A review of the significance of animal food products as potential pathways of human exposures to dioxins

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A Review of the Significance of Animal Food Products as Potential Pathways of Human Exposures to Dioxins[1]

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ABSTRACT: The polychlorinated dibenzo-*p*-dioxins and dibenzofurans (dioxins) are groups of compounds with similar chemical and toxicological properties. Carcinogenicity was considered the most serious toxic end point when setting previous regulatory policies, but recent concerns have focused on the possible endocrine-disrupting activities of the dioxins. Toxicity is related to the 2,3,7,8 pattern of chlorine substitution, a pattern that also leads to chemical and metabolic stability. Dioxins are practically insoluble in water and concentrate in lipids of biological systems, leading to low background concentrations in fat of the general human population. Major environmental sources of dioxins are emissions from industrial chlorination processes and combustion of materials containing chlorine. Inhalation and water have been ruled out as significant exposure pathways, which suggests that food is the primary source. Pathways of entry into food chains are atmospheric transport of emissions and their subsequent deposition on plants, soils, and water. The major food sources seem to be fat-containing animal products and some seafoods. This conclusion is based on evaluations of potential environmental pathways involving dioxins and related compounds. Generally, dioxins and other lipophilic compounds are not taken up and translocated by plants, so residues in foods and feeds derived from seeds should be negligible. Animals on high-roughage diets, or those that ingest contaminated soil, are the most likely to accumulate dioxin residues from the environment. The conclusion that animal products are a major source of human exposure requires verification by appropriate food sampling programs and animal metabolism studies. If it is desirable to reduce human exposure to dioxins via the food supply, reduction of sources would be a more effective strategy than changing agricultural practices and food consumption patterns.

Key Words: Dioxins, Food, Exposure, Animals

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Introduction

The health significance of human exposure to dioxins and related compounds has been the subject of extensive research and public controversy. The U.S. Environmental Protection Agency (EPA) has been engaged in an extensive reassessment of these compounds, which are now ubiquitous in the environment (Stone, 1994). The overall tenor of the reassessment leads to the conclusion that members of the general population have low body burdens due to background exposures of these compounds and that potential risks to human health may occur at exposures within one to two orders of magnitude greater than the average background exposure. Current information suggests that the major sources of human background exposures are foods, particularly animal products and fish from locally contaminated water bodies.

This paper provides an overview of the chemical and biological characteristics of dioxins, pathways of transport from environmental sources to animal food products, and the potential implications of the widespread occurrence of dioxins for livestock producers.

Background

Compound Classes

The term "dioxin" in general usage refers to the members of three chemical classes with similar biological and toxicological properties. These include the polychlorinated dibenzo-*p*-dioxins (**PCDD**), dibenzofurans (**PCDF**), and coplaner polychlorinated biphenyls (**PCB**), whose general structures are shown in Figure 1. The number of possible positional congeners are 75 PCDD, 135 PCDF, and 209 PCB. Of the 210 possible PCDD and PCDF congeners, only the

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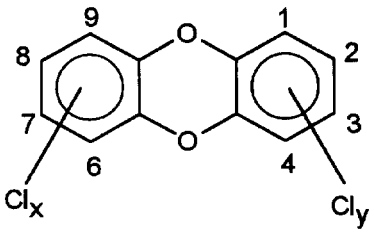
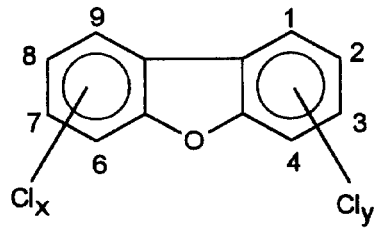
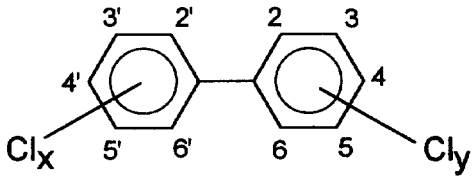


Polychlorinated Dibenzo-*p*-Dioxin



Polychlorinated Dibenzofuran



Polyclorinated Biphenyls

Figure 1. The general structures of the polychlorinated dibenzo-*p*-dioxins, polychlorinated dibenzofurans, and polychlorinated biphenyls.

