Science and the Law of Toxics
Scientists and Legislators
"Who are those Guys?"

Folk Heroes
or
Criminals

Union Pacific Posse

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Today …

- Distinguish between science and advocacy.
- Introduce 3 frameworks for evaluating scientific information.
  - Causal inference
  - Public health approach
  - Risk assessment approach
- Discuss some mercury issues related to air pollution, fish consumption, and vaccine safety

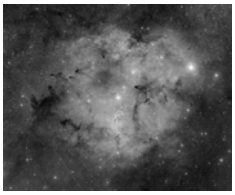
Science is **Not** Boring
(Hopefully)

- Astronomy and Astrology
- Causal Inference
- Public Health Approach
- Risk Assessment Approach
- Mercury in fish and vaccines

Boring Scientist

Can anyone confuse … Astronomy and Astrology?

Nebula IC 396 in the constellation of Cerbeus



Astronomists develop hypotheses to test astro-physical theories about the universe – the theories can be proven false!

Astrologists make predictions and do not test them for accuracy.

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We need both …

Science …

- Tests itself
- Always refines or reexamines its answers – never finishes.
- Creates novel questions.
- Success can be failure

Advocacy …

- Sets specific goals
- Takes sides
- Completion is the goal.
- Failure is never success.

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Judging Causal Inference

Austin Bradford Hill's Criteria

- Strength – 'A' has a strong effect on 'E'
- Consistency – 'A' effects 'E' in different experiments
- Temporality – 'A' precedes 'E'
- Preventability – removing 'A' also removes 'E'
- Dose-response – as 'A' varies so does 'E'
- Specificity – the association is specific
- Plausibility – the association has biologic plausibility
- Coherence – the association does not conflict with known biological facts
- Analogy – similar exposures will have similar effects

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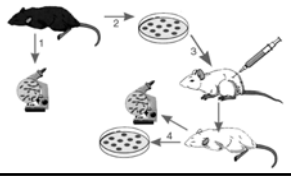
Types of Causes

- Necessary Cause – *Disease* 'D' cannot occur without *exposure* 'N'. (e.g. anthrax)
- Sufficient Cause – *Disease 'D'* **must** occur with *exposure* 'S'. (e.g. V-fibrillation)
- Component Cause – *Exposure* 'C' is one of several component causes that create a sufficient cause. (e.g. Hg and disability)



Koch's postulates

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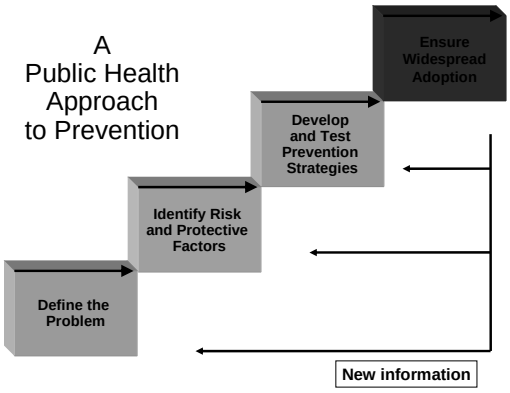
A Public Health Approach to Prevention



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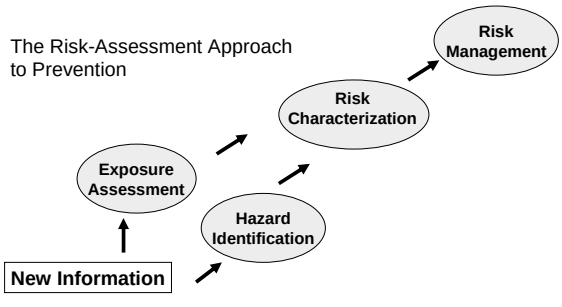
The Risk-Assessment Approach to Prevention



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Public Health Approach

- Goal is a change in morbidity/mortality
- Uses many studies
- Not assumption driven
- Accomplishment of goals are evaluated and adjustment in strategy expected.

Risk Assessment

- Goal is a critical value in the presence of uncertainty.
- Uses a single critical study
- Well defined assumptions
  - risk
  - uncertainty
  - people
- Critical value changed by redefining assumptions or new critical study.

