Background: Polychlorinated biphenyls (PCBs) are ubiquitous environmental toxicants, for which animal studies demonstrate immunotoxic effects, including thymic atrophy and suppressed immune responses; human investigations of similar end points are sparse. The thymus is essential for the differentiation and maturation of T-cell lymphocytes.

Objectives: The objective of this study was to examine the association between prenatal PCB exposures and estimated thymus volume in infants from eastern Slovakia, a region where PCBs were produced until 1984.

Methods: Mothers were enrolled at delivery, and maternal blood samples were collected for analysis of 15 PCB congeners, p,p’-DDT [1,1,1-trichloro-2,2’-bis(p-chlorophenyl)ethane], and p,p’-DDE [1,1-dichloro-2,2-bis(p-chlorophenyl)ethylene]. Each mother was interviewed to obtain information on sociodemographic characteristics, past pregnancies, occupational history, medication history, and living environment. Neonatal thymus volume was estimated using ultrasound measurements on the third or fourth day after birth. Thymic index was calculated on 982 newborns from mothers with PCB measurements. We developed a predictive model of the natural log of the thymic index using multiple linear regression with covariates selected from the bivariate analyses.

Results: Prenatal PCB exposure was associated with a smaller thymic index at birth \( \beta = –36 \) (natural log-transformed; nanograms per gram lipids); \( p = 0.047 \). District of residence and delivery also predicted thymic index. Male sex, later gestational age, larger birth weight z-score, and Roma ethnicity were associated with a larger thymic index, whereas respiratory illness was associated with a lower thymic index.

Conclusions: This study provides the first evidence to date that PCB exposure in neonates is associated with a smaller thymic volume, suggesting possible impaired immunologic development.

Key words: p,p’-DDE, p,p’-DDT, PCBs, thymic index, immune status, prenatal. Environ Health Perspect 116:104–109 (2008). doi:10.1289/ehp.9769 available via http://dx.doi.org/ [Online 14 August 2007]
capillary column (J&W Scientific, Folsom, MA, USA). Quantification was based on the calibration curve generated by authentic PCB standard solutions at five different concentration levels. Quality control activities consisted of analyses of samples in batches of 10 simultaneously with a blank sample and in-house reference material (spiked porcine serum). Response for a particular congener had to be in the range of 90–110% using the concentration of the middle point of the calibration curves for that congener. We determined the limit of detection for each analyte as the mean of background noise plus 3 standard deviations from five reagent blank samples.

Six of the individual PCB congeners were selected to be included into PCB sum (PCB IUPAC nos. 118, 153, 156, 170, and 180) based on having < 20% of samples below the limit of detection (LOD). When one of these PCB congeners was below the limit of detection in an individual’s sample, we imputed by assigning the LOD value divided by the square root of 2 (Persky et al. 2001; Weiskopf et al. 2005). PCB-sum concentrations were determined on a wet weight basis (nanograms per milliliter); subsequently these PCB concentrations were adjusted for lipids (nanograms per gram).

The Department of Toxic Organic Pollutants at the Slovak Medical University in Bratislava (SMU) performed the laboratory analyses. The laboratory has participated in intercalibration studies organized by the World Health Organization (2000) and the German Agency for Occupational and Environmental Medicine (Deutsche Gesellschaft fuer Arbeitsmedizin und Umweltmedizin e.V.).

**Lipids measurement.** We estimated total serum lipids (TL) using the enzymatic summation method (Akins et al. 1989). We measured serum total cholesterol (TC) and triglyceride (TG) using a DuPont Automatic Clinical Analyzer III analyzer (DuPont, Jemison, AR, USA), and cholesterol oxidase without cholesterol esterase was used to detect free cholesterol (FC). The method by Takayama et al. (1977) was used to determine serum choline-containing phospholipids (PL). Total serum lipids were calculated from the formula

\[ TL = 1.677 \times (TC - FC) + FC + TG + PL. \]

The lipids were measured at a biochemical laboratory accredited by the Slovak National Accreditation Service located at the Ministry of Defense Military hospital in Bratislava.