7 PCDD and 10 PCDF with chlorine substitutions in the 2, 3, 7, and 8 positions are considered to produce the characteristic "dioxin-like" toxicity (U.S. EPA, 1989). Eleven PCB congeners, which constitute only a small portion of the PCB residues in the environment, are thought to have dioxin-like toxicity. These congeners are unsubstituted or monosubstituted in the ortho positions and are referred to as coplaner PCB because the phenyl rings can rotate into the same plane.

The congeners of these classes that are included in the term "dioxin" exert biological effects through the mechanism of binding to a cytosolic protein termed the "Ah receptor." The Ah (aromatic hydrocarbon) receptor is an oligomeric 280-kDa protein that binds planer, nonpolar molecules such as the dioxins with high affinity and stereospecificity (Landers and Bunce, 1991). The Ah receptor evolved before the introduction of halogenated aromatic compounds (Czuczwa et al., 1984) and some other compound(s) must represent the natural ligand for the receptor. High-affinity ligands have been identified in plants (Gillner et al., 1985), and it is possible that the Ah receptor evolved as part of a substrate-inducible system for detoxifying dietary lipophilic substances.

The biological effects of dioxins are similar among species, but the dose required to elicit a response is variable. Mixed chlorinated-brominated and brominated congeners substituted in 2, 3, 7, and 8 positions also have dioxin-like activity. These compounds only occur at low concentrations or are confined to local areas and do not contribute significantly to exposure of the general population (Fries, 1985; Donnelly et al., 1990).

Toxicity equivalency factors (**TEF**) that relate the toxicity of all congeners to 2,3,7,8-tetrachloro-*p*-dioxin (**TCDD**), the most toxic congener, have been assigned to the biologically active PCDD and PCDF congeners (Table 1). There are no universally accepted TEF for the coplaner PCB. The TEF were assigned on the basis of binding affinities for the Ah receptor and short-term biological tests and are useful primarily because it is not realistic to carry out comprehensive toxicological evaluations for all congeners. The TEF are used most appropriately as intake values for predicting toxicity. Mixtures are often reported as the toxicity equivalent quantity (**TEQ**), which is the sum of the quantity of individual congeners multiplied by the respective TEF. Caution should be applied when TEQ are used to quantify remote sources and environmental pathways because of the differing environmental fates and pharmacokinetic properties of the individual congeners (McLachlan, 1993; Schlatter, 1994).

Historical Perspective

The PCDD and PCDF have never been synthesized as commercial products except for use as analytical standards and research materials. Synthesis of TCDD occurred as early as 1872, but the compound remained a laboratory curiosity until 1957 when it was linked to chloracne, a skin condition that occurred in workers who had been involved in a chemical plant accident (Kimmig and Schulz, 1957). At approximately the same time, the cause of several large outbreaks of chick edema disease in broilers was traced to toxic fat containing several dioxins that originated from pentachlorophenol (Higginbotham et al., 1968). The herbicide 2,4,5-T (2,4,5-trichlorophenoxyacetic acid) was found to be teratogenic in 1968, and it was later established that the effect was caused by TCDD contamination (Courtney et al., 1970; Sparschu et al., 1971). These findings provided the original impetus for dioxin research, which led to the detection of PCDD and PCDF as contaminants of many phenoxy herbicides and chlorophenol-based chemicals (Helling et al., 1973; Langer et al., 1973). Public awareness of

Table 1. Toxic equivalent factors (TEF) for the 2,3,7,8-substituted polychlorinated dibenzo-*p*-dioxins and polychlorinated dibenzofurans (U. S. EPA, 1989)

Chlorination	Dioxins	Furans
2,3,7,8-	1.0	.1
2,3,7,8-penta	.5	—
1,2,3,7,8-	—	.05
2,3,4,7,8-	—	.5
2,3,7,8-hexa	.1	.1
2,3,7,8-hepta	.01	.01
octa	.001	.001

dioxins also was heightened by the controversial use of phenoxy herbicides as defoliants in Viet Nam (Gough, 1986).

Several highly publicized incidents in the 1970s increased public awareness and concerns. The accidental release of a reaction mixture from a trichlorophenol plant in Seveso, Italy caused extensive dioxin contamination of surrounding agricultural and residential areas (Pocchiari et al., 1983). The deaths of horses and illness of riders at several riding areas in Missouri in 1975 was attributed to TCDD contamination in waste oil used for dust control (Carter et al., 1975). The oil contained waste from a hexachlorophene manufacturing plant, and it had also been used for dust control on the unpaved streets of Times Beach. The high concentrations of TCDD in the residential soils led to purchase and evacuation of the town by the U. S. Government (Kimbrough et al., 1984).

