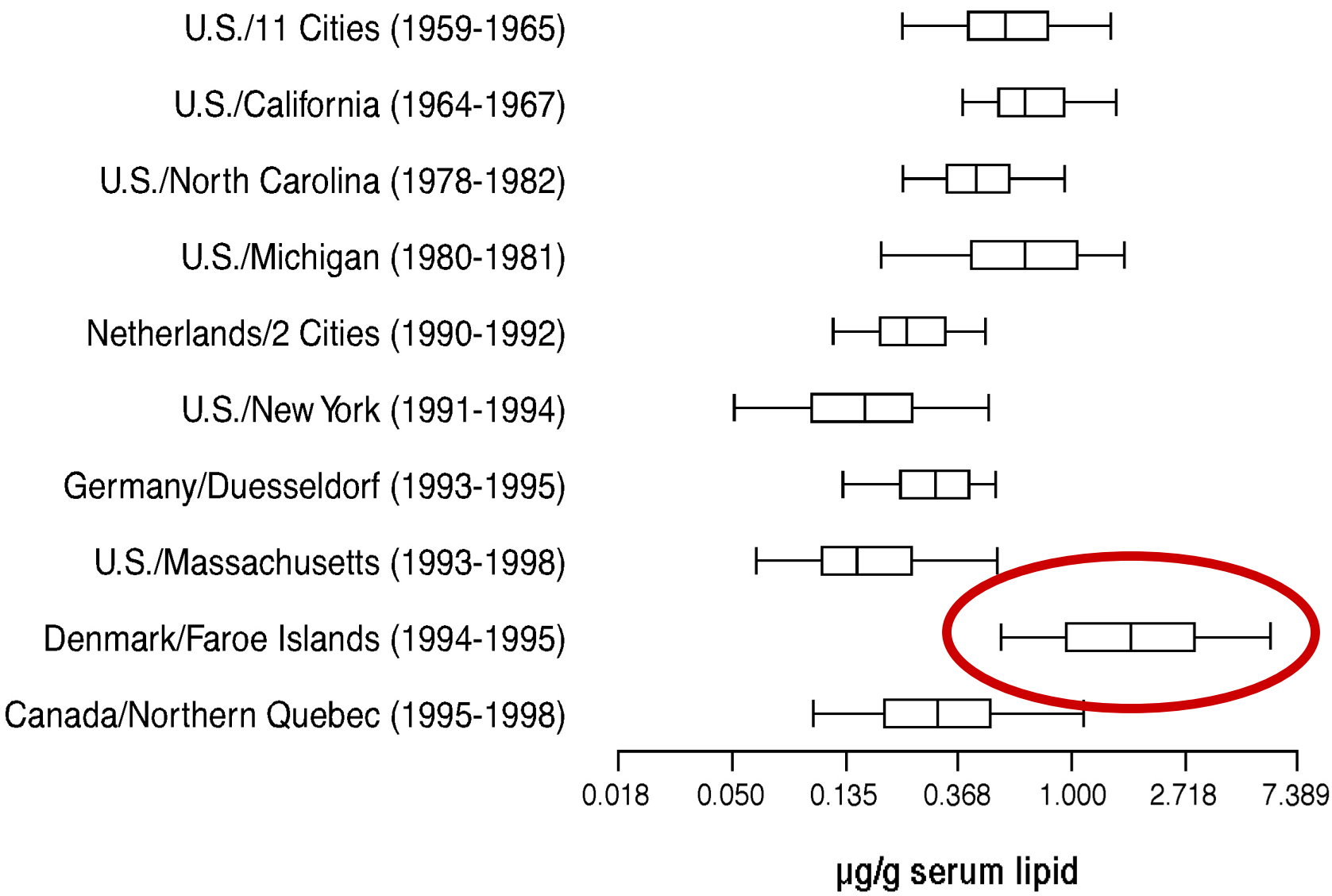
# Do Polychlorinated Biphenyls (PCBs) harm the human immune system?

## Distribution of total PCBs concentration in serum, 10 studies

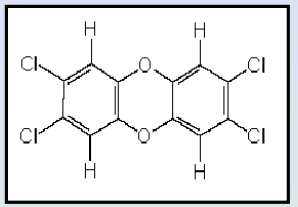


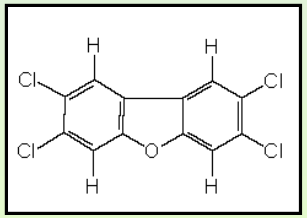
*"Although a number of systems can be affected by environmental contaminants, experimental animal data indicate that the immune system is one of the most sensitive targets for chemical-induced toxicity, especially for the chlorinated compounds TCDD and PCBs"*

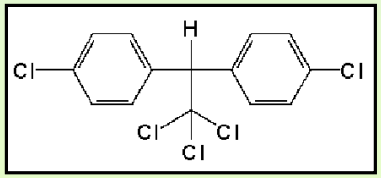
**Tryphonas H. Environ Health Perspectives, vol 109 suppl. 6, 2001**