**Thymus measurement.** The thymus was measured on the 3rd or 4th day after birth in 982 neonates from October 2002 through December 2004. Four radiologists from Michalovce and two radiologists from Švidnik measured the thymus using a sonographic scanner [in Michalovce: Esaote 580 FD Caris plus (convex probe 7.5 MHz); Esaote SpA, Genova, Italy; in Švidnik: Esaote AU 5 Harmonic (convex probe 7.5 MHz); Esaote SpA, Firenze, Italy]. The thymus is located in the anterior mediastinum in front of the large vessels, and is well delineated by sonography. The infant was examined on his or her back with the neck extended and head fixed in an optimal position for measurement. A trans-sternal approach was used to measure the maximal transverse diameter (width) of the thymus. In the plane perpendicular to this width, the largest sagittal area (longitudinal scan plan) was also measured. These two measurements were multiplied to obtain the thymic index. The thymic index was used as an estimate of the thymus volume.

**Data collection.** The two major data sources for covariates were an interview with the mother conducted by trained staff during the 5-day hospital stay, and the newborn medical record. The interview obtained information on sociodemographic characteristics, past pregnancies, occupational history, medical conditions, medication history before and during the pregnancy, and living environment. Romani ethnicity was attributed to the mother if the ethnic origin of either of her parents was Romani, the Romani language was spoken at the home of the child, or the mother was planning to raise her child with the Romani language. This definition of Romani was subsequently independently confirmed by a Slovak member of the research team who used additional information such as the family’s last name to confirm the ethnicity. Ethnicity was categorized into two groups: Slovakian/other eastern European or Romani. Smoking history during or before pregnancy was extracted from the interview data. Alcohol consumption was defined as one or more drinks of beer, wine, or liquor per week during pregnancy or in the 3 months before pregnancy. Maternal illness history included respiratory infection, asthma, or allergy during the same time period. Parity was coded as an ordinal variable (0–4).

The abstraction of the newborn’s medical records included birth weight and gestational age (weeks). The estimate of gestational age was based on last menstrual period (LMP) reported in the medical records and the clinical judgment made by the woman’s physician.

**Data analysis.** Univariate distributions were examined and implausible values were investigated and resolved by communication with field staff. The thymic index was highly skewed (test of normality by Shapiro-Wilk, p < 0.0001), so we used the logarithmic transformation (log) of the thymic index in the analysis as the outcome variable. As the primary predictor variable of interest, the total maternal PCB concentration based on the six most abundant congeners was adjusted for...
reduce the influence of extreme values. Birth values were log-transformed as well to reduce the influence of extreme values. Birth weight was expressed as a Z-score standardized for sex, parity, and gestational age based on all births in Slovakia in 2004.

As a first step in the data analysis, we conducted simple linear regressions (bivariate analyses) with the thymic index as the outcome. Possible confounders such as sex, socioeconomic status (parental education), smoking, alcohol consumption, ethnicity, and maternal medical history including such ailments as diabetes, hypertension, hypothyroidism, allergy, asthma, and respiratory disease were evaluated. Then a multiple linear regression model was developed with covariates selected from the bivariate analyses. Variables with low or no association with the thymic index at p > 0.3 were excluded from final multiple linear regression models. We used a backward selection approach to develop a final predictive model. After exponentiation from the final regression model, expected thymic indices were calculated; results are presented as percent change in thymic index across the interquartile range and for the 10th–90th increase in PCBs respectively.

