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COMPARATIVE EVALUATION OF XENOBIOTICS IN HUMAN AND DIETARY MILK: PERSISTENT ORGANIC POLLUTANTS AND MYCOTOXINS

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Abstract

Publications produced over the past 20 years regarding the concentration of xenobiotics in human and dietary milk were evaluated, focusing primarily on persistent organic pollutants (e.g. polychlorinated biphenyls, flame retardants), pesticides (e.g organochlorine) and mycotoxins. In general, countries of low industrialization rate present low levels of dietary milk contamination with dioxins compared to those with high rate of industrialization. According to published data, the most common persistent organic pollutants detected in breast and dietary milk are dichlorodiphenyltrichloroethane compounds, hexachlorocyclohexane, and hexachlorobenzene. Even though the potential risks of persistent organic pollutants in human milk have been acknowledged, the beneficial effect of breastfeeding as the optimal food source for newborn babies should not be disregarded. Especially when sharing information with the general public, it should be made clear that the presence of dioxins and persistent organic pollutants in human milk is not an indication for avoiding breastfeeding. The implications of xenobiotics in human and dietary milk is a matter of growing importance and warrants future work given its important health effects.

Key words: Health effects, dichlorodiphenyltrichloroethane, hexachlorocyclohexane, hexachlorobenzene, aflatoxins, silage, haylage.

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INTRODUCTION

Dietary milk is considered to be one of the most important products in the human diet. Its consumption displays a variety of advantages for the potential consumers of all ages. Milk not only is a valuable source of calcium, but it also provides the human body with vitamin D (95), B vitamins (50), carotenoids and retinoid (51). According to statistics from the Food and Agriculture Organization of the United Nations, the world production of cow milk for the year 2008 reached over 578 million tones, while USA, India, China, Russian Federation, Germany, Brazil, France, New Zealand, UK and Polland stood among the top ten cow milk producing countries (14).

Human breast milk is a special classification of milk and the only source of nutrients for newborns and infants. Breast milk provides all the vitamins, essential minerals and trace elements necessary for the proper development of the newborn (1). Apart from nutrients, human milk contains bioactive components and facilitates functional changes, protects infants from pathogenic infections and it can help reduce the risk of autoimmune disease development in the long run (19).

One of the most important factors affecting the quality of milk in terms of product safety is the presence of xenobiotics. Persistent organic pollutants (i.e. polychlorinated biphenyls, flame retardants), pesticides (i.e. organochlorine) and mycotoxins are some of the most commonly detected xenobiotics in both human and dietary milk (29, 31). Due to globalization, milk products with xenobiotics may travel all around the word. Because of the potential impact of the build-up of these xenobiotics in milk and its products in human health, consumers ought to be alert and well informed of the risks and possible adverse health effects. Moreover, diet, smoking habits, and environmental problems may affect the quantity of specific xenobiotics in human breast milk. In this paper, we review the available published evidence regarding the concentration of specific xenobiotics in human and dietary milk. Our review covers mostly papers and reports published during the past 20 years.

PERSISTENT ORGANIC POLLUTANTS IN HUMAN AND DIETARY MILK

Due to their fat content, both human breast and dietary milk could be polluted by many non-pharmaceutical xenobiotics characterized by lipophilic properties (6). Most of these xenobiotics are persistent, present a bioaccumulation activity and are toxic to humans. The category of persistanent organing pollutants (POPs) includes several xenobiotics such as organoclorine pesticides (OCPs),

polychlorinated biphenyls (PCBs), dioxins and furans and polybrominated diphenyl ethers (56). Substances included in POPs are either byproducts of incinerated waste, or may be manufactured for a specific purpose such as for flame retardants and pesticides (73).

According to the European Regulation EC No 396/2005 and the European Pesticide database for milk maximum residue limits have been set for as many as 332 active ingredients. Out of the reported maximum residue limits for pesticides, 14 (4.21%) are between 0.001 – 0.006, 288 (86.74%) are between 0.01 – 0.028, 28 (8.43%) are between 0.1 – 0.5, and 2 (0.62%) are above 1 mg/kg. The maximum residue limits for PCBs and dioxins in milk set by EC 1881/2006 are 3 and 6 pg/g of fat respectively.

