Environmental Pollution 169 (2012) 235–241

Contents lists available at SciVerse ScienceDirect

Environmental Pollution

journal homepage: www.elsevier.com/locate/envpol

Estimation of human body concentrations of DDT from indoor residual spraying for malaria control

Tenzing Gyalpo [a], Lukas Fritsche [a], Henk Bouwman [b], Riana Bornman [c], Martin Scheringer [a,*], Konrad Hungerbühler [a]

[a] Institute for Chemical and Bioengineering, ETH Zürich, Wolfgang-Pauli-Strasse 10, CH-8093 Zürich, Switzerland
[b] School for Environmental Sciences and Development, North-West University, Potchefstroom 2520, South Africa
[c] Department of Urology, Centre for Sustainable Malaria Control, University of Pretoria, Pretoria 0001, South Africa

ARTICLE INFO

Article history:
Received 28 April 2012
Accepted 29 April 2012

Keywords:
DDT
Indoor residual spraying
Human exposure modeling
Infant exposure
Reproductive characteristics

ABSTRACT

Inhabitants of dwellings treated with DDT for indoor residual spraying show high DDT levels in blood and breast milk. This is of concern since mothers transfer lipid-soluble contaminants such as DDT via breastfeeding to their children. Focusing on DDT use in South Africa, we employ a pharmacokinetic model to estimate DDT levels in human lipid tissue over the lifetime of an individual to determine the amount of DDT transferred to children during breastfeeding, and to identify the dominant DDT uptake routes. In particular, the effects of breastfeeding duration, parity, and mother's age on DDT concentrations of mother and infant are investigated. Model results show that primiparous mothers have greater DDT concentrations than multiparous mothers, which causes higher DDT exposure of first-born children. DDT in the body mainly originates from diet. Generally, our modeled DDT levels reproduce levels found in South African biomonitoring data within a factor of 3.

1. Introduction

Persistent organic pollutants (POPs) are found worldwide in human tissue samples such as blood, adipose tissue, and breast milk. In Europe and elsewhere, POPs such as DDT (dichlorodiphenyltrichloroethane) and PCBs (polychlorinated biphenyls) are decreasing in humans as their production and use were banned during the 1970s and 1980s (Solomon and Weiss, 2002). However, DDT as one of the initial twelve POPs regulated under the Stockholm Convention on POPs can still be produced and used for disease-vector control (UNEP, 2009). In South Africa, during the annual indoor residual spraying (IRS), 2 g of 75% water wettable technical DDT are applied per m^2 to the inner walls of all dwellings in malaria-endemic areas, resulting in 64–128 g of DDT applied per dwelling (Bouwman et al., 2011). Technical DDT used for malaria control is typically a mixture of the isomers *p,p′*-DDT (72–75%) and *o,p′*-DDT (21%) with traces of *p,p′*-DDE and *p,p′*-DDD (Bouwman et al., 2006). People living in DDT-treated dwellings have 100 times higher DDT concentrations in blood and human milk than the general population in Europe (Ritter et al., 2011a).

Infants experience high DDT exposure through breastfeeding (Bouwman et al., 1992; Bouwman and Kylin, 2009). Pre- and postnatal exposures are especially critical because they affect the early stages of the neural and physical development (Bouwman and Kylin, 2009; Eskenazi et al., 2009; Rogan and Chen, 2005). Recent studies from South Africa found reduced retinol-binding protein and thyroid hormone concentration, urogenital malformations in newborn boys, and impaired semen quality, associated with non-occupational exposure to DDT (Aneck-Hahn et al., 2007; Bornman et al., 2010; Delport et al., 2011).

To the best of our knowledge, no study has yet combined the empirical data specific for individuals who are currently exposed to DDT for malaria control with a pharmacokinetic (PK) model which predicts the DDT concentrations in human tissue over a full lifespan and which differentiates the exposure routes (diet, inhalation). Different PK model approaches have been used to determine infants' pre- and postnatal exposure under constant or time-variant exposure (Kreuzer et al., 1997; LaKind et al., 2000; Quinn et al., 2011). Here we present a one-compartment PK model that can be employed to quantify DDT lipid concentrations derived from estimated dietary and inhalation exposures (dermal exposure was not considered due to low importance found in Ritter et al. (2011a) for highly exposed populations). We used South African datasets from malaria-endemic areas based on samples collected since 1985 because of consistency of sampling, analyses, and documentation of exposure conditions.

The objectives of our study are: i) to quantitatively determine the concentrations of DDT and its transformation product,

* Corresponding author.
E-mail address: scheringer@chem.ethz.ch (M. Scheringer).

0269-7491/$ – see front matter © 2012 Elsevier Ltd. All rights reserved.
doi:10.1016/j.envpol.2012.04.032

dichlorodiphenyldichloroethylene (DDE), in South African women living in IRS-treated dwellings; ii) to evaluate the effects of breastfeeding duration, parity, and the mother's age at childbirth on the infant's body burden; and iii) to estimate the contribution of DDT and DDE from breast milk, diet, and inhalation at different stages of life. To this end, we defined different scenarios by varying the duration of breastfeeding, the parity as well as the mother's age and investigated the effects of these parameters on the mother's and infant's body burden.

2. Methods

It is a common approach to use PK models for lipophilic environmental contaminants and to assume that this type of contaminants partitions into the lipids of body organs, tissues, and fluids equally (Alcock et al., 2000; Lorber and Phillips, 2002; Quinn et al., 2011). This may also be applied to DDT and DDE (ATSDR, 2002; Ritter et al., 2009). In this type of model, the body is represented as one compartment containing a certain amount of lipids that changes with the age of a person (Alcock et al., 2000; Quinn et al., 2011). Consequently, lipid-normalized concentrations are assumed to be identical in different body compartments and organs. Empirical measurements support this assumption (Darnerud et al., 2010; Sapbamrer et al., 2008; Waliszewski et al., 2000, 2001).