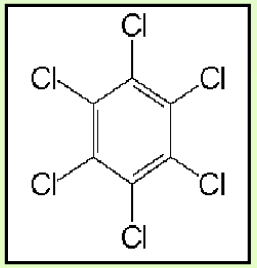
# Examples of Environmental Toxicants Influencing Immune Function

- Persistent Halogenated Organic Pollutants (POPs)*
  - Dioxins (TCDDs) (AhR binding)
  - Polychlorinated Biphenyls (PCBs, e.g. Aroclor 1254) (some AhR binding)
  - Pesticides (e.g. hexachlorocyclohexane, chlordane, diazinon, DDT, DDE, carbofuran (AhR binding))
  - Fugicides (e.g. hexachlorobenzene)



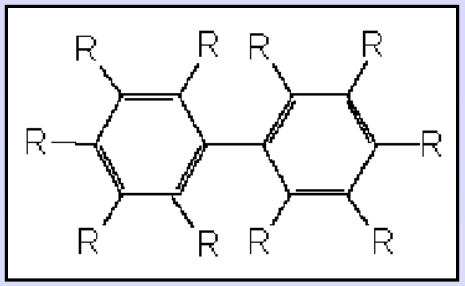




- Heavy metals (Hg*, Pb and Cd)

*Levels of Hg exposure often correlate with exposure to POPs

# Polychlorinated Biphenyls* (PCBs)




- **<u>Coplanar</u>** (Chlorine in ortho position, dioxin like)
  - AhR binding (Aryl hydrocarbon Receptor)
  - Measured in TEQ (total dioxin equivalents)
- **<u>Non-coplanar</u>** (AhR independent)
  - Probably also immunotoxic by other mechanisms than via AhR
  - **Most abundant in human tissues. Longer half life.**

•Trade names:Aroclor, Pyranol, Pyroclor, Phenochlor, Pyralene, Clophen, Elaol, Kanechlor, Santotherm, Fenchlor, Apirolio, Sovol.

# PCBs

## Animal:

- ✓ Several studies have suggested that PCBs have a **negative impact on antibody formation and T-cell function** in mammals, fish and birds. Most of these studies were performed in laboratory animals.

- ✓ E.G. **Reduced Ab response** to SRBC by aroclor1254 exposed monkeys (Tryphonas H et al 1991)

- ✓ Wild polar bears living in an area with high exposure levels to PCBs have **altered antibody responses** and **lymphocyte proliferative responses**. (Skaare JU et al 2002, 2004 and 2005)

- ✓ Influence of OC on **T-cell proliferation** in marine mammals and mice. (Mori C et al. J Toxicol environ health A. 2006;69:283.)

# PCBs

## Human:

- ✓ Yu-Cheng, Taiwan (Chang KJ et al. 1981) suggests focus on of perinatal exposure: **Low IgA and IgM levels** and **total T cells and cytotoxic T cells levels.**
  - ✓ Later (1997) decreased **delayed type skin reactions** and **pneumonia, bronchitis and otits media** more frequently than control infants.

- ✓ Great Lakes North America: Mothers with high PCB levels in milk had infants with **increased numbers of infections** first 4 months of life (Swain WR 1991).

- ✓ Canada Quebec: Inuit infants highly exposed to marine toxicants have been found to have changes in **T-cell subsets** (Dewailly E et al 1996)

- ✓ Canadian Inuit infants. An Increased **risk for otitis media** was observed among those with the highest levels of organochlorine exposure (Dewailly E et al. 2000).

- ✓ Dutch children (Weisglas-Kuperus N et al. 2000 and 2004) **Increased risk for otitis media** and **reduced risk for allergic reactions**. **Post-vaccination antibodies to mumps and rubella** correlated negatively to PCB levels in cord blood.

- ✓ Canada St. Lawrence River: Cord blood **T-cell subsets and T-cell proliferative response** influenced by high levels of blood PCBs. Furthermore *in vitro* TNF-secretion correlated negatively with plasma PCBs (Belles-Isles M et al. 2002 and Bilrha et al. 2003).

- ✓ Non-coplanar PCBs suppress *in vitro* **phagocytosis** by human leucocytes (Levin M et al. 2005)

# PCBs

- PCBs influence predominantly T-cell function and T-cell composition possibly via an influence on thymic function.
- Antibody production to T-dependent protein antigens is reduced.

Loveren H.V. et al.

