

## Causality Assessment: Is There a Role for Biomonitoring?

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## Key Questions

1. Can biomonitoring data provide a basis for hypothesis generation regarding causes of disease?
2. Can biomonitoring data provide a basis for associating diseases with exposures?
3. Can biomonitoring data satisfy the requirements for a scientific assessment of causality?
4. Under what conditions / what types of biomonitoring data provide such bases?

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## Objective Thought Process

- Consider the nature of a cause
- Consider the means of assessing a cause
- Consider the consequences of different assessment concepts
- Consider the nature of scientific evaluations
- Leave the conclusions to you

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## Causality: 1800's - 1900's

Henle-Koch, 1882  
[In Scheutz & Poulsen, 1999]

- 1) Cause always present in disease
- 2) Cause NOT in other diseases
- 3) Cause is isolable from diseased individual
- 4) Isolated cause produces same disease in other individuals (animals)

Hill, 1965

- 1) Strength
- 2) Consistency
- 3) Specificity
- 4) Temporality
- 5) Biological Gradient
- 6) Plausibility
- 7) Coherence
- 8) Experiment
- 9) Analogy

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## Linear Causalism

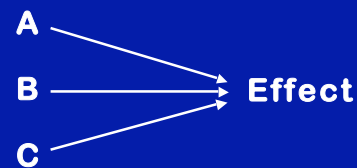
- One-to one correspondence between cause and effect;
- The same cause always produces the same effect and vice versa; a.k.a. mechanical determinism.
- Essential properties of linear causalism include:
  - 1) Sufficient cause: X always produces Y
  - 2) Necessary cause: X always precedes Y
  - 3) Specificity: X produces Y only
  - 4) Dose-response relationship: increasing X also proportionally increases Y
  - 5) Unidirectionality: the direction of the relation is from X to Y
  - 6) Externality: X is external to Y

Attena, 1999

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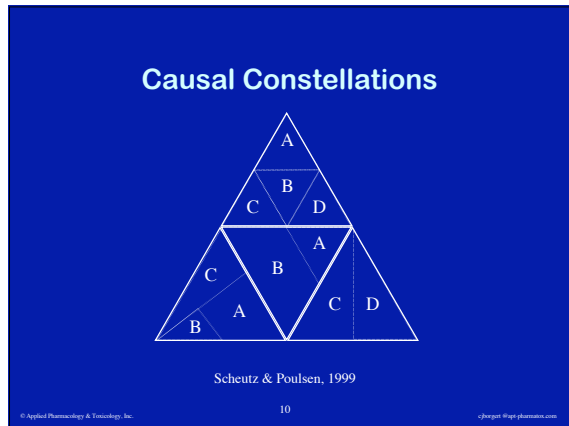
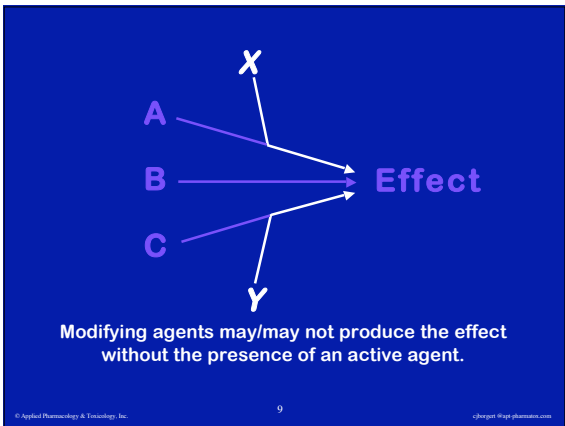
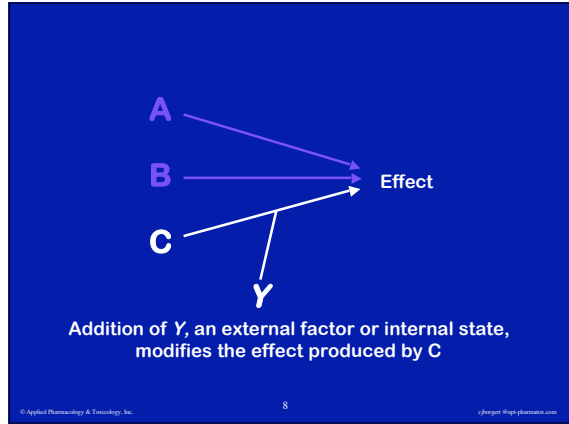
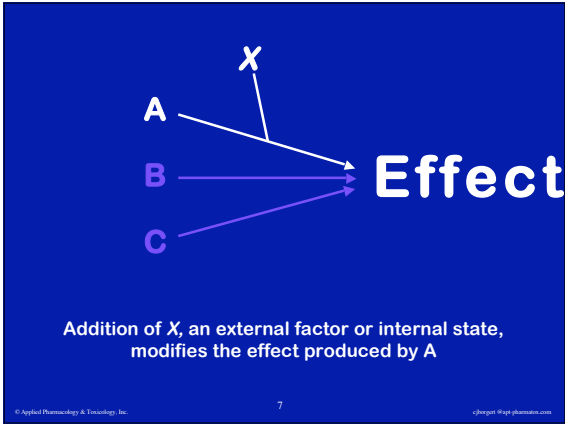