Human breast milk, characterized by relatively high lipid content, may be used as an indicator of human long term exposure to POPs and provides us with valuable information concerning POPs body load. In monitoring studies, results are expressed as the amount of chemical per gram of lipids in human milk in order to overcome the problem of lipid variations in breast milk among different mothers (72). For the current review, the main challenges in comparing different monitoring programs for POPs in breast milk were: (i) different monitoring design i.e. studies designed for a localized problem, and (ii) different techniques for the collection of samples i.e. time of sampling, samples originating from areas with different levels of POPs pollution and samples from people with different dietary patterns (56).

According to published data, the OCPs most often detected in breast and dietary milk are dichlorodiphenyltrichloroethane compounds (DDTs), hexachlorocyclohexane (HCH) and hexachlorobenzene (HCB). Aldrin, dieldrin, chlordane, heptachlor have also been reported in monitoring studies, although not as often. OCPs are covered under the Stockholm Convention on persistent organic pollutants. The vast majority of results of human breast milk and dietary milk for DDTs, HCHs, PCBs and dioxins published from 1992 up to 2010 are provided below:

Dichlorodiphenyltrichloroethane compounds (DDTs): the reported levels of DDTs in developing countries present higher numbers compared to those in developed countries. Moreover, in developing countries, a higher exposure to DDTs is observed in urban areas rather than in rural areas, probably due to the ongoing usage of DDT for public health purposes (i.e. 10 000 ton/annum in India) (92). Countries encountered with malaria outbreaks present high levels of DDTs in breast milk (77). Despite the tendency to reduce DDTs detection limits worldwide, India constantly presents one of the highest levels of contamination. 1, I-bis[p-chlorophenyl]-2,2-dichloroethylene (p,p´-DDE) appears to be the major metabolite retained and detected in the body, and its increased concentration indicates chronic exposure to DDT (16). In some studies conducted in developing countries, the levels of DDT appear to be inversely related to the mother's age (69). In contrast, DDT levels in developed countries are linearly related to the age of the mother, and inversely related to the number of breastfed infants per mother (6)**.** The reported values in developing and developed countries during the last decade vary from 470 up to 2100 ng/g lipid wt, and from 170 up to 610 ng/g lipid wt, respectively (92). Interestingly, in developed countries the concentrations of DDT are often higher in mothers that were born in developing countries than in mothers born in developed countries.

p,p´-DDE appears to be the major metabolite of OCPs detected in dietary milk. Indeed, p,p´-DDE was detected in milk samples in Greece during 1992 [22 ng/g lipid wt (59)], as well as in milk samples in Germany during 1983 (7 ng/g lipid wt) and Spain during 1996 (5 ng/g lipid wt) (85). However, more recent studies in Italy (37) and Greece (96) did not detect DDTs in dietary milk samples. In developing countries, DDTs have been detected more often in higher concentrations, for instance 36 ng/g lipid wt in Indian milk samples and 24 ng/g lipid wt in Mexican milk samples (85). Moreover, recent evidence suggest differences in DDT/DDE values among different areas of developing countries which may be related to differences between past and current uses of DDT (40). Indeed, a more intensive use of DDT has been observed in areas where the milk is used for the production of cheese (40). Although a tendency for reduction is observed in DDTs concentrations in dietary milk, mostly due to limited usage, the decline of p,p´-DDE seems to be slower and, at times, does not reach statistical significance. This finding is probably due to DDT degradation and p,p´-DDE bioaccumulation (103).

Hexachlorocyclohexane (HCHs): HCH are actually consisted of eight isomers α-, β-, γ-, and –δ. The pesticide lindane contains more than 99% of γ- isomer. Usually the β- isomer is the most prevalent HCH in breast milk probably due to the fact that it is more persistent and prone to bioaccumulation (90). The detection of the α-isomer may be an indication of recent exposure to technical HCH (2009). The reported HCH levels in recent years present a decline both in the developing and the developed countries. Apart from a few exceptions, based on the listed bibliography, the reported levels of HCH in breast milk are lower compared to those of DDTs, but higher compared to other POPs. These differences possibly reflect variations in exposure sources and metabolic capacities (97). The levels of HCHs in milk are also linearly related to the mother's age. Moreover the grouping of women based on nationality during the monitoring may help in the case of HCHs and DDTs monitoring studies by reducing the standard deviations within the groups (79).

