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GLOBAL SURVEILLANCE OF DDT AND DDE LEVELS IN HUMAN TISSUES

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Abstract. The organochlorine insecticide dichlorodiphenyltrichloroethane (DDT) was initially introduced for control of vector-borne diseases. It was banned in the United States by the Environmental Protection Agency in 1972 because of potential harmful effects on humans, wildlife and the environment. Since it is a potential human carcinogen, the United Nations Environmental Program (UNEP) has recently restricted the use of DDT in developing countries until alternative methods of vector control are sought. DDT and its metabolite, dichlorodiphenyltrichloroethylene (DDE) are lipid soluble, and bioaccumulate more in human adipose tissue, than breast milk and serum. This article is a review of DDT and DDE levels in human tissues from different countries in the world. Data on p,p'-DDT and p,p'-DDE levels in human adipose tissue, breast milk and serum were selected from more recent literature. It was discovered that countries in Africa, Asia, and Latin America with more recent exposure to DDT and DDE have higher levels in human tissue than in Europe and the United States. The global concern for DDT and DDE is the environmental spread and persistence in the food chain. Hypothetically, there is a potential risk of harmful effects of DDT and DDE to human health. UNEP has cautiously taken action to protect human health, the environment and the earth from further destruction by persistent organic pollutants. Further exposure to DDT should be prevented to achieve this goal.

Key words:
DDT, DDE, Human tissues, Exposure, Environmental exposure

INTRODUTION

We have reached a stage where there is no conclusive answer on the health effects of the organochlorine insecticide, dichlorodiphenyltrichloroethane (DDT). At this point, even though there has been no scientific evidence that DDT causes cancer in humans, it remains a global public health issue [1,2]. Historically, DDT was introduced as an insecticide to control malaria, a vector-borne disease in the 1950s. In the United States, DDT was banned in 1972 by the Environmental Protection Agency, because of the potential harmful effects on wildlife and humans [2,3]. Likewise the use of DDT gradually declined in the developed countries, but its use increased substantially in developing countries for malaria control and in agriculture. Presently, twenty-three countries in Africa, Asia and Latin America use DDT for vector control, with restrictions in some of these countries [4].

The concern is that DDT and its principal metabolite dichlorodiphenyltrichloroethylene (DDE) pervade the environment in all forms of life, humans, plants, animals, water, air, and soil [2,5]. DDT is known to have affected wildlife by causing the thinning of eggshells in bald eagles in the United States, and reproductive failures in other bird species [6]. Humans are to a large extent exposed to DDT and

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DDE through diet. Both DDT and DDE are highly lipid soluble, accumulate in fat-containing foods, and travel through the food chain [2,5]. Bioaccumulation of DDT and DDE in humans occurs in adipose tissue at much higher levels, and to a lesser extent in the bloodstream and breast milk [1,7]. A potential effect of DDE in humans is the risk of breast cancer [8], since it is a xenoestrogen or described as an endocrine disruptor with estrogen-like effects [9,10]. Other possible effects of DDT are low sperm counts [11], testicular anomalies [12], premature delivery of fetus [13] and small for gestational age fetuses [14].

The United Nations Environmental Program (UNEP) held their fifth session on persistent organic pollutants (POPs) in Johannesburg, South Africa in December 2000 [15]. Diplomats from 122 countries negotiated on a legally binding treaty requiring governments to minimize and eliminate some of the most toxic chemicals ever created. The mission of the treaty is to protect present and future generations from cancer, birth defects, and other effects caused by persistent organic pollutants. At that meeting, the precautionary principle to protect the environment was kept in place [16]. DDT, which is included in the list of POPs was granted a health exemption for use in countries where malaria is still a major public health concern. The restricted use of DDT in needy countries will be permitted until the concerned countries replace DDT with chemical and non-chemical alternatives that are cost effective and environmentally friendly. The use of the remaining organochlorine insecticides are now banned.

In May 2001, at the Stockholm Convention in Sweden, the treaty on POPs was adopted and signed by respective governments and other plenipotentiaries [17]. This convention was to reinforce the protection of human health and environment from POPs. With respect to DDT, the implementation of the treaty applies strict regulations on the use of DDT. This includes limitations on the production and use of DDT. The introduction of a DDT Register advocates the monitoring of the use of DDT, its availability, regulation and safety. Participating countries on the DDT register would form a Conference of Parties for the use of DDT for malaria control in accordance with the World Health Organization (WHO) recommendations and guidelines. The goal is to reduce and ultimately eliminate the use of DDT from the world [15,17].

