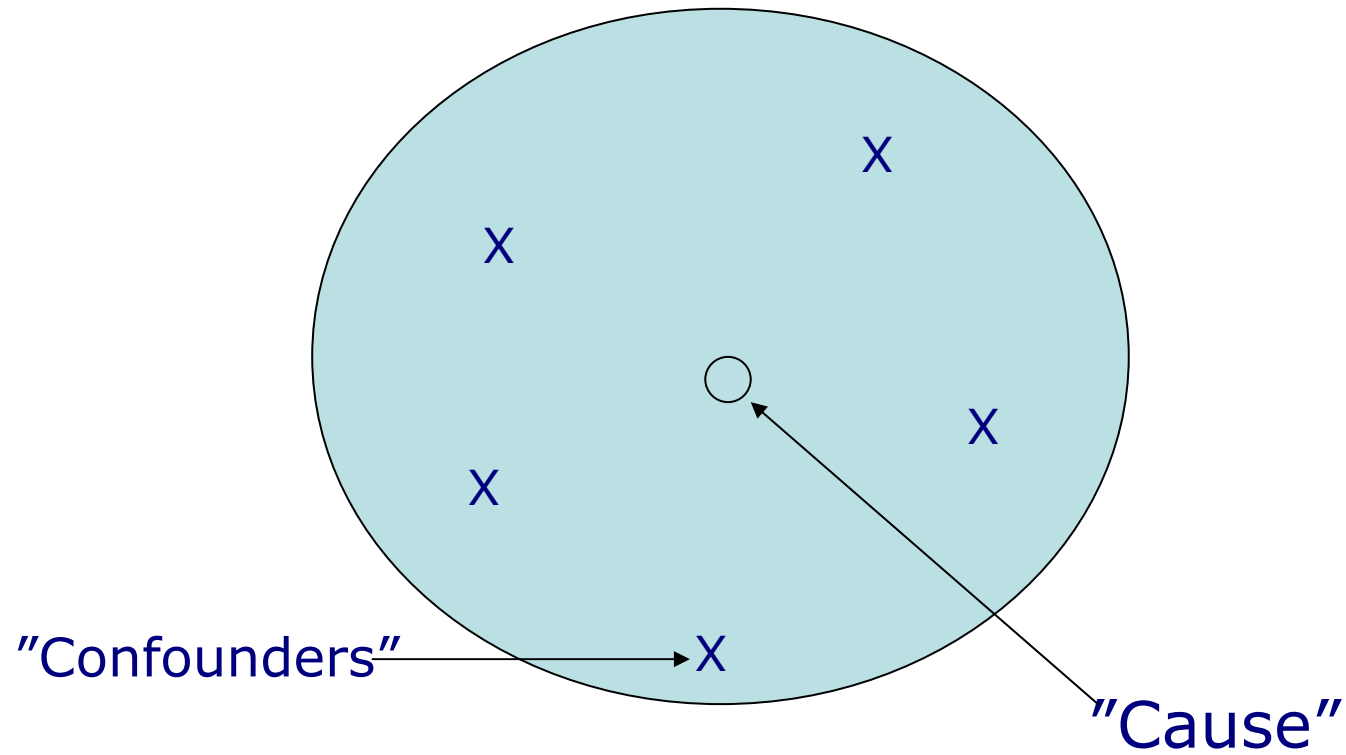
- “Rather than having a single function, most genes probably play a small part in lots of tasks.... by dissecting biology into its genetic atoms, reductionism failed to account for these multi-tasking genes”
- “Instead of focusing on key control points, **systems biologists look at the system properties of the entire network**”