The most recent available milk sample data from Brazil suggest that HCHs are detected in only 1.1% of samples and at levels of 0.01 mg/kg, which suggests a decline from previous years probably due to strict regulations (11). In contrast, a number of studies from Mexico confirm no significant changes in the levels of detection from 1993 to 2001, and present β-HCH as the major metabolite detected (76, 103). A recent study in India confirmed a decline in the frequency and detection of HCHs, yet contaminated milk samples are still found probably due to fact that the use of HCHs is restricted but not banned (71).

Polychlorinated biphenyls (PCBs): PCBs are technical mixtures characterized by different levels of chlorination and can be used in a wide range of products including building materials, plasticizers, capacitors, and transformed hydraulic systems. PCBs use has recently been put under strict regulations, with dioxins and brominated flame retardants considered as the most potent chemicals (66). Some, but not all (58), reports conclude that the levels of PCBs tend to be lower in developing countries (most reported values are lower than 100 ng/g lipid wt)

compared with those of developed/industrialized countries (reported values ranged from 140 up to 550 ng/g lipid wt) (92). This is in line with the results from a recent study which showed that German mothers born abroad present lower concentrations of PCBs in their breast milk than that of mothers born in the country (6). A recent Danish market monitoring study reported 4.4 μg/kg lipid wt for Danish milk and 1.0 μg/Kg lipid wt for foreign milk which, in both cases, was lower than the Acceptable Daily Intake (31).

Overall, the levels of PCBs reported in European studies range from 0.01 ng/g lipid wt (Germany, Switzerland, Denmark, Netherlands) up to 50 ng/g lipid wt (Italy) (43). Within the same country, location (i.e., rural or urban) does not seem to significantly influence the levels of PCBs. In a recent study in Italy, PCBs were detected in dietary milk samples from two different areas without any statistically significant difference (47). Moreover, evidence shows that within the same country the mother's exposure to PCBs is usually similar regardless of the location, mainly due to low levels of accumulation and due to the fact that dietary intake – which constitutes more than 90% of the total PCB intake – is not altered significantly within a country (33, 93). Also the primiparous women seem to have higher concentrations of PCBs in their milk compared with multiparous women (79). With regard to changes across time, studies performed in Germany present a decline in PCBs concentration in breast milk probably due to the implementation of strict EU regulations concerning their usage, disposal and destruction (33).

Worldwide, there is variability in the reported PCB levels in breast milk which may be partly explained by differences in technical products, the extent of use and dietary habits (79). The compounds considered as primary indicators of biological PCB burdens were PCB nos. 28, 52, 101, 118, 138, 158, 180 (39). PCB 180 was found to be the major contributor to ΣPCB in milk samples from Brazil (43), while according to the European Food Safety Agency, PCB 138, 153 and 180 are the most common compounds in European milk samples that are used to estimate the total concentration of PCBs (28).

Dioxins: Dioxins are a group of chemicals characterized by high persistence in the environment. The most toxic compound is 2,3,7,8 tetrachlorobibenzo-p-dioxin, also known as TCDD. Dioxins are commonly formed under burning processes and during industrial processes. Usually they are detected as a mixture of several different dioxin compounds. In order to compare the results from different studies it is essential to take note of the details of the toxic equivalent factor (TEF) model that was applied in order to convert the analytical results into toxic equivalents (TEQ). Thus in recent studies the daily intake of dioxins expressed in pg/Kg/day is very important (33). In developing countries dumping sites of municipal wastes may be a significant emission source. In these countries, the majority of dioxins in milk originate from deposition in adipose tissue (86%) and a small fraction from dietary habits 14% (55). Thus only the next generation may reduce the exposure levels through food consumption (55). In studies with no specific pollution outbreaks, the levels of dioxins in breast milk between urban and rural areas do not present significant difference (33). The concentration of dioxins tends to be lower with an increased lactation period probably due to continuous excretion via breast milk (94)**.** Although the levels of dioxins in multiparous mother's breast milk are lower than those in primiparous mothers, no significant differences are observed in cases of continuous exposure (91). Overall, there seems to be a decline across time in the levels of dioxins in human breast milk which is in accordance with the reduction of dioxins levels in milk.

Despite the fact that most monitoring studies for dioxins are focused on human breast milk, a number of studies have also investigated dietary milk. The Belgian milk shows a reduction in the concentration of dioxins during the last decade, probably due to the measures taken in order to reduce the exposure (105). Moreover low industrialized countries such as Greece show low levels of milk contamination with dioxins compared with highly industrialized (75). As the contribution of main contaminant sources (municipal solid waste incinerators) has been eliminated, consumed food seems to be the most widespread source of dioxin milk pollution (20).