Since DDT remains a controversial issue for reasons described, answers to the potential health effect of persistent DDT and DDE need further exploration. Till then, limited use of DDT will be permitted in developing countries. What would be the result of, or what is the risk of long standing DDT accumulated in human tissues? The aim of this paper is to discuss the public health implications of bioaccumulation of DDT and DDE in the human population after reviewing the more recent literature on the status of DDT and DDE levels in human tissues from different countries in the world.

DDT IN HUMAN TISSUES

Environmental exposure to DDT and DDE or exposure from dietary sources results in the bioaccumulation of these chemicals in the human body in adipose tissue, serum and breast milk [1,5]. Higher exposure to DDT increases the extent of its bioaccumulation in the body [1,2]. DDE is also metabolized from DDT in the circulation and accumulates in fatty tissue, and in breast milk by its high lipid solubility [1,18]. DDT has a very long half-life in the body because of its persistent nature. But DDE tends to persist much longer in the body, and is the metabolite, which is of more concern with regard to bioaccumulation, since it is a marker of chronic exposure to DDT [2,18]. A high DDT/DDE ratio is an indication of chronic, but ongoing exposure to DDT. Conversely, a low DDT/DDE ratio implies high environmental persistence and ongoing bioaccumulation [7].

DDT levels increase with age; older age groups above 60 years have higher levels than younger people [1,7]. This was also confirmed in Ludwicki's study in Poland [19]. With the slow elimination rate, it may take approximately 10–20 years for DDT to disappear from the body after the use of DDT ceases [4]. In countries with more recent use of DDT, the levels are higher than in countries, which have ceased to use DDT. However, studies have shown that levels of DDT in human tissue have decreased remarkably worldwide with the decline in the use of the insecticide [1,2].

Analytical techniques for detection of DDT in human tissues vary. But, the general method includes: extraction, separation and purification and identification, and quantification of organochlorines using gas-liquid chromatography with electron capture detection using Nickel (^{63}Ni) or mass spectrometry [20,21]. This principle is applied in measuring DDT or DDE in adipose tissue, serum, and breast milk. Strict quality control methods with specific detection limits are applied in this experimental technique.

DDT in adipose tissue

The high lipid solubility of DDT enables it to accumulate in all fatty tissues (adipose) in the body. The levels of DDT in adipose tissue are at least one hundred times greater than the levels in breast milk or serum [1,2]. The extent of fatty tissue throughout the body in various organs and areas of the body could be a reason for the higher magnitude of DDT and DDE in adipose tissue. Extraction of adipose tissue for DDT or DDE analysis involves biopsy specimens of fatty tissue, but post-mortem samples of adipose tissue have been used in many studies [1,7]. The levels of these chemicals in fatty tissue are usually expressed in parts per billion (ppb), which is equal to nanograms per gram (ng/g) of fat tissue.

DDT in human breast milk

Since DDT and DDE accumulate in breast tissue, they are transported through the ductal system and are secreted into breast milk [22]. The concentration of DDT or DDE in breast milk is affected by lactation and associated factors such as age, parity, menopausal status, diet and social and environmental factors [22,23]. The study by Czaja [23] in Poland showed that increased lactation decreased the levels of DDT in mothers' breast milk. Breast-feeding of DDT contaminated milk is also a form of exposure to DDT in the infant from the mother [24], where DDT enters the circulation of infants [25,26].

DDT in serum

Exposure to DDT results in its entry into the circulation, where it is transported in the lipophilic component of the plasma in the body by its high lipid solubility [1,18]. The half-life of DDT in serum is about 10 years [4]. Levels of DDT or DDE found in serum are far lower than those in adipose tissue. However, measurements of these chemicals are reliable and are good indicators of exposure. One study done by Lopez-Carrillo et al. [27] showed that there was a very good correlation between measuring DDE in adipose tissue and in serum. Measurement of DDT or DDE in serum or plasma is a more viable method than using adipose tissue, which requires a biopsy specimen of fatty tissue or post mortem sample of tissue, which may not be easily available. Blood sampling by venupuncture for serum preparation is less invasive than a tissue biopsy [27]. Serum DDT or DDE levels have been used in several epidemiological studies measuring the risk of breast cancer from DDT or DDE exposure [8,28].

MATERIALS AND METHODS

Studies with information on measurements of DDT or DDE in humans from different countries in the world were reviewed from Medline [29]. Forty-seven studies from the literature were selected for this review. They included more recent scientific studies on DDT in different regions of the world, which included the five continents and major islands. The period selected for DDT and DDE measurements was during the last decade 1990–2000. Tissue sampling for measurements on DDT and DDE in the selected studies had been done during that period. In instances where several studies were done in a particular country, only the more recent studies were selected.