Scatterplots of residuals (the difference between the observed thymic index values and those predicted by the regression equation) for thymic index were plotted from the final regression model, expected thymic index from six radiologists in two districts. The measurements of radiologists 5 and 6, both from Svidnik area, seemed to be larger and had wider variation than those of radiologists from Michalovce. Radiologist 5 was the most experienced of all of them. The mean, median, and 10th and 90th percentiles of the PCB sum were 620, 440, and 1,170 ng/g serum lipids respectively. Table 3 shows the final multiple regression model predicting the log thymic index as a function of the lipid-adjusted PCB sum, adjusting for sex of infant, maternal smoking and alcohol history, Romani ethnicity, gestational age, Z-score of birth weight, district of residence, and maternal respiratory infection history during pregnancy or the 3 months before pregnancy. Higher serum PCB concentrations were associated with a smaller thymic index. For an increase in PCB across the interquartile range [280–700 ng/g (ug/g) serum lipids], the thymic index decreased by 3% (p = 0.047). An increase from the 10th to 90th percentile [190–1,170 ng/g serum lipids] was associated with a 7% reduced thymic index. Female infants had a smaller thymic index by 10% in comparison with male infants. Maternal smoking, alcohol, and respiratory infection histories were associated with a smaller thymic index by 3%, 5%, and 6% respectively; however, smoking and alcohol consumption were not statistically significant. The district differences observed in the crude data were upheld after adjusting for covariates. Each unit of Z-score of birth weight adjusted for gestational age (1 SD increase) and each week of gestational age increased thymic index by 13% and 3%, respectively.

We tested p,p'-DDE and p,p'-DDT in the multiple linear regression models. Although the same direction of effect was observed as was seen in PCBs, the coefficients were small and not significant (results not shown). Table 4 presents a separate final multiple linear regression model in which we focused on the measurements (n = 187) from the radiologist who is the most experienced. Applying the beta coefficient from this model to the population interquartile range of PCBs yielded a decrease in the thymic index of

---

**Table 1.** Characteristics of the study cohort consisting of 982 mother–infant pairs with deliveries 2002–2004 in two districts of eastern Slovakia.

| Characteristic                        | No. (%)       |
|---------------------------------------|---------------|
| **District**                          |               |
| Michalovce                            | 702 (71.5)    |
| Svidnik                               | 280 (28.5)    |
| **Maternal age (years)**               |               |
| < 19                                   | 84 (8.6)      |
| 20–29                                  | 689 (70.1)    |
| ≥ 30                                   | 209 (21.3)    |
| **Maternal education**                 |               |
| Basic schooling                       | 294 (20.8)    |
| High school without graduation         | 260 (26.5)    |
| High school with graduation            | 443 (45.1)    |
| More than college/university           | 72 (7.3)      |
| Missing                               | 3 (0.3)       |
| **Sex of child**                       |               |
| Male                                  | 503 (61.2)    |
| Female                                | 479 (48.8)    |
| **Ethnicity**                         |               |
| Slovakian/other eastern European       | 757 (77.1)    |
| Romani                                | 215 (21.9)    |
| Missing                               | 10 (1.0)      |
| **Marital status**                    |               |
| Married or living with partner         | 905 (92.2)    |
| Never married                         | 59 (6.0)      |
| Divorced                              | 7 (0.7)       |
| Missing                               | 11 (1.1)      |
| **Maternal smoking**                  |               |
| No                                    | 613 (62.4)    |
| Yes                                   | 357 (36.4)    |
| Missing                               | 12 (1.2)      |
| **Maternal alcohol consumption**      |               |
| No                                    | 673 (68.5)    |
| Yes                                   | 298 (30.4)    |
| Missing                               | 11 (1.1)      |
| **Parity**                            |               |
| 0                                     | 404 (41.2)    |
| 1                                     | 328 (33.4)    |
| 2                                     | 171 (17.4)    |
| 3                                     | 75 (7.6)      |
| 4                                     | 2 (0.2)       |
| Missing                               | 2 (0.2)       |
| **Maternal allergy history**          |               |
| No                                    | 937 (95.4)    |
| Yes                                   | 35 (3.6)      |
| Missing                               | 10 (1.0)      |
| **Maternal asthma history**           |               |
| No                                    | 973 (89.1)    |
| Yes                                   | 9 (0.9)       |
| **Maternal respiratory history**      |               |
| No                                    | 774 (78.8)    |
| Yes                                   | 198 (20.2)    |
| Missing                               | 10 (1.0)      |
8.9\% (p = 0.033). If PCBs increased from the 10th to the 90th percentile, the thymic index was reduced by 16.9\%.

