Epidemiology of Childhood Overweight and Obesity

Is there a role for factors other than the 'usual suspects'?

NIEHS Workshop, January 23, 2007

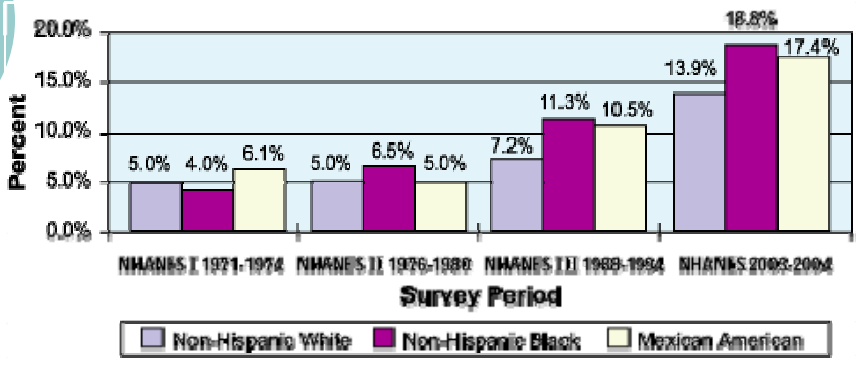
Overview

- Prevalence and time trends of childhood obesity and metabolic syndrome
- Review of 'established' risk factors
- Alternative hypotheses -- endocrine disruptors
- Limitations of epidemiologic studies
- Future directions

Definitions of childhood obesity

- Definition straightforward in adults
  - Overweight ⇨ body mass index (BMI) ≥25-29.9 kg/m^2
  - Obese ⇨ BMI≥30 kg/m^2
- In children, based on percentiles
  - 'At risk for overweight' ⇨ BMI ≥ 85th percentile for age, sex and height, based on CDC growth charts
  - 'Overweight' ⇨ BMI ≥ 95th percentile
- Inconsistent definitions across studies
- BMI has poor sensitivity and specificity for level of body fat; measures of central obesity may be preferable

Prevalence of childhood overweight and obesity, 1971-2004, by racial/ethnic group, U.S.

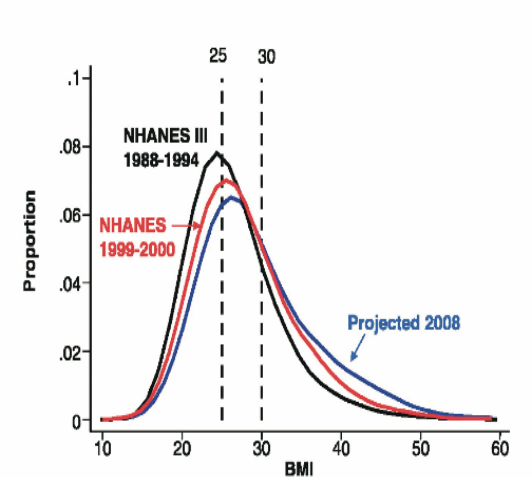


http://www.cdc.gov/nccdphp/dnpa/obesity/childhood/prevalence.htm

Figure 1. Trends in Child and Adolescent Overweight

Note: Overweight is defined as BMI >= gender- and weight-specific 95th percentile from the 2000 CDC Growth Charts.
Source: National Health Examination Surveys II (ages 6-11) and III (ages 12-17), National Health and Nutrition Examination Surveys I, II, III and 1999-2004, NCHS, CDC.