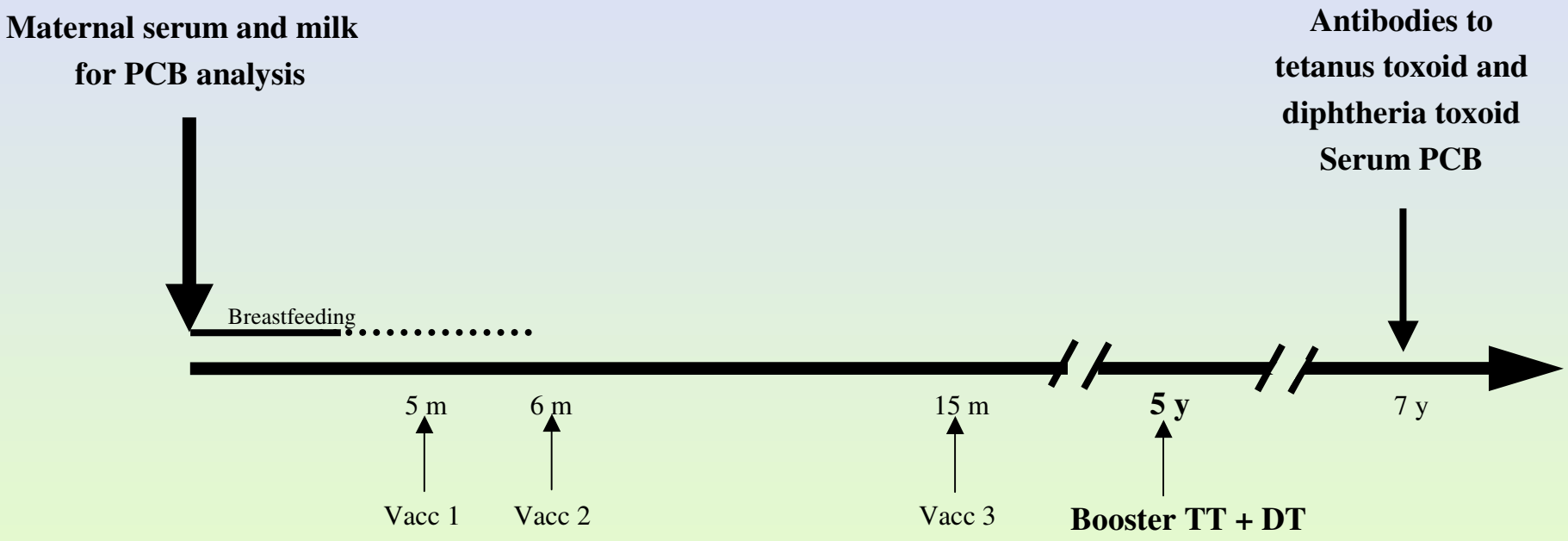
(Report of the Bilthoven Symposium 1999):

“for suppression of immune function, the system is best assessed by vaccination with an antigen to which no prior exposure has occurred ….

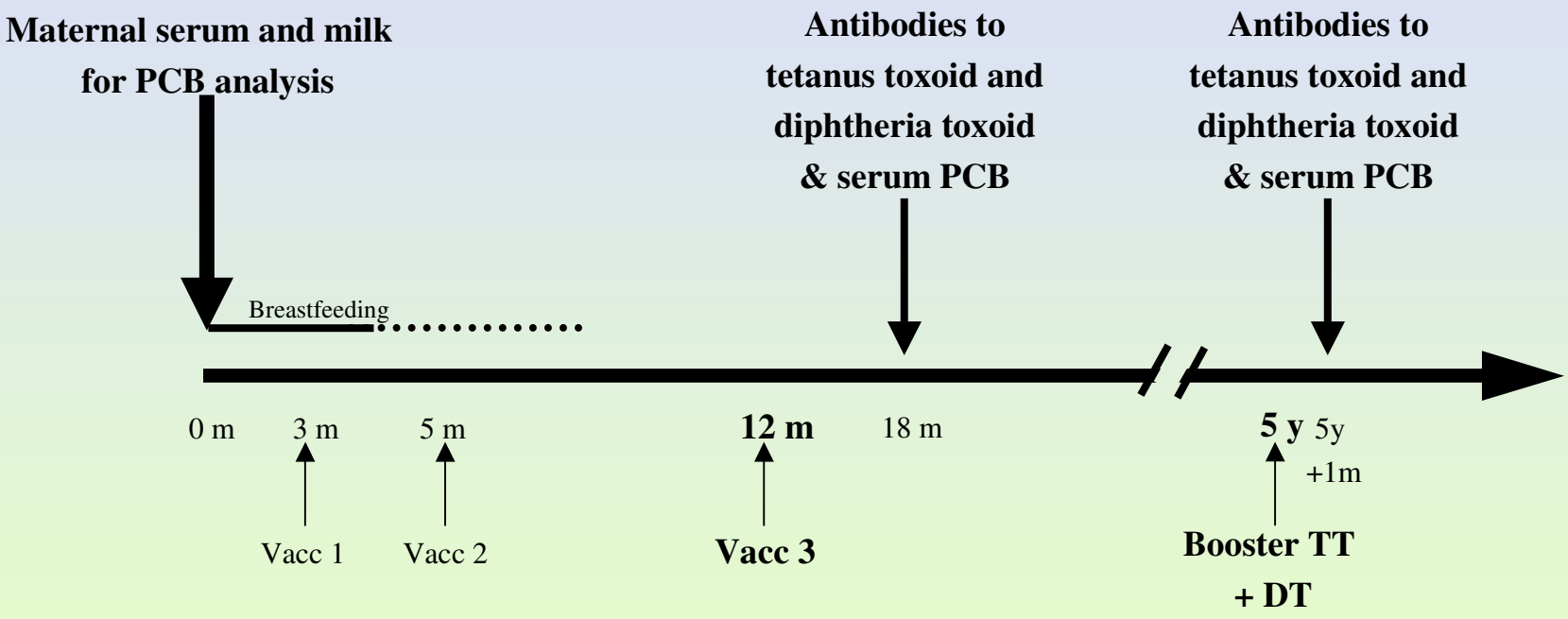
A strong recommendation is therefore to make a greater use of paediatric vaccination programs.”