Because individuals living in malaria-endemic regions in South Africa have experienced DDT exposure from annually performed IRS for more than 60 years (Bornman et al., 2010), we assumed that different generations experience identical exposure patterns. That is, a first-born mother would show the same DDT concentration profile as her first-born child (under the assumption that factors such as the mother's age at delivery and the duration of breastfeeding remain the same). Hence, our base case scenario is a South African woman who was the first-born of a 20-year-old woman and was breastfed for 2 years. She in turn gives birth for the first time at the age of 20 and also breastfeeds for 2 years. In addition, a nulliparous woman was included and assumed to have been breastfed for 2 years as the first-born child of a 20-year-old mother. We investigated the effect of breastfeeding duration (0.5, 1, or 2 years), parity (from one child to four children) and the mother's age (16, 20, or 25 years old) on the mother's and infant's body burden by modifying the base case scenario accordingly. We present concentration–age profiles of total DDT, which includes ΣDDT (= *p,p′*-DDT and *o,p′*-DDT) and ΣDDE (= *p,p′*-DDE and *o,p′*-DDE).

2.1. Calculation of total DDT concentration in women

Our one-compartment PK model is represented by the first-order differential equation (Eq. (1)), describing the mass balance in a South African woman, and the conversion equation (Eq. (2)) to obtain lipid-normalized concentrations:

$$\frac{dm_i(t_{age})}{dt} = U_{i,diet}(t_{age}) + U_{i,inh}(t_{age}) - \Big(k_{i,met}(t_{age}) + k_{ex}(t_{age}) + k_{i,bf}(t_{age}, t_{bf})\Big) \times m_i(t_{age}) \quad (1)$$

$$c_i(t_{age}) = \frac{m_i(t_{age})}{bw(t_{age}) \times f_{lip}(t_{age}) \times 1000} \quad (2)$$

where $m_i(t_{age})$ is the mass (ng) of substance i (i = ΣDDT or ΣDDE) in the body as a function of age, $U_{i,diet}(t_{age})$ is the uptake (ng/d) via diet, $U_{i,inh}(t_{age})$ is the uptake (ng/d) via inhalation, $k_{i,met}(t_{age})$ is the first-order rate constant (1/d) for metabolic elimination, $k_{ex}(t_{age})$ is the first-order rate constant (1/d) for non-metabolic elimination (i.e. excretion) (identical for ΣDDT and ΣDDE), $k_{i,bf}(t_{age}, t_{bf})$ is the first-order rate constant (1/d) for breastfeeding as a function of the mother's age and breastfeeding time (t_{bf}), $c_i(t_{age})$ is the lipid-normalized concentration (ng/g$_{lip}$) in the body, $bw(t_{age})$ is the body weight (kg), and $f_{lip}(t_{age})$ is the lipid fraction of the body (dimensionless).

$k_{i,met}(t_{age})$ and $k_{ex}(t_{age})$ were calculated according to Kreuzer et al. (1997) (Eqs. (3) and (4)) by using the overall intrinsic elimination half-life of DDT ($t^{1/2}_{DDT,elim}$ = 2.2 years) and DDE ($t^{1/2}_{DDE,elim}$ = 6.2 years) reported by Ritter et al. (2009):

$$k_{i,met}(t_{age}) = k^{ref}_{i,met} \times \left(\frac{V^{ref}_{lip}}{V_{lip}(t_{age})}\right) \times \left(\frac{V_{liv}(t_{age})}{V^{ref}_{liv}}\right)^{0.667} \quad (3)$$

$$k_{ex}(t_{age}) = \frac{r_{lip,feces}(t_{age})}{bw(t_{age}) \times f_{lip}(t_{age}) \times 1000} \quad (4)$$

where $k^{ref}_{i,met}$ is the first-order rate constant (1/d) for metabolic elimination of the reference subject (= 40-year-old South African woman), V^{ref}_{lip} is the lipid volume (L) and V^{ref}_{liv} is the liver volume (L) of the reference subject, $V_{lip}(t_{age})$ and $V_{liv}(t_{age})$ are the age-dependent lipid volume (L) and liver volume (L), respectively, and $r_{lip,feces}(t_{age})$ is the daily excretion rate of lipids in feces (g$_{lip}$/d). Metabolic conversion of DDT to DDE in the body was not modeled because most of the DDE present in the human body originates from uptake via diet and inhalation (Baselt and Cravey, 1989), with supporting indication from Van Dyk et al. (2010). Further, DDT is much faster degraded to DDD than to DDE (Morgan and Roan, 1971). Therefore, we concluded that the formation of DDE in the body is negligible.

When the mother starts breastfeeding, the amount of ΣDDT and ΣDDE removed via breast milk is equal to the amount taken up by her infant. The first-order rate constant for breastfeeding ($k_{i,bf}$), is described as (Eq. (5)):

$$k_{i,bf}\left(t_{age},\ t_{bf}\right) = \frac{r_{milk}(t_{bf}) \times f_{lip,milk}(t_{bf})}{bw(t_{age}) \times f_{lip}(t_{age}) \times 1000} \quad (5)$$

where $r_{milk}(t_{bf})$ is the rate of the consumed amount of breast milk (g/d) and $f_{lip,milk}(t_{bf})$ is the lipid fraction (dimensionless) of the breast milk as a function of time during the breastfeeding period. Whenever the woman is not breastfeeding, the breastfeeding term in the mass balance (Eq. (1)) is zero. All model calculations were performed in Matlab R2010b; all input parameters for this PK model are provided in the Supplemental Material (SM).