Prediction of BMI distribution in adults, 2008



Hill et al. Science 299:853, 2003

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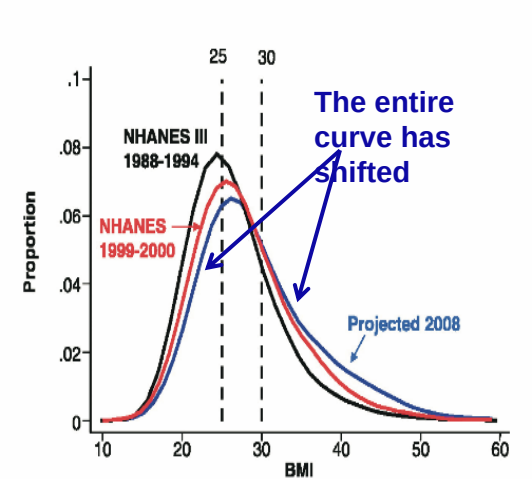
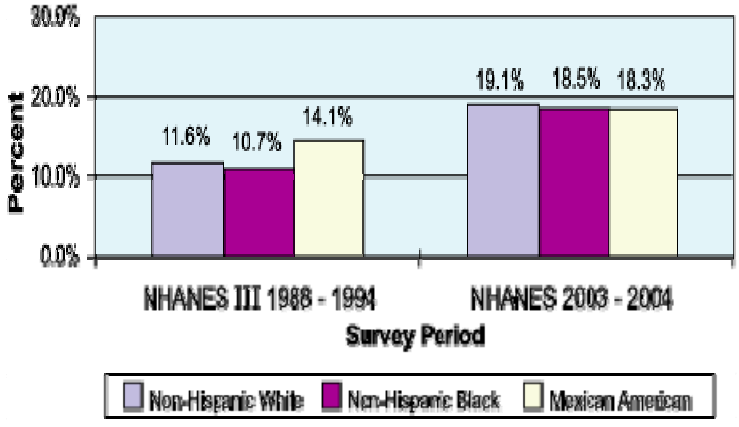
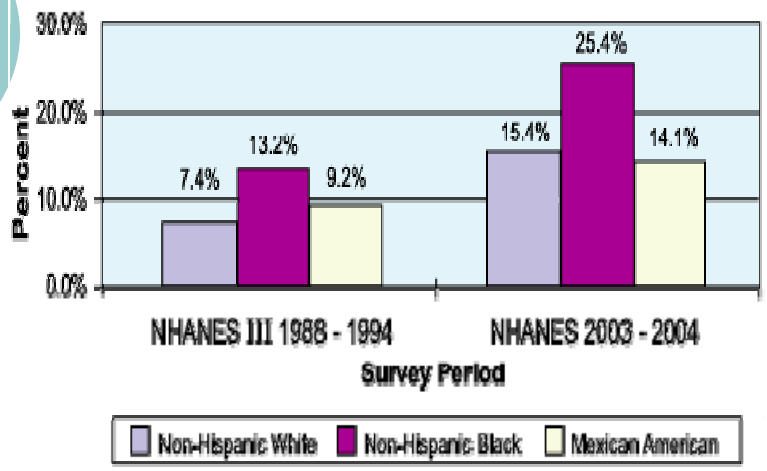


Hill et al. Science 299:853, 2003

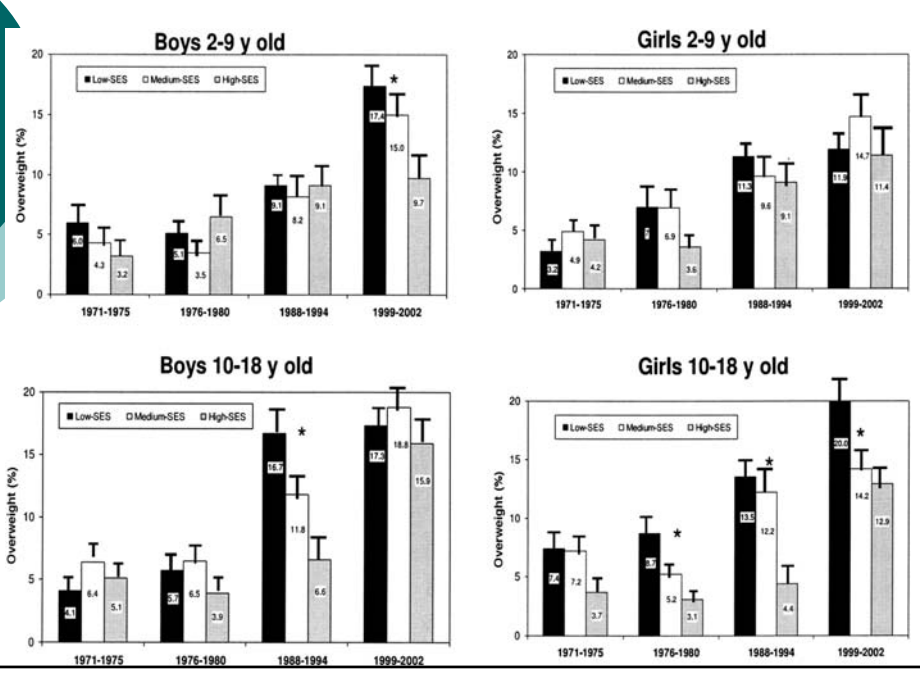
Trends in overweight in adolescent boys, aged 12-19, 1988-2004