...where multi-causality dominates

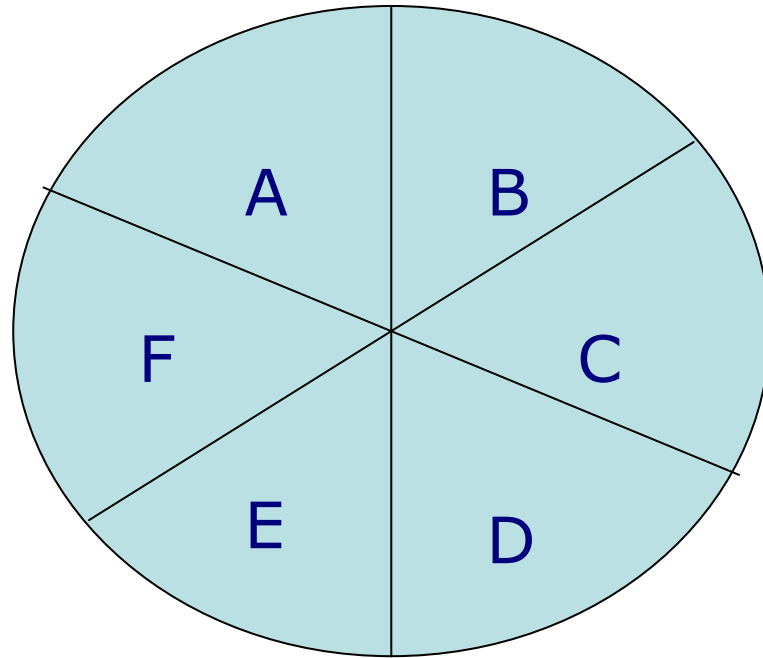
- “Few genes play more than a minor role in complex traits like heart disease, autism, schizophrenia or intelligence – maybe such genes do not exist...”
- “Rather than being “caused” by single genes these traits may represent a **network perturbation** generated by small, almost imperceptible, changes in lots of genes”

(J. McFadden, Professor of Molecular Genetics,
Surrey University, “Guardian”, May 6, 2005)

