

Environmental Epidemiology Studies: New Techniques & Technologies to Find Environmental Triggers

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Historical Overview of Epidemiologic Designs

1. Focused clinical studies

- self-selected study populations, or
- clinical convenience samples
- descriptive
- small n's
- *a posteriori* hypotheses

Clinical studies: what we've learned

1. Focused clinical studies

Clues:

- Ø Family studies - sibling recurrence
- Ø Twin concordance
- Ø Male/female
- Ø Co-morbidities: seizure disorders, GI symptoms
- Ø Heterogeneity of onset pattern
- Ø Head circumference

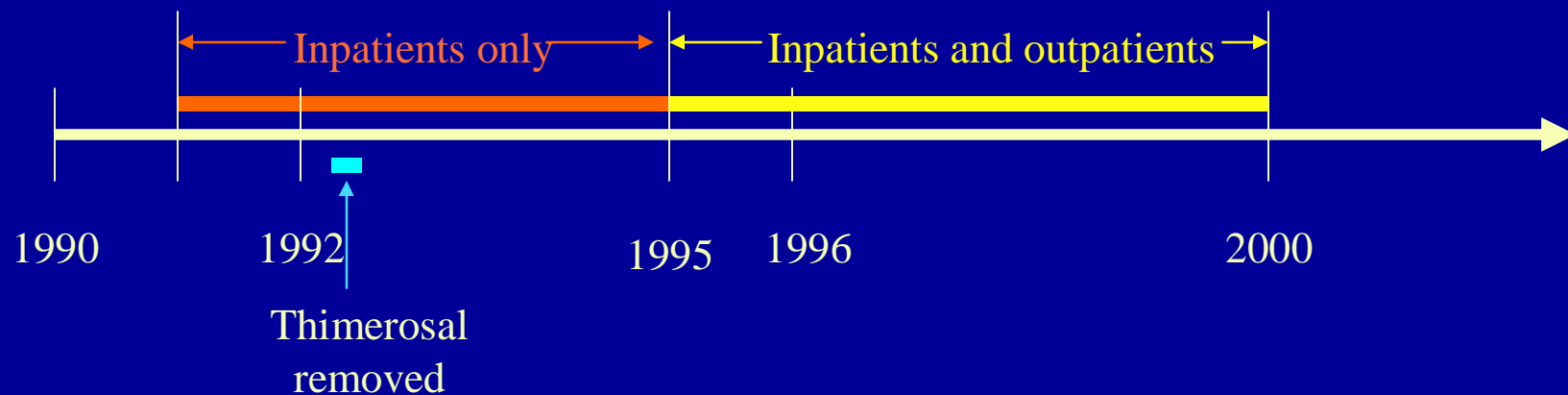
Epidemiologic Designs, con't

2. Administrative databases

- uncertain diagnoses
- demographics
- perinatal factors
- time trend: ecologic, or individual design

Example: Administrative database Time trend - ecologic analysis

Hviid et al 2003



Example: Administrative database

Perinatal case-control study:

Hultman et al. 2002

- Swedish Birth Register linked to Swedish Inpatient Register
- 408 cases
- 2040 matched controls

Findings of increased risk:

- Ø Foreign born
- Ø Small for gestational age
- Ø Low APGAR score
- Ø C-section

Administrative database analyses: what we've learned

2. Administrative databases

Clues:

- Ø Increased diagnoses over last two decades
- Ø Socio-economic pattern
- Ø Maternal & paternal age
- Ø Obstetric complications, suboptimal birth condition
- Ø Auto-immune disorders

Epidemiologic Designs, con't

3. Genetic studies

- volunteer samples
- twin studies
- multiplex families

Genetic studies what we've learned

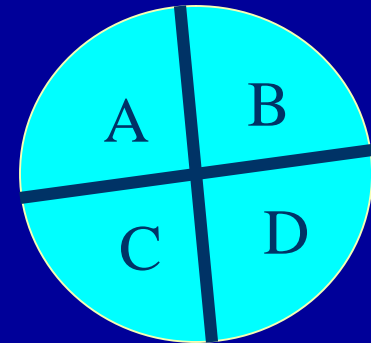
3. Genetic studies

Findings:

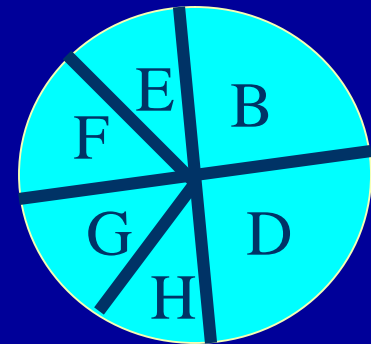
- monozygotic twins highly concordant, but not entirely
- not simple Mendelian inheritance
- regions on nearly every chromosome: multiple genes
- multiple genes
- so far, genes in isolation - not combined with environmental information

Why Study Environmental Factors in Autism?