Some of the studies were surveys on DDT and DDE levels in human tissues in different populations. Others included case control studies on DDT or DDE exposure and the risk of cancer in humans, mainly breast cancer. Relevant data on DDT and DDE measurements in adipose tissue, serum, and breast milk were retrieved from the studies. Since the p,p'-DDT isometric form of DDT is the predominant form of technical DDT (77.1%) [18] and p,p'-DDE is the principal metabolite, they were selected for review [1,18]. The sum total of DDT comprises p,p'-DDT + p,p'-DDE + o,p'-DDT + o,p'-DDE + p,p'-DDD and

other derivatives of DDT [1,18]. Data on total DDT and other isometric forms of DDT were not consistently available; therefore only data on p,p'-DDT and p,p'-DDE were selected. Some of the studies only had data on measurements of either p,p'-DDT or p,p'-DDE and not both.

The mean values of DDT and DDE from the literature were used for this review, while in some studies the median values were the only available data. Where data on the mean DDT or DDE values were recorded separately for cases and controls, the average of the two combined measurements were used to represent the mean of the total population group. Similarly, where data on DDT and DDE were separated by age groups, or between males and females, the average values of DDT or DDE in the total population were used. The units of measurement for DDT or DDE from the literature were converted to ng/g or ng/l for purposes of this review. With adipose tissue the values were converted to a standardized unit in ng/g of fat tissue [30]. Depending on the method of measurement, expressed values of DDT and DDE in breast milk or serum were converted to ng/l for the wet method or ng/g after the lipid adjustment [27]. DDT and DDE measurements in breast milk were recorded in ng/g of milk fat and ng/l of whole milk [31]. The results were tabulated by country, year of study, number of subjects, mean p,p'-DDT and mean p,p'-DDE measurements, the sum of the means of DDT and DDE and DDT/DDE ratio. If the year of tissue sampling was not stated then either the year of submission of the article or the year of publication was used. Studies with specimen collections, which had been done prior to 1990, were not included for this review with the exception of two studies. They were by Alawi et al. [32], during 1989–1990 in Jordan, and Ludwicki et al. [19] during 1989–1992 in Poland. In cases where the period of specimen collection was through 1990, then data on DDT and DDE, which specifically corresponded to 1990 and later years were selected.

Review of human data on DDT and DDE levels

An ideal comparison of DDT and DDE between the countries was not viable for several reasons. This was because of vast sets of measurements of DDT and DDE across the globe with differences in: regions and population groups, number of subjects, characteristics of exposure to DDT, study periods, experimental techniques and methods of analysis of DDT and DDE. There was no uniformity or general consistency in study objectives, methods or results amongst such a large collection of studies. The extensive literature available on DDT and DDE levels in humans over time is a representation of the spread of DDT and DDE across the globe. This paper is a bird's eye view of the status of DDT exposure and bioaccumulation in humans around the world over the past decade. Regions of high exposure and bioaccumulation of DDT and DDE were identified in addition to regions with lower levels or exposure.

The studies reviewed were from 34 countries; Europe – 11, North America – 3, Africa – 4, Asia – 9, Australia – 1, South America – 1, Central America – 1, Greenland – 1, and Middle East – 3. Data on DDT in adipose tissue, which was expressed in ng/g of fat, was available from a total of 20 population groups, with information on both p,p'-DDT and p,p'-DDE from 15 groups (Table 1). Five groups had information available on p,p'-DDE only. Most of the measurements were mean values with the exception of a set of median values of DDT and DDE in a study done in the USA during 1994–1996 [33]. DDT and DDE were measured in ng/g of milk fat in breast milk from 21groups of women, with information on p,p'-DDT and p,p'-DDE from 17 groups (Table 2A). The measurements of DDT and DDE in ng/l of milk were available from 4 groups of women (Table 2B), one group had data on p,p'-DDT only. A total of 16 groups of people had information on serum DDT or DDE, 11 studies measured in ng/g (Table 3A), and 6 studies in ng/l of serum (Table 3B). Data on DDT and DDE in breast milk and serum were predominantly mean measurements.

