The "Environmental" in Occupational and Environmental Medicine: The Present and the Future

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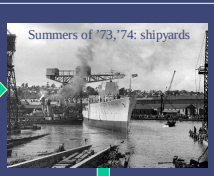
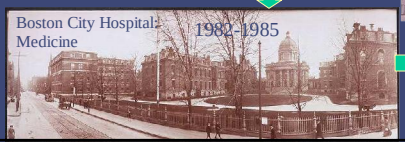
Topics

- A. Personal perspective: my journey
- B. Conventional "Environmental Medicine" (Air pollution, children, toxic waste, etc.)
  - Contemporary issues and the latest science
- C. Broadening the definition of "Environmental Medicine"
  - The built environment, climate change, etc.
- D. Incorporating environmental medicine into daily practice

Introduction: My journey

To Ann Arbor: 2006





Faculty: 1988

Harvard OEM & Epi: 1985-1988

Research: The Metals Epidemiology Research Group (now a Michigan-Harvard Collaboration)

- Pediatricians, Internists
- Neuroscientists,Toxicologists
- Epidemiologists, Statisticians
- Chemists, Physicists
- ***Forte:***

Multi-disciplinary Environmental Epidemiology Using Novel Techniques for Measuring Dose and Early Effects

- ***Application:***

Research on Aging adults and Newborns/Infant development

JAMA

PEDIATRICS

Circulation

American Journal of EPIDEMIOLOGY

Environmental Health perspectives

Training

- The Harvard Occupational/Environmental Medicine Residency, 1996-2006
  - Total overhaul of curriculum; growth of Env Med curriculum; ACGME accredits x 2
  - Domination of OPSFs, Military scholars
  - New rotations at OH&R, ATSDR, Ministry of Labor, NRDC, Johnson Space, etc.
  - 50 trainees, outstanding research, 86% pass rate on Boards
  - Careers in OEM services, NIOSH, Academia, State Health Depts, WHO, NRDC, etc.
  - Successful transition to new leadership: *Stefanos Kales*

Teaching

- Introduction to Environmental Health

- Human Health and Global Environmental Change

Founding Medical Editor (1998): *Environmental Health Perspectives*

- Environmental medicine section
  - Original Research (with clinical outcomes)
  - Grand Rounds
  - Case Reports
  - Reviews
- Impact score: now 5.4
  - Top EH journal

Clinical—in the trenches…

- Kindred Health Care (AKA, Northeast Specialty, Olympus Specialty, Mass Respiratory, Norfolk County Hospitals!!)

- *Clinical OEM with David Christiani for 21 years….*
- *…and Dianne Plantamura, Tom Gassert, Uma Dhanabalan, Karen Cassidy, and a generation of trainees…*

What is Environmental Medicine?

- ACOEM: "*Occupational and environmental medicine is the medicine specialty devoted to prevention and management of occupational and environmental injury, illness and disability, and promotion of health and productivity of workers, their families, and communities.*"
- QUESTION: What is Environmental "Injury, Illness, and Disability"?
- FOCUS OF THIS TALK: on what is *new*
  - "Conventional" Environmental Medicine
    - Axes of Discovery
  - "Unconventional" Environmental Medicine

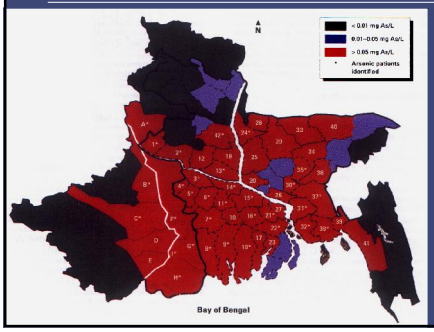
"Conventional" Environmental Medicine: AXES OF DISCOVERY

- NEW and NEWLY-RECOGNIZED toxicant exposures
- Diseases NEWLY-RECOGNIZED as possibly or probably environmental
- Sub-populations NEWLY-RECOGNIZED as being susceptible/vulnerable
- Other NEWLY-RECOGNIZED interactions
- UNKNOWN mechanisms of disease