Figure 1 shows the scatterplot of the log-transformed maternal serum PCBs against the residuals of the log thymic index from a multiple linear regression model with all predictor variables except PCBs. This plot visually presents the degree of negative slope explained by PCBs alone.

Discussion

The thymus is a flat, bi-lobed organ located above the heart. It plays a critical role in the differentiation and maturation of T-cell lymphocytes in immune system. These T lymphocytes are mainly responsible for cell-mediated immunity, which does not involve antibodies but protects against cancer cells, intracellular bacteria, and viruses. T lymphocytes secrete cytokines that can contribute to activating other immune cells or can serve a cytotoxic or regulatory function (Goldbly et al. 2003).

It has been reported that certain risk factors such as malnutrition, zinc depletion, stress, HIV or other infection, preterm birth, and seasonality [e.g., birth during hungry season, July–December, in Gambia (Collinson et al. 2003)] are associated with a smaller thymus size (Collinson et al. 2003; Dominguez-Gerpe and Rey-Mendez 2003; Jeppesen et al. 2003; Malpuech-Brugere 2001). Information is more limited on possible mechanisms to support these reported associations. Suggested hypotheses (Dominguez-Gerpe and Rey-Mendez 2003) include enhanced apoptosis in thymocytes, or reduced migration of precursor T lymphocytes from bone marrow to thymus. A small thymic index at birth was associated with reduced interleukin-7 in breast milk of the mother.

In vivo rodent experiments and in vitro studies have shown loss of thymocytes or thymic atrophy induced by certain PCB congeners (Beineke et al. 2005; Robertson et al. 1984; Tan et al. 2003). Other studies suggest this occurs by enhanced differentiation with impaired proliferation of thymocytes (Esser et al. 1994; Kremer et al. 1994; Lai et al. 1994). PCBs may interfere with the interaction of stromal cells that interact with the developing thymocytes rather than acting directly on thymocytes themselves (Esser et al. 1994; Kremer et al. 1994; Lai et al. 1994). Thymocytes develop in a three-dimensional stromal-cell network that consists of epithelial cells, dendritic cells, and macrophages (Goldbly et al. 2003). The interaction between stromal cells and thymocytes leads to proliferation and maturation of a repertoire of T cells (Van 1991). Fine et al. (1989, 1990) reported from an in vitro study with BALB/c mice that TCDD, chemical compounds structurally similar to PCBs, caused thymic atrophy through changes in lymphocyte precursors in the bone marrow and in the fetal liver. Camacho et al. (2004) showed that in C57BL/6 mice after perinatal exposure, TCDD induced increased apoptosis causing thymic atrophy.

Before sonographic examination became available, thymic size measurements were possible only on autopsy. Several earlier studies using sonographic measurements were either case reports or used their own estimates of thymus size such as thickness. Since Hasselbalch et al. (1996) suggested the thymic index as an estimate of the size of thymus, this approach has been adopted by several researchers (Aaby et al. 2002; Iscan et al. 2000; Jeppesen et al. 2003; Yekeler et al. 2004).

Our findings are consistent with previous studies showing the thymic index to be positively correlated with birth weight (Hasselbalch et al. 1997; Iscan et al. 2000; Yekeler et al. 2004) and gestational age (Jeppesen et al. 2003). Male infants had larger thymic index even after adjustment for birth weight in our study; Aaby et al. (2002) also reported a larger thymic index in boys, though this study did not adjust for birth weight. We also observed that maternal smoking, alcohol consumption, and respiratory infections during pregnancy or the 3 months before conception were associated with a lower thymic index, although smoking and alcohol consumption were not statistically significant in our data.