Loveren H.V. et al. Report of the Bilthoven Symposium: Advancement of Epidemiological Studies in Assessing the Human Health Effects of Immunotoxic Agents in the Environment and the Workplace. Biomarkers, Volume 4, Number 2, 1 March 1999, pp. 135-157(23)

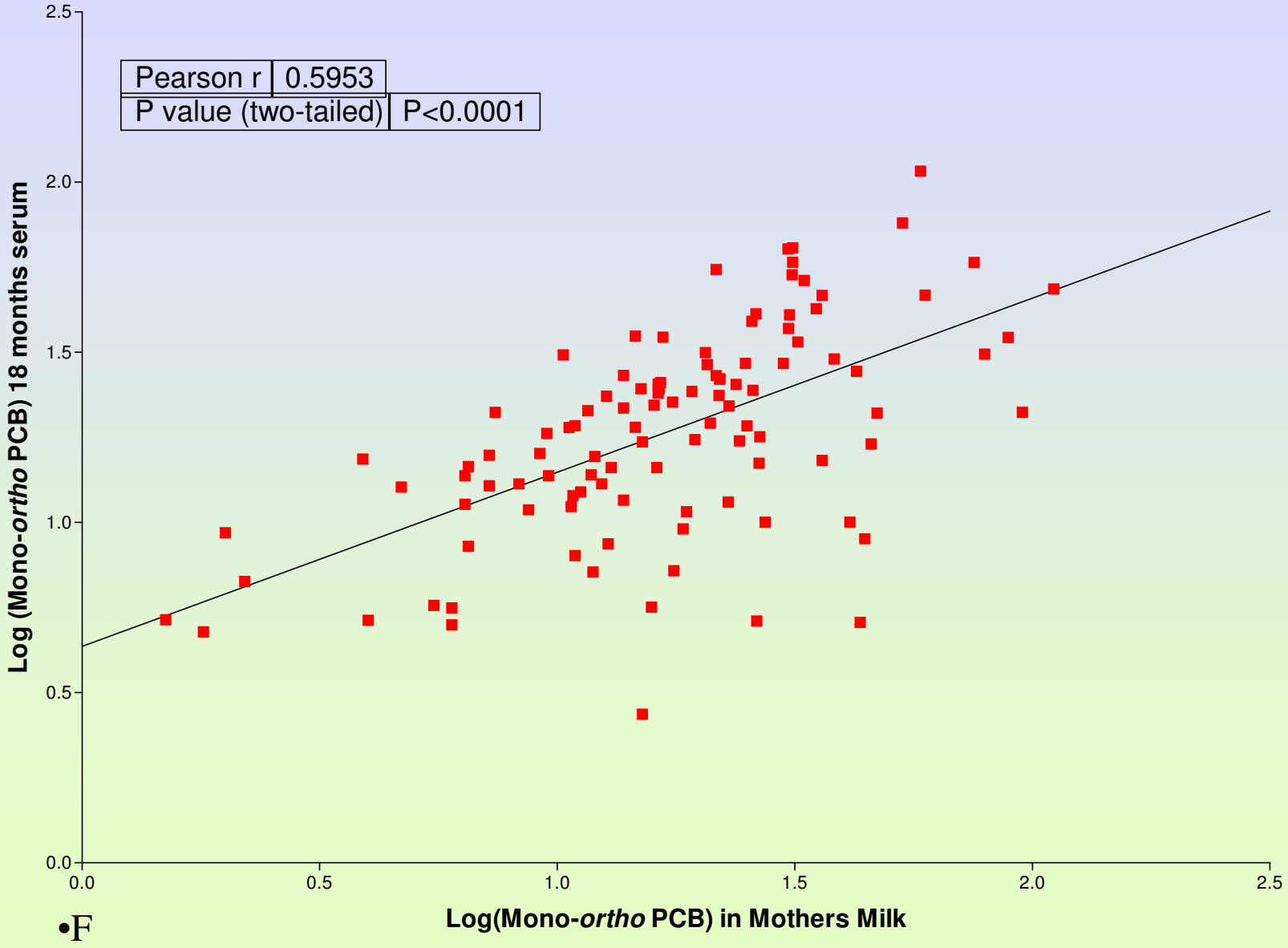
# Group A


Maternal serum and milk
for PCB analysis
Antibodies to
tetanus toxoid and
diphtheria toxoid
Serum PCB
Breastfeeding
5 m
6 m
15 m
5 y
7 y
Vacc 1
Vacc 2
Vacc 3
Booster TT + DT