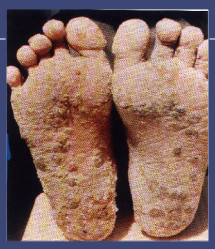
New and Newly-recognized Toxicant Exposures

- Well-recognized exposures
  - E.g. Outdoor air pollution, lead paint poisoning, pesticides, indoor air pollution, water pollution
- Newly recognized exposures
  - E.g., Arsenic in water (Bangladesh, Taiwan, Chile, New England, Arizona)
- New exposures
  - E.g., PBDFs, phthalates, manganese gas additive, nanoparticles…

Bangladesh: One environmental "solution" creates another environmental disaster



Arsenic poisoning in West Bengal from contaminated well water (EHP: 108, 2000)



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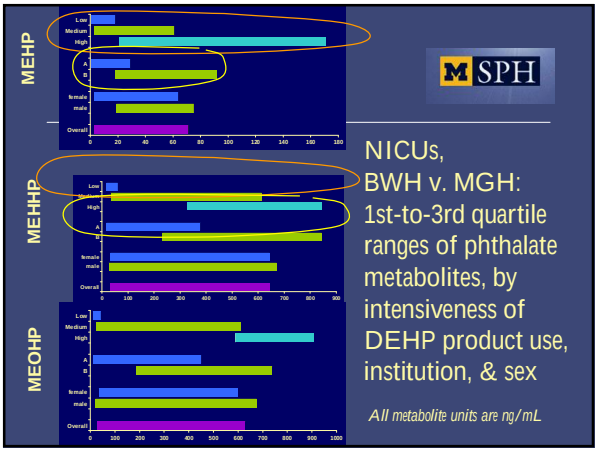
Arsenic poisoning in West Bengal
(EHP: 108, 2000)

Where are phthalates?

Building materials

Phthalates: Probable human endocrine disruptors

- Animal studies: some phthalates (at very high doses) are reproductive and developmental toxins
  - Data are most consistent and abundant for testicular development and function
- Human studies: extremely limited
  - See Hauser & Calafat. *Occup Environ Med* 2005.
- Are there human populations that have unusually high exposure to phthalates?



NICUs, BWH v. MGH: 1st-to-3rd quartile ranges of phthalate metabolites, by intensiveness of DEHP product use, institution, & sex

All metabolite units are ng/mL

Diseases NEWLY-RECOGNIZED as possibly or probably environmental

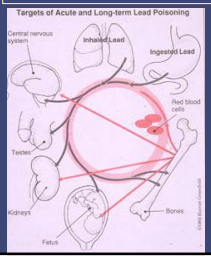
- Cardiovascular Disease
  - Hypertension
  - Heart attacks, stroke
- Dementia, Parkinson's Disease, ALS
  - Other neurodegenerative diseases
- Other chronic degenerative conditions
  - Cataracts
  - Osteoporosis
- Reproductive abnormalities
  - Declines in sperm counts
- Cancer
  - Brain, testicular, leukemia, breast, etc.

Linking exposures to Chronic disease

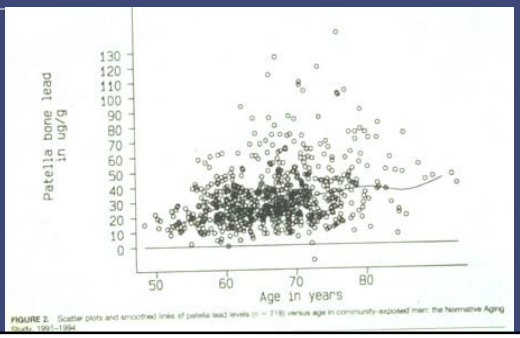
- *The lack of chronic exposure dosimeters*
  - *"Exposure, exposure, exposure"---the mantra of all environmental epidemiologists*
  - Poor characterization of dose extent, initiation, termination, windows of vulnerability…
    - "The definition of a public health disaster---one in which the effect is so huge that even an environmental epidemiologic study can detect it."
      - …David Ozanoff, fomer Chair of EH at Boston University