Production processes were altered to reduce the formation of dioxin contaminants in chlorophenol-based products, and many uses were restricted or banned as the potential health significance of dioxins was established. Improved analytical methods led to the identification of other sources of dioxins, and these sources are now the major focus of public concern and controversy. In 1977, dioxins were identified in incinerator fly ash, which is the fine particles of ash carried out of the fuel bed by the draft (Olie et al., 1977). Subsequently, it was determined that PCDD and PCDF are formed in many combustion processes when suitable precursors and temperatures are present (Bumb et al., 1980). Municipal and hazardous waste incinerators are now considered to be the major sources of PCDD and PCDF in aerial emissions (Fiedler and Hutzinger, 1992; Harrad and Jones, 1992; Rappe, 1992). Hospital incinerators, chlorine paper bleaching processes, metal refineries, and exhausts of automobiles using leaded fuel also are significant sources.

Because dioxins are products of combustion, it has been suggested that such natural processes as forest fires are important sources of environmental contamination (Gribble, 1994). Evidence for this suggestion is not conclusive. The traces of PCDD and PCDF detected in the smoke of controlled burns could have arisen from resuspension of background material (Tashiro et al., 1990). Concentrations in tissues of ancient mummies were much lower than present background tissue concentrations (Ligon et al., 1989). Low concentrations of dioxins are present in sediment cores from as early as 1860. Concentrations increased rapidly after 1920, reached a peak in about 1980, and have declined since, suggesting that industrial activity has been the major source (Czuczwa et al., 1984; Smith et al., 1992). The apparent decline has coincided with the reduced use of chlorophenol-based products.

Chemical and Toxicological Properties

Three physical chemical characteristics are important in determining the fate and transport of PCDD and PCDF in the environment. Water solubility is low, ranging from 317 ng/L for TCCD to .074 for OCDD (octa-CDD) and the log K_{ow} (octanol-water partition coefficients) range from 6.8 for TCDD to 8.2 for OCDD and OCDF (Shiu et al., 1988). The PCDD and PCDF are characterized as semivolatile to nonvolatile with vapor pressures ranging from 10^{-8} atm for TCDD to 10^{-12} atm for OCDD (Eitzer and Hites, 1988). Nearly all PCDD and PCDF with the 2,3,7,8-chlorine substitution pattern are chemically and metabolically stable under normal environmental conditions. As a result, PCDD and PCDF persist and concentrate in the lipids of biological systems, including food-producing animals.

The dioxins exhibit a wide range of biological effects, all of which are thought to be mediated through initial binding to the Ah receptor. Some biochemical changes, such as induction of cytochrome P450 enzymes, occur at very low exposures, but the clinical significance of these subtle changes is uncertain (Whitlock, 1991). The carcinogenicity of TCDD has been established in several rodent species (Kociba et al., 1978; Kociba, 1991). Typically, epidemiological studies of accidently and occupationally exposed humans have been inconclusive because of small populations and uncertainties concerning exposure levels (Fingerhut et al., 1991; Bertazzi et al., 1993). Extrapolation of carcinogenicity results from rodents has been the primary basis for establishing regulations and policy actions up to this time (Kimbrough et al., 1984; U. S. EPA, 1990).

Reproductive and immunotoxicological effects have drawn the most concern among non-cancer effects (Mably et al., 1991; Vos et al., 1991). A three-generation rat reproduction study has been the basis for assessing the hazards of the non-cancer effects (Murray et al., 1979). More recent work suggests that the fetus is very sensitive to exposure to TCDD at the 16th d of gestation in rats (Mably et al., 1991, 1992). The adverse postnatal effects in rats exposed *in utero*

are most pronounced in males and occur at dose rates that do not cause adverse effects in the parent.

The reproductive effects have been attributed to the estrogen-like activity of the dioxins, but this interpretation has been controversial (Colborn et al., 1993; Stone, 1994). The dose rates that produce adverse reproductive effects would produce body burdens closer to background body burdens in the general population than the level of concern previously established for cancer effects. An important area of uncertainty is the appropriateness of extrapolating of single-dose results to chronic exposure scenarios. Additionally, uncertainties are associated with the use of the TEF concept for effects other than cancer, for which the TEF concept was developed.