# Group B


Maternal serum and milk for PCB analysis
Antibodies to tetanus toxoid and diphtheria toxoid & serum PCB
Antibodies to tetanus toxoid and diphtheria toxoid & serum PCB
Breastfeeding
0 m
3 m
5 m
12 m
18 m
5 y
5y +1m
Vacc 1
Vacc 2
Vacc 3
Booster TT + DT

## Correlation between Mono-*ortho* PCB in Mothers Milk and Infant Serum at age 18 Months.

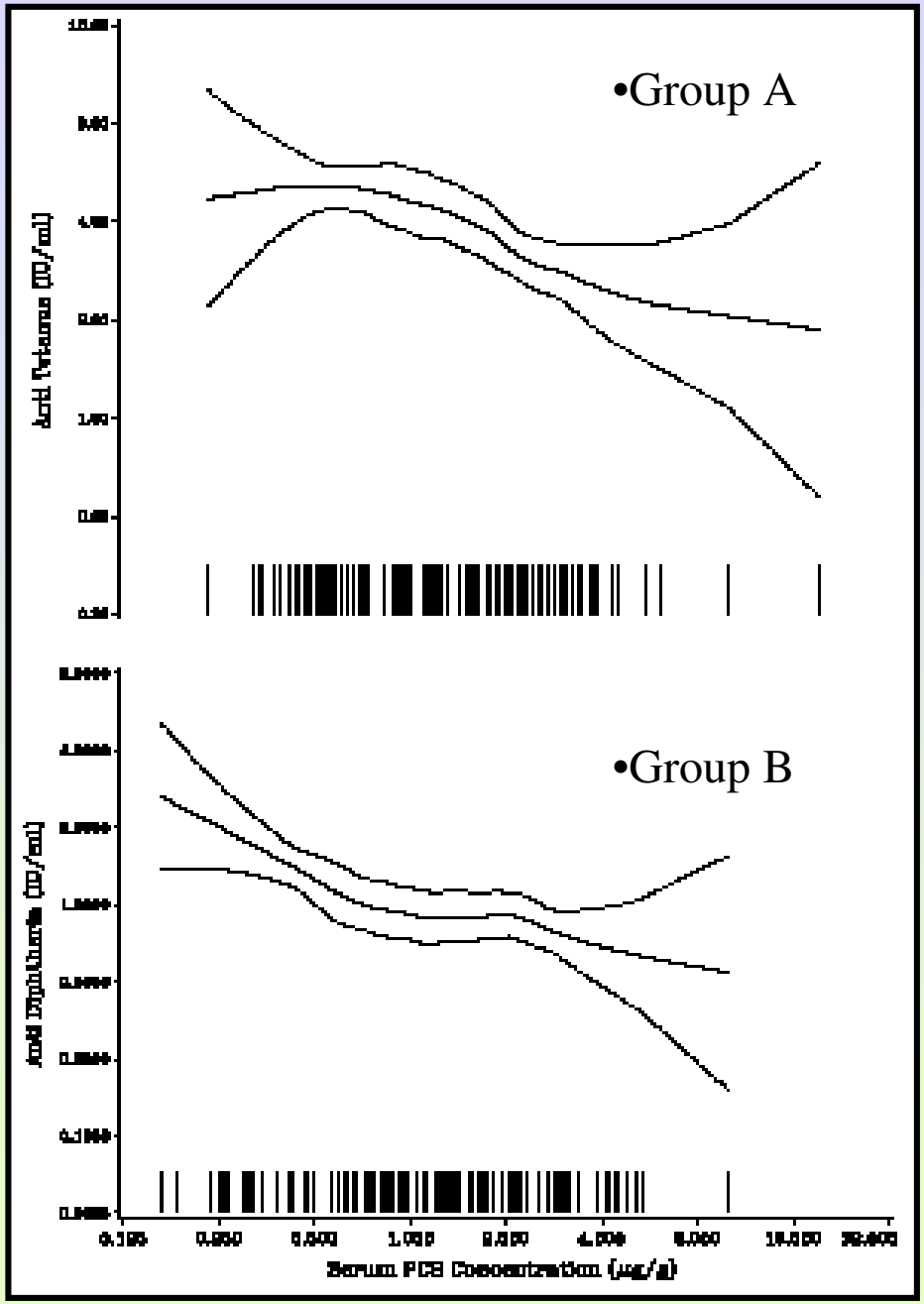



•F

# Dose-effect relationship between PCB exposure and antibody response to antigens from routine childhood vaccinations.

Upper panel: Maternal serum concentration of sum BCBs plotted against serum tetanus antibody concentrations at 7 years of age.

Lower panel: Serum concentrations of sum PCBs against serum diphtheria antibody concentrations, both at 18 months of age.