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Forms of Mercury

Attribute	Elemental Hg	Inorganic Hg	Methyl Hg	Ethyl Hg
Common forms	Quicksilver	Hg^{+}& Hg^{++} salts, cinnabar, calomel	Bio-organified, manmade	Manmade
Sources	Dental amalgams, manometers, thermometers, switches, mining precious metals	Disinfectants, stool fixatives, skin creams, preservatives, batteries, lab reagents, folk meds, historical uses	Seafood, fungicides, (Other organic Hg: diuretics, antiseptics, phenyl Hg in paints)	Thimerosal in immuni-zations
Routes of Exposure	Inhaled monoatomic	Oral (accidental) dermal	Oral, dietary	IM

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Total Blood Hg and Methyl Hg Effects

Level (μg/L)	Associated Effects
< 1.9	95th percentile for children 1-5 yrs
< 4.6	95th percentile for women of childbearing age
58	Lower 95% confidence bound of level (85 μg/L) of cord blood associated with 5% increase in prevalence in abnormal Boston Naming Test (NRC)
50-100	Increasing prevalence of abnormal test components on neurodevelopmental testing in kids (cord blood). Complaints in adults of malaise, weakness, and reduced cognitive abilities.
100-500	Low prevalence of paresthesias, ataxia (100 μg/L = chelation w/ symptoms; 200 μg/L = chelation w/o symptoms)
>500	Increasing prevalence of paresthesias, ataxia, tremor, visual and auditory deficits. Low prevalence renal injury. Highest levels leading to brain damage, retardation, paraplegia, blindness, deafness, seizures, death

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Public Health and Risk Assessment methyl-mercury

Public Health ….

- High levels of methyl-Hg cause severe neurodevelopmental damage to the fetus (Iraq and Minimata)
- Low levels from eating lots of fish in Seychelles show no adverse effect.
- Low levels from eating whale in Faroese show subtle effect.
- Fish is a healthy source of vitamin and protein

Risk Assessment …

- NRC – used Faroese Island study
- CDC determines ~ 5% women 16-49 above RfD.
- RfD is 1/10th a conservative estimate of the LOAEL

CDC

methyl mercury (Hg)

Intervention Goals

- Decrease Hg releases
- Preserve fisheries
- Fish advisories and bans

Areas for additional Science

- Burden of disease from Hg emissions or fish consumption
- Utility of intervention strategies

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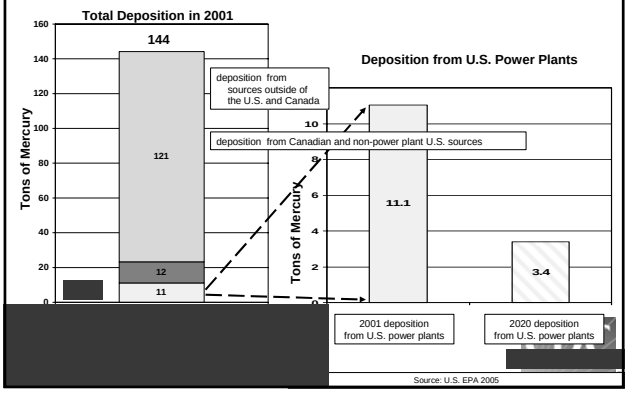
Mercury Deposition in the U.S.



Geometric mean and selected percentiles of blood concentrations (in µg/L) for males and females aged 1 to 5 years and females aged 16 to 49 years in the U.S. population, National Health and Nutrition Examination Survey, 1999-2002.

