



USC

ENVIRONMENTAL CHALLENGES TO REPRODUCTIVE HEALTH AND FERTILITY

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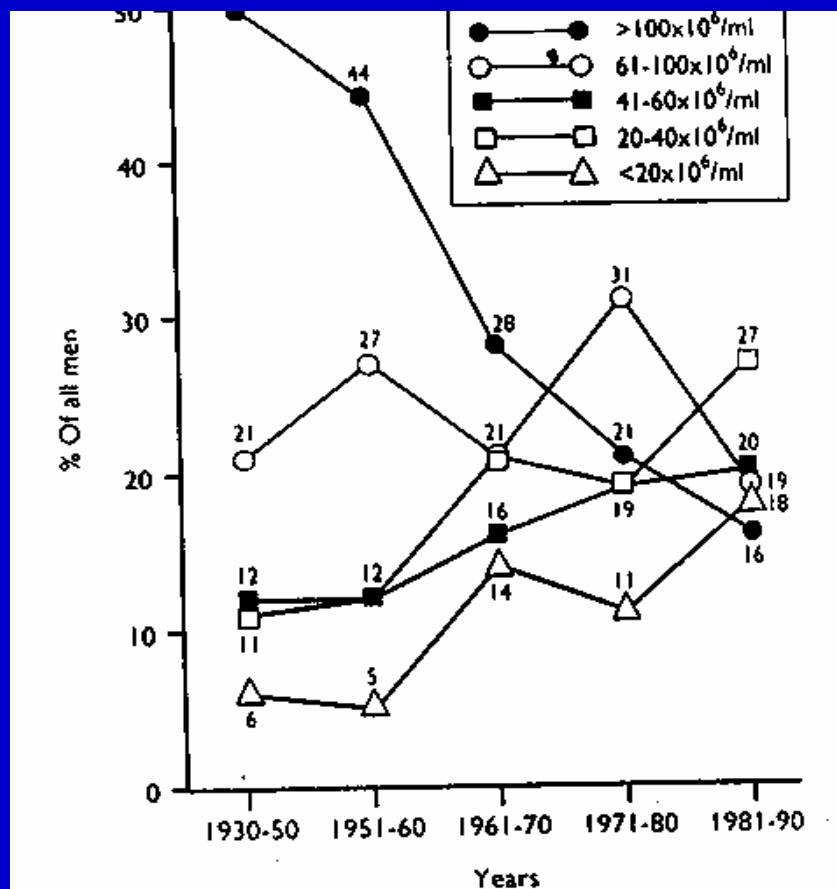
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HX OF REPRODUCTIVE TOXICOLOGY

- **Roman Times: Lead Toxicity**
 - Abortifacient
 - Male and female infertility
- **1975 (Lancranjan)**
 - First extensive study reports reproductive toxicity of lead in men
- **1977 (Whorton)**
 - DBCP
- **1992 (Carlsen, et. al.)**
 - Decrease in sperm quality
 - Endocrine disruption hypothesis