Lead and chronic disease: Novel methods for measuring cumulative dose

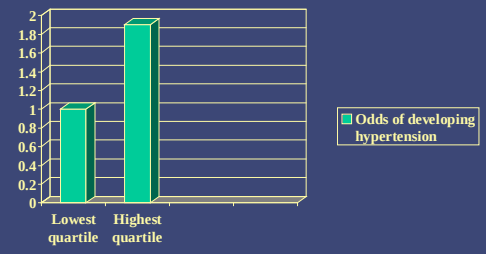
- K-x-ray fluorescence instruments for measuring levels of lead in bone…



Population data: the Normative Aging Study

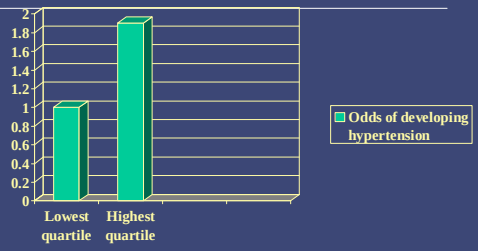


Example of *adult exposure, aging outcome*: Hu et al. (JAMA, 1996). Bone lead and risk of hypertension in community-exposed men.*



*Adjusted for age, body mass index, family history of hypertension, smoking, alcohol ingestion, dietary calcium, dietary sodium

Korrick et al. (Am J Public Health, 1999). Bone lead and hypertension in nurses.*

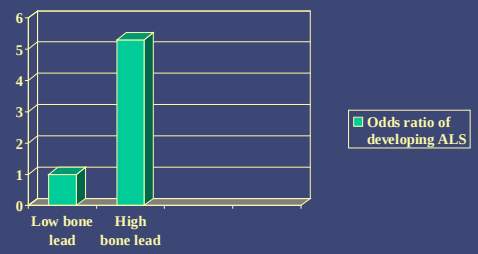


*Adjusted for age, body mass index, family history of hypertension, smoking, alcohol ingestion, dietary sodium, dietary calcium

Weisskopf et al. (AJE, 2004). Bone lead and prospective change in MMSE.

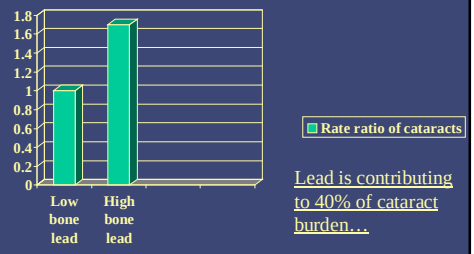
- Interquartile increase in bone lead (20 µg/g) associated with 0.3 point/year steeper decline in MMSE.
- Equivalent to 5 years of excess aging.

Bone Lead and Specific Neurologic Diseases: Kamel et al. (Epidemiology, 2002). Bone lead and Amyotrophic Lateral Sclerosis.*



*Case-control study; adjusted for age, sex, region.

Schaumberg et al. (JAMA, 2004).
Bone lead and risk of cataracts in the NAS.*



Lead is contributing to 40% of cataract burden…

*Adjusting for age, smoking

On the horizon: cadmium

- Staessen et al., Lancet 1999
  - Modest cadmium exposures in Belgium
    - ↑risk of osteoporosis, height loss in men & women
    - ↑risk of bone fracture in women

Sub-populations NEWLY-RECOGNIZED as being susceptible/vulnerable

- Vulnerable because of biology
  - Children
  - Elderly, pre-existing disease
  - Genetic sub-types

Children: Our Hopes and Fears— Does exposure to common pollutants impact their development?

- Neurodevelopment
- Behavioral development
- Physical development
- Sexual maturation

Preview of cutting edge topic:

- Do early life exposures impact the risk of late-life disease?????
  - The Barker hypothesis

Vulnerability-Why? Reason #1: poverty=exposures

- 13% of Americans live in poverty
- 20% of American Children live in poverty
  - Higher rates of exposure to toxic chemicals
  - Poorer nutrition- itself toxic, but can also increase internal dose of some toxicants
  - Fewer opportunities for recreation/education
  - Decreased access to Medical care