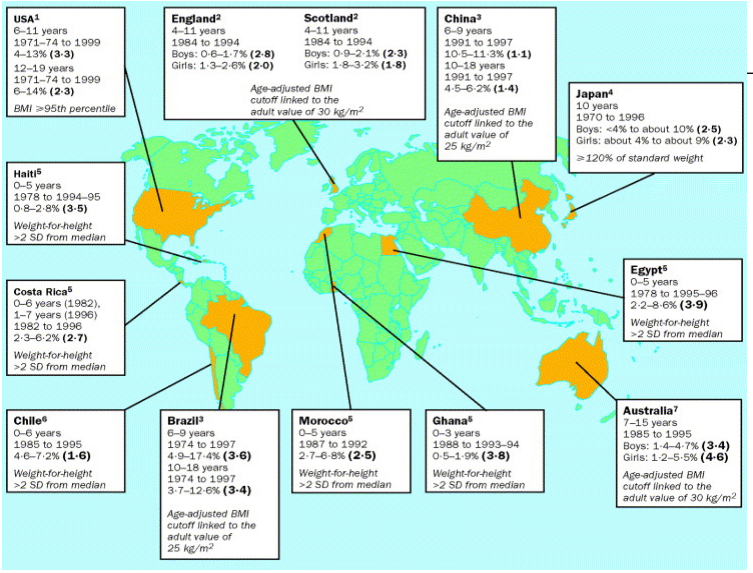
Trends in overweight in adolescent girls, aged 12-19, 1988-2004



Obesity trends by Socioeconomic level, NHANES surveys



Global increases in the prevalence of childhood obesity



Ebbeling, C et al, Lancet 2002

Summary of obesity statistics

- In U.S., "epidemic" didn't start until the early 1980's
- Racial and ethnic disparities, particularly in females
- Shift in entire BMI distribution, not only in the right tail
- Global increases in obesity have occurred
- Increased trends in other countries started later than in the U.S.

Metabolic syndrome

- Linked to high risk of Type 2 diabetes and cardiovascular disease
- Defined by 3 or more of following abnormalities:
  - Elevated triglycerides
  - Low HDL
  - Elevated fasting glucose
  - Large waist circumference
  - Elevated systolic blood pressure

Changing prevalence of metabolic syndrome in adolescents, 1988-2000

- Overall prevalence of 3 or more abnormalities increased from 9.2% to 12.7%
- Prevalence of syndrome in overweight teens was 38.6% in 1999-2000 survey
- Prevalence in non-whites increased more sharply than in whites (3 fold increase in blacks)
- Waist circumference (above 75% in NHANES 3) increased from 25% to 34%

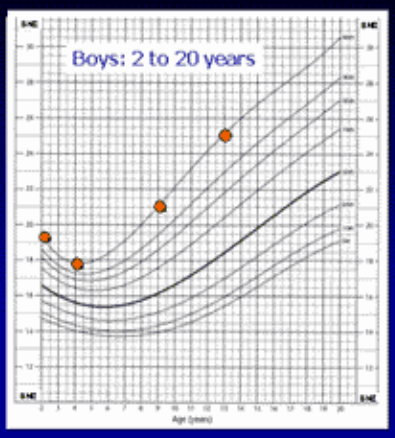
Ferranti SD et al; Clinical Chemistry, 2006

Critical periods of increased risk for development of obesity

- Prenatal
- Adiposity rebound
- Puberty/adolescence

- Childhood overweight and obesity strongly linked to adult overweight and obesity
- Therefore, early life prevention of obesity is critical—treatment is difficult and mostly ineffective