We found increased thymic index among infants with Romani ethnicity. Considering the deficient nutrition (e.g., the estimated average daily intake of vitamin C is 44\% of recommended daily allowance) (Brazdova et al. 1998); social conditions for the Romani in eastern Slovakia including low socioeconomic status, slum housing, and suboptimal hygienic conditions; and a high prevalence of smoking and alcohol consumption (Brazdova et al. 1998; Koupilova et al. 2001; Krajcovickova-Kudlackova et al. 2004; Vivian and Duncds 2004), a reduced thymic index might have been expected. Because we adjusted for smoking and alcohol consumption (as well as birth weight, which is also lower in Romani children), the mechanism leading to increased thymic index remains unclear. Interestingly, in our data, the Romani group showed lower prevalence, compared with non-Romani, of maternal illness history such as respiratory infections (17.2 vs. 21.3\%, asthma (0.5 vs. 1.1\%), or allergy (0 vs. 4.6\%) during pregnancy or in the 3 months before pregnancy.
Therefore, the possibility of selection bias (e.g., participation of more healthy subjects from Romani background) cannot be excluded in this study. In utero exposures to unmeasured environmental factors/pollutants during critical windows of gestation in the Romani ethnic group might play a role in the increased thymic index as well.

Despite the long time period since their arrival to Europe from Asia, the Romani maintain significantly smaller stature in terms of body height and weight and percentage of body fat, and a trend toward lower concentrations of the thyroid hormone thyroxine (Ginter et al. 2001); thus genetic differences might be related to an unbalanced establishment of the peripheral T-lymphocyte system.

Six radiologists measured the thymic index from the two districts where different instruments were used. Inter- or intrareliability comparisons among these six were not performed. Inclusion of a set of indicator variables for radiologist in the final model did not influence the parameter estimates for PCBs or for other covariates. We also tested models for the PCB association with thymic index within radiologists, and our finding was most strongly confirmed with infants examined by the most experienced radiologist (no. 5, from Svidnik).

Also, they observed that significant recurrent otitis media and higher prevalence of chicken pox were associated with a higher PCB body burden at 42 months of age. The median level of the sum of PCBs 118, 138, 153, and 180 in the Dutch study (Weisgals-Kuperus et al. 1995, 2000) was 2.07 µg/L, whereas in our study population it was 3.67 µg/L. If we compare the median concentration of PCB-153, the major congener, among different studies, it ranged from 30 to 140 ng/g lipid (Longnecker et al. 2003) in general populations from the United States, the Netherlands, Germany, and Canada, and in our study the concentration was 140 ng/g lipid. Considering half-lives of PCBs and the general decline in body burdens in most parts of the world (Cerna et al. 2007; Noren and Meirnyone 2000), and noting the fact that the specimens from the Netherlands study were measured in the early 1990s, the residents in eastern Slovakia are currently exposed to high levels of PCBs.

The clinical implication of this reduced thymic index remains to be clarified. Nonetheless, the reduction in thymic index associated with an increase across the interquartile range of PCBs was comparable to the reduction associated with a 1-week premature delivery: both were ~3%. Thus, the magnitude of the impact of this level of PCBs might be equivalent to a one-week delay in thymic maturation, although the actual mechanism and consequences are unknown. Because we are following the children in this birth cohort, in future analyses, we will examine longitudinal data for thymic index measured at 6 and 16 months to determine whether prenatal or postnatal PCB exposures influence the trajectory of this organ, and to evaluate associations of PCBs with other immune parameters as well as with clinical outcomes.

References

Aaby P, Marx C, Trauern S, Rudas D, Hasselbach H, Jensen H, et al. 2002. Thymus size at birth is associated with infant mortality: a community study from Guinea-Bissau. Acta Paediatr 91(6):699–703.

Akins JR, Waldep K, Bentern JT, Jr. 1989. The estimation of total serum lipids by a completely enzymatic ‘summation’ method. Clin Chim Acta 184(3):219–226.