AFLATOXINS – MYCOTOXINS

Aflatoxins are a group of chemical substances produced as byproducts by certain species of fungi (mainly *Aspergillus flavus* and *Aspergillus parasiticus*). These naturally occurring mycotoxins are produced during fungi growth in feed grains, processed feed, and food products, while high moisture and high temperature promote growth. Aflatoxins can be highly toxic to livestock and are considered carcinogenic to both animal and human populations (8, 46, 38). Aflatoxins B1&B2 (produced by *Aspergillus flavus* and *Aspergillus parasiticus)* and aflatoxins G1&G2 (produced by *Aspergillus parasiticus),* are the most common types to be found in nature. Aflatoxin B1 is considered to be the most toxic and can be metabolized to aflatoxin M1 in people and animals, while aflatoxin B2 can be metabolized to M2 in milk. Once entering the human body (liver, intestine, bone marrow) they are converted to an epoxide by P450 cytochrome enzymes and react with nucleic acids, DNA and RNA, leading to depurination and inhibition in protein and DNA synthesis. DNA damage can be mutagenic and carcinogenic, with liver being the main target organ for aflatoxin toxicity (aflatoxicosis) (88, 24, 107, 32, 87). The International Agency for Research on Cancer (IARC) has classified the aflatoxin B1 as a group 1 carcinogen and M1 as a group 2B carcinogen (49)**.**

Aspergillus flavus and *Aspergillus parasiticus* are widespread in tropics and subtropics and are associated with a wide range of food products consumed worldwide (e.g. cereals, oilseeds, spices and tree nuts). Aflatoxin production is mainly observed after post harvest food spoilage (due to abnormal humidity and temperature), although plant tissue contamination during field growth can also occur (65)**.** Aflatoxins can pass through the food chain to humans; B1 found in animal feeds is metabolized to M1 and secreted into milk. Consumption of M1 contaminated milk is a public concern issue, especially since neonates and children experience an increased health risk (74). Aflatoxin M1 has been detected in raw milk in concentrations lower than 100ng/l in Europe (15, 5) and more than 1000ng/l in India and Equador (78), and in pasteurized Ultra High Temperature (UHT) milk (17, 71). B1 and M1 have also been identified in human breast milk samples, in concentrations varying from 95-4100 ng/l and 60-300 ng/l for B1 and M1 respectively (84, 36, 42).

Maximum residue levels have been established through-

out the world, in order to provide a legal basis to minimizing health risk during food marketing and consumption. However, these limits vary across countries. The European Commission Regulation No 1881/2006 states the maximum permitted levels of aflatoxins in foodstuffs (27), the Directive 2002/32/EC specifies the levels of aflatoxin B1 in feed materials (25), while the European Commission Regulation No 401/2006 describes the official methods for sampling and analysis of aflatoxins (26). In the European Union 4 μg/Kg and 50 ng/Kg are the acceptable limits of total aflatoxins for ready to eat tree nuts and milk products respectively, while Codex Alimentarius Commission (FDA) has set the maximum level at 10 μg/Kg and 500 ng/Kg of total aflatoxins respectively (13). On the contrary, there are countries (e.g., in Asia) where no legal limits for aflatoxin M1 in milk and milk products exist.

Various methods for aflatoxin analysis have been reported. Enzyme linked immunosorbent assay methods provide rapid screening, but they are associated with false positive results, hence there is a need for additional confirmation (98, 86). High performance liquid chromatography combined with fluorimetric detectors (44, 22) or coupled with tandem mass spectrometry (7) are preferred by researchers, while the introduction of ultra high pressure liquid chromatography coupled with triple quadrupole mass spectrometer allows for faster, more sensitive and efficient identification with little sample manipulation (major cut in clean up protocols, solvent usage and laboratory labor) (45, 4).