For Children, BMI Changes with Age



Example: 95th Percentile Tracking

Age	BMI
2 yrs	19.3
4 yrs	17.8
9 yrs	21.0
13 yrs	25.1

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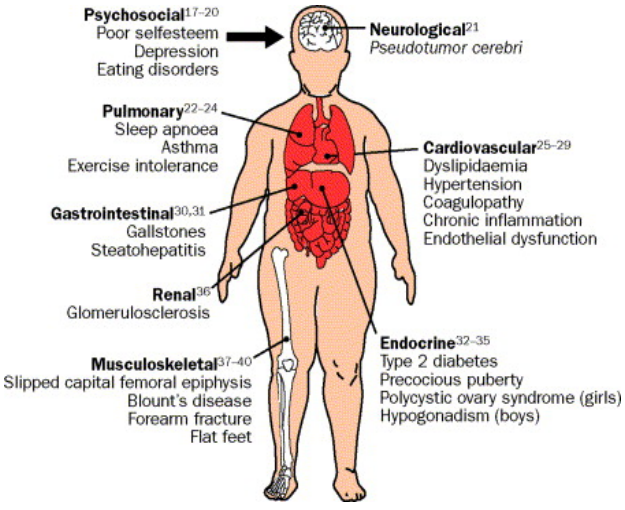
Complications of childhood obesity



Ebbeling C et al, Lancet, 2002

Early life risk factors for development of overweight and obesity

- Genetic factors
- Maternal factors
  - Pre-pregnancy BMI
  - Pregnancy weight gain
  - Diet
  - Gestational diabetes
  - Smoking in pregnancy
- Pre- and perinatal factors
  - Low birth weight
  - High birth weight
  - Breast feeding (protective)

Childhood risk factors: 'the usual suspects'

- Energy balance
  - Activity
    - Decreased physical activity
    - Increased sedentary behavior (TV etc)
  - Diet
    - Fast food intake
    - Increased portion sizes
    - Fat intake/type of fat consumed
    - Changing balance of carbohydrates vs. fat
    - Sugar sweetened beverages
    - High fructose corn syrup
- The 'built environment'
- Social/demographic/family factors

Relationship between overweight and TV viewing

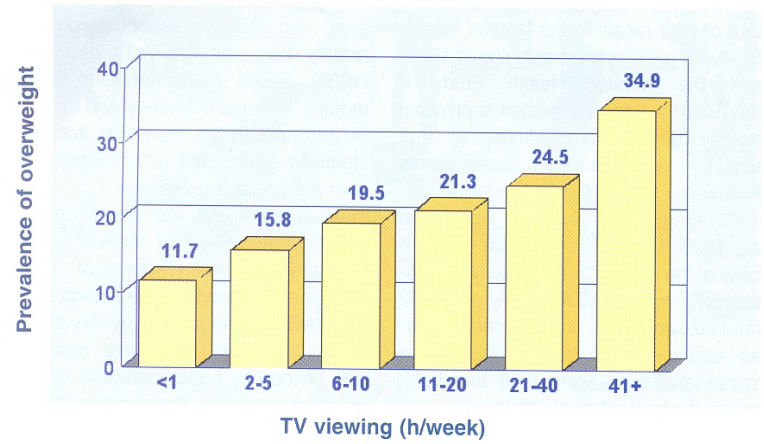


Figure 11 Relationship between overweight and TV viewing
Data from Ching *et al.* (1996)

Limitations of current epidemiologic studies

- Mostly cross-sectional to date
- BMI is a proxy measure of obesity--misclassifies some individuals
  - Is central adiposity (waist circumference or waist to hip ratio) a better measure?
- Analytic challenges
  - What are the critical time periods for exposure?
    - Different risk factors operate during different time periods
  - Are risk factors independent of each other or interacting over the life course (in epi-speak, is there confounding or effect modification?)

Results from Avon longitudinal study, Reilly JJ et al, BMJ 2005

Risk Factor	OR (95% CI)
Birth weight	1.05 (1.03-1.07)
Maternal Smoking >20/day	1.80 (1.01-3.39)
Parental obesity (both parents)	10.4 (5.11-21.32)
TV at age 3	
≤ 4	1.00
4-8	1.37 (1.02-1.83)
>8	1.55 (1.13-2.12)
Sleep duration (hrs) at age 3	
<10.5	1.57 (1.23-1.99)
10.5-10.9	1.31 (1.02-1.69)
11-11.9	0.94 (0.71-1.25)
12 +	1.00
*all results adjusted for maternal education	

Results from Avon longitudinal study, Reilly JJ et al, BMJ 2005

Risk Factor	OR (95% CI)
Std dev score for weight	
Top quartile, 8 mos	3.03 (1.89-4.85)
Top quartile, 18 mos	3.71 (2.29-6.00)
Adiposity rebound	
Late (>61 mos)	1.00
Early (by 61 mos)	2.85 (1.53-5.33)
Very early (<43 mos)	12.0 (6.01-24.03)
Catch up growth	2.21 (1.30-3.80)
Weight gain first 12 mos (per 100 gram increase)	1.07 (1.05-1.10)

What else might contribute to increases in childhood obesity?

