Breastfeeding has been the norm throughout primate evolution. Breastfeeding stimulates both the mother and the infant physiologically. Maternal effects include the release of oxytocin, which is essential for milk ejection but also induces a lower threshold to pain and stimulates positive feelings, hence its nick name the ‘love’ hormone. The skin-to-skin contact and the act of breastfeeding also modulates infant temperament, heart rate, temperature and acid–base balance. In addition, there are a myriad of positive effects on both the mother and infant that can in many cases be attributed to the unique species specific composition of human milk (HM) (1,2).

The short-term benefits of HM for the infant are extensive, where meta-analyses show a lower incidence of infection including necrotising enterocolitis (NEC), gastrointestinal tract infections and a reduction in infant mortality with increased doses of HM (3). Further, the lifetime programming effects of HM include a lower risk of obesity and diabetes later in life (4,5), which are precursors to metabolic disease as well as better neurological development and cognitive function compared to infants that were formula-fed (6,7). Indeed mothers also reap significant health benefits, particularly if they breastfeed their infants for more than 12 months, with a significant reduction in risk of cardiovascular disease, hypertension, diabetes and cancer (breast and ovarian) compared to those who have never breastfed (8-10).

The benefits of HM to infant are still therefore undeniable. However, the mechanisms associated with the transfer and/or production of nutritional and protective components in milk also act as pathways for the passage of environmental contaminants into the milk. Indeed persistent organic pollutants (POPs) and heavy metals have been detected in HM. The question is: does this pose a risk to the infant? Further, is the monitoring of these contaminants worldwide sufficient to safeguard not only the infants, but also everyone that lives in the same environment?

**Persistent Organic Pollutants**

POPs, such as pesticides, polychlorinated biphenyls (PCBs) and polychlorinated dibenzo-p-dioxins (dioxins), are synthetic chemicals that are ubiquitously present in the environment (11,12). These pollutants are usually by-products from industrial processes or agrichemicals used for pest and weed control on farms. As many of these xenobiotics have lipophilic properties and are resistant to environmental degradation, they can be transported over a long distances via the atmosphere and water. Hence, these chemicals are then absorbed into mammals via inhalation, ingestion and dermal contact, followed by bioaccumulation in organs with higher lipid contents, such as the liver and breast, as they are not easily metabolised in the body (12).

Pesticides, such as organochlorine pesticides (OCPs), organophosphate pesticides (OPPs) and carbamates, are used to control pests in agriculture and in homes. Besides their primary action as pesticides, many of these OCPs and OPPs can interfere with the functions of normal endocrine systems by mimicking, blocking, modulating or altering the synthesis, metabolism or transport of hormones (12,13). Long term pesticide exposure has also been associated with neuropsychiatric sequelae (14), chronic diseases such as Parkinson’s disease (15), cancer (16) and asthma (17), as well as congenital disorders (18,19).

While many of these pesticide groups, such as OCPs and OPPs, have been banned since the 1980s/90s due to their persistence and long half-lives (over seven years), many of these pesticides are still detected in the environment and in biofluids. A variety of pesticides, such as \( p,p' \)-dichlorodiphenyldichloroethylene (\( p,p' \)-DDE), \( p,p' \)-dichlorodiphenyldichloroethane (\( p,p' \)-DDT) and hexachlorocyclohexane (HCH), have been detected in various biofluids of the inhabitants of different countries. \( p,p' \)-DDE, which is a metabolite of \( p,p' \)-DDT, is one of the most commonly detected OCPs in humans as DDT was widely used around the world in agriculture and domestic households in the 1940s/50s. Since the 1980s, many of these banned pesticides have been replaced by more ‘human-friendly’ pesticides, such as pyrethroids, which can be easily metabolised by mammals and have shorter half-lives of 2.5 to 12 hours in blood plasma (20).

As humans are not only exposed to a single chemical, but to a multitude of different chemicals simultaneously, it is important to continuously measure the level of environmental contaminants, both banned and legalised, to ensure that the total environmental pesticide exposure is within the safe threshold limits.

**Impact of Pesticide Exposure on Infant Health**

The fetus and infants are recognised as being more susceptible to the harmful effects of pesticides due to their small size and rapid growth as well as their immature immune and metabolic systems (21). Many of the studies designed to investigate the adverse effects of pesticides on infants have focused on maternal exposure to pesticides by measuring pesticide levels in maternal biofluids, such as blood (22,23), cord blood (24) and HM (25,26). Associations are then drawn between these measures and prenatal, infant and child development measures such as
Table 1. Concentrations of DDTs (ng/g fat) in human milk from various countries. Adapted from (25).