Beinke A, Siebert U, McLaughlin M, Bruhn R, Thron K. 1994. Induction of apoptosis in T cells from murine fetal thymus embryos. J Toxicol Environ Health A 68(6):485–500.

Benn CS, Jeppesen DL, Hasselbalch H, Jeppesen AB, Nielsen SD, Ersboll AK, Valerius NH, et al. 2003. Thymic size in preterm neonates: a sonographic study. Acta Paediatr 92(7):817–822.

Cerna M, Svec vaskova B, Bartova A, Smid J, Cejchanova M, Ocdalikova D, et al. 2007. Human biomonitoring system in the Czech Republic. Int J Hyg Environ Health 210(3–4):485–499.

Chevrier C, Sevilla R, Zalles L, Seasj E, Belmonte G, Parent G, et al. 1996. Immuno-nutritional recovery of children with severe malnutrition. Sanite 6(4):201–208.

Collinson AC, Moore SE, Cole TJ, Prentice AM. 2003. Birth season and environmental influences on patterns of thymic growth in rural Gambian infants. Acta Paediatr 92(9):1014–1028.

Conk K, Droba B, Kocan A, Petrlik J. 2005. Simple solid-phase extraction method for determination of polychlorinated biphenyls and selected organochlorine pesticides in human serum. J Chromatogr A 1084(1–2):23–38.

DeCaprio AP, McDevitt ON, O’Keefe FW, Rej R, Silbchester JW, Kaminsky LS. 1988. Subchronic oral toxicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin in the guinea pig: comparisons with a PCB-containing transformer fluid pyrolysate. Fundam Appl Toxicol 6(3):454–466.

Dominguez-Garpe L, Rey-Mender M. 2003. Evolution of the thymus size in response to physiological and random events throughout life. Microsc Res Tech 62(6):464–476.

Elliott JE, Mascher MM, Wilson LJ, Henny CJ. 2000. Concentrations in esophageal aspirates of: II. Organochlorine pesticides, polychlorinated biphenyls, and mercury, 1991–1997. Arch Environ Contam Toxicol 38(1):50–106.

Esser C, Lai ZW, Gleimchen E. 1994. Proliferation inhibition and C4d/C8d thymocyte subset skewing by in vivo exposure of C57BL/10 mice to Ah receptor-binding, 3,3’,4’,4’-tetrachlorobiphenyl. Exp Clin Immunogenetics 11(4):7-15.

Fine JS, Gasiewicz TA, Silverstone AE. 1989. Lymphocyte stem cell alterations following perinatal exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin. Mol Pharmacol 35(1):18–25.

Fine JS, Silverstone AE, Gasiewicz TA. 1990. Impairment of pro-thymocyte activity by 2,3,7,8-tetrachlorodibenzo-p-dioxin. J Immunol 144(4):1169–1176.

Fraker PJ, King LE, Laakka T, Vollmer TL. 2000. The dynamic link between the integrity of the immune system and zinc status. J Nutr 130(Suppl:1399S–1405S.

George AJ, Ritter MA. 1996. Thymic involution with ageing: obsolescence or good housekeeping? Immunol Today 17(6):267–272.

Ginter E, Krajcovickova-Kudlackova M, Kacala O, Kovacic V, Valachovickova M. 2001. Health status of Romany (Gypsies) in the Slovak Republic and in the neighbouring countries. Bratisl Lek Listy 102(10):479–484.

Goff KA, Hulse BE, Grasmann KA. 2005. Effects of PCB 126 on primary immune organs and thymocyte apoptosis in chicken embryos. J Toxicol Environ Health A 68(8):485–500.

Goldsky RA, Knibb TJ, Osbourne BA, Kubiak BJ. 2003. Immunology. New York:W.H.Freeman and Company.

Hasselbalch H, Jeppesen DL, Ersboll AK, Engellman MD, Nielsen MB. 1997. Thymus size by sonography. A longitudinal study on infants during the first year of life. Acta Radiol 38(2):222–227.