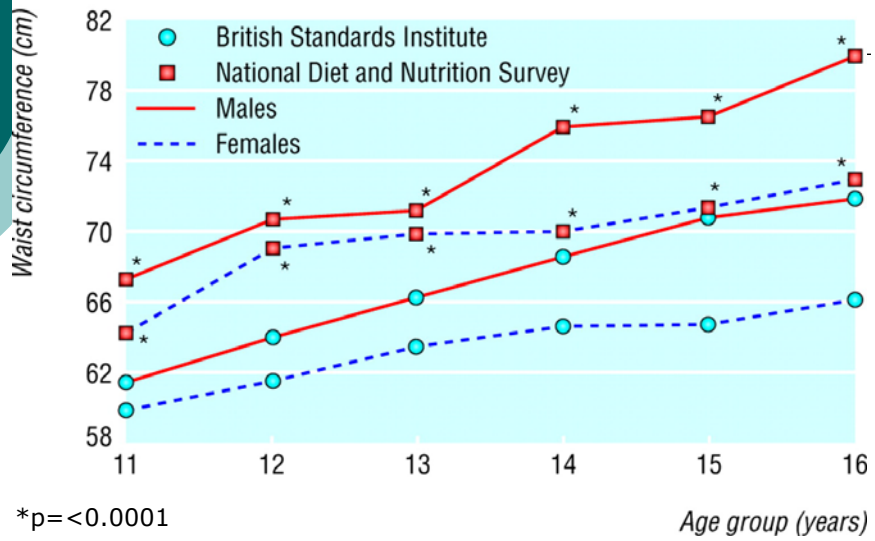
- Sleep patterns
- Air conditioning and heating
- Increased medication use
- Increased stress
- Viruses
- Endocrine disrupting chemicals

Keith SW et al, Int J Obesity 2006; 30:1585-1594

Central adiposity

- Has there been a disproportionate increase in central obesity?
- If so, why? What factors are related to location of body fat stores?
- Central obesity related to hormone levels
- Could exposure to endocrine disrupting chemicals play a role due to fetal programming, or by interfering with the action of hormones?

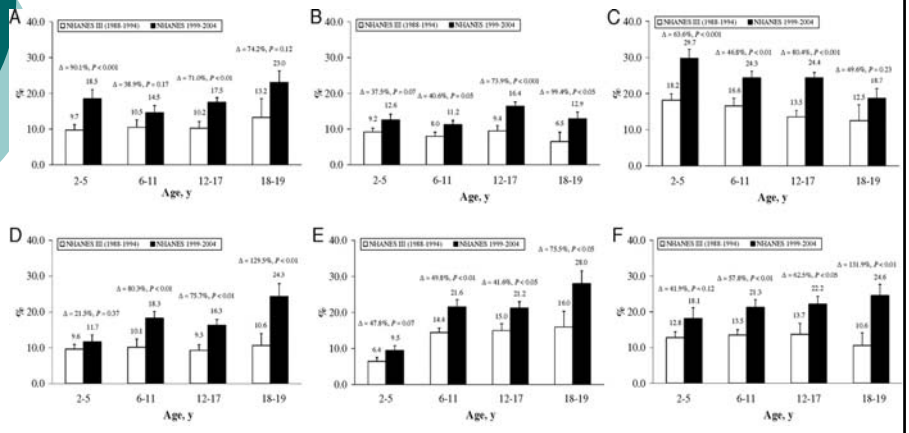
Trends in Waist Circumference in British children, aged 11-16, 1977-1997



*p=<0.0001

McCarthy HD et al, British Medical Journal 2003

FIGURE 4 Changes in the prevalence of abdominal obesity as defined by the 90th percentile of WC between NHANES III (1988-1994) and NHANES 1999-2004 according to gender, race/ethnicity, and age



Li, C. et al. Pediatrics 2006;118:e1390-e1398

PEDIATRICS

Central obesity and hormones

- Estrogen plays a major role in regulation of adipose tissue deposition in both males and females
- Hormone receptors present in adipose tissue (ER, PR, and AR)
- ER's also present in hypothalamus—primary site in brain that regulates appetite
- Females with central obesity: higher androgens, insulin resistance, lower SHBG
- Hormone replacement therapy results associated with lower BMI and lower central adiposity

Do EDCs affect hormone levels?