<table>
<thead>
<tr>
<th>Country/region</th>
<th>Year of sampling</th>
<th>Mothers (number)</th>
<th>Human milk samples</th>
<th>Fat content (g/L)</th>
<th>DDTs (ng/g fat)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Asia</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>China</td>
<td>2006/07</td>
<td>60</td>
<td>60</td>
<td>31</td>
<td>583&lt;sup&gt;a&lt;/sup&gt;</td>
<td>(52)</td>
</tr>
<tr>
<td>India</td>
<td>2011</td>
<td>53</td>
<td>53</td>
<td>32</td>
<td>1914&lt;sup&gt;b&lt;/sup&gt;</td>
<td>(47)</td>
</tr>
<tr>
<td>Taiwan</td>
<td>2000/01</td>
<td>36</td>
<td>36</td>
<td>31</td>
<td>333&lt;sup&gt;c&lt;/sup&gt;</td>
<td>(53)</td>
</tr>
<tr>
<td>Korea</td>
<td>2008</td>
<td>&gt;50</td>
<td>50</td>
<td>22</td>
<td>225&lt;sup&gt;e&lt;/sup&gt;</td>
<td>(54)</td>
</tr>
<tr>
<td>Japan</td>
<td>2008/09</td>
<td>90</td>
<td>9#</td>
<td>32</td>
<td>119&lt;sup&gt;e&lt;/sup&gt;</td>
<td>(55)</td>
</tr>
<tr>
<td>Malaysia</td>
<td>2003</td>
<td>17</td>
<td>17</td>
<td>17</td>
<td>1600&lt;sup&gt;i&lt;/sup&gt;</td>
<td>(37)</td>
</tr>
<tr>
<td>Philippine</td>
<td>2004</td>
<td>33</td>
<td>33</td>
<td>22</td>
<td>170&lt;sup&gt;b&lt;/sup&gt;</td>
<td>(56)</td>
</tr>
<tr>
<td>Turkey</td>
<td>2009</td>
<td>47</td>
<td>47</td>
<td>36</td>
<td>338&lt;sup&gt;e&lt;/sup&gt;</td>
<td>(57)</td>
</tr>
<tr>
<td>Iran</td>
<td>2006</td>
<td>10</td>
<td>10</td>
<td>15</td>
<td>3560&lt;sup&gt;e&lt;/sup&gt;</td>
<td>(36)</td>
</tr>
<tr>
<td><strong>Australian and New Zealand</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>New Zealand</td>
<td>2007/2010</td>
<td>39</td>
<td>37</td>
<td>39</td>
<td>385&lt;sup&gt;j&lt;/sup&gt;</td>
<td>(58)</td>
</tr>
<tr>
<td>Australia/WA</td>
<td>2013/15</td>
<td>40</td>
<td>40</td>
<td>33</td>
<td>63&lt;sup&gt;k&lt;/sup&gt;</td>
<td>(25)</td>
</tr>
<tr>
<td><strong>Europe</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Poland</td>
<td>2002/05</td>
<td>28</td>
<td>28</td>
<td>14</td>
<td>1621&lt;sup&gt;b&lt;/sup&gt;</td>
<td>(59)</td>
</tr>
<tr>
<td>Slovakia</td>
<td>2003</td>
<td>12</td>
<td>12</td>
<td>27</td>
<td>665&lt;sup&gt;i&lt;/sup&gt;</td>
<td>(60)</td>
</tr>
<tr>
<td>Norway</td>
<td>2002/06</td>
<td>377</td>
<td>377</td>
<td>36</td>
<td>53&lt;sup&gt;j&lt;/sup&gt;</td>
<td>(61)</td>
</tr>
<tr>
<td>Latvia</td>
<td>2002/04</td>
<td>15</td>
<td>15</td>
<td>na</td>
<td>267&lt;sup&gt;e&lt;/sup&gt;</td>
<td>(62)</td>
</tr>
<tr>
<td>Denmark</td>
<td>1997/01</td>
<td>43</td>
<td>43</td>
<td>na</td>
<td>82&lt;sup&gt;e&lt;/sup&gt;</td>
<td>(63)</td>
</tr>
<tr>
<td>Belgium</td>
<td>2009/10</td>
<td>84</td>
<td>84</td>
<td>44&lt;sup&gt;*&lt;/sup&gt;</td>
<td>60&lt;sup&gt;i&lt;/sup&gt;</td>
<td>(64)</td>
</tr>
<tr>
<td>Germany</td>
<td>2007/08</td>
<td>516</td>
<td>516</td>
<td>36</td>
<td>125&lt;sup&gt;i&lt;/sup&gt;</td>
<td>(65)</td>
</tr>
<tr>
<td>Croatia/Zagreb</td>
<td>2009/10</td>
<td>20</td>
<td>29</td>
<td>na</td>
<td>278&lt;sup&gt;k&lt;/sup&gt;</td>
<td>(66)</td>
</tr>
<tr>
<td>UK</td>
<td>2001/03</td>
<td>54</td>
<td>54</td>
<td>na</td>
<td>157&lt;sup&gt;i&lt;/sup&gt;</td>
<td>(67)</td>
</tr>
<tr>
<td><strong>North and South Americas</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>USA</td>
<td>2004</td>
<td>38</td>
<td>38</td>
<td>22</td>
<td>65&lt;sup&gt;j&lt;/sup&gt;</td>
<td>(68)</td>
</tr>
<tr>
<td>Brazil</td>
<td>2001/02</td>
<td>69</td>
<td>69</td>
<td>na</td>
<td>493&lt;sup&gt;b&lt;/sup&gt;</td>
<td>(69)</td>
</tr>
<tr>
<td><strong>Africa</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>South Africa</td>
<td>2001</td>
<td>28</td>
<td>28</td>
<td>na</td>
<td>6320&lt;sup&gt;b&lt;/sup&gt;</td>
<td>(70)</td>
</tr>
<tr>
<td>Ethiopia</td>
<td>2010</td>
<td>39</td>
<td>29</td>
<td>na</td>
<td>14460&lt;sup&gt;b&lt;/sup&gt;</td>
<td>(71)</td>
</tr>
</tbody>
</table>

