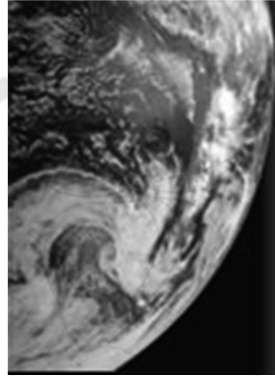


Environmental epidemiology II.

How do we know
when the
environment is
harmful?



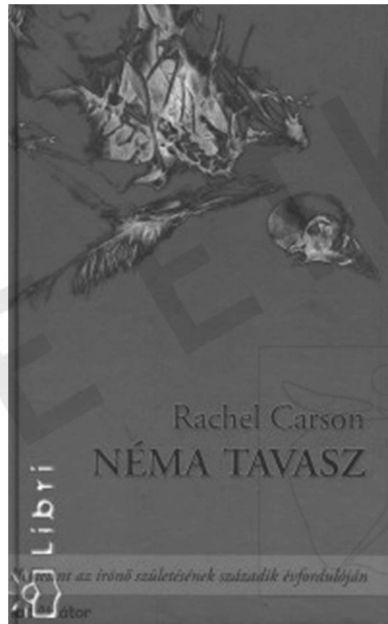
Rachael Carson



- English, Biology
- *The Sea Around Us*: 1951 best seller
- Full-time writer, Maine
- DDT magazine story
- *Silent Spring*, 1962
- Died 1964



Rachel
Carson



DDT: Regulatory Arena

- Paul Muller (1948)
 - Nobel prize
- Amount applied in U.S. (1950-72)
 - 675,000 tons
- Banned in U.S. 1972
- National Academy of Sciences
 - *Saved 500 million lives worldwide*

Internal Body Exposure?



Exposure Data

- Biologic sample (blood, urine)
- Personal air sample
- Measurements in vicinity
- Est. of air, water, food intake
- Distance from point source

Best



Poorest

DDT in Breast Milk

Country	Year	Microg/kg	
U.S.	1950	5200	
U.S.	1961	3300	
U.S.	1973	880	
U.S.	1974	2360	Smith D
U.S.	1980	2500	Int J Epidemiol. 1999
U.S.	1986	990	Apr;28(2):179-88.
U.S.	1989	550	

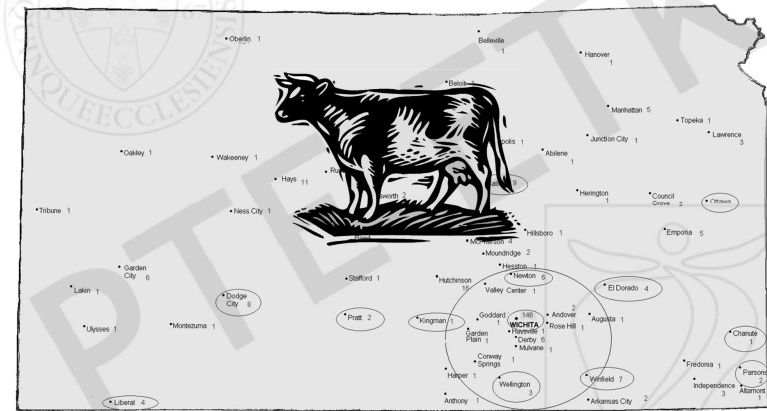
DDT in Breast Milk

Country	Year	Microg/kg	
Kenya	1986	4800	
India	1989	3740	
Mexico	1989	6250	Smith D
Viet Nam	1989	11,400	Int J Epidemiol. 1999
Jordan	1990	6420	Apr;28(2):179-88.
Zimbabwe	1990	6000	

Kansas, USA: Nitrate, Drinking Water Wells



Kansas Feedlots



Kansas, USA: Drinking Water Wells



- Nitrate exposure
 - US Nitrate standard: < 10 mg/L
 - Private wells exempt
 - Of 110,000 private wells, estimated 25% are above 10 mg/L = **27,500 wells**
 - Public perception: OK if no baby
 - But chronic effects may occur
- Environ Health Perspect* 2005;113:1607-14



Methemoglobinemia in Transylvania

Catherine Zeman, Burton Kross, Marianna Vlad. *Environ Health Perspect* 2002;110:817-22

- Case control study by:
 1. Institute of Public Health, Cluj-Napoca, Romania
 2. University of Northern Iowa, USA
 3. University of Iowa, USA
- Led to KSOHIA Project



Methemoglobinemia

Environ Health Perspect 2002;110:817-22



- Case-control design

- Participants with/without the disease
- Look for exposures & risk factors

	Cases	Controls
Well nitrate, ppm	253	28
Breast feeding, months	0.75	4



WHO Case Studies: Drinking Water Wells



- Campaign, Romania:

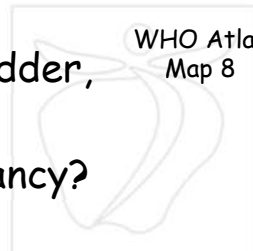
- Survey: 2,480 people
- Hydro-geological study
 - Municipal wells
 - Mean nitrate: 120 mg/L
- Preventive solutions
 - Water purification
 - Education
 - Address pollution: farms, other sources



Atlas of Children's Health & the Environment

- Drinking Water & Arsenic
- Skin pigmentation, hyperkeratosis
- Cancer (skin, lungs, bladder, kidney)
- Problems during pregnancy?