Uni-causality in environment & health

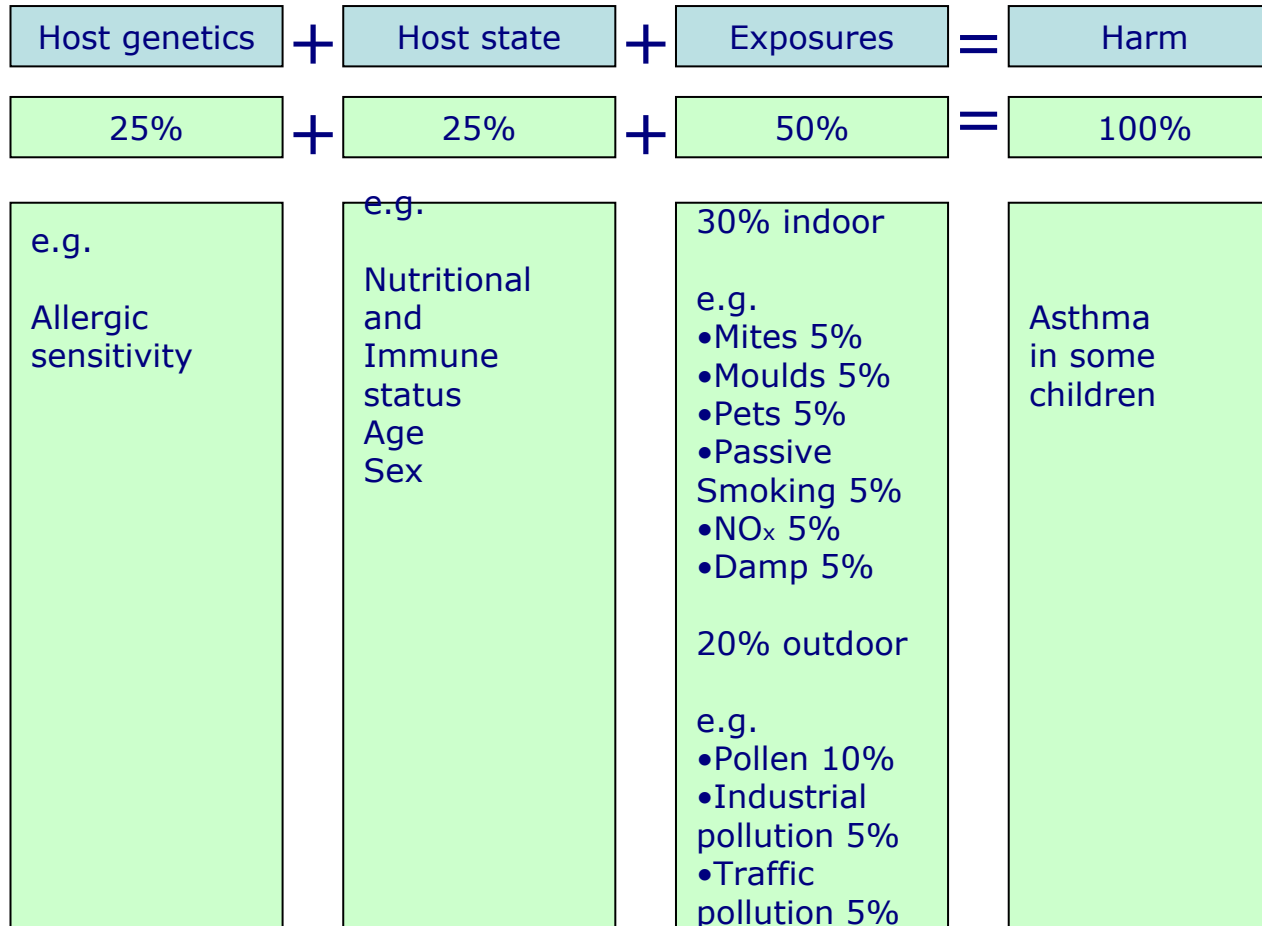


Multi-causality



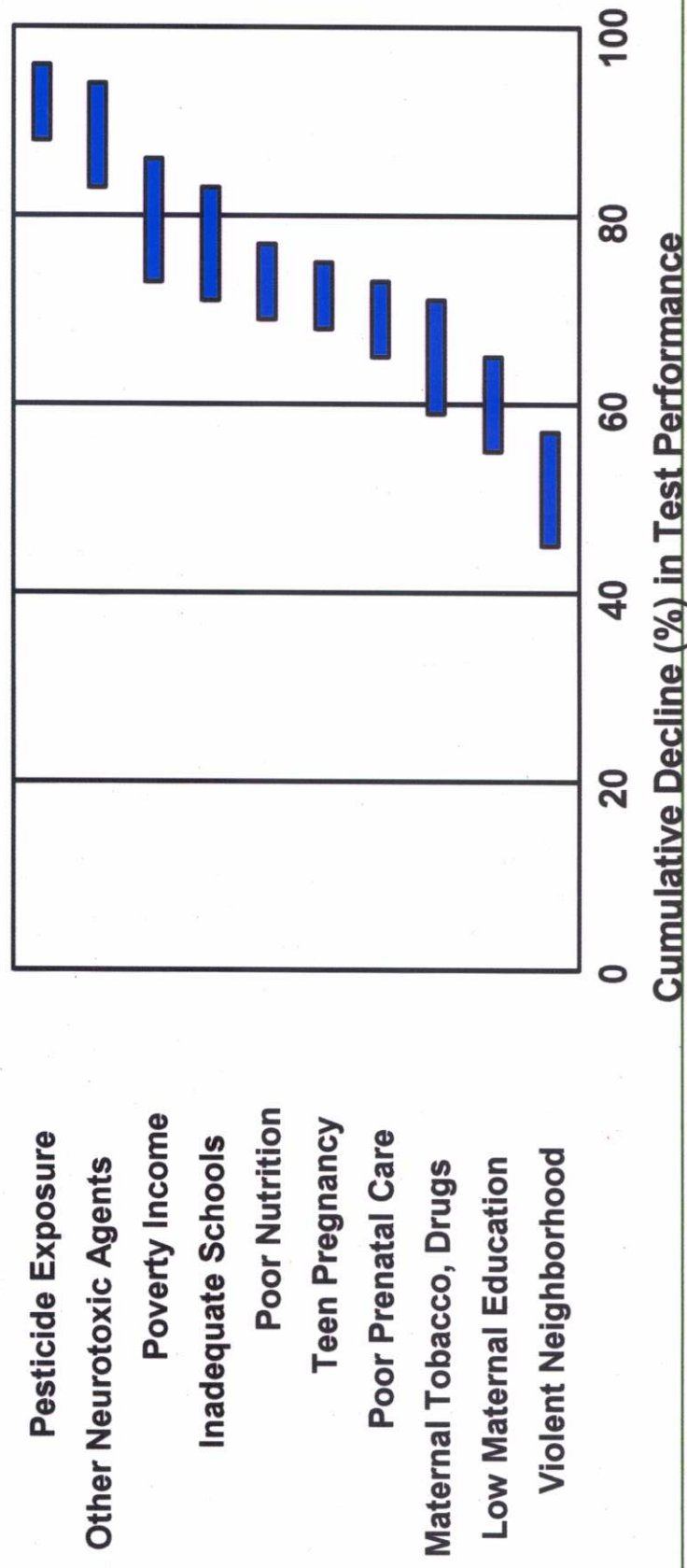
A-F: Co-causal factors

Illustrations of multi-causality in childhood asthma



Source: EEA, 1999

Schematic model to show how individual components of a stressful environment might cumulate individual stressors are overlapping to suggest a lack of independence. No single component is overwhelming in isolation.



Some Implications of Multi-Causality and Complexity

1. **Timing** of the dose can make the poison
2. “**Confounders**” are sometimes co-causal factors
3. Simple genetic determinism becomes **complex systems dynamics**
4. “**Consistency**” of scientific results can be unusual.

Environmental Stressors: Confounders or Co-causal factors?

- “what we have labelled as **co-variates, confounders and effect modifiers possess a biological reality** that we have yet to resolve”

*Weiss & **Bellinger**, "Social Ecology of Children's Vulnerability to Environmental Pollutants", Env Health Perspectives, V 114, 2006*

On Consistency..

”Consistency in nature does not require that all, or even a majority of studies find the same effect. **If all studies of lead showed the same relationship between variables, one would be startled, perhaps justifiably suspicious**”

Source: Needleman (1995) *“Making Models of Real World events: the use and abuse of inference”*, *Neurotoxicology and Teratology*, vol 17, no. 3.

5. "Small" environmental causes can be very important:
 - a. As **links** in an interdependent causal chain
 - b. As "**triggers**" of diseases, however caused eg. Asthma
 - c. For large "**secondary**" **benefits** eg. Noise improvement from traffic reduction
 - d with low RR and widespread exposure
6. **Effectiveness evaluation** of policy interventions will be difficult
7. Increased relevance of the **precautionary principle and different strengths of evidence for different purposes..**

A definition of the PP based on “Late Lessons”