Individual Characteristics

- Pound for pound children
  - Drink more water
  - Eat more food
  - Breathe more air in a given day
- Infants specifically
  - Drink 7 times as much water (the major constituent of formula and breast milk)
  - Breathe 3 times faster than an adult and per body weight- breathe twice as much air
- Unique food patterns
  - 21 x apple juice; 11 x more grape juice

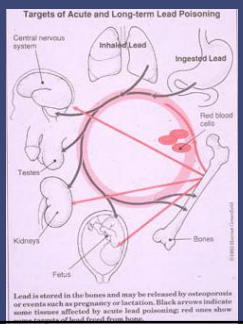
Individual Characteristics (continued)

- Children like to put their hands in their mouths
  - Hand to mouth activity begins almost immediately and does not begin to dissipate until age 3-4 years
- Children are low to the ground
  - Whatever is on the floor(dust) or soil will get ingested
  - Some toxicants sequester in low-lying layers of air, such as pesticide vapors

Biological Characteristics

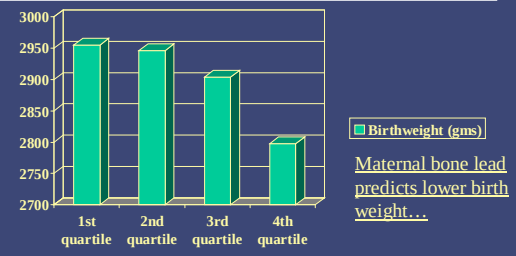
- Children's bodies are developing
  - Metabolic pathways are immature, different ability to detoxify and excrete toxicants (usually, worse)
- Each system (brain, liver, heart, lungs, immune etc) develops at a different rate
  - Periods of key development comprise windows of vulnerability
- Chemicals can:
  - Cause cell loss
  - Alter the process of neuronal connections
    - Anatomically appears normal, but functionally altered
  - Inappropriately, turn on or off signals which regulate DNA transcription

Back to the example of lead: Fetal Exposures



- The maternal skeleton dissolves itself to provide calcium to the fetus…
- Lead is mobilized with the calcium…

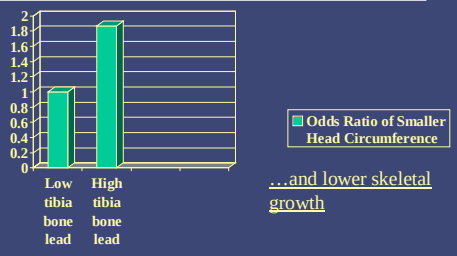
Gonzalez-Cossio et al. (Pediatrics, 1997). Bone lead and birth weight in 272 mothers in Mexico.*



Maternal bone lead predicts lower birth weight…

*Adjusted for gestational age, parity, smoking, maternal calf circumference, education

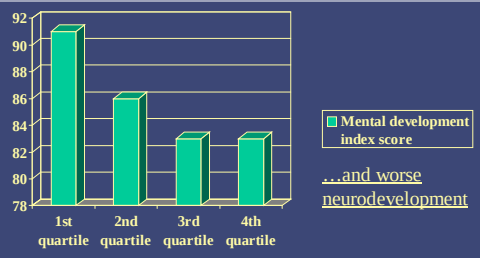
Hernandez-Avila et al. (Arch Env Health, 2002). Maternal bone lead and head circumference at birth.*



…and lower skeletal growth

*Adjusted for maternal age, cord blood lead, birth weight.

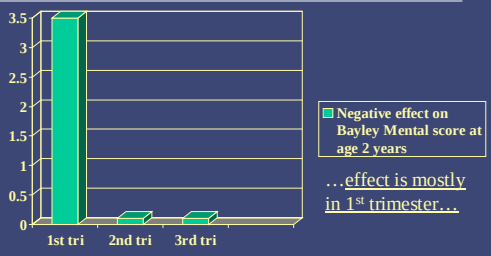
Gomaa et al. (Pediatrics, 2002). Maternal bone lead and offspring IQ (Bayley scales) at age 2.*



…and worse neurodevelopment

*Adjusted for maternal age, IQ, gender, maternal education, paternal education, parental marital status, breast feeding duration, cord blood lead.