na no data available  
* Values represented as median value  
# Pooled sample  
<sup>a</sup> Sum of o,p'-DDE + p,p'-DDE + p,p'-DDD + p,p'-DDT  
<sup>b</sup> Sum of p,p'-DDE + p,p'-DDD + p,p'-DDT  
<sup>c</sup> Sum of p,p'-DDE + p,p'-DDD + o,p'-DDT + p,p'-DDT  
<sup>d</sup> Sum of p,p'-DDD + p,p'-DDT  
<sup>e</sup> Sum of o,p'-DDE + p,p'-DDE + o,p'-DDD + p,p'-DDD + o,p'-DDT + p,p'-DDT  
<sup>f</sup> Sum of o,p'-DDE + p,p'-DDE + p,p'-DDD + o,p'-DDT + p,p'-DDT  
<sup>g</sup> p,p'-DDE only  
<sup>h</sup> Sum p,p'-DDE + o,p'-DDT + p,p'-DDT
growth, immune and metabolic status. Studies have shown an association between higher concentrations of the insecticide chlorpyrifos in maternal prenatal plasma and smaller infant birth weight and length (23). Similarly, smaller infant birth weight and head circumference have been observed in mothers with high prenatal urinary DDE concentrations (27). Further, recent studies have associated high exposure of OPPs with attention deficit/hyperactivity disorder in five-year-olds (28), and poor intellectual development and cognitive performance in seven-year-olds (29). Sex differences have also been identified where male infants were more susceptible to OPP exposure with smaller head circumference, delayed adaptive skills and social and motor development skills respectively (30). It is still difficult however to decide whether the associations are due to prenatal or postnatal pesticide exposure, therefore, one should exercise caution in the interpretation of these studies.

While many studies have used maternal pesticide levels and infant anthropometrical data at birth as a proxy measure of in utero development, our recent epidemiological longitudinal and cross-sectional studies have shown no significant associations between \( p,p' \)-DDT concentrations in milk from mothers in Western Australia and infant growth outcomes such as weight, length, head circumference and percentage fat mass (estimated using bioimpedance spectroscopy and ultrasound skinfolds) at 2, 5, 9 and 12 months postpartum (25). Furthermore, the concentration of \( p,p' \)-DDE significantly decreased by 68% from 70.9 ± 70.6 ng/g fat at 2 months to 22.4 ± 14.0 ng/g fat at 12 months (31), indicating that maternal bioburden is reduced via breastfeeding. Interestingly, expected relationships between maternal age (increased HM pesticide levels) and parity (reduced HM pesticide levels) are not always confirmed in the literature, however this is likely due to differences in study design and analysis. (22,25,27). One is tempted however, to speculate that the reduction of maternal bioburden during lactation could potentially contribute to the reported reduced incidence of breast and ovarian cancer in women that have breastfed (32-34). Whilst the Western Australia data is encouraging, the question is whether the dramatic reductions in POPs in HM are paralleled globally?