The sum of p,p'-DDT and p,p'-DDE values was considered as the total DDT. This value is close to the true sum total DDT because the remaining isomers (o,p'-DDT, o,p'-DDE) form a very small percentage of this true sum total [1,18]. Figure 1 is a graphical plot of the levels of p,p'-DDT and p,p'-DDE from different countries using a logarithmic scale. It is a representation of the DDT/DDE ratio

Table 1. DDT and DDE measurements in adipose tissue

Country	Year	Number of subjects	p,p'-DDT (ng/g)	p,p'-DDE (ng/g)	DDT+DDE (ng/g)	DDT/DDE (%)	Reference
Mexico	1996	40	31000	60980	91980	50.8	30
Mexico	1991	87	4020	10000	10420	40.2	34
Poland	1989–1992	277	537	5745	6282	9.3	19
Tanzania	1992	9	3034	2547	5581	119.1	35
Mexico	1997–1998	60	1224	4335	5559	28	38
Mexico	1997	30	560	4040	4600	13.8	39
Greenland	1990–1994	26	142	3194	3336	3.8	36
Jordan	1996	50	701	2475.6	3176.6	28.3	37
Japan	1999	22	61.77	1600	1661.77	3.8	41
United States	1995–1996	146	264.45	752.5	1016.95	35	42
Germany	1992	6	73.9	906	979.9	8.1	35
United States	1994–1997	590	53.7	790.3	844	6.8	43
Finland	2000	27	110	567	677	19	45
Canada	1999	430	20.15	644.5	664.65*	3.1	44
United States	1994–1996	555	12.2	396.65	408.85	3	33
Spain	1990–1991	110		2845			46
Germany	1990–1991	62		1360			46
Holland	1990–91	118		1350			46
Switzerland	1990–1991	121		1245			46
New Ireland	1990–1991	185		1010			46

* Median values of p,p'-DDT and p,p'-DDE.

in adipose tissue. Where data was available from more than one study in a particular country, only information of the most recent study was included for this figure.

The highest values for the sum of DDT and DDE were from people in Mexico [30,34], followed by Poland [19], Tanzania [35], Greenland [36] and Jordan [37]. The study in Mexico with the highest value of DDT and DDE was measured from adipose tissue of 40 malaria control workers [30]. Therefore, these figures were far higher than the values of the other groups of people as shown in Table 1. Workers exposed to DDT by occupation with close contact to the chemical are expected to have higher bioaccumulation than the general population [1,18]. Between 1991 and 1997, the values of DDT and DDE appear to have decreased in Mexico, showing a general decline [34,38,39] (Table 1). The WHO reported that 1000 tons of DDT were used in Mexico in 1992 [12]. Currently, DDT is used in Mexico for public health purposes, with relatively higher exposure than in other countries [4]. Even though its use is restricted, DDT is still a serious public health problem in Mexico.

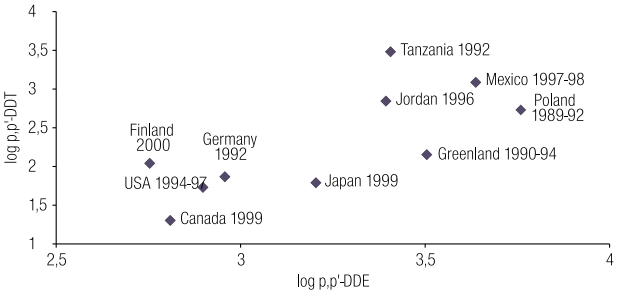

Fig. 1. Logrithmic representation of p,p'-DDT and p,p'-DDE measurements in adipose tissue.

In Poland, DDT was banned in 1975/1976. The high levels are more likely a result of dietary exposure to p,p'-DDE [19]. Tanzania is a country endemic with malaria, where

Table 2A. DDT and DDE measurements in breast milk of women in ng/g of milk fat

Country	Year	Number of subjects	p,p'-DDT (ng/g)	p,p'-DDE (ng/g)	DDT+DDE (ng/g)	DDT/ DDE (%)	Reference
Jordan	1992	59	2522	5680	8202	44	32
Zimbabwe	1991	40	2390	2530	4920	94	48
Mexico	1997–1998	60	651	3997	4648	16.3	39
Ukraine	1993–1994	197	336	2457	2793*	13.6	49
Jordan	1989–1990	59	700	2040	2740*	34.3	32
Kazakhstan	1997	76	300	1960	2260	15.3	50
Turkey	1997	104	106.5	2055	2161.5	5.2	31
Czechoslovakia	1993	26	716	1129	1845	63.4	31
Uzbekistan	2000	41	70	873	943*	8	52
Kuwait	2000	32	12.4	833	845.4	8	53
Greece	1995–1997	112	65.9	721.21	787.11	9.1	31
Mexico	1994–1996	50	162	594	756	27.2	58
UK	1997–1998	168	40	430	470	9.3	57
Japan	1998	49	17.8	270	287.8	6.6	55
Saudi Arabia	1998	115	64.5	183	247.5	35.2	31
Canada	1996	497	22.1	222	244.1	9.9	31
Egypt	1996	60	2.93	21.47	24.4	13.6	54
Uganda	1999	143	3510				51
Germany	1995–1997	3500	202*				56
Holland	1997	89			330*		55
Nicaragua	2000	52			7.12		59

* Median values of p,p'-DDT and p,p'-DDE.