2.2. Total DDT uptake via diet and inhalation

We calculated the daily uptake of ΣDDT and ΣDDE via diet ($U_{i,diet}$) and inhalation ($U_{i,inh}$) as described by Eqs. (S1)–(S3) in the SM. Dietary uptake was calculated by using all available ΣDDT and ΣDDE concentrations measured in local food items such as chicken (muscle and fat), fish (fat) and leafy vegetables (Barnhoorn et al., 2009; Van Dyk et al., 2010). Further, we included ΣDDT and ΣDDE concentrations from recent measurements in chicken eggs in South Africa (R. Bornman, unpublished data). For concentrations of ΣDDT and ΣDDE in chicken fat, a high variability is present in the data reported by Van Dyk et al. (2010) and Barnhoorn et al. (2009). Therefore, we decided to use the median concentrations of Van Dyk et al. (2010) as the upper and the median concentrations of Barnhoorn et al. (2009) as the lower bound. The average of the medians was set as our default concentration for the chicken fat (Table S6, SM). Consumption rates of the food items considered have been reported by Nel and Steyn (2002). The reported consumption rates were extrapolated to obtain age-adjusted consumption rates according to the age-dependent calorific intake reported in Rose et al. (2002). The following age groups were used in this calculation: 0.5–3 years, 3–6 years, 6–10 years, 10–50 years, and >50 years.

Uptake via inhalation of indoor air was calculated by using age-dependent inhalation rates (U.S. EPA, 1997) with constant ΣDDT and ΣDDE concentrations in indoor air of 5.0 μg/m^3 and 0.185 μg/m^3, respectively; the ratio of ΣDDT/ΣDDE = 27 was taken from Van Dyk et al. (2010). We assumed constant concentrations in indoor air because ΣDDT and ΣDDE were still detected 84 day after an IRS intervention in South Africa (Bouwman et al., 2009; Van Dyk et al., 2010). During this period the total DDT concentration decreased quickly from initially 16.5 μg/m^3 to 3.4 μg/m^3. Further, it was assumed that the inhabitants spend 8 h/d inside their dwellings (Bouwman et al., 2009). Uptake efficiency from diet, inhalation, and breast milk was set to 100%.

2.3. Implementation of pregnancy, birth, and breastfeeding

We assumed a weight gain of 0.3 kg/week during pregnancy (Williamson, 2006). At delivery, a woman loses about 4.5 kg (= newborn baby, placenta, and amniotic fluid; ICRP (1975)) immediately and thereafter she continuously loses 0.5 kg/week until she reaches her pre-pregnancy weight (IOM, 1996). The newborn's initial ΣDDT and ΣDDE concentrations were assumed to be identical to the mother's body concentrations at the time of birth; in this way, we accounted for prenatal exposure (Sapbamrer et al., 2008; Verner et al., 2009). The amount of breast milk consumed was assumed 800 g/d for the first year and 600 g/d for the second year (Bouwman et al., 2006; Da Costa et al., 2010). Further, the lipid content of the breast milk was assumed to increase from 3.3% (month 0–4), 3.8% (month 5–8), 4.2% (month 9–12) to 5.0% (month 13–24) (Bouwman, 1990). The concentrations of ΣDDT and ΣDDE in the breast milk over the course of breastfeeding were predicted by the model itself.

2.4. Biomonitoring data

We compared our model results with biomonitoring data of non-occupationally exposed inhabitants who live in dwellings where IRS with DDT is applied once per year. Bouwman et al. (1991, 1992) and Bouwman and Schutte (1993) reported concentrations in blood or blood serum. These concentrations had to be converted to make them comparable with our modeled ΣDDT and ΣDDE concentrations. To this end, whole weight-based concentrations were doubled to yield serum-based concentrations (Bouwman et al., 1992). For the conversion of the serum-based concentrations to lipid-normalized concentrations, we used the factors proposed by the WHO (WHO, 2011), namely 200 for children under 19 years old and 160 for adults over 19 years old which were derived from the average lipid fraction of the blood serum (~0.5–0.65%). The measured total DDT concentrations consist of DDT, DDE, and DDD isomers, but DDD isomers accounted for <3% of the total DDT measured in breast milk and blood (Bouwman et al., 1990, 1992). For this reason and

also because DDD is less persistent in humans than DDT and DDE (Kirman et al., 2011), we only included ΣDDT and ΣDDE in our investigation.

2.5. Hypothetical complete post-ban situation

To describe a scenario of a total ban of DDT in 2020, we calculated ΣDDT and ΣDDE concentrations in 20-year-old primiparous mothers until 2100. In this calculation, the half-life of ΣDDT and ΣDDE was set at 10 years for soils (ATSDR, 2002). The dietary exposure was assumed to decline according to a first-order exponential decrease with the same half-life of 10 years (Ritter et al., 2009).

3. Results

3.1. Total DDT concentration profile over lifetime of a nulliparous woman

Fig. 1 shows the modeled age-dependent lipid-normalized concentration of total DDT (= ΣDDT + ΣDDE) for a nulliparous woman who was breastfed for two years. The sharp increase in total DDT concentration after birth is due to the lactational transfer of ΣDDT and ΣDDE, which is greater than the rate of growth during the first two years of life according to the model. The peak concentration of total DDT is reached at the age of 1.7 and is 75 $\mu g/g_{lip}$, which consists of 21% ΣDDT and 79% ΣDDE. After the age of 2, the total DDT concentration in the child declines due to the weight gain during childhood until the age of 10. During this period, growth dilution is the dominant process and exceeds the rate of contaminant uptake via diet and inhalation. After the age of 10, the uptake exceeds growth dilution resulting in an increase of total DDT concentration until it stabilizes around the age of 20. After this age, the woman's body weight and lipid fraction stabilizes, resulting in a total DDT steady state concentration of approximately 30 $\mu g/g_{lip}$.

We compared our modeled concentrations of total DDT with measured concentrations in blood serum of both genders living in DDT-sprayed areas (Bouwman et al., 1991, 1992). Our model results agree with the measurements within a factor of 1.5 except for the ages of 25 and 35, which fit within a factor of 3.3. The drop in the measured concentration for the age group of 20–40 years might have been caused by including women who already had children, whereas we present model results for a nulliparous woman.