Mercury in blood	Survey years	Geometric mean (95% conf. interval)	Selected percentiles (95% confidence interval) 50th	75th	90th	95th	Sample size
Age Group							
1-5 years (females and males)	99-00	.343 (.297-.395)	.300 (.200-.300)	.500 (.500-.600)	1.40 (1.00-2.30)	2.30 (1.10-3.50)	705
	01-02	.318 (.268-.377)	.300 (.200-.300)	.700 (.500-.800)	1.20 (.900-1.60)	1.90 (1.40-2.90)	872
Females	99-00	.377 (.299-.475)	.200 (.200-.300)	.800 (.500-1.10)	1.60 (1.00-2.80)	2.70 (1.30-5.50)	318
	01-02	.329 (.285-.407)	.300 (.200-.300)	.700 (.500-.800)	1.30 (1.00-2.10)	2.60 (1.30-4.90)	432
Males	99-00	.317 (.269-.374)	.200 (.200-.300)	.500 (.500-.600)	1.10 (.800-1.60)	2.10 (1.10-3.50)	387
	01-02	.307 (.256-.369)	.300 (.200-.300)	.600 (.400-.700)	1.30 (.900-1.70)	1.70 (1.40-2.00)	440
16-49 years (females only)	99-00	1.02 (.835-1.27)	.900 (.800-1.20)	2.00 (1.50-3.00)	4.90 (3.70-6.30)	7.10 (5.90-11.3)	1709
	01-02	.833 (.756-.940)	.700 (.700-.800)	1.70 (1.40-1.90)	3.00 (2.70-3.50)	4.60 (3.70-5.90)	1928
Race/ethnicity (females, 16-49 years)							
Mexican Americans	99-00	.820 (.684-1.01)	.900 (.700-1.00)	1.40 (1.20-2.00)	2.60 (2.00-3.60)	4.00 (2.70-5.50)	579
	01-02	.667 (.541-.824)	.700 (.500-.800)	1.10 (1.00-1.40)	2.10 (1.70-3.00)	3.50 (2.30-4.40)	527
Non-hispanic blacks	99-00	1.35 (1.06-1.73)	1.30 (1.10-1.70)	2.60 (1.80-3.40)	4.80 (3.30-6.60)	5.90 (4.20-11.7)	370
	01-02	1.06 (.871-1.29)	1.10 (.800-1.20)	1.80 (1.50-2.20)	3.20 (2.20-3.90)	4.10 (3.30-6.00)	436
Non-hispanic whites	99-00	.944 (.726-1.23)	.900 (.700-1.10)	1.90 (1.30-3.30)	5.00 (3.00-6.90)	6.90 (4.50-12.0)	588
	01-02	.800 (.697-.919)	.800 (.700-.800)	1.50 (1.30-2.00)	3.00 (2.20-3.70)	4.60 (3.30-6.80)	806

Calculated Exposure Limits for Mercury:
Using Various Agency Guidelines for Exposure to Methylmercury
Infants ≤ 6 Months of Age by Percentile Body Weight

Agency	Percentile Body Weight		
	5th	50th	95th
EPA	65 µg	89 µg	106 µg
ATSDR	194 µg	266 µg	319 µg
FDA	259 µg	354 µg	425 µg
WHO	305 µg	417 µg	501 µg

CDC

Cumulative Exposure to Mercury from Vaccines
U.S. Children @ 6 months of age

	Total Minimum Mercury Dose	Total Maximum Mercury Dose
1999	12.5 µg	187.5 µg
2005	< 3.0 µg	28.0 µg

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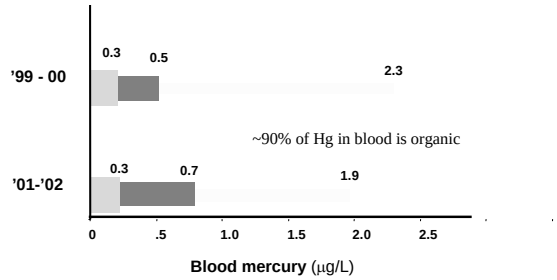
Total Blood Mercury in Children Aged 1 to 5, United States, 1999-2000 and 2001-2002

50th, 75th and 95th percentiles



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Fetal/child development and Hg in Fish and Vaccines Causal Criteria

	Methyl Hg in fish	Ethyl Hg - Autism
Strength	yes and no	no
Consistency	yes and no	no
Temporality	yes	yes
Preventability	yes and no	no
Dose-response	yes	no
Specificity	no	unknown
Plausibility	yes	unknown
Coherence	yes	no
Analogy	yes	no

CDC

Today we …

Distinguished between science and advocacy.

Introduced 3 frameworks for evaluating scientific

Discussed mercury issues related to air pollution, fish consumption, and vaccine safety

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