Table 2B. DDT and DDE in breast milk of women in ng/l of whole milk

Country	Year	Number of subjects	p,p'-DDT (ng/l)	p,p'-DDE (ng/l)	DDT+DDE (ng/l)	DDT/DDE (%)	Reference
India	1994	25	158000	672000	830000	23.5	25
Egypt	1996	42	8900	119100	128000	7.5	31
Spain	1999		2620	37520	40140	6.9	21
Poland	1997	253	2160	24900	27060	8.6	31
Thailand	1998	25	23200*				60

* Median value of p,p'-DDT.

DDT is utilized for vector control and in agriculture [35]. The very high levels and DDT/DDE ratio above 100% is an indication of current and ongoing use of DDT. People in African countries are highly exposed to DDT and have higher levels of these chemicals. Recent data on DDT and DDE levels in humans from African countries is limited. Studies have been done in Nigeria in the 1970s [37], and in Kenya [40] and South Africa [26] in the 1980s. In Kenya, the mean p,p'-DDT in human adipose tissue was 2490 ng/g and mean total DDT was 5910 ng/g in a study done in 1986. Kenya is also a country in East Africa with high exposure to DDT for malaria control and in farming.

Table 3A. DDT and DDE measurements in serum

Country	Year	Number of subjects	p,p'-DDT (ng/g)	p,p'-DDE (ng/g)	DDT+DDE (ng/g)	DDT/DDE (%)	Reference
Mexico	1990–1995	246	190	3125	3315	6.1	63
Mexico	1994–1996	359	356	533	889	66.8	64
Sweden	1996–1997	359	20.4	663.2	683.6	3	65
Canada	1994–1997	532	12.6	485.8	498.4	2.3	66
Egypt	1996	48	3.9	38	41.9	10.2	67
USA	1996–1997	190		1813			68
USA	1992	744		792*			69
Brazil	1995–1996	493		692			70
Brazil	1999	33		357			71
Nicaragua	2000	52		7.12			73
Australia	1999	68		3.9*			72

* Median values of p,p'-DDT.

Table 3B. DDT and DDE measurements in serum

Country	Year	Number of subjects	p,p'-DDT (ng/l)	p,p'-DDE (ng/l)	DDT+ DDE (ng/l)	DDT/DDE (%)	Reference
Mexico	1999	24	2900	21800	24700	13.3	74
Vietnam	1994	42	2495	17040	19535	14.6	75
China	1998	30	600	17000	17600	3.5	76
Spain	1992–1995	77	940	9100	10040	10.3	77
Uzbekistan	2000	16	266.5	4710.5	4977*	5.6	52

* Median values of p,p'-DDT and p,p'-DDE.

The high bioaccumulation of DDT and DDE in people in Greenland and Jordan could be explained by their dietary consumption of p,p'-DDE in fat-containing foods, particularly meat or animal fat [36], since DDT has not been recently used in these countries. Eskimos in Greenland have been exposed to DDT and DDE by the drift of these chemicals into the environment across the globe. Hence, it is evident that they have accumulated high levels of lipid soluble DDE. The levels of DDT and DDE have decreased in Jordan since the earlier years when DDT exposure was high [37].

Lower levels of DDT and DDE in human adipose tissue were observed in Japan [41], the United States [33,42,43], Canada [44] and the European countries [35,45,46]. DDT has not been used in Europe since the 1970s, particularly in Germany that prohibited its use in 1972 [35]. This is clearly evident by the low levels of DDT and DDE in the European population. The levels of DDT and DDE in adipose tissue in Japan though moderately low compared to people in other countries were a result of the maximum use of DDT in the 1970's, when the concentration of DDT in humans was also at its maximum [41]. Levels of DDT in the Japanese population have decreased considerably since then. Dietary exposure to DDT has resulted in the persistence of DDE. But the lower levels may be a result of consumption of more seafood and shelled fish in Japan [41], compared to countries with high fat consumption of meat, milk and other dairy products.

The studies in the United States also show that DDT and DDE levels in humans have decreased considerably since DDT was banned in 1972. In 1980, total DDT in adipose tissue in the USA was reported to be 3000 ng/g [4]. A study

by Adhesina and Todd [47] in the USA during 1987–1988 measured DDT in human adipose tissue from autopsy samples in a survey where the mean p,p'-DDT was 294 ng/g and the mean total DDT was 987 ng/g. These values are comparable to other studies done in the 1990's. The prevalence of exposure to p,p'-DDE through a high fat diet prevails in the USA.