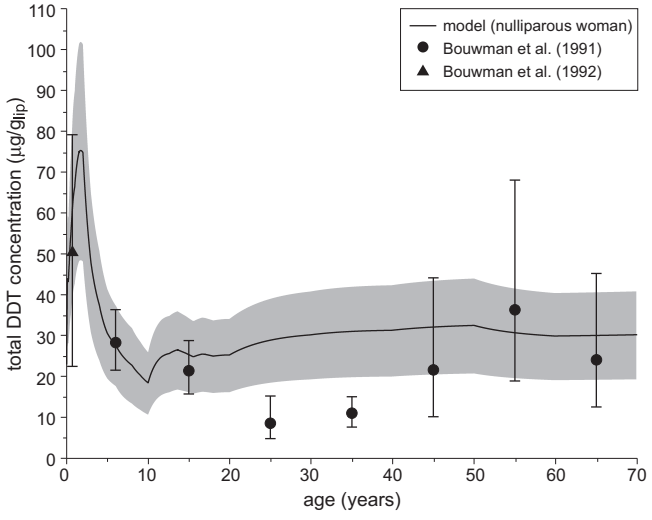

Fig. 1. Total DDT lipid-normalized concentration profile of a nulliparous woman who was breastfed for 2 years as the first-born child of a 20-year-old mother. The shaded area represents the variability caused by the range of median ΣDDT and ΣDDE concentrations measured in chicken fat (Barnhoorn et al., 2009; Van Dyk et al., 2010) (see Methods and Sensitivity analysis in SM). The biomonitoring data are the lipid-normalized total DDT concentrations converted from mean serum and blood concentrations with 95% confidence intervals reported in Bouwman et al. (1991, 1992).

3.2. Effect of breastfeeding duration, parity, and mother's age at childbirth

Fig. 2a shows the total DDT concentration of a nulliparous woman in contrast to a primiparous mother with different durations of breastfeeding (6 months, 1 year or 2 years). When the woman becomes pregnant at the age of 20, her body lipid weight starts to increase causing a drop in the total DDT concentration from the beginning of her pregnancy (gestation of 270 days). After giving birth, the steep decrease in maternal total DDT concentration is caused by the transfer of contaminants to the infant, which exceeds the mother's contaminant uptake via diet and inhalation. The longer the breastfeeding lasts, the more the total DDT concentration decreases in the mother. When the breastfeeding ends, the mother's total DDT concentration rises again approaching finally the level of the nulliparous woman.

The corresponding postnatal exposure of the first-born child is shown in Fig. 2b. We assumed that the infant is exclusively breastfed for 6 months, 1 year, or 2 years and then receives a normal diet. In each case the maximum of total DDT concentration is reached at the end of the breastfeeding period and increases with its duration from 54 to 66 and 75 $\mu g/g_{lip}$, respectively. The amounts of ΣDDT, ΣDDE, and total DDT that are transferred during breastfeeding are shown in Table 1. Bouwman et al. (1992) investigated the transfer of total DDT to infants via breast milk and reported concentrations in infant blood (μg/L). Fig. 2b shows additionally the adjusted total DDT concentrations in infants investigated by Bouwman et al. (1992). Most measured concentrations differ by a factor of less than 2, few by a factor of less than 3 from the model results.

Fig. 2c and d show the effect of parity on the total DDT concentration of the mother as well as on her children. In this case, the woman was assumed to give birth to four consecutive children who are born in 3-year intervals when the mother is 20, 23, 26, and 29 years old. Each child is breastfed for 2 years. During these reproductive years, the total DDT concentration profile of the mother is determined by the interplay of different processes, namely weight gain during pregnancy, weight loss after pregnancy, breastfeeding, and contaminant uptake via diet and inhalation. According to Fig. 2c, the model predicts a fast decrease in the mother's body burden with the first child and a further decrease in total DDT concentration with subsequent births.

Bouwman et al. (1990) examined 132 breast milk samples of women living in IRS-treated dwellings to identify possible factors (i.e. parity, infant's age, and mother's age) affecting the levels of total DDT in breast milk. They found that mothers aged 17–20 years had higher total DDT concentrations than older mothers (blue triangles in Fig. 2c) and that primiparous mothers had significantly higher total DDT concentrations than multiparous mothers (green dots in Fig. 2c). Although the breast milk samples labeled for parity are not labeled for age, we here assumed that parity is positively correlated with the mother's age. Especially in the case of rural areas in South Africa this assumption is valid where women have four children on average (Department of Health, 2007). Therefore, we arranged these data points (green dots) accordingly. Our model results agree well with these findings.

As revealed by Fig. 2d, the first-born child experiences the highest load of contaminants: the steep decrease in the mother's concentration corresponds with the steep increase in the first-born's concentration (identical case as the 2-year breastfeeding scenario in Fig. 2b). The subsequent children receive considerably less contaminant via breastfeeding (Fig. 2d and Table 1). With