Many other effects, such as immunosuppression, induction of cytochrome P450 enzymes, and alteration of hormone levels, have been noted in laboratory animals, and it could be presumed that similar effects could occur in humans at some specific dose (Whitlock, 1991). At this time, however, the rodent cancer and reproductive studies are of the greatest concern for assessing risks to humans.

Background Exposure Levels

Body Burdens

Members of general population have low body burdens of dioxins due to exposure to background sources that cannot be specifically identified. The ranges of background concentrations in fat on a TEQ basis are similar in all industrial countries, and limited evidence suggests that concentrations are lower in less-developed countries (Schecter, 1991). Results of one U. S. study of composite fat samples from surgical patients and cadavers is presented in Figure 2. Only four congeners were important contributors to the total TEQ. The hepta- and octachlorinated congeners, although present in high concentrations, did not contribute greatly to the total burden because of their low TEF. Age was an important demographic factor affecting concentrations. This finding is expected because the half-lives of TCDD in humans are in the range of 7 to 12 yr (Poiger and Schlatter, 1986; Pirkle et al., 1989). The distribution of the congeners did not change greatly with age, which suggests that sources have remained comparable in congener distribution over time.

Differences in concentrations were not associated with demographic factors such as sex, geographical area, and ethnic background. Because the samples were composites, the statistical distribution of background concentrations is not known, but distributions are typically log normal, so one might expect the 90th percentile to be approximately three times the average (Sielken, 1987). Orban et al. (1994) suggested that concentrations had declined when the 1987 data set (Figure 2) was compared with a similar 1982 data set. The conclusion is uncertain because of changes in analytical methodology and because the two data sets would not necessarily represent the same population.

Exposure Sources

Estimates of the contributions of various sources to background exposures have been made in a number of countries. The typical conclusion was that approximately 95% of the exposure was from food, and the remainder was attributed to inhalation and dermal exposure to contaminated soil (Gilman et al., 1991; Theelen, 1991). Estimates of the contributions of various food sources in Germany and the Netherlands are summarized in Table 2. It can be concluded that foods of animal origin, fish, and other seafoods are the major sources of background human exposure. The relative importance of the food classes reflects differences in measured concentrations in food and dietary habits. Data for the U. S. are inadequate for drawing reliable inferences concerning the relative contributions of different food classes, but the major sources would be expected to be comparable to the European data.

Sources and Transport Processes

Overview

The major environmental sources of dioxins since the phaseout of the chlorophenol-based products are emissions from combustion, incineration, and industrial processes using chlorine (e.g., chlorine bleaching of paper). Aerial transport of emissions from these processes is now considered the primary pathway of PCDD and PCDF entry into the environment and food chains. A schematic diagram of the potential pathways of dioxin transport from sources to humans is shown in Figure 3. Minor introductions may occur occasionally in local situations, such as application of sewage and paper mill sludges to land (Weerasinghe et al., 1985; Rappe et al., 1989) and the use of facilities constructed of wood treated with pentachlorophenol (Firestone et al., 1972; Shull et al., 1981; Ryan et al., 1985). In addition, residues in the food chain may arise from the release of dioxins from sediment and soil that were sinks for past introductions into the environment.

Characterization of contaminant transport from sources to animal products requires the evaluation of multifactor pathways involving soils, plants, and animals (Figure 3). The three most important pathways are 1) introduction of the chemical on plants by deposition of vapors and particles, with consumption of the plants by animals; 2) introduction of the chemical to soil, transfer to plants by root uptake and translocation or by volatilization from soil and deposition, with consumption of the plants by animals; and