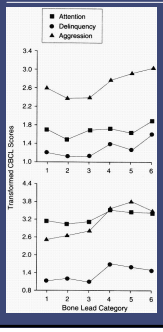
Specificity of maternal/fetal exposures:
Hu et al. (EHP, 2006). Trimester-specific maternal plasma lead as predictor of IQ at age 2.*



…effect is mostly in 1st trimester…

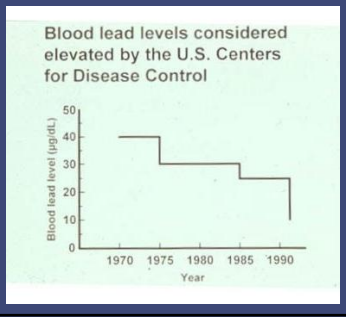
*Adjusted for maternal age, IQ, gender, maternal education, paternal education, parental marital status, breast feeding duration, cord blood lead.

Needleman et al., (JAMA, 1996): Bone lead and behavior



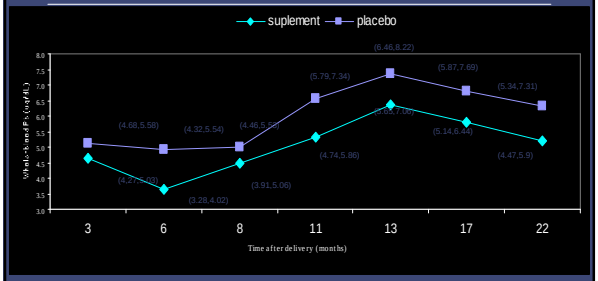
- Bone lead levels in adolescents predicted:
  - Increased attentional disorders
  - Increased aggression
  - Increased risk of juvenile delinquency acts
    - Parents scores (top)
    - Teachers scores (bottom)

Progressive decline in allowable levels of lead in a child's blood…



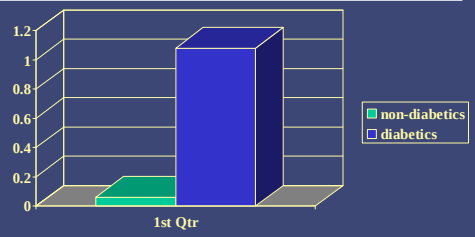
- Have we missed the boat by ignoring fetal exposures?
- CDC committee currently meeting to figure out…

Preliminary results: calcium trial during *pregnancy*



Study month (9 mo= delivery)

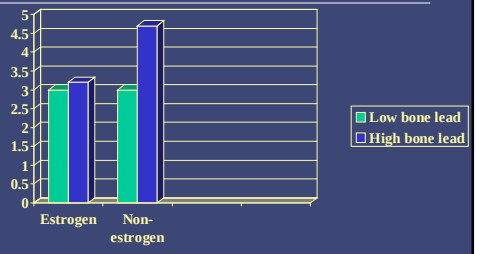
LEAD-AGING INTERACTIONS: Increase in serum creatinine associated with an increase in bone lead: non-diabetics v. diabetics* (Tsaih et al., 2004)



Type II Diabetics do much worse!!!!!

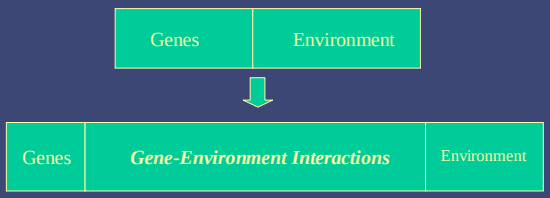
*Adjusting for age, hypertension, baseline serum creatinine, smoking, use of analgesics, diuretics, body mass index

Korrick et al. (AJE, 2002). Estrogen replacement as modifier of the bone lead-blood relationship in Nurses. *



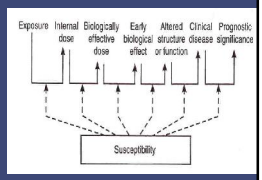
*Adjusted for age, smoking, alcohol ingestion, parity