Hasselbalch H, Nielsen MB, Jeppesen D, Pedersen JF, Korkov J. 1996. Sonographic measurement of the thymus in infants. Eur Radiol 6(5):700–703.

Iscan A, Tarhan S, Guven H, Bilgi Y, Yuncu M. 2000. Sonographic measurement of the thymus in newborns: close association between thymus size and birth weight. Eur J Pediatr 159(3):223–224.

Jeppesen DL, Hasselbalch H, Nielsen SD, Sorensen TU, Ersboll AK, Valerius NH, et al. 2003. Thymus size in preterm neonates: a sonographic study. Acta Paediatr 92(7):817–822.

Kerkvliet NJ, Steppan LB, Brauner JA, Deyo JA, Henderson MC, Tomar RS, et al. 1990. Influence of the Ah locus on the humoral immunotoxicity of 2,3,7,8-tetrachlorodibenzop-dioxin: evidence for Ah-receptor-dependent and Ah-receptor-independent mechanisms of immunosuppression. Toxicol Appl Pharmacol 105(1):26–36.

Kocan A, Petrik J, Draba B, Chovancova J. 1994. Levels of PCBs and some organochlorine pesticides in the human population of selected areas of the Slovak Republic. I. Blood. Chemother Pharmacov 29(8):1123–2235.

Kosova I, Epstein H, Holick MC, McKee M. 2001. Health needs of the Roma population in the Czech and Slovak Republics. Soc Med Sci 53(9):1191–1204.

Krajcovickova-Kudlackova M, Blazicek P, Spustova V, Valachovickova M, Ginter E. 2004. Cardiovascular risk factors in young Gypsy population. Bratisl Lek Listy 105(7–8):256–259.

Kremer J, Gleimchen E, Esser C. 1994. Thymic stroma exposed
to arylhydrocarbon receptor-binding xenobiotics fails to support proliferation of early thymocytes but induces differentiation. J Immunol 153(6):2778–2786.

Lei ZW, Kremer J, Gleichmann E, Esser C. 1994. 3,3’,4,4’-Tetrachlorobiphenyl inhibits proliferation of immature thymocytes in fetal thymus organ-culture. Scand J Immunol 39(5):480–488.

Longnecker MP, Wolff MS, Gladen BC, Brock JW, Grandjean P, Jacobson JL, et al. 2003. Comparison of polychlorinated biphenyl levels across studies of human neurodevelopment. Environ Health Perspect 111:95–70.

Malpuech-Brugere C. 2001. Immunonutrition and the thymus. Nutrition 17(11-12):972–973.

Noren K, Meironyte D. 2000. Certain organochlorine and organobromine contaminants in Swedish human milk in perspective of past 20–30 years. Chemosphere 40(9–11):1111–1123.

Olesen AB, Andersen G, Jeppesen DL, Benn CS, Juul S, Thestrup-Pedersen K. 2005. Thymus is enlarged in children with current atopic dermatitis. A cross-sectional study. Acta Derm Venereol 85(3):240–243.

Persky V, Turyk M, Anderson HA, Hanrahan LP, Falk CM, Steenport DM, et al. 2001. The effects of PCB exposure and fish consumption on endogenous hormones. Environ Health Perspect 109:1275–1283.

Robertson LW, Parkinson A, Bandiera S, Lambert I, Merrill J, Safe SH. 1984. PCBs and PBBs: biologic and toxic effects on C57BL/6J and DBA/2J inbred mice. Toxicology 31(3–4):191–206.

Ross PS, Jeffries SJ, Yunker MB, Addison RF, Ikonomou MG, Calambokidis JC. 2004. Harbar seals (Phoca vitulina) in British Columbia, Canada, and Washington State, USA, reveal a combination of local and global polychlorinated biphenyl, dioxin, and furan signals. Environ Toxicol Chem 23(1):157–165.