- Genetics: ~60-90%
- Environment: 10-40% = minimum
- Sum not 100%



- Risk Ratios of 10+:
 - Congenital rubella
 - Thalidomide
- Risk Ratios ~4 to 5:
 - Maternal age
 - Male sex



Epidemiologic Designs, con't

4. New generation case-control studies

- population-based
- diagnoses confirmed
- broad range of factors
- retrospective exposure assessment
- specimen collections -- linkage to laboratory scientists

Example: New generation case-control studies

Hertz-Picciotto et al 2006

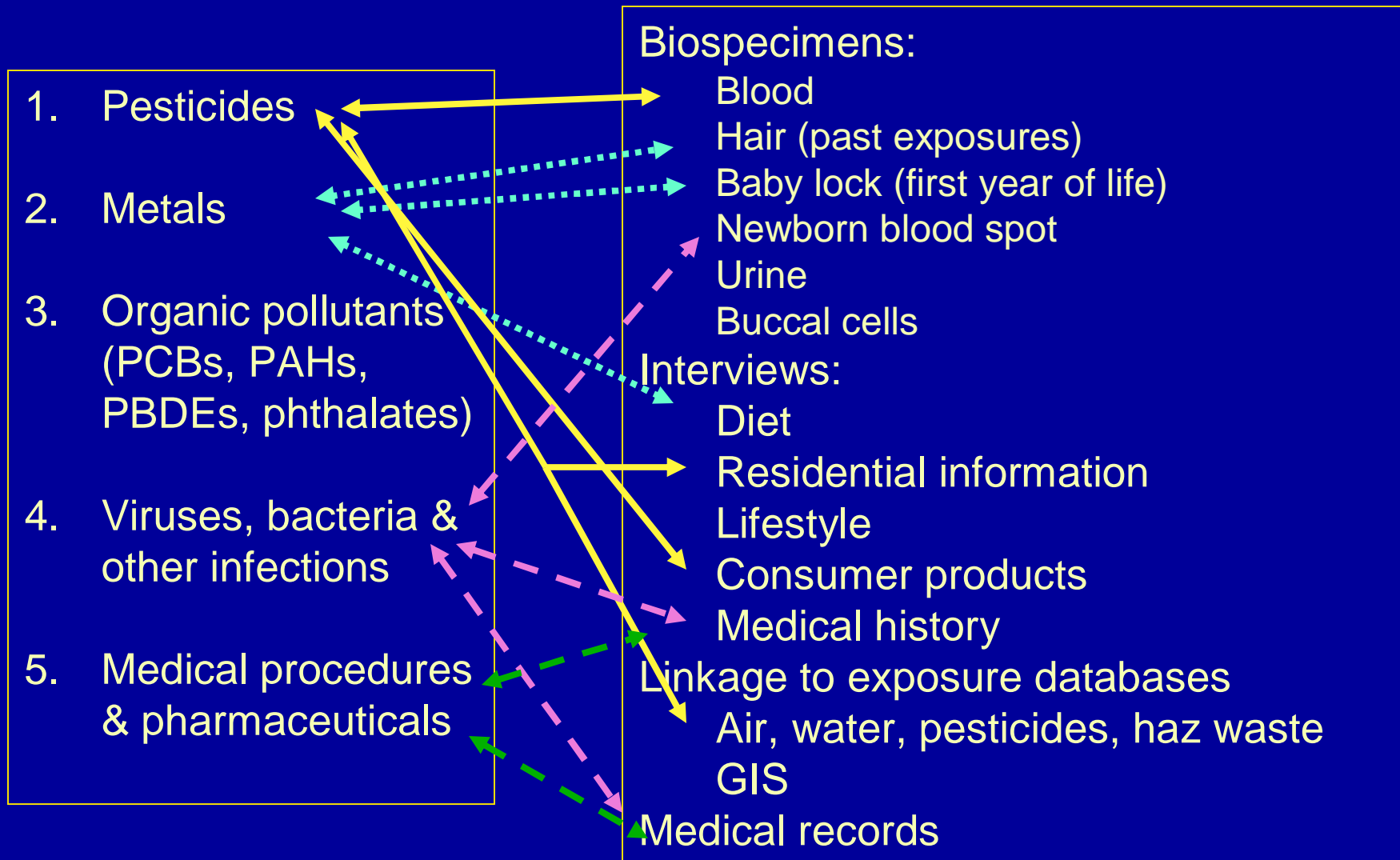
- CHARGE study
- >700 participating families to date: 3 groups
- Autism dx confirmed: ADOS and ADI
- Tests of cognitive and adaptive development
- Physical examination, medical hx
- Structured interview
 - Ø Demographics, socioeconomic status
 - Ø Reproductive hx
 - Ø Index pregnancy
 - Ø Household products
 - Ø Residential history
 - Ø Metal exposures

Example: New generation case-control studies

Hertz-Picciotto et al 2006

- Self-administered forms: sleep, GI, auto-immune
- Blood, urine, hair, baby lock (first haircut) on index child
- Blood, urine, hair on 1st degree relatives
- Medical records
 - Ø Prenatal
 - Ø Labor & delivery
 - Ø Neonatal
 - Ø Pediatric
 - Ø Mental health
 - Ø Dental
 - Ø Pre-conception
- Ø Newborn blood spots

Environmental Exposures in CHARGE



Case-control studies, new generation: what we've learned

4. In-progress case-control studies

- CHARGE (Childhood Autism Risks from Genetics & Environment)
- APP (Autism Phenome Project)
- Seattle study
- CADDRE

Clues:

- Ø Immunology: lower IgG, altered cytokines
- Ø Transcriptional gene expression, esp NK cells
- Ø Obstetric factors
- Ø Dysmorphology
- Ø Electrophysiology & brain imaging

Epidemiologic Designs, con't

5. Prospective cohort studies

- Temporality: potential etiologic exposures
- Infant sib studies
- MARBLES & EARLI Network } High risk cohorts
- National Children's Study

Epidemiologic Designs, con't

5. Prospective cohort studies

Promise

- Ø Understand time course: critical windows?
- Ø Biomarkers
 - to identify high risk children
 - mechanisms → targets to intervene

Goal - to discover environmental causes & triggers of autism...

New technologies?

- Last 2 decades: psychologists & psychiatrists, -improvements in diagnosis, early behavioral markers
- Developmental pediatricians and neuroscientists
- Incentives for new blood, environmental and perinatal epidemiologists & toxicologists
- State of the art, population-based molecular epidemiology