“The PP provides justification for public policy actions in situations of scientific complexity, uncertainty and ignorance, where there may be a need to act in order to avoid, or reduce, potentially serious or irreversible threats to health or the environment, using an appropriate level of scientific evidence, and taking into account the likely pros and cons of action and inaction”.

EEA, 2002

Some strengths of evidence..

- Beyond all reasonable doubt
- Reasonable certainty
- **Balance of probabilities/evidence**
- Strong possibility
- Scientific suspicion of risk
- Negligible/insignificant

..that are appropriate for different purposes

Bradford Hill on different strengths of evidence, 1965

The “case for action”... leads us to “**differential standards before we convict**” e.g.

- “**relatively slight evidence**” for pregnancy pill ban
- “**fair evidence**” for reduced/eliminated exposure to probable carcinogenic oil at work
- “**Very strong evidence**” for public restrictions on smoking or diets.

Bradford Hill, The Environment & Disease: Association or Causation?”, Proc Roy. Soc. Med , 1965, 58, 295-300.

Choosing an “appropriate “ strength of evidence

...involves accepting **the costs of being wrong**, in both directions (i.e. acting and not acting) and ,critically, on their **distribution** between groups and generations.

Who benefits and who gains from being wrong in acting not acting to prevent harm?

Choosing the ratio between FPs
and FNs..

This is generated by the **strength of evidence** chosen to justify precautionary action...which is an ethical choice between the costs of being wrong in acting/not acting

A Science/Policy Conflict?

Scientists generally prefer to avoid False Positives.....(which bring damaged reputations; “unsound” science..) by using high strengths of evidence..

Policymakers generally prefer to avoid False Negatives...(which bring damaged people; reduced public trust in politicians & scientists..)