What causes disease? The evolution of a paradigm…



Vulnerability due to genetic subtype

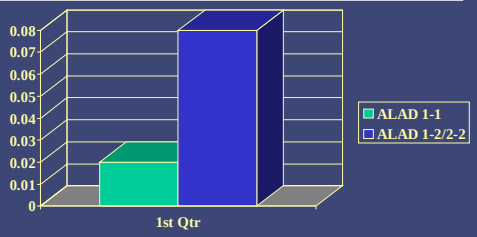
- Our strategy for discovery: selecting candidate genetic polymorphisms
  - Functional polymorphisms
  - Phenotype is well-known to be involved in metabolism of lead or other metals



Example: The δ-aminolevulinic acid dehydratase (ALAD) polymorphism

- 2nd enzyme in heme synthesis
- Polymorphic, single nucleotide mutation
- Wild type: ALAD 1-1
- ~15% population has ALAD 1-2 or 2-2
- ALAD-2 subunit appears to bind lead more tightly than the ALAD-1 subunit
- ALAD-2 carriers seem to have higher blood lead levels

Wu et al., (EHP, 2003). ↑ serum creatinine (mg/dL) assoc. with ↑bone lead of 40 µg/g, by ALAD*



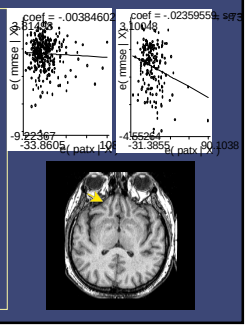
*Adjusting for age, BMI, hypertension, alcohol consumption, current smoking, analgesic meds; interaction p-value=0.025

But: Bellinger et al. (Arch Env Health, 1994). ALAD carriers had attenuated effects of lead on cognition in kids.

Test	Performance, ALAD2 gene carriers
Digit span, Arithmetic, Digit symbol	Better
Cancellation	Better
Trail-making	Better
Stroop	Same
CPT, correct, errors, reaction time	Better
Wisconsin sort test	Better
IQ	Better

Similar paradoxes

- The hemachromatosis genes (C282Y, H63D)
  - Accelerated lead-associated declines in renal function and cognition in elderly men (in preparation)
  - BUT less lead-associated effects on hematopoiesis and weight in infants (Wright et al., 2002)
- The APOE4 gene
  - Well-known as risk factor for Alzheimer's in the elderly
  - BUT less lead-associated declines in cognition amongst 2-year old children (Wright et al., 2003)



What is going on?

- Could this be evidence for the *antagonistic pleiotropy* theory of aging?
  - Some genes put humans at risk for chronic disease
  - Why would such genes be retained during the course of evolution?
    - *…because they might confer selective advantages when the organism is young*

Vulnerable because of Other interactions

- Vulnerable because of other interactions
  - Toxicant-toxicant
    - Asbestos, smoking and cancer
    - Other interactions? Yes, probably so.
  - Nutrient-toxicant
    - Toxic metals, dietary iron, zinc, calcium
  - Toxicant-stress

Vulnerable because of where one lives

- Environmental justice in our communities
  - Superfund siting
- The exportation of hazardous industries, products and wastes
  - Joe LaDou, last year's Harriett Hardy awardee

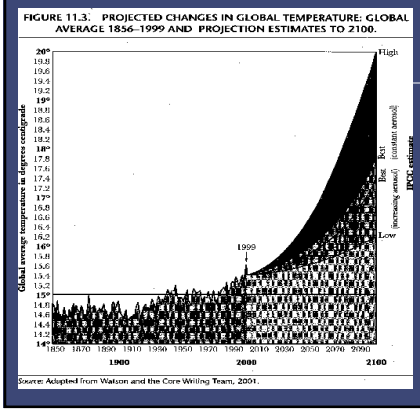
Unknown Mechanisms of Disease

- Air pollution and heart disease
  - Ischemic heart disease, arrythmias, heart failure
  - Environmental oxidants→
    - ↑synthesis of nitric oxide
    - ↑endogenous production of reactive oxygen species
  - BUT which pollutants? Do they act independent of other risk factors? Who is susceptible?
- Metals and cognitive delays and declines
  - Pro-oxidant damage?
- Environmental carcinogenesis
  - Epigenetic change as well as DNA damage?
- Chronic illness syndromes (e.g., MCS/IEI)
  - My view: NOT just ψ, although ψ plays a co-morbid role
  - Likely at least partly neurogenic