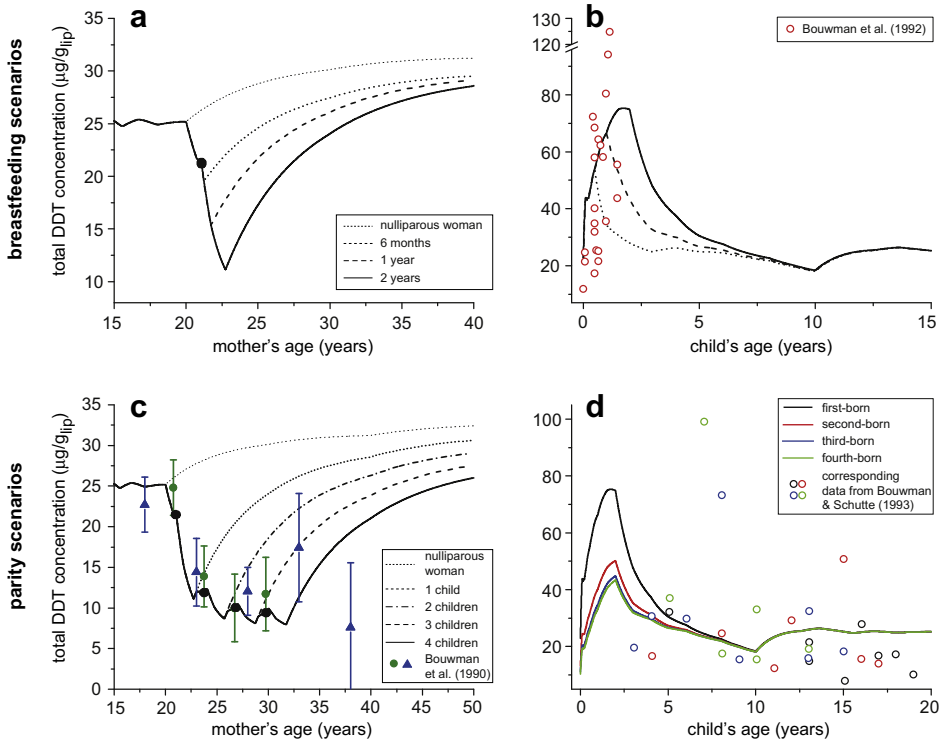

Fig. 2. Effect of breastfeeding duration and parity on the total DDT concentration of the mother (a, c) and her children (b, d); see Eq. (S5) in the SM for the mass balance equation for infants. Births are indicated with black dots. The biomonitoring data presented in panel c) are the mean concentrations (with 95% confidence interval) of total DDT in breast milk of mothers at different ages (blue triangles) and with different parity (green dots) reported by Bouwman et al. (1990). The parity data were assigned according to the age of the model mother. Biomonitoring data in panel b) and d) represent measurements from individual children (Bouwman et al., 1992; Bouwman and Schutte, 1993).

increasing number of children, the mean level of total DDT contamination in the breast milk decreases from 16 μg/g_{lip} to 10 μg/g_{lip}, 9.2 μg/g_{lip} and 8.8 μg/g_{lip}. The maximum concentrations in the children are reached around the age of 2 with the first-born child showing almost twice the maximum concentration of the subsequent children. The effect of parity on the total DDT concentrations among siblings was investigated by Bouwman and Schutte (1993) in eight families by measuring total DDT in blood serum. The total DDT concentrations measured in girls and boys aged 3–19 years are shown in Fig. 2d. The model results differ by a factor of less than 4.3 from these measured concentrations.

Finally, the difference in the mother's age at childbirth has a smaller effect on the infant's chemical burden than breastfeeding duration and parity (Table 1). This difference in lactational transfer is caused by the age-dependent total DDT concentration of the mother prior to pregnancy (Fig. 1). The latter is a direct result of the fluctuation of the body lipid volume at this age.

Table 1
Transfer of ΣDDT and ΣDDE from mother to child over the full duration of breastfeeding; shown is the effect of the duration of breastfeeding (A), the order of children born (B), and the mother's age (C).

	ΣDDT (mg)	ΣDDE (mg)	Total DDT (mg)
A: Duration of breastfeeding			
6 months	26	81	107
1 year	51	159	210
2 years (base case)	88	265	352
B: Parity			
First-born child (base case)	88	265	352
Second-born child	66	162	228
Third-born child	62	139	202
Fourth-born child	61	134	194
C: Mother's age			
16 years	82	229	310
20 years (base case)	88	265	352
25 years	91	302	393

3.3. Contribution of breast milk, diet and inhalation to the overall uptake of total DDT

The overall uptake of total DDT was calculated as the sum of ΣDDT and ΣDDE uptake via breast milk, diet and inhalation. For children under 2 years, the contributions of ΣDDT and ΣDDE to this uptake are 26% and 74%, respectively. In this age group, 7% of ΣDDT originate from inhalation and 93% from breast milk, while ΣDDE comes mainly from breast milk (>99%). Also in older age groups, more than 99% of ΣDDE stem from food (this is because technical DDT consists of mainly DDT isomers). For the age 2–10 years, ΣDDT contributes 43% and ΣDDE 57% to the total DDT uptake, and 24% of the ΣDDT uptake originates from inhalation (diet: 76%). For the age >10 years, the contribution of ΣDDT and ΣDDE is similar as in the younger age group but the fraction of ΣDDT from inhalation is only 15% (diet: 85%). In conclusion, the inhalation route is important for ΣDDT uptake (7–24%), but is less relevant for the total DDT uptake (2–10%) because, firstly, the contribution of ΣDDT to total DDT uptake is smaller than the contribution of ΣDDE, and secondly, uptake via diet is more important than via inhalation even for ΣDDT.

3.4. Hypothetical post-ban situation from 2020

A hypothetical situation in which DDT use in IRS would be terminated was modeled in order to predict the evolution of the total DDT concentration of future generations. Fig. 3 illustrates the initial concentrations in breast milk of 20-year-old primiparous mothers under the assumption that IRS with DDT was abandoned in 2020. Swedish levels (total DDT below 0.15 μg/g_{lip}) were reached after more than 80 years (Norén and Meironyté, 2000).

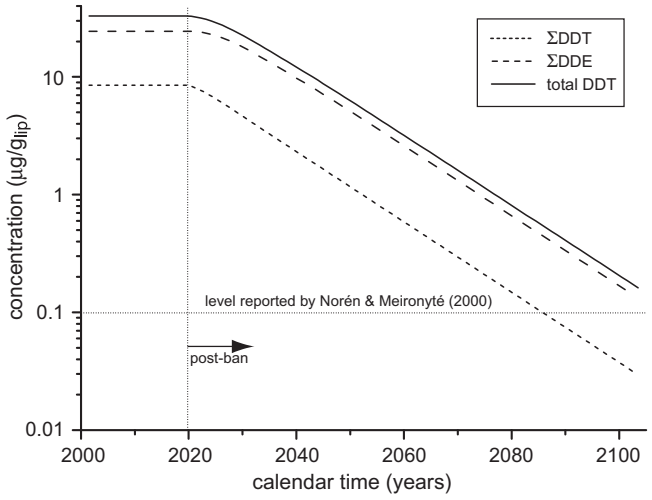

Fig. 3. Model prediction of cross-sectional trend data of ΣDDT, ΣDDE, and total DDT in 20-year-old primiparous women in a hypothetical post-ban scenario after 2020.

