Biological effects of low level exposure to trichloroethylene (TCE): Recent findings from the National Cancer Institute

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Rationale

• To study early biologic effects of TCE at airborne exposure levels below the U.S. occupational standard, 100 ppm as an 8-hour time weighted average.

• To provide insight into carcinogenic mechanism of TCE exposure, especially for non-Hodgkin lymphoma and kidney cancer.
Molecular Epidemiology Study of TCE

Study design:

- **40** factories in Guangdong, China were screened to identify factories that used TCE with *none to minimal* use of other chlorinated solvents.

- **6** metal cleaning factories selected: 80 workers exposed almost exclusively to TCE were enrolled.

- **96** unexposed controls were enrolled from 2 clothes and 1 food factory.

- Extensive personal air monitoring for TCE.

- Blood and urine samples collected.
Leucocyte (white blood cells) Subsets

- Myeloid lineage
  » Granulocytes
  » Platelets
  » Monocytes

- Lymphoid lineage
  » T-cell subsets
  » B cells
  » NK cells
TCE Exposure and Peripheral Blood Cell Counts and Lymphocyte Subsets

**Myeloid lineage**

- Granulocytes: p=0.96
- Platelets*100: p=0.31
- Monocytes: p=0.54

**Lymphoid lineage**

- Lymphocytes: p<0.0001
- CD4+ T cells: p=0.003
- CD4+ T cell EMC: p=0.0003
- CD8+ T cells: p=0.0010
- B cells: p=0.0002
- NK cells: p<0.0001

*p values are for trend*

Lan et al., Carcinogenesis 2010
Hosgood…Lan, Front Oncol 2012
Cytokines and Antibodies in Peripheral Blood Serum

• **Cytokines** are cell signaling molecules that aid cell to cell communication in immune responses:
  - sCD27
  - sCD30
  - IL-10

• **Antibodies:**
  - IgG
  - IgM
TCE Exposure and Immunologic Markers

*: p<0.05; **: p<0.01; ***: p<0.001; ****: p<0.0001

Lan et al., Carcinogenesis 2010; Bassig...Lan, Environ Mol Mutagen 2013; Zhang...Lan, Carcinogenesis 2013
Conclusions and Implications of TCE Study

• TCE exposure → alterations in multiple immune markers

• Supports biological plausibility that TCE may cause NHL

• All effects occurred at exposures < 12 ppm, raising a concern about the current US OSHA standard of 100 ppm
Impact of Research Findings

  - TCE causes kidney cancer, and possibly NHL

- EPA risk assessment of TCE exposure (2014)
  - TCE is carcinogenic to humans

• Hosgood et al. (2012) Decreased numbers of CD4+ naïve and effector memory T cells, and CD8+ naïve T cells, are associated with trichloroethylene exposure. Frontiers in Oncology 1:1-6.


• Bassig et al. (2013) Occupational exposure to trichloroethylene and serum concentrations of IL-6, IL-10, and TNF-alpha. Environ Mol Mutagenesis 54: 450-4.