DIETARY INTAKE OF OTHER MYCOTOXINS

The effects of aflatoxins have been well investigated and acknowledged due to the extensive research conducted by medical mycologists. Less understood is the role of other mycotoxins, which are produced by fungi that directly enter the human food chain via an animal feed, known as silage. These mycotoxins include classes of toxins of high interest such as Zearalenones, Trichothecenes, and Fumonisins. Human exposure to these mycotoxins via milk, dairy products and beef is initiated through a combination of grain and grass feedstuffs (silage) present with mycotoxin producing fungi**.**

Silage is a fermented, high-moisture fodder that is commonly fed to ruminant cud-chewing animals including cattle and sheep. It is fermented and stored in a process called silaging, made from grasses, including corn, sorghum, and other cereals. Silage can also be made from many field crops including oats and alfalfa. Silage involves anaerobic fermentation conducted by many microorganisms including inoculants to accelerate fermentation. The fermentation process converts sugars into acids and exhausts any oxygen available in the crop material. Silage inoculants may be one or more strains of lactic acid bacteria, commonly employing the genera of Lactobacillus including plantarum and buchneri sp. and strains, Enterococcus sp. and Pediococcus sp. When these naturally occurring and highly beneficial bacteria are present, they expectedly produce a nutritious feed. However, the production of secondary metabolites and mycotoxins of other species of Aspergillus flavus (aflatoxin), and other genera such as the Fusarium producing toxins of trichothecene B: deoxynivalenol, zearalenone, fumonisins B1 and B2 and T-2 and HT-2 toxins are not wanted. Moreover, the presence of fungi such as Penicillium species that produce the nephrotoxic *ochratoxin* A, the tremorgenic roqufortine and the carcinogen citrinin is unwelcome (30).

DAIRY HERD EXPOSURE TO MYCOTOXINS

Dairy herds affected by mycotoxins display symptoms of exposure to mycotoxins and are often associated with a reduction in milk production, failing to respond to veterinary therapy, lowered resistance to disease (18) and may not demonstrate any adjustments or changes in nutrition. Although symptoms may be vague or nonspecific they may include a reduction of feed (silage) consumed, refusing feed, roughened cow-hair or coat, weakened body condition, jaundice, disorientation (neurotoxicity) and reproductive disorders including metritis, the inflammation of the endometrium. Researchers have also associated the presence of mycotoxins with an increase in cow problems including displaced abomasum, ketosis, and retained placenta, fatty liver and bovine mastitis (104).

HUMAN DIETARY MYCOTOXIN INTAKE IN MILK AND GRAIN

Extensive data is available for detectable levels of mycotoxin in grain cereals but for milk and its products only the U.K. provides consumption data for zearalenone in milk. For all populations, consumers, males and females the dietary intake from milk varied between 2.0 and 4.8 ng/kg body weight (bw)/day among adult consumers. Dietary intake of zearalenone from milk among the younger age groups varied between approx.1.8 ng/kg bw/day (15-18 year old adolescents) to 46.5 ng/kg bw/day (infants aged 6-12 months). Intake among the elderly ranged between 2.0 to 4.5 ng/kg bw/day. Results: (N = 100; 3,0 % positive) wherein the mean 1 was 0,50 μg/kg and 0,63 μg/kg. The highest value was 5,5 μg/kg, thus the number of reported results was rather small and only 3% were contaminated with zearalenone (13).

Zearalenone toxicity is probably of little significance due to the rapid biotransformation and excretion of zearalenone in animals. Only a minimal transmission of zearalenone to dairy cows milk has been found after exposure to low doses of zearalenone, and there is no evidence of zearalenone in milk intended for human consumption. It is therefore assumed that the main dietary sources of zearalenone are cereals and related products. This finding should also apply to meat and eggs.

CEREALS AND GRAINS

Levels of mycotoxins monitored and levels set for human dietary cereal grains including corn, oats, wheat, barley and reported in the U.S. are limited to the presence of aflatoxin. EU regulations also exist for monitoring and surveillance of additional mycotoxins including aflatoxin M1; the Trichothecenes deoxynivalenol (DON), diacetoxyscirpenol, T-2 toxin and HT-2 toxin; the Fumonisins B1, B2, Nivalenol (NIV) and B3; agaric acid; ergot alkaloids; Ochratoxin A; patulin; phomopsins; sterigmatocystin, and zearalenone (35).

Most recent data of the EU occurrence of mycotoxins in food (35) suggest that among cereals, corn and wheat contribute the most to the total intake of Fusarium mycotoxins whereas wheat and wheat containing products are the primary source of DON, NIV T-2 toxin and HT-2 toxin intake.