4. Discussion

We used a one-compartment PK model to predict the lipid-normalized total DDT (= ΣDDT and ΣDDE) concentrations in mothers and in their children living in IRS-treated areas in South Africa. This approach yields total DDT concentrations in women and in their children that agree within a factor of less than 3.3 and less than 4.3 with the biomonitoring data reported by Bouwman et al. (1990, 1991, 1992) and Bouwman and Schutte (1993), respectively. The factor of 4.3 is due to siblings of two families who had much higher levels compared to the other children. Different exposure level and/or pharmacokinetic elimination pattern might have caused this variability in children (Bouwman and Schutte, 1993).

We identified first-born children to experience both the highest pre- and postnatal exposure compared to later-born children. Breastfeeding caused elevated concentrations in infants that are twice as much as the concentrations in adults. Additionally, the mean concentration of total DDT in primiparous mothers was found to be 36–45% higher than that of multiparous mothers (Fig. 2c). These findings agree with the outcomes of the biomonitoring studies by Bouwman et al. (1990, 2006) who also found that primiparous mothers have higher concentrations than multiparous mothers and considered first-born children as a possible high-risk group. Both the birth interval (three years) and the two years of breastfeeding (our base case) are realistic values for the rural population in South Africa (Bouwman et al., 1992, 2006; Bouwman and Schutte, 1993; Department of Health, 2007).

Infant exposure to TCDD was investigated by using differential elimination half-life of TCDD based on age-dependent liver volume, lipid volume, and fecal lipid excretion (Kreuzer et al., 1997; LaKind et al., 2000; Lorber and Phillips, 2002). In our investigation of infant exposure to total DDT, this approach also yields a better agreement with the biomonitoring data in infants and children than using constant elimination half-lives. The overall intrinsic half-life of ΣDDT and ΣDDE increased from 0.2 to 0.6 years and from 0.3 to 1.2 years, respectively, during the first two years after birth. In adults (>20 years old), the elimination half-lives correspond to those reported in Ritter et al. (2009). Due to the very short half-lives in infants and children (Fig. S6, SM) the maximum modeled concentrations in infants differ only by a factor of less than 2.

In addition, the total amount of total DDT transferred during breastfeeding depends on the duration of breastfeeding, parity, and mother's age at delivery (Table 1). Bouwman et al. (1990) calculated 559 mg of total DDT that was transferred to the first-born child during a breastfeeding period of 2 years. Our estimate is lower by a factor of 0.63. However, according to the model the concentration in the breast milk decreases over the course of breastfeeding (see Fig. 2a and c), which was not taken into consideration by Bouwman et al. (1990). Exceptionally high concentrations can be found in breast milk such as of a 21-year-old primiparous mother from KwaZulu-Natal, South Africa, whose total DDT (= ΣDDT and ΣDDE, ΣDDD was not considered) concentration was measured to be 117 $\mu g/g_{lip}$ (Bouwman et al., submitted for publication) after 381 days of breastfeeding. In this case, at least 2 g of total DDT was transferred from mother to child throughout the 381 days of breastfeeding that was not finished at the time of sampling. This high amount of DDT transferred during the postnatal phase together with the prenatal exposure indicates serious risk of long-lasting adverse health effects. Evidence for adverse health effects has been discussed elsewhere (Bouwman et al., 2006, 2011; Eskenazi et al., 2009; Longnecker et al., 2001).

According to our results, dietary uptake is the dominant exposure route for both ΣDDT and ΣDDE. Among the food items considered, chicken muscle and chicken fat were highly contaminated (Van Dyk et al., 2010; Barnhoorn et al., 2009). Further, a high variability in the *p,p′*-isomers of DDT and DDE concentrations differing by four orders of magnitude were observed, probably caused by uptake of contaminated dust and soil particles with their feed (Van Dyk et al., 2010). This variability in chicken levels might also be caused by different age, sex, husbandry conditions, and import from non-sprayed areas. Since we identified the concentration in chicken fat as a highly influential model input parameter that also exhibits the highest actual variability (Fig. S4, SM), we chose this parameter for estimating the variability in the concentrations in the human body (Fig. 1).

For inhalation exposure, we used a constant indoor air concentration since total DDT was detected in indoor air long after its application (Bouwman et al., 2009; Singh et al., 1992; Van Dyk et al., 2010). In our calculations, the contribution of inhalation to the overall uptake of total DDT is small (2–10%). Ritter et al. (2011a), in contrast, estimated that inhalation contributes 70% to the overall uptake of total DDT for adults in regions with IRS. This discrepancy originates from the different concentrations used for the dietary uptake: Ritter et al. (2011a), in their compilation of data before 2009, found typical concentrations in various food groups on the order of 100 ng/g_{lip}, while the chicken fat concentrations, according to Van Dyk et al. (2010) and Barnhoorn et al. (2009), are on the order of 10^4 ng/g_{lip}. Further, the influence of the constant indoor concentration chosen on the model results is low (see Sensitivity analysis, SM).

If DDT were ever completely phased out, the exposure to total DDT via diet would exponentially decrease as it has done in developed countries in the last 40 years (Ritter et al., 2009). The cross-sectional trend concentration profile displayed in Fig. 3 is governed by the slower one of two processes, namely intrinsic elimination from the body and decrease in exposure (Ritter et al., 2011b). With our assumption of an environmental half-life of 10 years, the decrease in exposure is slower than intrinsic elimination (half-lives of 2.2 and 6.2 years for ΣDDT and ΣDDE, respectively). The model results suggest that it would take more than 80 years until the total DDT concentration of women living in formerly IRS-treated regions are in the similar range as those of today's women (below 0.15 $\mu g/g_{lip}$) in Sweden (Norén and Meironyté, 2000).