EVIDENCE FOR DECREASING QUALITY OF SEMEN OVER PAST 50 YEARS

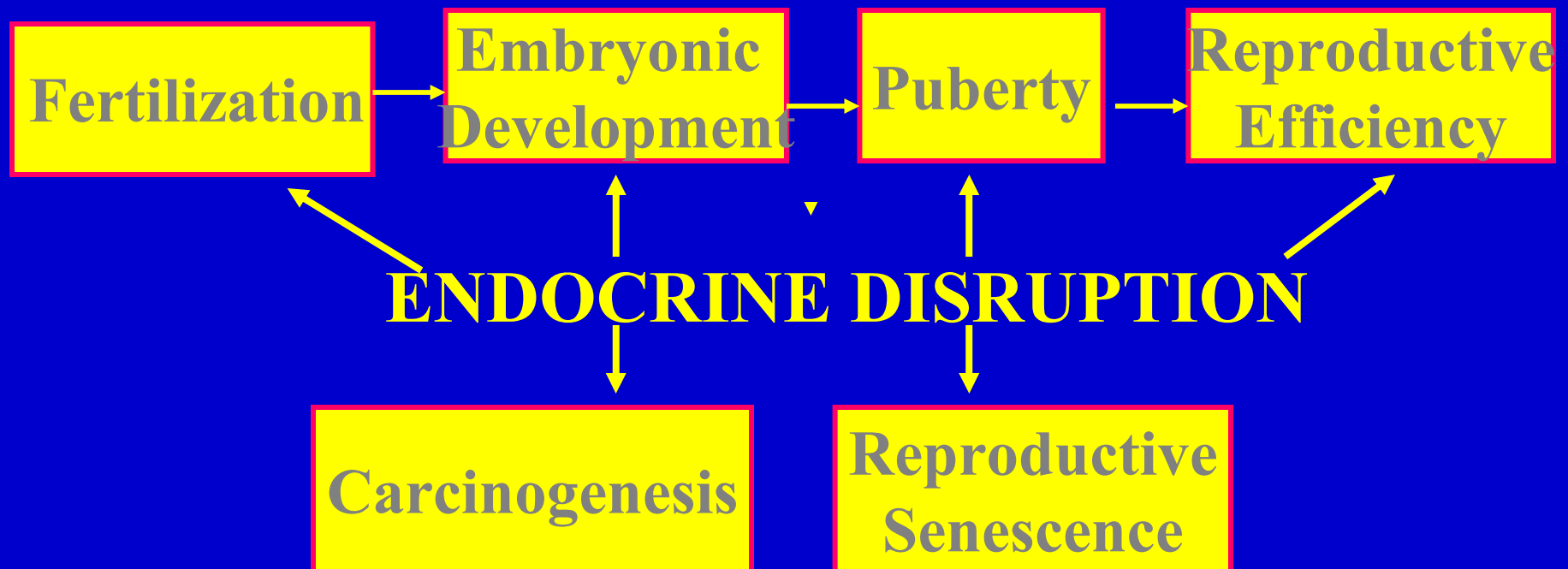


- Study decline in men with sperm conc. $> 100 \times 10^6$ sp/cc
- Increase in men with sperm conc $< 40 \times 10^6$ sp/cc
- Concl: “There has been a genuine decline in SQ over the past 50 years”

ENDOCRINE DISRUPTION HYPOTHESIS

- **Environmental or occupational exposures to compounds with endocrine disruptive properties may account for changes in male reproductive health**

POTENTIAL SITES OF ENDOCRINE DISRUPTOR ACTION



REPRODUCTIVE TOXICANTS

- **Therapeutic/pharmacologic agents**
- **Recreational drugs**
- **Environmental/Occupational chemicals**

ENVIRONMENTAL/OCCUPATIONAL CHEMICALS

- **Heavy metals**
- **Agricultural chemicals**
 - **Pesticides**
 - **Fungicides**
- **Industrial chemicals**
 - **Phthalates**
 - **PCBs**
 - **Bisphenol A**

RISK ASSESSMENT

- **Hazard identification**
 - **Clinical observation/ studies**
- **Dose-response assessment**
 - **Animal studies**
- **Exposure assessment**
 - **Animal and epidemiologic studies**
- **Risk characterization**
 - **Clinical and epidemiologic studies**

LEAD EXPOSURE

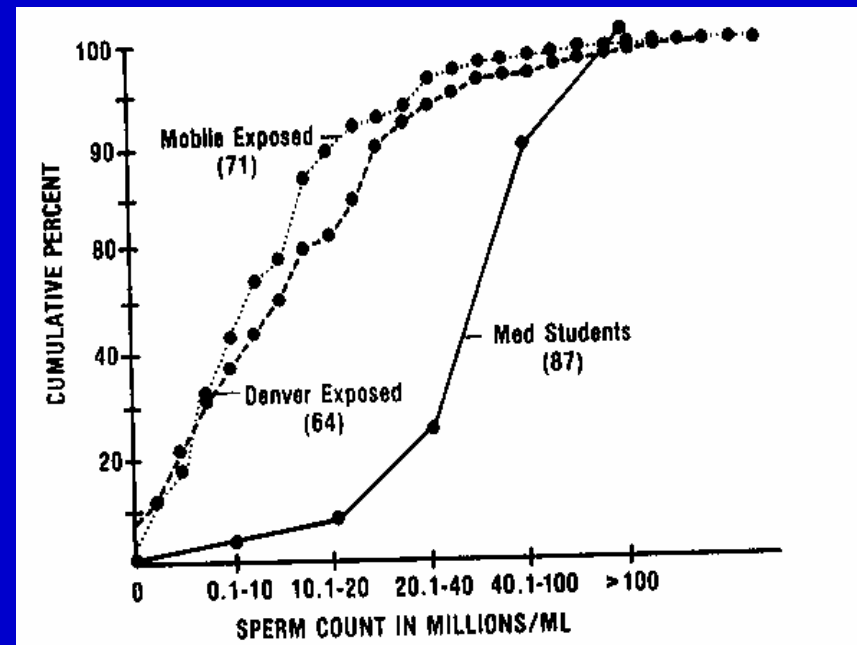
- **Male Reproductive Toxicity**
 - **Subclinical suppression of LH, FSH, T**
 - **Abnormal spermatogenesis**
 - **Conc**
 - **Morphology**
 - **Abnormal sperm function**
 - **No data on fertility**

LEAD EXPOSURE

- **Female Reproductive Toxicity**
 - **Subclinical suppression of LH, FSH, E₂**
 - **Delayed Puberty**
 - **Disruption of menstrual cycle**
 - **Delayed time to pregnancy**
 - **Fewer pregnancies**
 - **Early menopause**