ON BEING WRONG: Environmental Health Sciences and Their Directions of Error

SCIENTIFIC STUDIES	SOME METHODOLOGICAL FEATURES	MAIN ¹ DIRECTIONS OF ERROR-INCREASES CHANCES OF DETECTING A:
Experimental Studies	<ul style="list-style-type: none"> •High doses 	<ul style="list-style-type: none"> •False positive
(Animal)	<ul style="list-style-type: none"> •Short (in biological terms) range of doses •Low genetic variability •Few exposures to mixtures •Few Foetal-lifetime exposures •High fertility strains 	<ul style="list-style-type: none"> •False negative •False negative •False negative •False negative (Developmental/reproductive endpoints)

¹ Some features can go either way (e.g.inappropriate controls) but most of the features mainly err in the direction shown in the table

Observational Studies (Wildlife & Humans)	<ul style="list-style-type: none"> •Confounders •Inappropriate controls •Non-differential exposure misclassification •Inadequate follow-up •Lost cases •Simple models that do not reflect complexity 	<ul style="list-style-type: none"> •False positive/negative •False positive/negative •False negative •False negative •False negative •False negative
Both Experimental And Observational Studies	<ul style="list-style-type: none"> •Publication bias towards positives •Scientific cultural pressure to avoid false positives •Low statistical power (e.g. From small studies) •Use of 5 % probability level to minimise chances of false positives 	<ul style="list-style-type: none"> •False positive •False negative •False negative •False negative

(Gee, Bailer, Grandjean,2004)

Bradford Hill on Statistical Significance

“Too often I suspect we waste a deal of time, we grasp the shadow and lose the substance, we weaken our capacity to interpret the data and to take reasonable decisions whatever the value of P.”

Bradford Hill. 1965, *“Environment and Disease: Association or Causation”?*

Asymmetry arises from Complexity

- The **presence** of a causal criteria (consistency, temporality, strong association), is generally more robust than its **absence**.
- .
- Recognised by Bradford Hill.....
- But more pronounced now given complex systems

Complexity and MC: implications for Communications

- Clear & consistent **terminology** for Cause/Effect links
- Communication of **Uncertainties**
- Clear **rules for translating Knowledge into Evidence**, using types of argumentation, and evaluating strengths of evidence for different purposes.

Asymmetry in costs and benefits..

- **Costs of reducing risks** are usually easily quantified, short term ,and specifically distributed (*and they have been shown to have been much exaggerated because of dynamic efficiency gains*)
- **Benefits of reducing risks** are often hard to quantify, are usually long term, (discounting is an ethical issue), and are diffusely distributed
- And **losers shout whilst gainers don't**

Some costs of delays in acting on an EW

- 400b Euro for asbestos in Europe (cancers only, by 2030)
- 15b (2000-2017) for PCBs in Europe (soil cleaning only) Compare to cost of REACH, c.5b over 10 years
- 000's of jobs and billions of \$ for N.Atlantic . Fish stocks collapse.

Some benefits of “late” actions on EWs..

- \$22 trillion for 1970 Clean Air Act over 20 years.
- CFCs controls ..300,000 lives saved over some decades (plus other benefits eg agricultural productivity losses avoided)
- Health gains from reduced lead,SO2 etc

Evidence of success?

“the change in incidence of NHL in Sweden and other countries may serve as a good example of how prohibition and limitation of exposure may be reflected in cancer statistics some decades later”

Lennart Hardell, Mikael Eriksson, 2003.

Some Research Options for "Integrative Biology within socio-ecological systems"

- Identify emerging health issues from Wildlife; lay/local knowledge.
- long term monitoring of "surprise sensitive " parameters e.g. fetuses, fish, frogs and bees
- Effectiveness evaluation of such EW systems e.g. LTM (Avon study; Strat ozone monitoring)
- Identify scientific and statistical methods that achieve more economically efficient/ethically acceptable balance between FPs and FNs

Research Options...

- Dissolve the “effects /adverse effects” dichotomy with development of robust, predictive **biomarkers** of exposure/effects rooted in **epigenetics** (NHANES,US; Newgeneris)
- Evaluate/design human/ecological **tissue/biomarker banks** via European co-operation (Germany; Nordics)

Research Options

- Identify susceptible sub-groups via age, sex , location, host state (resilience reserves) (Ross Anderson, SAHSU, Dec 07)
- Investigate Use of clear, transparent, cause /effect terminology and “rules” for translating Knowledge into Evidence (EEA/ECDC)
- Implications of Multi-causality for human/economic burden of diseases methodologies.