Most of the studies in Table 2A with measurements on DDT and DDE in human breast milk were measured in ng/g of milk fat. The sums of DDT and DDE in human breast milk were higher in Jordan [32], Zimbabwe [48], Mexico [39], Ukraine [49], Kazakhstan [50], Turkey [31] and Czechoslovakia [31] than in the other countries. The DDT/DDE ratio on a logarithmic scale for human breast milk is shown in Fig. 2. Uganda had a high mean value for p,p'-DDT in breast milk amongst a group of women. It is a country in East Africa, where DDT was introduced in 1946, and is still used for malaria control with wide intradomicilary use as well [51].

Zimbabwe had a high DDT/DDE ratio close to 100%, indicating an ongoing exposure to DDT and bioaccumulation. It is a country in southern Africa with extensive agricultural farming, where DDT was widely used [48]. Mexico had persistently high levels of DDT and DDE in human breast milk. Similarly levels were moderately high in the Ukraine, Kazakhstan and Czechoslovakia.

Lower levels of DDT and DDE in human breast milk were observed in people in Uzbekistan [52], the Middle East [31,53,54], Japan [55], Germany [56], Greece [31], Holland [52], Canada [31], and the United Kingdom, where DDT is banned [57]. In most of these countries, DDT had been used many years ago. In the former Soviet Union, the production and use of DDT in agriculture was banned in 1981, but its use was permitted for public health purposes [4]. However, there seems to be some environmental persistence through dietary exposure in these countries. The study by Torres et al. [58] in Mexico during 1994–1996 showed lower levels of DDT and DDE in breast milk. The population group in that study were possibly from a region in Mexico with lower exposure to DDT, even though it is expected that DDT levels in Mexico would be higher than those in other countries. There was a similar situation in Nicaragua [59].

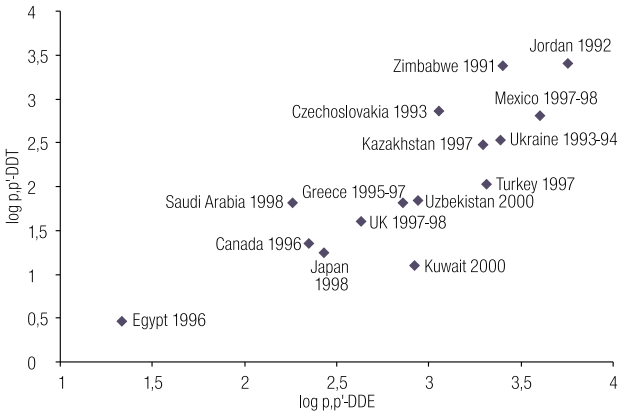

Fig. 2. Logarithmic representation of p,p'-DDT and p,p'-DDE measurements in human breast milk.

A few studies measured DDT and DDE in whole breast milk of humans in ng/l (Table 2B). Since the unit of measurement is different from that of ng/g, these data were compared separately. The higher values of DDT in human breast milk were in India [25] and Thailand [60] compared to Poland [31], Spain [21] and Egypt [31]. India is one country that has very high exposure to DDT. It was reported that DDT is still produced in India [4]. Between 1999–2000, 7500 tons of DDT had been used for malaria control in India [61]. Reports have shown that exposure to DDT formed 70% of total pesticide consumption in India [25]. With adverse publicity about DDT, its use is restricted in this country [62]. Despite a relatively high exposure to DDT in India compared to many countries in the world, recent data on DDT and DDE in human tissues is limited. The levels of DDT and DDE in breast milk in Nair's [25] study are a clear indication of high DDT exposure, and bioaccumulation in India considering the history of DDT use. Likewise, Thailand also being in Asia has a situation very similar to India; high levels of DDT would be expected. In Egypt, DDT was widely used and is still used for malaria control. It was reported by the WHO that 3457 metric tons of DDT were used in Egypt in 1970 [18]. Of the data on p,p'-DDT and p,p'-DDE in human serum, Mexico had the largest value of total DDT [63,64], followed by Sweden [65], Canada [66] and Egypt [67]. As already explained, Mexico is a country with high exposure to DDT. Sweden was the first country to ban DDT