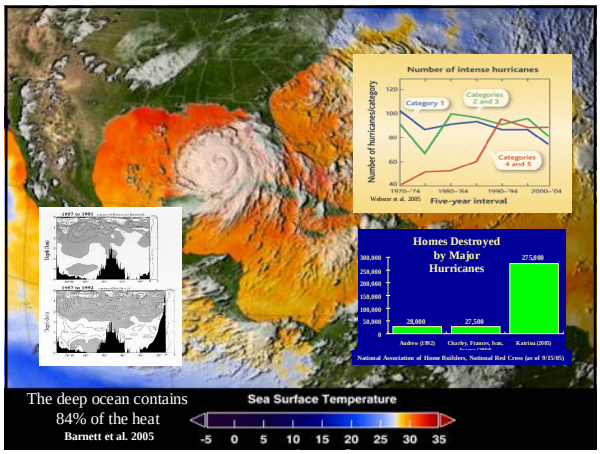
"Unconventional" Environmental Medicine

- Global environmental change
  - Climate change, warming, extremes of weather
  - Destruction of habitat, over-hunting, over-fishing, human encroachment

    →Loss of biodiversity
  - The built environment, megacities



The "debate" is over…



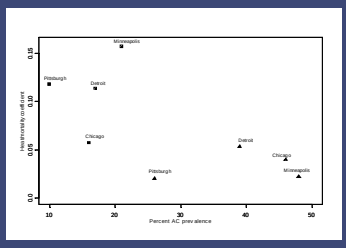
Mortality from the 2003 Heat Wave in Europe

Source: Kovats, Wolf and Menne, 2004.

Country	Heatstroke Deaths	Excess Deaths (%)	Time Period	Method for Estimating Baseline Mortality
England/ Wales	1	2,045 (16%)	August 4 to 13	Deaths in same period in years 1998 to 2002
France	n.a.	14,802 (60%)	August 1 to 20	Average of deaths in same period years 2000 to 2002
Italy	n.a.	3,134 (15%)	June 1 to August 15	Deaths in the same period in year 2002
Portugal	7	2,099 (26%)	August 1 to 31	Deaths in same period in years 1997 to 2001
Spain	59	?		

Heat related deaths in the U.S.: race as a modifier---

Marie O'Neill and colleagues…



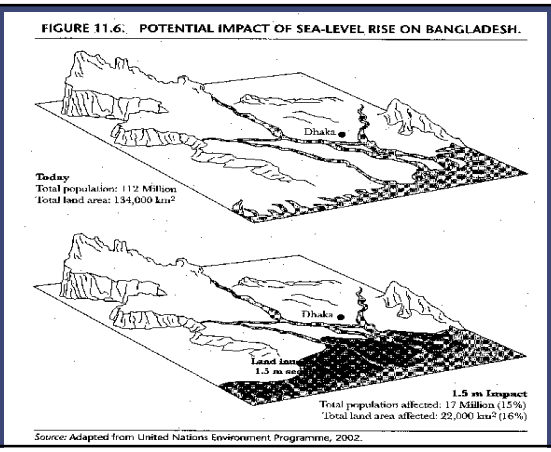
Relative risk of mortality on hot days by prevalence of air conditioning, race and city. △ Whites ■ Blacks

Conclusion: Access to air conditioning and correlated socio-economic factors explains much of the mortality during hot weather among African Americans

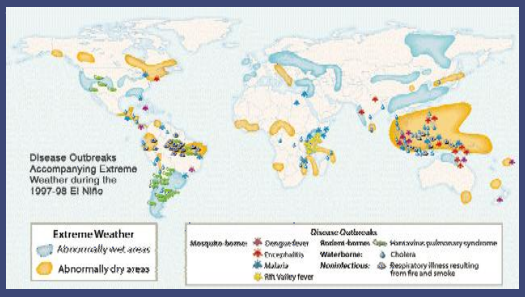
O'Neill MS, et al. (2005) Disparities by race in heat-related mortality in four U.S. cities: The role of air conditioning prevalence. Journal of Urban Health 2005;82(2):191-197