MYCOTOXINS IN WHEAT AND WHEAT-BASED PRODUCTS

Wheat as a dietary staple is common through western Europe and as such its importance to human diet and the presence of mycotoxins studied is of high interest (35). Positive occurrence for given Limit of Detection (LOD) of selected mycotoxins:

Trichothecenes (DON) in 11 countries (Austria, Belgium, Denmark, Finland, France, Germany, The Netherlands, Norway, Portugal, Sweden and UK) provided data for a total number of results was 6358 with 61 % of positive samples, which ranged from LOD 2 μg/kg (Sweden) to 50000 μg/kg (France). The mean 1 ranged between 8 (Belgium) to 1427 μg/kg (Sweden). The weighed mean 1 was 205 μg/kg and the weighed mean 2 was 293 μg/kg.

Zearalenone in eight countries provided data on similar wheat products. The total amount of samples was N =1900 samples. These samples were divided into respective products and resulting wherein cereal grains (N = 847; 30 %positive), milling wheat fractions (N = 768; 24 % positive) and wheat based products (N = 285; 10,5 % positive). LOD ranged from 1 to 30 μg/kg.

Fumonisins with two participating countries (France and Italy) provided results. The total number of results was 110 for FB1, with 79.1 % of positive samples, and they ranged from LOD (10 ug/kg) to 736 ug/kg (France). No weighed means for Europe were calculated due to the paucity of data. As for FB2 only France provided data FB2 resulted in 88,4 % of total samples.

MYCOTOXINS PRESENT IN HUMAN MILK

Aflatoxin and other mycotoxins have been found in human breast milk (53). When breast milk in Sierra Leone was tested for the presence of mycotoxins only 10 out of 113 breast milk samples were mycotoxin-free. Eighty-eight percent of samples contained various aflatoxins and 35% contained Ochratoxin. Very few samples (15%) had only a single mycotoxin. Thirty-six samples (32%) had two mycotoxins; 50 samples (40%) had three or more. It was concluded that infants in Sierra Leone are exposed to aflatoxins and other mycotoxins at levels that, in some cases, far exceed those levels permissible in animal feed in developed countries.

This is not a problem unique to African nations, as has been all too often claimed by the developed nations. The following report also documents that the problem also exists in Europe. This suggests that if the human breast milk in other countries were to be checked, similar findings would be found.

Ochratoxin was found in human breast milk from nursing Italian mothers (63). Fifty samples of human milk were collected randomly over the course of one year from Italian nursing mothers and analyzed for Ochratoxin. Nine samples (18%) were found to contain Ochratoxin. This study highly suggests the possibility that Ochratoxin could be transmitted from mother to child through milk during breast-feeding (63).

HEALTH EFFECTS OF MYCOTOXINS IN HUMAN AND DIETARY MILK

Mycotoxins, particularly cyclosporine, found in human milk demonstrate immunosuppressive effects and have been used to minimize organ rejection and only recently a reduction in their use has been observed due to the carcinogenic properties of cyclosporine. Other immunosuppressive toxins of Aspergillus *flavus* produce aflatoxin that suppresses the function of macrophages (57), while Aspergillus *ochraceus* produces ochratoxin that is known to be cytotoxic to lymphocytes and it suppresses many functions of lymphocytes, monocytes, and granulocytes (67, 68). As observed by researchers, trichothecene of the genus Fusarium has similar immunosuppressive effects (60).

Neurotoxicity: *Cyclopiazonic acid* (CPA) is an indoletetramic acid *neurotoxin* produced by some of the same strains of A. *flavus* that produce aflatoxins and Penicillium species growing on feedstuffs (9).

Aflatoxin in breast milk causes liver cancer in young rats. Several published studies on breast-fed rats have shown cases of liver cancer in offspring as a result of the ingestion of aflatoxin from the breast milk (41, 102).

Previous researches point out that infant exposure to aflatoxin result in liver at the age of 30 (99). It has been postulated that one factor contributing to this early onset of the disease could be exposure to environmental carcinogens at or soon after birth. The presence of various mycotoxins, especially a highly toxic one like aflatoxin, in human breast milk provides proof of a very early exposure of humans to mycotoxin carcinogens.