- Decreased testosterone with high levels of 2 phthalates (DBP and DEHP) found in study Chinese workers
- Phthalates in breast milk correlated with hormone levels in male infants
- Decreased estrogen and progesterone in females with increases in DDT levels
- Effects on thyroid hormones: PCBs, PDBEs, phthalates and others

Phthalates and Obesity

?

Phthalate exposure as a possible risk factor—Exposure Sources and Levels

- Exposure to phthalates is widespread
- Supported by data from NHANES
  - 4 phthalates are detected in over 90% of study population
  - Broad range of exposure
  - Interesting patterns with age and sex
- Reason for high levels of exposure is because of multiple uses:
  - Plasticizers in manufacture of consumer products such as plastic toys, medical equipment, food packaging
  - Used in cosmetics, lotions, shampoos, nail polish to hold color and scent
  - Used as solvents in paints, glue, insect repellants, lubricants, and adhesives
  - Does not covalently bind to plastic and may leach into food, beverages or environmental media
- Many potential routes of exposure, although ingestion is thought to be the main route

Phthalate exposure as a possible risk factor—Known or suggested health outcomes

- Very few human studies!
- Lower sperm count and altered motility (Hauser R et al, Epidemiology 2006)
  - Dose response relationships between MBP quartiles and both sperm count and motility
  - Confirmed an earlier smaller study
  - No effects for DEHP metabolites
- Reduced anogenital distance in male infants (Swan S et al; EHP 2005)
  - Exposure to phthalates measured in maternal urine during pregnancy
  - Levels of 4 monoester phthalate metabolites were inversely related to AGD
  - When exposures to phthalates were combined in the analysis, effects were even stronger

Phthalate exposure as a possible risk factor—potential mechanisms of action

- PPARγ agonist
  - Plays a key role in lipid and glucose metabolism
- Ovarian toxin
  - Decreased estradiol secretion and caused prolonged estrous cycles and anovulation in female rats
  - May disturb the estrogen/androgen balance
  - Androgen/estrogen balance may be associated with central adiposity

Geometric means, selected EDCs, by overweight status in young girls (Wolff et al, 2007)

Biomarker	BMI < 85%	BMI ≥85%
Enterolactone	513.0	174.0*
MECPP	86.6	93.4
MEHHP	43.0	56.1
MEOHP	28.8	35.8
MEHP	5.5	6.5
MEP	102.0	144.0
Bisphenol A	3.7	2.2*

*difference significant at $p<0.05$

Other clues for role of EDCs in obesity

- Diabetes associated with POP's?
  - 2 suggestive studies
- Diethylstilbestrol (DES)
  - In utero exposure to DES resulted in fatter offspring (R. Newbold et al)
  - DES used extensively in agriculture to fatten cows and chickens
  - DES may affect adult hormone levels (higher androgens)
  - DES and third generation effects
- Several drugs (especially psychiatric) related to weight gain and central adiposity
  - Could exposure to low levels of multiple environmental chemicals have similar effects?
  - If so, what are the mechanisms of action?

Challenges in studying possible role of EDC's and obesity

- How do we prioritize chemicals to study?
  - Which ones have biologic plausibility for association with obesity
- Measurement issues, especially for chemicals which are not persistent
- Time period of exposure—effects may be important in one life stage but not in others
  - Life course epidemiologic approach necessary

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Approaches to study environmental chemical exposure and obesity in epidemiologic studies

- Existing cross-sectional data
  - NHANES
- Special exposure cohorts
  - DES, Agent Orange, PCB exposure cohorts, Seveso, others?
- On-going cohort studies (especially pregnancy cohorts) with stored biological specimens
  - Incorporate hypotheses for specific environmental chemicals
- Initiate new cohort studies
- Interdisciplinary collaboration