Rising sea levels

- 13 of world's 20 megacities are at sea level
- Rise of 1 meter of sea level would affect
  - 18.6 million people in China
  - 13-17 million people in Bangladesh
- Also, would cause salination of coastal freshwater aquifers
- *Think: migration, civil conflict*



Extreme Weather Events & Disease Clusters



Work of Paul Epstein and colleagues…

Biodiversity

- Relationship between area of protected wildlife and species biodiversity is exponential
- Accelerating loss of species
  - Implications for food supply, pharmaceuticals, genetic diversity
- Eric Chivian and colleagues…

Ecology and Human Disease

Richard Osterman and colleagues…

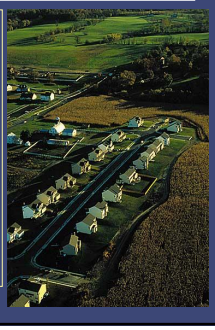
Raptors

Rodents

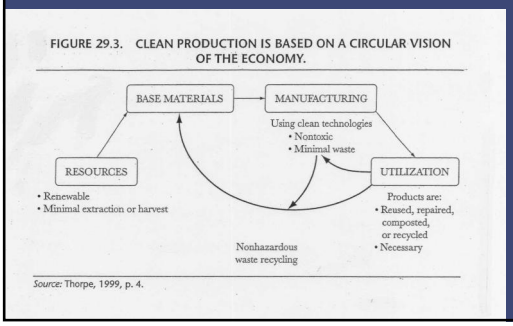
Lyme disease
Hantaviruses
Arenaviruses
Leptospirosis
Toxoplasmosis
Plague

Megacities, Built Environment

- Consider *Design*
  - *Urban sprawl/Urban design*
  - *Less walking---obesity???*
  - *Howard Frumkin and colleagues…*

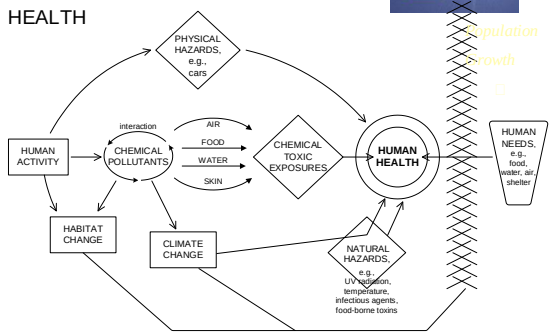


The design of our products…



Should we embrace this????????

THE UNIVERSE OF ENVIRONMENTAL HEALTH



Population growth

Environmental Medicine: The Future

- The practice of Medicine
  - Cannot escape the realities of cost-benefit
  - Everyday make difficult choices
- The practice of Occ-Env Medicine
  - The same realities, often with focus on employers and employees
  - *But in addition: balance between public health/prevention and medicine*

Advocacy in Medicine, Advocacy in Occ-Env Medicine

- Medicine
  - Sounding the alarm on patient care quality, patient rights
  - Research on health care impacts, quality of care
  - Clinicians and the control of third party insurance, HMO's, clinical practice groups
- Occ-env Medicine
  - Sounding the alarm on the broader issues of our environment
  - *Developing metrics of environment-health connection beyond the molecular*
    - *CHALLENGE: metrics of "Planetary health"*
  - *Getting onto Boards, Governmental agencies, etc.*

Global environmental change: Apocalypse in slow-motion

- International Physicians for the Prevention of Nuclear War (IPPNW)
  - Physicians, nurses, allied health
  - Highlighted absurdity of "planning" a medical response to nuclear war
  - Nobel Peace Prize, 1985
- Clinicians for Environmental Sustainability?????

Conclusions

- "Environmental Medicine"
  - Enormous amount still to learn about the impact of toxicants on our health
    - New chemicals, new insights on chronic disease and development, vulnerabilities, mechanisms
  - The mega-picture is part of our universe
    - Climate change, biodiversity, megacities, design
  - Can we make a difference?
    - Connecting public health and medicine
    - Planetary health metrics
    - Engage in the debate and outreach
    - YES!!

Thanks!