5. Conclusion

The finding that diet contributes significantly to the DDT body burden indicates that exposure reduction efforts should target this

uptake route. Domesticated animals kept near the homestead are a plausible DDT source because they are kept in the same vicinity where DDT is applied. It seems that chicken (and possibly other domesticated food animals such as pigs and goats where they occur) that reside on or near homestead premises act as a major vector of DDT to humans. A better understanding of the Total Homestead Environment (THE) as advanced by Van Dyk et al. (2010), and modeled here, may therefore support the design of exposure reduction strategies leading to reduced impacts on human and environmental health. Finally, it is of high importance to not only continue the regular biomonitoring of DDT in breast milk, but also to focus on determining actual health effects from DDT, especially in infants and children.

Appendix A. Supplementary material

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.envpol.2012.04.032.

References

Alcock, R.E., Sweetman, A.J., Juan, C.-Y., Jones, K.C., 2000. A generic model of human lifetime exposure to persistent organic contaminants: development and application to PCB-101. Environmental Pollution 110, 253–265.

Aneck-Hahn, N.H., Schulenburg, G.W., Bornman, M.S., Farias, P., de Jager, C., 2007. Impaired semen quality associated with environmental DDT exposure in young men living in a malaria area in the Limpopo Province, South Africa. Journal of Androlgy 28, 423–434.

ATSDR (Agency for Toxic Substances and Disease Registry), 2002. Toxicological Profile for DDT, DDE, and DDD. Available at: http://www.atsdr.cdc.gov/toxprofiles/tp.asp?id=81&tid=20 (accessed 06.11.11.).

Barnhoorn, I.E.J., Bornman, M.S., van Rensburg, C.J., Bouwman, H., 2009. DDT residues in water, sediment, domestic and indigenous biota from a currently DDT-sprayed area. Chemosphere 77, 1236–1241.

Baselt, R.C., Cravey, R.H., 1989. Disposition of Toxic Drugs and Chemicals in Man, third ed. Year Book Medical Publishers Inc., USA.

Bornman, R., de Jager, C., Worku, Z., Farias, P., Reif, S., 2010. DDT and urogenital malformations in newborn boys in a malarial area. British Journal of Urology International 106, 405–410.

Bouwman, H., Kylin, H., 2009. Malaria control insecticide residues in breast milk: the need to consider infant health risks. Environmental Health Perspectives 117, 1477–1780.

Bouwman, H., Schutte, C.H.J., 1993. Effect of sibship on DDT residue levels in human serum from a malaria endemic area in Northern KwaZulu. Bulletin of Environmental Contamination and Toxicology 50, 300–307.

Bouwman, H., Reinecke, A.J., Cooppan, R.M., Becher, P.J., 1990. Factors affecting levels of DDT and metabolites in human breast milk from KwaZulu. Journal of Toxicology and Environmental Health 31, 91–115.

Bouwman, H., Cooppan, R.M., Becher, P.J., Ngxongo, S., 1991. Malaria control and levels of DDT in serum of two populations in KwaZulu. Journal of Toxicology and Environmental Health 33, 141–155.

Bouwman, H., Becker, P.J., Cooppan, R.M., Reinecke, A.J., 1992. Transfer of DDT used in malaria control to infants via breast milk. Bulletin of the World Health Organization 70, 241–250.

Bouwman, H., Sereda, B., Meinhardt, H.M., 2006. Simultaneous presence of DDT and pyrethroid residues in human breast milk from a malaria endemic area in South Africa. Environmental Pollution 144, 902–917.

Bouwman, H., Bornman, R., van Dyk, C., Barnhoorn, I., Kylin, H., 2009. Dynamics and Risks of DDT Applied Indoors for Malaria Control [Abstract]. Available at: http://www.certh.gr/dat/6C584BD8/file.pdf (accessed 19.12.11.).

Bouwman, H., van den Berg, H., Kylin, H., 2011. DDT and malaria prevention: addressing the paradox. Environmental Health Perspectives 119, 744–747.

Bouwman, H., Kylin, H., Sereda, B., Bornman, R. High levels of organochlorines in breast milk: intake, risk, lactation duration, and involvement of gender. Environmental Pollution, submitted for publication.

Bouwman, H., 1990. Malaria vector control and occurrence, levels and dynamics of DDT in breast milk in certain rural areas of KwaZulu. PhD thesis. Potchefstroom University for Christian Higher Education (now, North-West University). Unpublished.

Da Costa, T.H.M., Haisma, H., Wells, J.C.K., Mander, A.P., Whitehead, R.G., Bluck, L.J.C., 2010. How much human milk do infants consume? Data from 12 countries using standardized stable isotope methodology. The Journal of Nutrition 140, 2227–2232.

Darnerud, P.O., Lignell, S., Glynn, A., Aune, M., Törnkvist, A., Stridsberg, M., 2010. POP levels in breast milk and maternal serum and thyroid hormone levels in mother–child pairs from Uppsala, Sweden. Environment International 36, 180–187.

Delport, R., Bornman, R., MacIntyre, U.E., Oosthuizen, N.M., Becker, P.J., Aneck-Hahn, N.H., de Jager, C., 2011. Changes in retinol-binding protein concentrations and thyroid homeostasis with nonoccupational exposure to DDT. Environmental Health Perspectives 119, 647–651.

Department of Health, Medical Research Council, 2007. South Africa Demographic and Health Survey 2003. Department of Health, Pretoria. Available at: http://www.mrc.ac.za/bod/sadhs.htm (accessed 16.12.11.).

Eskenazi, B., Chevrier, J., Goldman Rosas, L., Anderson, H.A., Bornman, M.S., Bouwman, H., Chen, A., Cohn, B.A., de Jager, C., Henshel, D.S., Leipzig, F., Leipzig, J.S., Lorenz, E.C., Snedeker, S.M., Stapleton, D., 2009. The pine river statement: human health consequences of DDT use. Environmental Health Perspectives 117, 1359–1367.

ICRP International Commission on Radiological Protection, 1975. Report of the Task Group on Reference Man No 23. Pergamon Press, Oxford, Great Britain.

IOM (Institute of Medicine), 1996. WIC Nutrition Risk Criteria: a Scientific Assessment. National Academy Press, Washington, D.C., USA.