Temporal Trends and Worldwide Comparisons of Pesticides in HM

The ratio of \( p,p' \)-DDE to \( p,p' \)-DDT concentration indicates exposure history where a high DDE/DDT ratio (>5) represents historical exposure and a low DDE/DDT ratio (<5) suggests continuous exposure (35). This provides valuable insight into the maternal environment, lifestyle and dietary habits but also allows early intervention to minimize infant (and maternal) exposure to these pesticides if present at high concentrations. HM pesticide concentrations vary widely between countries (Table 1) and these are largely dependent on the extent of pesticide use and the timing of legal bans. Higher total DDT concentrations (sum of DDTs and its metabolites, DDE and DDD) are typically observed in malaria-prone countries such as Iran (36) and Malaysia (37), where DDTs were widely used to combat mosquitoes and were only recently banned (1990s to 2000s). Limited use of DDT is also still allowed indoors in malaria endemic countries, such as South Africa and India (38). We have shown a declining trend in the total DDTs in HM from women in Western Australia since the 1970s (Fig. 1) (39-43). This is in agreement with Muller et al., where an annual decrease of approximately 12–13% of DDTs was observed in earlier years (1960s to 1980s) slowing to around a 5% annual decrease since the 1990s (40). On a national level, the HM \( p,p' \)-DDE concentrations observed in WA are 2.4 to 7.5 times lower than corresponding \( p,p' \)-DDT concentrations in other states and territories such as South Australia, Victoria and New South Wales, and is reflective of the inconsistent timing of legislation for pesticide control prior to the 1990s. Since levels of pesticides are declining in HM, it stands to reason infant dose is also declining.

Infant Daily Dose of Pesticides Via HM

It is essential to monitor HM pesticide concentrations to ensure that the daily infant pesticide intake is within the tolerable limit of 0.5–10 µg/kg body weight/day (44-46) recommended by regulatory agencies (e.g. EPA, FAO, RIVM, WHO) to decrease the risk of impaired infant growth and development. Calculation of infant dose requires infant weight, concentration of the pesticide,
milk fat and the volume of milk consumed. Many studies have used estimated values of milk fat, infant milk intake and infant weight, to estimate daily intake (EDI) of the infant (36,47,48). In our recent cross sectional study we calculated daily intake (CDI) by using the average milk intake based on the infant age (49) and measuring milk fat (25). This was further improved by calculating the actual daily intake (ADI) which is based on the actual measurements of milk fat, 24 hour milk intake and infant weight in our longitudinal study (Fig. 2) (31). The EDI significantly overestimates the overall daily intake over the first 12 months postpartum compared to both CDI and ADI by 53% and 44%. While Du et al. (31) observed a significant decrease in pesticide intake by the infant throughout the 12 months, they also observed that the ADI from several mothers exceeded the tolerable limit (>0.5 µg/kg body weight/day) in the earlier months of lactation (two and five months). This could be considered concerning, however this is counterbalanced by the fact that infant exposure to pesticides in HM via breastfeeding is a relatively short period as compared to a lifetime living in the same environment. Overall, the ADI we calculated was approximately three times lower than the tolerable limit. Thus, the benefits of HM, such as the immunological and nutritional benefits, far outweigh the potential negative effects that are yet to be adequately demonstrated. Therefore breastfeeding should continue to be encouraged for up to two years and beyond, as recommended by WHO (50).

Conclusions and Future Directions

The maternal environment, diet and body composition before and during pregnancy play a major role in fetal programming and the future health of the infant (51). As part of a continuum, lactation represents a period of further infant programming for optimum health outcomes. Whilst the presence of pesticides in HM is of concern, the use of HM can provide a non-invasive avenue to monitor pesticide exposure and to measure infant daily intake. Further, while new data does not show detrimental effects of POPs in HM on early infant growth, longitudinal studies should be conducted for longer periods (beyond three years of life) to elucidate relationships with infant growth and developmental outcomes, including cognitive function. As many countries now source commodities, such as food produce, from various countries, it is essential that global restrictions are implemented and adhered to in order to reduce population contaminant exposure via diet.

References
44. FAO/WHO (2000)