Aflatoxin in infant powdered milk: Previous reports have investigated the problems associated with the presence of potential mycotoxin producing fungi in powdered milk preparations marketed for infants (55). The study was prompted by the finding of aflatoxin in the livers of deceased children and in some samples of milk powder. Commercial samples of domestic and foreign milk powder intended for babies were examined and, as expected, 29 different species of molds were isolated. The authors concluded that these results must lead to a revision of views on the microbiological standards and the production and packaging technologies for baby foods. Aflatoxicosis traced to aflatoxin-contaminated infant milk food (1977) in their studies of encephalopathy with fatty degeneration of viscera (Reye's syndrome) found that the disease appeared to be associated with aflatoxin-contaminated milk food, a finding supported by a number of other researchers.

HEALTH EFFECTS OF XENOBIOTICS IN HUMAN AND DIETARY MILK

It has been known for some time that xenobiotics in human and dietary milk have profound effects on human health. Although the use of persistent organic pollutants and mycotoxins has been declining in recent decades, concerns regarding their health effects remain due to the existing human data demonstrating unfavourable associations with several health markers coupled with recent evidence for continued population exposure.

As a group, POPs are of great concern for both environmental and human health issues. That is because, at high concentrations, POPs cause severe environmental effects, such as reproductive and developmental affects in wild and laboratory animals (101, 106, 64). There is more uncertainty regarding human health effects, especially at the present environmental levels, because the intakes of humans are much lower than those of some animal species. The World Health Organization recognizes the concern about the potential risks of POPs in human milk (100). Nevertheless, the beneficial effect of breastfeeding as the

optimal food source for newborn babies should always be emphasized. In particular, when sharing information with the general public it should be made clear that the presence of dioxins and PCBs in human milk is not an indication for avoiding breastfeeding (81). Body load is clearly age-dependent and is lower in the young age groups most at risk during pregnancy or breastfeeding (54).

A number of human epidemiological studies have assessed the relationship between environmental PCB exposure and markers of male reproductive health, namely semen quality parameters (sperm concentration, motility, and morphology), sperm DNA integrity (DNA damage or chromatin fragmentation), and circulating reproductive hormone levels. The most recently published evidence on this topic show that, despite a wide range of study designs and locations, measurement methods, and PCB exposure levels, the inverse associations between PCBs and sperm motility have been consistent which may suggest a lack of exposure threshold for a PCB-related effect on sperm motility (62). Moreover, several studies have reported inverse associations between PCBs and circulating testosterone levels in men.

Probably the most well studied health effects arise from DDT inherent in milk. In 1991, the International Agency for Research on Cancer (IARC) rated DDT as "possibly carcinogenic to humans (Group 2B)" (48). Indeed, DDT has been linked with liver cancer (61), pancreatic cancer (34, 80, 2), breast cancer (89, 10, 83), colorectal, lung, bladder, prostate, endometrial, and stomach cancers (12, 82, 23). Moreover, recent evidence suggests that DDT may be involved in pathophysiological mechanisms leading to diabetes, miscarriage, preterm birth, low birth weight, urogenital birth defects, as well as reproductive and neurodevelopmental abnormalities (23).

CONCLUSIONS

- DDTs levels in breast milk are higher in developing countries compared to developed countries and a worldwide declining tendency is observed. p-p´-DDE is the major metabolite detected in both human and dietary milk.
- β-isomer of HCH is the most frequently detected in breast milk samples. Generally a declining tendency is presented in reported levels both in developing and developed countries.
- Worldwide PCB levels in breast milk vary among studies. In dietary milk the estimated PCB intake is lower than the Acceptable Daily Intake.
- Low industrialized countries show low levels of dietary milk contaminations with dioxins compared with high-industrialized countries.
- Aflatoxins maximum residue levels have been established in order to provide a legal basis for minimizing health risk during food marketing and food consumption, yet these limits vary across countries.
- The potential risks of POPs in human milk have been recognized, yet the beneficial effect of breastfeeding as the optimal food source for newborn babies should always be emphasized. In particular, when sharing information with the general public it should be made clear that the presence of dioxins and PCBs in human milk is not an indication for avoiding breastfeeding.
- PCBs are inversely associated with sperm motility and circulating testosterone levels in men.
- DDT has been linked with a number of cancers, while recent evidence suggests that DDT may be involved in pathophysiological mechanisms leading to diabetes, miscarriage, preterm birth, low birth weight, urogenital birth defects, as well as reproductive and neurodevelopmental abnormalities.
- Mycoxins are introduced into dairy herds primarily through feed including grains and silage mix.
- Toxicity from mycotoxins includes immunosupression, oncogenesis and both cyto and neurotoxicity.

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