Kirman, C.R., Aylward, L.L., Hays, S.M., Krishnan, K., Nong, A., 2011. Biomonitoring equivalents for DDT/DDE. Regulatory Toxicology and Pharmacology 60, 172–180.

Kreuzer, P.E., Csanády, Gy.A., Baur, C., Kessler, W., Päpke, O., Greim, H., Filser, J.G., 1997. 2,3,7,8-Tetrachlorodibenzo-*p*-dioxin (TCDD) and congeners in infants. A toxicokinetic model of human lifetime body burden by TCDD with special emphasis on its uptake by nutrition. Archives of Toxicology 71, 383–400.

LaKind, J.S., Berlin, C.M., Park, C.N., Naiman, D.Q., Gudka, N.J., 2000. Methodology for characterizing distributions of incremental body burdens of 2,3,7,8-TCDD and DDE from breast milk in North American nursing infants. Journal of Toxicology and Environmental Health Part A 59, 605–639.

Longnecker, M.P., Klebanoff, M.A., Zhou, H., Brock, J.W., 2001. Association between maternal serum concentration of the DDT metabolite DDE and preterm and small-for-gestational-age babies at birth. Lancet 358, 110–114.

Lorber, M., Phillips, L., 2002. Infant exposure to dioxin-like compounds in breast milk. Environmental Health Perspectives 110, A325–A332.

Morgan, D.P., Roan, C.C., 1971. Absorption, storage, and metabolic conversion of ingested DDT and DDT metabolites in man. Archives of Environmental Health 22, 301–315.

Nel, J.H., Steyn, N.P., 2002. Report on South African Food Consumption Studies Undertaken Amongst Different Population Groups (1983–2000): Average Uptakes of Foods Most Commonly Consumed. Pretoria, South Africa. Available at: http://www.mrc.ac.za/chronic/foodstudies.htm (accessed 13.11.11.).

Norén, K., Meironyté, D., 2000. Certain organochlorine and organobromine contaminants in Swedish human milk in perspective of past 20–30 years. Chemosphere 40, 1111–1123.

Quinn, C.L., Wania, F., Czub, G., Breivik, K., 2011. Investigating intergenerational differences in human PCB exposure due to variable emissions and reproductive behaviors. Environmental Health Perspectives 119, 641–646.

Ritter, R., Scheringer, M., MacLeod, M., Schenker, U., Hungerbühler, K., 2009. A multi-individual pharmacokinetic model framework for interpreting time trends of persistent chemicals in human populations: application to a postban situation. Environmental Health Perspectives 117, 1280–1286.

Ritter, R., Scheringer, M., MacLeod, M., Hungerbühler, K., 2011a. Assessment of nonoccupational exposure to DDT in the tropics and the north: relevance of uptake via inhalation from indoor residual spraying. Environmental Health Perspectives 119, 707–712.

Ritter, R., Scheringer, M., MacLeod, M., Moeckel, C., Jones, K.C., Hungerbühler, K., 2011b. Intrinsic human elimination half-lives of polychlorinated biphenyls derived from the temporal evolution of cross-sectional biomonitoring data from United Kingdom. Environmental Health Perspectives 119, 225–231.

Rogan, W.J., Chen, A., 2005. Health risks and benefits of bis(4-chlorophenyl)-1,1,1-trichloroethane (DDT). Lancet 366, 763–773.

Rose, D., Bourne, L., Bradshaw, D., 2002. Food and Nutrient Availability in South African Households – Development of a Nationally Representative Database. Medical Research Council, South Africa. Available at: http://www.mrc.ac.za/healthdevelop/foodnutrientavail.pdf (accessed 13.11.11.).

Sapbamrer, R., Prapamontol, T., Prakobvitayakit, O., Vaneesorn, Y., Mangklabruks, A., Hock, B., 2008. Placental transfer of DDT in mother-infant pairs from Northern Thailand. Journal of Environmental Science and Health Part B 6, 484–489.

Singh, P.P., Udeaan, A.S., Battu, S., 1992. DDT and HCH residues in indoor air arising from their use in malaria control programmes. The Science of the Total Environment 116, 83–92.

Solomon, G.M., Weiss, P.M., 2002. Chemical contaminants in breast milk: time trends and regional variability. Environmental Health Perspectives 110, A339–A347.

U.S. EPA, 1997. Exposure Factors Handbook (1997 Final Report). U.S. Environmental Protection Agency, Washington, DC. EPA/600/P-95/002F a-c. Available at: http://cfpub.epa.gov/si/si_public_record_report.cfm?dirEntryId=12464 (accessed 13.11.11.).

UNEP, 2009. Stockholm Convention on Persistent Organic Pollutants. Available at: http://www.pops.int (accessed 10.12.11.).

Van Dyk, J.C., Bouwman, H., Barnhoorn, I.E.J., Bornman, M.S., 2010. DDT contamination from indoor residual spraying for malaria control. Science of the Total Environment 408, 2745–2752.

Verner, M.-A., Ayotte, P., Muckle, G., Charbonneau, M., Haddad, S., 2009. A physiologically based pharmacokinetic model for the assessment of infant exposure to persistent organic pollutants in epidemiologic studies. Environmental Health Perspectives 117, 481–487.

Waliszewski, S.M., Aguirre, A.A., Infanzon, R.M., Siliceo, S.J., 2000. Carry-over of persistent organochlorine pesticides through placenta to fetus. Salud Publica De Mexico 42, 384–390.

Waliszewski, S.M., Aguirre, A.A., Infanzon, R.M., Siliceo, S.J., 2001. Organochlorine pesticide levels in maternal adipose tissue, maternal blood serum, umbilical blood serum, and milk from inhabitants of Veracruz, Mexico. Archives of Environmental Contamination and Toxicology 40, 432–438.

WHO, 2011. DDT in Indoor Residual Spraying: Human Health Aspects. Environmental Health Criteria 241. Available at: http://www.who.int/ipcs/publications/ehc/ehc241.pdf (accessed 06.11.11.).

Williamson, C.S., 2006. Nutrition in pregnancy. Nutrition Bulletin 31, 28–59.