AGRICULTURAL CHEMICALS

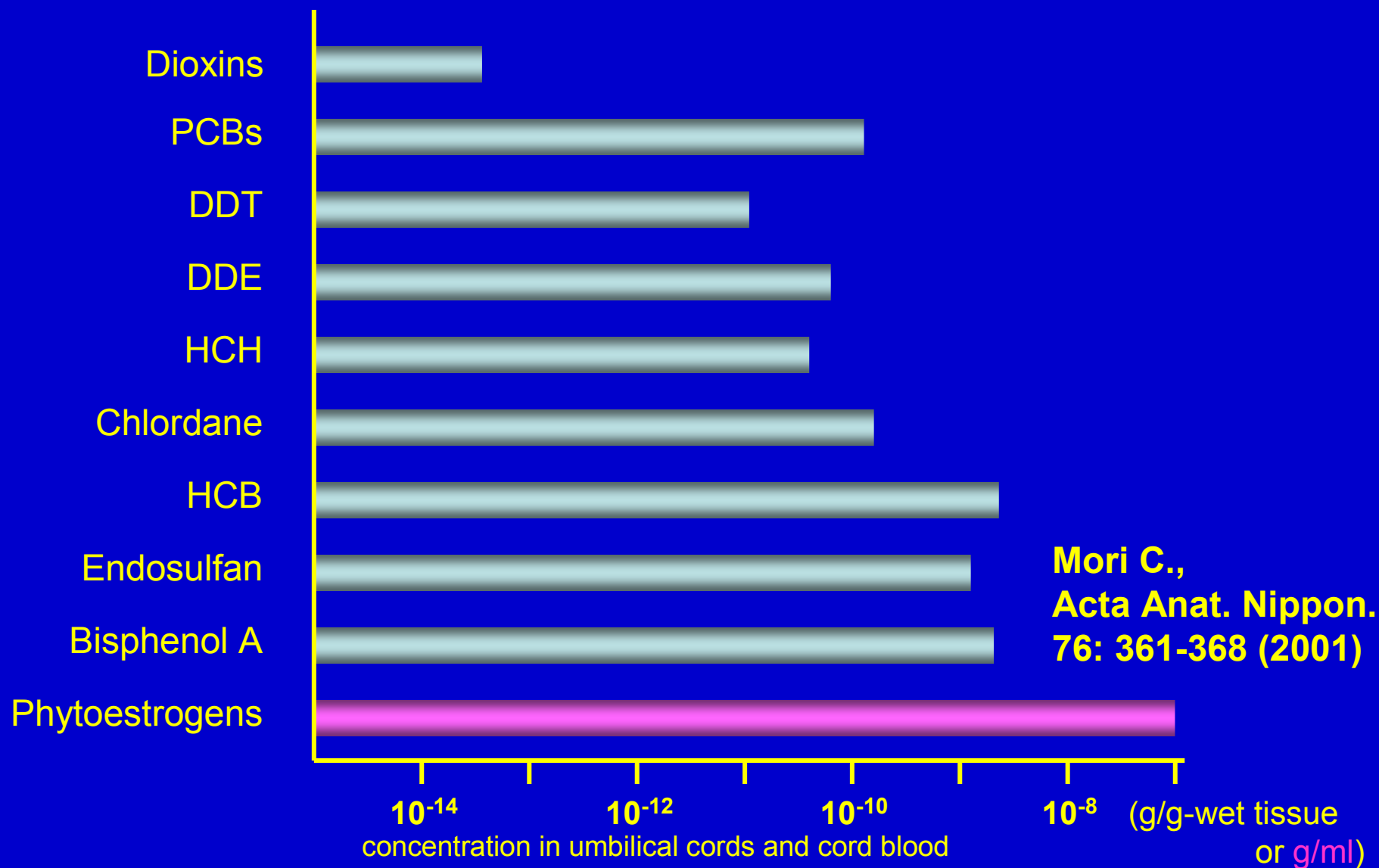
- 1977: Whorton reports DBCP sperm toxicity
- 1980-1995: Confirming studies
- 1990s
 - Use prohibited in U.S.A. and Europe



INDUSTRIAL CHEMICALS

- **Polycyclic aromatic hydrocarbons**
 - Antiandrogen in vitro
- **Polychlorinated biphenyls**
 - Feminization of trout
 - Great lakes
 - Inhibition of spermatogenesis
 - rodents
- **Phthalates**

CHEMICALS IDENTIFIED IN NEWBORNS IN JAPAN



PHTHALATES AND HUMAN SEMEN QUALITY

- **Two studies with inconsistent results:**
 - **U.S. infertility clinic study** (Hauser et al., Epidemiology 2006)
 - **Higher the dose, lower the sperm count**
 - **Swedish conscripts study** (Jonsson et al., Epidemiology 2005)
 - **Possible decline in sperm motility**

ROLE OF CLINICIAN

- **Identify the exposure and the potential health effects.**
- **Characterize the extent of exposure.**
- **Assess the degree of risk to the patient.**
- **Initiate a plan to control or prevent the exposure.**