**Change (in %) in Antibody Concentrations after Childhood Vaccinations (18 months) Associated with a Doubling in Prenatal or Postnatal Exposure to Polychlorinated Biphenyls (PCBs).**

| Exposure parameter | Diphtheria tox | |
|---|---|---|
| | Change | P |
| **Transitional milk** | | |
| Total PCB | -19 | **0.04** |
| Weighted mono-*ortho* PCB congeners | -20.7 | **0.02** |
| **Child serum postnatally (18months)** | | |
| Total PCB | -20.3 | **0.01** |
| Weighted mono-*ortho* PCB congeners | -17.3 | 0.062 |

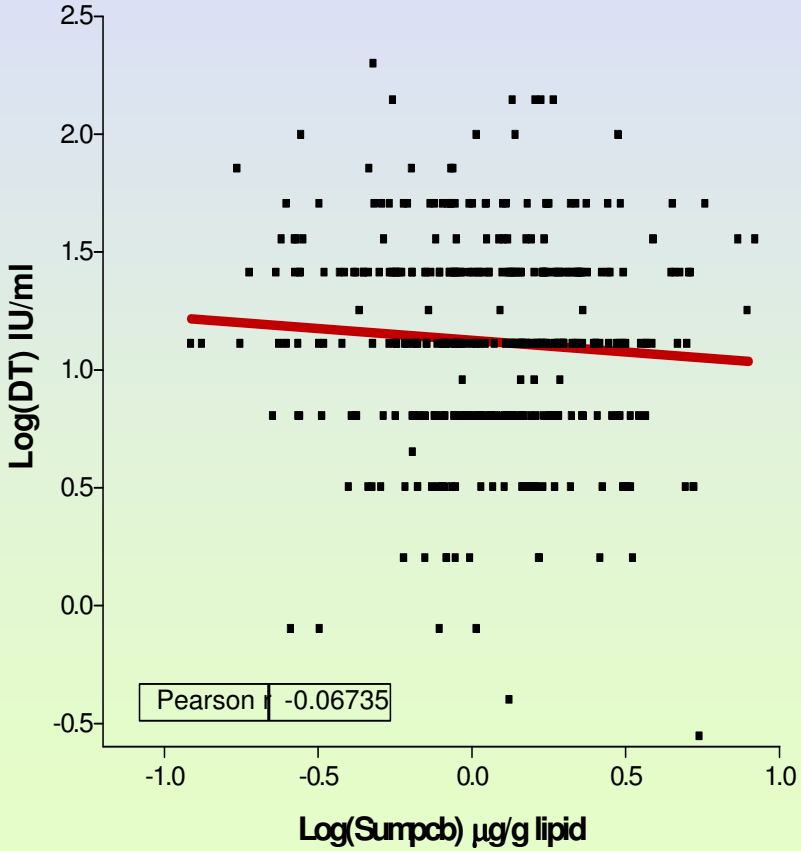
# Change (in %) in Antibody Concentrations after (2y) Childhood Vaccinations (5 years) Associated with a Doubling in Prenatal or Postnatal Exposure to Polychlorinated Biphenyls (PCBs).

| Exposure parameters | Tetanus tox | |
|---|---|---|
| | Change | P |
| **Maternal serum** | | |
| Total PCB | -16.5 | **0.029** |
| Weighted mono-*ortho* PCB congeners | -1.72 | 0.800 |
| | | |
| **Child serum postnatally (7 years)** | | |
| Total PCB | -13.8 | 0.081 |
| Weighted mono-*ortho* PCB congeners | -13.8 | 0.099 |

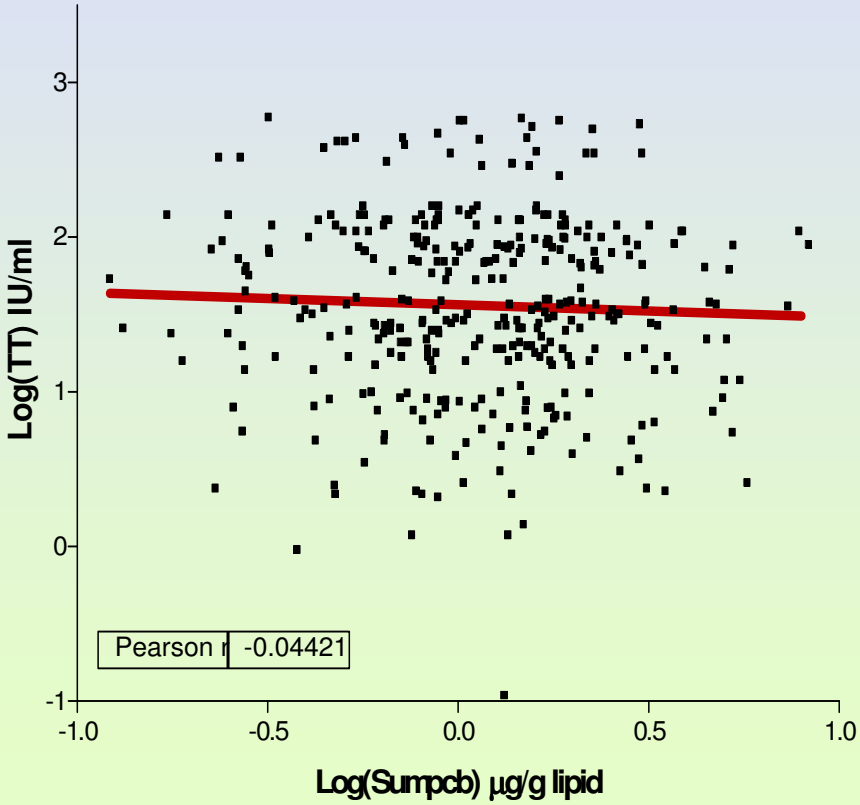
# Serum antibody concentrations at different time points in relation the source of PCB measurement