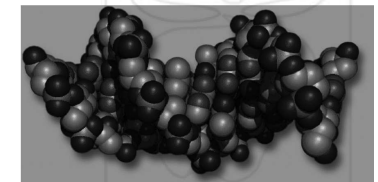
WHO Atlas
Map 8



When is an association causal?

Multicausality of disease

- Epidemiologic triad
- Miscarriage or preterm birth
 - ✓ Exposure to chemical?
 - ✓ Other risk factors?
 - ✓ Genetic vulnerability?



Applying Causality Criteria



- Bangladesh
Arsenic in drinking water and pregnancy outcomes
Ahmad et al. *Environ Health Perspect* 2001;109:629-31
- Cross-sectional study
 - Well water mean 0.240 mg/L (guideline: 0.05 mg/L)
 - Random sample of villagers, home visit, interview



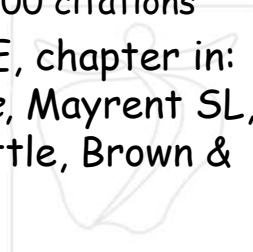
Origin of Causality Assessment Guidelines

- Koch's postulates (1880s)
 - Specificity of association
 - One bug, one disease
 - Experimental exposures
- Sir Bradford Hill
 - Proc Royal Soc Med 1965;58:295-300



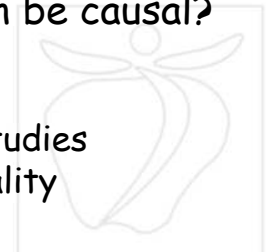
CH Hennekens, MD, DrPH

- Updated the Bradford Hill Criteria
- PubMed:
 - Hennekens CH [AU]: > 500 citations
- Hennekens CH, Buring JE, chapter in: *Epidemiology in Medicine*, Mayrent SL, editor. 1987, Boston, Little, Brown & Co., p. 45



Causality Criteria

- Is there a valid statistical association?
 - Chance
 - Bias
 - Confounding
- Can this valid association be causal?
 - Strong association
 - Biologic credibility
 - Consistency with other studies
 - Time sequence / Temporality
 - Dose-response



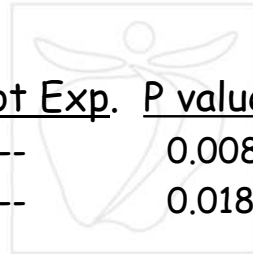
Chance



- Was the relationship between the purported causal factor and the health outcome statistically significant?

Arsenic study: **Very good**

	<u>Exposed</u>	<u>Not Exp.</u>	<u>P value</u>
Miscarriage	--	--	0.008
Preterm birth	--	--	0.018



Bias



- Could the relationship between the purported causal factor and the health outcome be the result of bias?

Selection bias

Non-representative participants?

Arsenic study: Random sample-- **Very good**



Bias



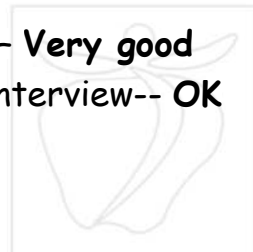
Misclassification bias

Mistakes in exposure, disease assessment

Arsenic study:

Water arsenic measured- **Very good**

Pregnancy outcomes by interview-- **OK**



Confounding

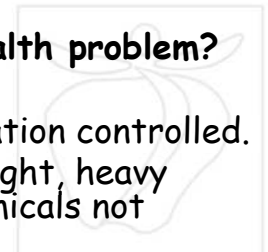


- Could the relationship between the purported causal factor and the health outcome be the result of confounding?

What else causes this health problem?

Arsenic study: **OK**

- Maternal age, SES, education controlled.
- Parity, pre-pregnancy weight, heavy physical work, other chemicals not controlled.



Strong Association

- Check size of the effect

Arsenic study: **Moderately strong**

	<u>Exposed</u>	<u>Not Exp.</u>	<u>Ratio</u>
Miscarriage*	68.8	23.7	2.9
Preterm birth*	68.8	27.1	2.5

per 1,000 live births



Biologic Credibility

- Supporting evidence from animal studies?
- Molecular mechanism known?

Arsenic study: **Very good**

Arsenic is known teratogen

Also is a human carcinogen; carcinogens often are reproductive toxicants



Consistency

- Other studies agree?
- PubMed search:

Arsenic study: **Good**

Epidemiology 2005;16:82-6

Several other studies



Time Sequence

- Did the exposure really happen before disease onset?

Arsenic study: **Good**

Water chronically contaminated. Asked about migration history. Cohort study design would have been stronger



Dose-response



- Separate population into subgroups by amount of exposure

Arsenic study: **Very good**

Years drinking arsenic-contaminated water:

	< 15 yrs	> 15 yrs	P Value
Miscarriage*	43.5	133.3	0.003
Preterm birth*	47.8	122.2	0.021

per 1,000 live births

Causality Summary: Arsenic



Chance	Very good
Bias	Good to very good
Confounding	OK
Strong association	Moderate
Biologic credibility	Very good
Consistency, other studies	Good
Time sequence	Good
Dose-response	Very good

Causality Assessment:

Try applying criteria to this article

Maternal exposure to low-level air pollution and pregnancy outcomes: A population based study

Marozziene et al. *Environ Health* 2002;1:6
[e-pub]



DDT & Children Today

- Men, sperm DNA breaks: Sweden
 - *Environ Health Perspect* 2005
- Low birth weight: India, Sweden
 - *Int Arch Occup Environ Health* 2003
 - *Scand J Work Environ Health* 1995



To be continued...
KSOHIA sessions,
Human Reproduction and
the Environment



**Thank You For Your
Attention**