in 1970 [4]. Therefore, it would have the least exposure and lower levels of DDT and DDE. Dietary exposure to DDT and DDE possibly accounts for the levels shown in the Swedish population. The levels of DDT and DDE in people in Egypt were unusually low compared to the other countries. These results may have been from a population who had low exposure to DDT, despite the use of DDT in Egypt [67]. Amongst the groups with only measurements on p,p'-DDE, the one study in the United States (1996–1997) had higher values than those in the other studies [68]. This was because of previous occupational exposure to DDT in the study population in the USA. The dietary exposure to persistent p,p'-DDE from a high fat consumption also accounts for this level of bioaccumulation. The other study done in 1992 by Laden et al. [69] had lower levels of DDE in human serum in the USA. Similar levels were observed in the studies done in Brazil [70,71]. DDT was banned in Brazil in 1985 for agricultural use, but it was permitted for public health programs till 1998 [71]. The WHO reported the use of DDT in Brazil in 1992 [12]. The other studies done in the USA, Australia [72] and Nicaragua [73] showed very low levels of DDE. Australia had used DDT many years ago; the WHO reported the use of 1000 metric tons of DDT in 1970 [18]. Therefore, DDT exposure is not a major public health problem like in countries with high exposure. Nicaragua, which is situated in Central America, had unusually low levels of DDE in human serum. DDT was widely used in these countries and is still in use in Latin America today [62]. The low levels are perhaps the result of measuring DDE in a population not as highly exposed as the one that would be in an area where DDT is frequently applied.

The measurements of human serum expressed in ng/l showed higher values of DDT and DDE in Mexico [74], Vietnam [75] and China [76] (Table 3B). All these countries are currently using DDT, and their populations are more exposed to DDT than people in other countries. Lower levels of DDT and DDE in human sera were in Spain [77] and in Uzbekistan [52].

The DDT/DDE ratio, which is an indication of environmental exposure to DDT, also reflects occupational exposures. Mexico in particular had the highest level of bioaccumulation of p,p'-DDT and p,p'-DDE in humans, being a country with recent high exposure to DDT even though its use is restricted [64]. In Africa, Uganda, Tanzania and Zimbabwe there are also high exposure and bioaccumulation of DDT and DDE in human tissues. Similarly, Asia, India, China, Vietnam and Thailand are countries, which currently use DDT and the body burden of DDT and DDE is high. Kashyap [78] measured DDT in human adipose tissue from cadavers in India, and found that the total mean DDT concentration in males was 3967 ng/g and 4054 ng/g in females. Countries, which had previous exposure to DDT had moderate to lower levels of DDT and DDE in their population than the countries with current exposure. These include some European countries like Poland, and Czechoslovakia, Middle Eastern countries, Japan, Turkey, Uzbekistan and Kazakhstan. Lower levels of DDT and DDE were observed in the population in most of Europe, the USA, the UK, Australia and Canada.

DISCUSSION

We are aware that DDT and DDE are present in every part of the world, with higher concentrations in certain areas. On the whole, the levels of bioaccumulation in humans has decreased since the reduction in the use of DDT. This may not be so apparent from the data presented in this review. However, in comparison to the 1970–1980s, there is a general decline in DDT levels in the human population [1]. Exposure to DDT is directly proportional to the degree of bioaccumulation in human tissues, but DDT levels decrease years after exposure has ceased. Theoretically, the relationship between exposure to DDT and bioaccumulation in a single population could be explored quantitatively if the appropriate information on DDT levels in the environment in a particular area is known.

The global spread of DDT and DDE in the environment is a source of low-level exposure of people in developed countries. The environmental persistence of p,p'-DDE is also a public health concern [4], since it travels through the food chain in fat contained in food, which is consumed by humans [5]. The major concern to human health and

the environment is the potential effect of persistent DDT and DDE. What are the risks of high levels of DDT and DDE in the body? On the other hand with the long half-life of these chemicals what would be the risk to human health?

Epidemiological research has not proven that DDT causes cancer or other harmful effects in humans [79]. It is known that DDT and DDE are carcinogenic in animals [2,18]; they bind with estrogen receptors, mimic the action of estrogen [9], and accumulate in lipid soluble tissue [2,7]. Yet, there is no scientific evidence in the literature to show that DDT is harmful to man. The research completed in humans in developed countries was done with the understanding that previous high exposure to DDT would possibly have a delayed effect in humans. The population in developed countries had been exposed to very high levels of DDT or DDE more than 20 years ago. Therefore, recent research on DDT and health effects including cancer, in retrospect took into consideration the latent period for the development of cancer since the period of toxic exposure in the general population.