| Parameter | Group A (7 years) Tetanus | | Group B (18 months) Diphtheria | |
|---|---|---|---|---|
| | Mean | p | Mean | P |
| **Maternal serum PCB** | | | | |
| Above median | 4.61 | | 1.15 | |
| Below median | 7.03 | **0.035** | 2.25 | 0.13 |
| **Current serum PCB** | | | | |
| Above median | 4.74 | | 1.37 | |
| Below median | 6.70 | 0.088 | 2.39 | **0.032** |

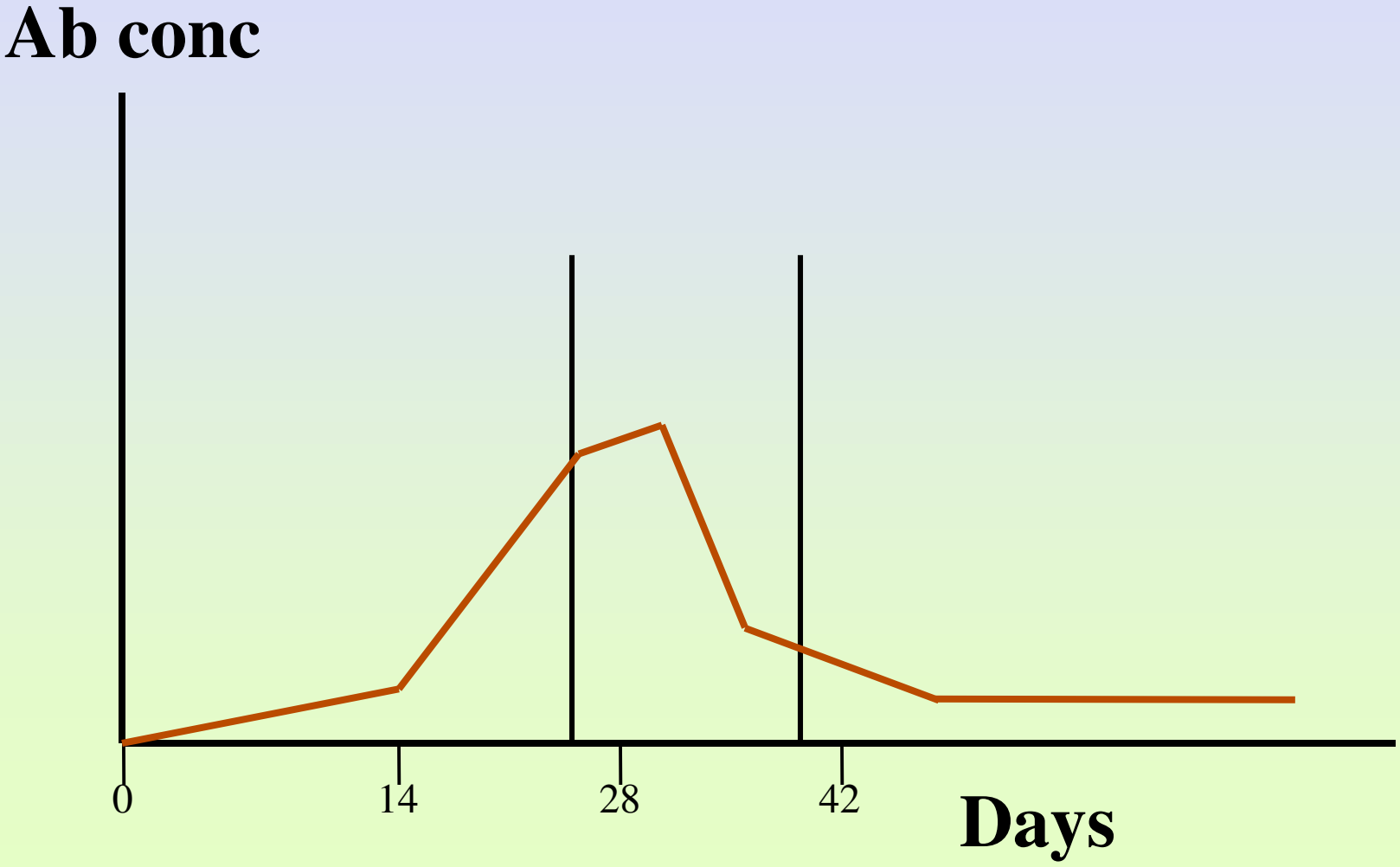
## Correlation between anti DT Ab and SumPCB 1 month post 5y boost