Causes A, B, C produce the same effect

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### Ranges of Rigor

<i>Stringent Causal Criteria</i>	<i>Relaxed Causal Criteria</i>
<ul style="list-style-type: none"> <li>Based on linear causalism</li> <li>Implies chain of connected events</li> <li>Implies necessity of each event</li> <li>Can be refuted by disproving a link in the chain</li> <li>Causal propositions insecure</li> <li>May reject real causes</li> </ul>	<ul style="list-style-type: none"> <li>Based on causal mosaic</li> <li>Implies web of related events</li> <li>No single event necessary or sufficient</li> <li>Refutation requires disproving all events</li> <li>Causal propositions tenured</li> <li>May accept unfounded causes</li> </ul>

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### Causality: Legal Analogy

“Another view of the causal relationship of an agent to disease might be framed in legal terms. ...In criminal law, the presence of the criminal at the scene of the crime would be equivalent of the presence of the agent in a lesion of the disease.”

“The proof of the guilt must be established beyond a reasonable doubt. The proof of causation must be established beyond reasonable doubt or role of chance.”

Evans, 1978 [Reprinted in 1995]

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## Causal Propositions vs Causal Assessment

“Hill, Susser, and others recognize that these criteria do not define cause *per se*, but merely provide guidelines for assessing it. Nonetheless, the criteria are occasionally used by epidemiologists and clinical researchers as though they provide an operational definition of causality: A causes B if and only if there exist studies for which the criteria are fulfilled. But this substitution of assessment criteria for the underlying meaning of causality can produce incorrect causal inferences.” Kramer & Lane, 1992

## Definitions of “Cause”

: that which produces an effect.

Oxford Dictionary [In Podrebarac et al. 1996]

: that which brings about any condition or produces any effect.

Dorland's Medical Dictionary, 27th Edition

: that which makes a difference.

: ‘...an object followed by another ... where, if the first object had not been, the second never had existed.’

David Hume, 1748 [In Maldonado & Greenland 2002]

## Hume’s Definition of “Cause”

“A key innovation of this definition was that it pivoted on a clause of the form ‘if C had not occurred, D would not have either,’ where C and D are actually what occurred.”

Maldonado & Greenland, 2002

## Types of Causal Propositions

Type	Locus (where)	Time Frame (when)
Retrodictive ( <i>it did</i> )	1 specific locus (i.e. dental caries)	Past
Potential ( <i>it can</i> )	Population	Past or Future
Predictive ( <i>it will</i> )	Specific individual or population	Future

Kramer & Lane, 1992

## Constructing the Counterfactual

- An alternative to the world observed;
- An alternative world that cannot be observed epidemiologically;
- The truth of a retrodictive causal proposition depends on the choice of the alternative world;
- “This principle applies to all three types of causal proposition; when a causal proposition interests us because we face a decision to which it is related, the choice of alternative world will be determined by the actions available to us.” Kramer & Lane, 1992
- Clinical trials [*experiment*] creates the counterfactual.

## Fundamental Tenets of Science

1. The identity of the measurements are demonstrable and amenable to estimation of error
2. The elimination of extraneous factors that can affect the measurements is certain
3. The result is repeatable in independent hands

✓ Satisfied by Henle-Koch

✓ May be satisfied by Hill, but requires criterion 8!

## Decisions, Decisions

### Clinical vs Public Health vs Legal Decisions

#### **Idiopathic Hepatotoxicity - Potentially Drug-Induced**

1. Remove potentially toxic drug
2. Do not remove drug
  - Treat with a lower dose of the drug
  - Treat with a different drug, nutrition change, etc. (each carries different risks)
  - ✗ Don't treat at all
3. Insufficient information to assess . . .
  - precaution includes the option to do nothing.

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## Is Biomonitoring a Scientific Assessment of Causality?

1. Is the identity of disease certain?
2. Is the measurement of chemical levels an accurate reflection of exposure . . . of dose?
3. Can it be demonstrated that those individuals with the larger dose are the individuals with disease?
4. Have the various factors that might affect measurements of disease or dose been eliminated?

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### What is *YOUR* Conclusion?

*Thanks for your attention!*

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