To further explore the risks of high exposure to DDT, more research is required in countries that use DDT. Latin America, Mexico, African, and Asian countries are regions where scientific research is required and should be given priority. In addition to the extensive research on the effects of DDT in animals, and the environment [5,18], more research on the human population would be invaluable. Most of the human epidemiological studies have been done in developed countries that have very low exposure to DDT. This could be a reason for the inconclusive evidence of harmful effects of DDT in humans. Since such research on DDT toxicity in humans is limited in developing countries, the high exposure to DDT is the more reason why such research should be expedited. The effects of DDT could be specifically studied in high-risk populations with exposure to DDT and high bioaccumulation of DDT and DDE. They could be occupational exposures to DDT in malaria prevention spraying operations or in the pesticide industry where DDT is manufactured [1,18]. The use of DDT on farms for agricultural purposes in developing countries is also a major source of exposure. There may be a high probability of observing effects of DDT in humans in developing countries, which would reveal answers to the many questions on DDT toxicity and human health. This research should be administered and regulated by appropriate organizations, including governmental health agencies and academic institutions, which will require extensive research grants with large sources of funding in order to accomplish this goal.

The persistent nature of DDT and DDE in the environment and dispersal through the food chain is a form of ongoing exposure in humans. It is the presence of long standing DDT and DDE over many years in the human body, which is the health concern. Scientifically, there is no definite answer to the risk of DDT exposure and any long-term effect on human health. Hypothetically, the possibility of DDT causing cancer or other harmful effects cannot be excluded. We are faced with a no risk to minimal risk situation of the harmful effects of DDT exposure in humans. However small the risk maybe, the odds of ill health to humans cannot be ignored.

Based on the risk assessment of DDT and DDE exposure in humans, the UNEP negotiations on POPs agreed to ultimately phase out or ban the use of DDT in the world. This step was taken with the concern for DDT effects on the environment and all forms of life. They included government representatives from all over the world, WHO, non-governmental organizations: Physicians for Social Responsibility, Green Peace, World Wildlife Fund and many other interested parties. At the Stockholm Convention on POPs, 127 governments agreed on elimination or restriction on the production and use of all intentionally produced POPs, and continued use of DDT is allowed for vector control until safe, affordable and effective alternatives are in place. As a precaution to human health, the objective of the Stockholm Convention is to prevent any further potential damage of DDT to man, animals and the environment as a whole. The World Wildlife Fund set the year 2007, by when DDT should be totally phased out from the world [80].

During the process of the UNEP negotiations for banning DDT from the globe, there was some resistance from countries that require the use of DDT for public health

programs, including the Malaria Foundation International. Malaria is a vector-borne infectious disease highly prevalent in tropical and subtropical countries. It affects more than 300 million people resulting in more than a million deaths in the world [81]. The killing of mosquitoes hosting the malaria parasite by DDT, very much encouraged its use to combat malaria. With the action taken by UNEP and WHO and other supporting organizations, many of the developing countries would be affected by the decisions made to ban DDT. The reason being that a decrease in the use of DDT increased the incidence of malaria in some countries, raising health concerns in malaria endemic countries [61]. South Africa is one country, which experienced this change with malaria in endemic areas after DDT spraying was temporarily stopped [81]. Alternatives to malaria control have been tried in some countries, but are not economically viable for poorer nations [61]. Taking into consideration the needs of developing countries, their public health issues and financial restraints, the POPs treaty agreed on a partial ban on DDT till alternatives to the use of DDT are discovered and accepted. At the same time the WHO Roll Black Malaria initiative is devoted to reduce the incidence of malaria in affected countries, which will eventually benefit affected countries [81].

The action taken at the Stockholm Convention in May 2001 marks a step forward in safeguarding human health against pesticide toxicity. The restrictions and regulations applied to the use of DDT in the world were done in anticipation of any unknown or potential harmful effect of DDT on life, human health and the environment. It was an act to prevent further damage to human life, by saving more lives from potential adverse effects of DDT. It is not known when DDT may prove to be carcinogenic in humans. If this theory is shown through scientific research, it may be too late for mankind by then. Therefore, the responsible action taken unanimously by several countries will only protect human health and well being from the unanswered questions of DDT exposure. Ignorance of the risks of DDT exposure, and passive decision making with regard to DDT would indirectly allow more harm to human health, animal species, plant life, elements of the earth, and the total environment.

DDT was once thought to be the "miracle insecticide" [3], and its use was encouraged across the globe. At this point in time we have DDT and DDE present in the environment in every part of the world in all living species, in the food we consume, and in our bodies where they lie dormant. We are unaware of what harm they may cause to human health. To save the earth from further damage caused by organic persistent pollutants, the solution would be to prevent further exposure to DDT and DDE in the environment, in addition to what already exists.

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