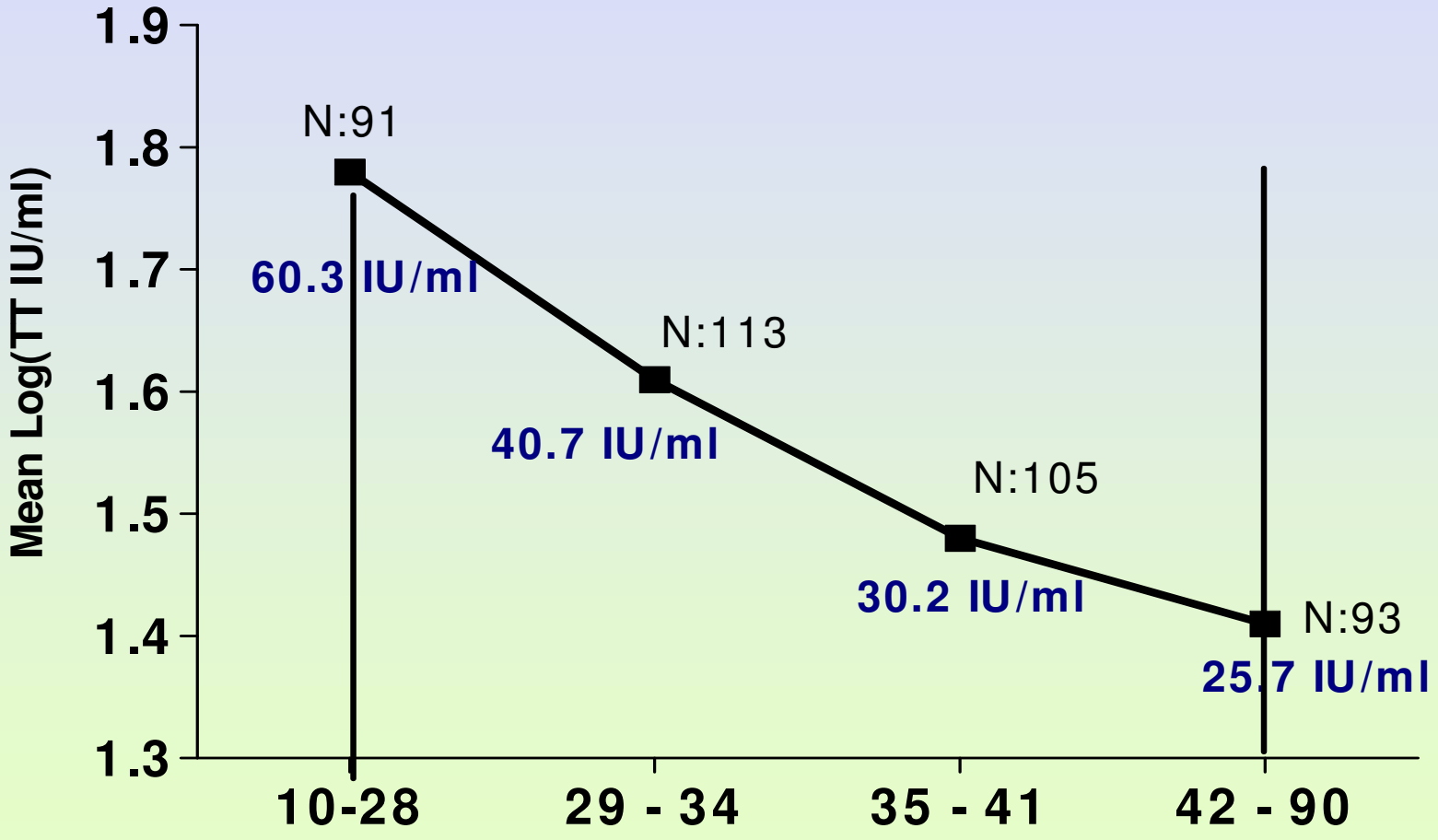

## Correlation between anti TT Ab and SumPCB 1 month post 5y boost



# Variation in Ab Concentartion Shortly after Vaccination



# TT ab concentrations in relation to numbers of days from booster vaccination




Diff. birth - boost vacc.: >4.5y And <6y

# Conclusions

- Environmental maternal PCB exposure negatively influence antibody response in infants in a dose dependent way.
- Environmental maternal PCB exposure negatively influence recall antibody response in children in a dose dependent way.
- Recall antigen response is probably mainly influenced by a diminished priming of infants elicited by exposure through maternal PCBs intrauterinly and via mothers milk.

# Immunotoxicological study on the Faeroe Islands:

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