Shimada T. 1987. Lack of correlation between formation of reactive metabolites and thymic atrophy caused by 3, 4, 3’, 4’-tetrachlorobiphenyl in C57BL/6N mice. Arch Toxicol 59(5):301–306.

Silkworth JB, Antrim L. 2005. Relationship between Ah receptor-mediated polychlorinated biphenyl (PCB)-induced humoral immunosuppression and thymic atrophy. J Pharmacol Exp Ther 335(3):606–611.

Silkworth JB, Antrim LA, Sack G. 1986. An receptor mediated suppression of the antibody response in mice is primarily dependent on the Ah phenotype of lymphoid tissue. Toxicol Appl Pharmacol 86(3):380–390.

Steinmann GG, Klaus B, Muller-Hermelink HK. 1985. The involution of the ageing human thymic epithelium is independent of puberty. A morphometric study. Scand J Immunol 22(5):563–575.

Takayama M, Itoh S, Nagasaki T, Tanimizu I. 1977. A new enzymatic method for determination of serum choline-containing phospholipids. Clin Chim Acta 79(1):93–98.

Tan Y, Li D, Song R, Lawrence D, Carpenter DD. 2003. Ortho-substituted PCBs kill thymocytes. Toxicol Sci 76(2):328–337.

Tryphonas H, Feeley M, Robertson LW, Hansen LG. 2001. Polychlorinated biphenyl-induced immunomodulation and human health effects. In: PCBs: Recent Advances in the Environmental Toxicology and Health Effects. Lexington/University Press of Kentucky, 193–209.

Van EW. 1991. T-cell differentiation is influenced by thymic microenvironments. Annu Rev Immunol 9:591–615.

Venkataraman P, Siddhar M, Dhanammal S, Vijayababu MR, Srinivasan N, Arunakumar A, Srinivasan N, et al. 2004a. Effects of vitamin supplementation on PCB (Aroclor 1254)-induced changes in ventral prostatic androgen and estrogen receptors. Endocr Res 30(3):469–480.

Venkataraman P, Siddhar M, Dhanammal S, Vijayababu MR, Srinivasan N, Arunakumar A. 2004b. Antioxidant role of zinc in PCB (Aroclor 1254) exposed ventral prostate of albino rats. J Nutr Biochem 15(10):608–613.

Vivian C, Dunlop L. 2004. The crossroads of culture and health among the Roma (Gypsies). J Nurs Scholarsh 36(1):89–91.

Weisglas-Kuperus N, Patandin S, Berbers GA, Sas TC, Mulder PG, Sauer PJ, et al. 2000. Immunologic effects of background exposure to polychlorinated biphenyls and dioxins in Dutch preschool children. Environ Health Perspect 108:1203–1207.

Weisglas-Kuperus N, Sas TC, Koopman-Esseboom C, van der Zwan CW, de Ridder MA, Beishuizen A, et al. 1995. Immunologic effects of background prenatal and postnatal exposure to dioxins and polychlorinated biphenyls in Dutch infants. Pediatr Res 38(3):404–410.

Weiskopf MG, Anderson HA, Hanrahan LP, Kanarek MS, Falk CM, Steenport DM, et al. 2005. Maternal exposure to Great Lakes sport-caught fish and dichlorodiphenyl dichloroethylenne, but not polychlorinated biphenyls, is associated with reduced birth weight. Environ Res 97(2):149–162.

World Health Organization. 2000. Interlaboratory Quality Assessment of Levels of PCBs, PCDDs and PCDFs in Human Milk and Blood Plasma. Fourth Round of WHO- Coordinated Study. WHO Report EUR/00/5020352. Copenhagen:World Health Organization Regional Office for Europe.

Yekeler E, Tambağ A, Tunaci A, Gencelhac H, Dursun M, Gokce G, et al. 2004. Analysis of the thymus in 101 healthy infants from 0 to 2 years of age. J Ultrasound Med 23(10):1321–1326.