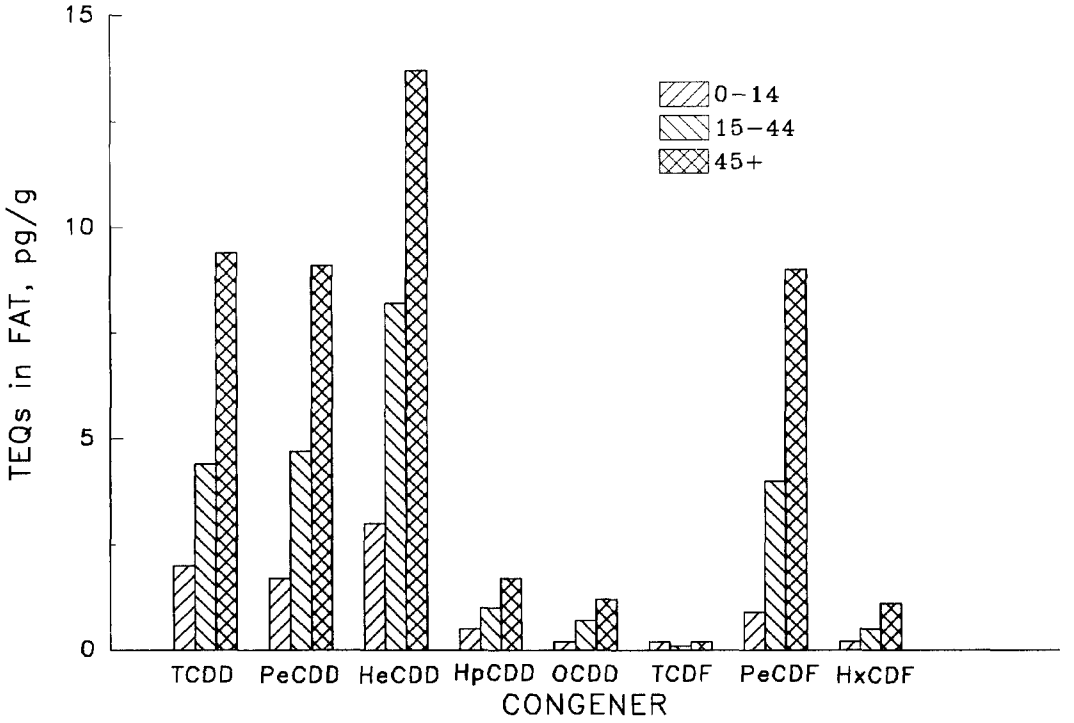


Figure 2. Concentrations of toxic equivalents (TEQ) of polychlorinated dibenzo-*p*-dioxins and polychlorinated dibenzofurans in fat of the U. S. population. Adapted from Orban et al. (1994).

3) introduction of the chemical to soil, with ingestion of the soil by animals. Evaluations of these pathways in the context of specific chemicals and agricultural and industrial practices are available (Connett and Webster, 1987; Fries, 1987; Stevens and Gerbec, 1988; Fries and Paustenbach, 1990).

Aerial Transport and Deposition

Evidence of aerial transport from sources to the environment is the presence of PCDD and PCDF in soils and sediments in areas remote from potential sources (Czuczwa et al., 1984). Vapor-phase transport predominates in PCDD and PCDF congeners with the higher vapor pressures, and particle transport predominates in congeners with lower vapor pressures (Bidleman, 1988; Eitzer and Hites, 1989a). The ratios of transport by the two phases also are dependent on the ambient temperature. The deposition processes are categorized as wet and dry, and each process has different implications for plant contamination and retention. Scavenging by precipitation is most efficient with particle-bound PCDD and PCDF (Eitzer and Hites, 1989b). The distribution between wet and dry deposition of PCDD and PCDF was about equal in two locations in Indiana, but the distribution may differ in areas with different climatic conditions (Koester and Hites, 1992).

Air-borne lipophilic chemicals in the vapor phase accumulate on plant surfaces in cuticle waxes, which are present in all terrestrial plants (Bacci et al., 1990a). The amount adsorbed depends on the concentration in air, physical and chemical characteristics of the congener, and the plant species. Modeling studies have led to the conclusion that the octanol-air partition coefficient is the key descriptor for accumulation of lipophilic compounds from air (Bacci et al., 1990b; Paterson et al., 1991). A great deal of uncertainty is related to the application of these models to the field. Photodegradation is an important dissipation mechanism for TCDD on plant leaves (McCrady and Maggard, 1993), and the large differences in uptake among plant species require experimental characterization (Buckley, 1982).

Table 2. Estimated contributions of various food classes to intake of toxic equivalents (TEQ) of dioxin-like compounds in Germany and The Netherlands[a]

Food	Germany, pg/d	Netherlands, pg/d
Fluid milk	8.1	17
Other dairy products	13	26
Beef and veal	19	13
Pork	7.6	4.2
Poultry and eggs	1.4	4.8
Fish and seafood	27	31
Vegetable oils	3.8	14
Leafy vegetables	No estimate	4.4
Total	79	115

[a]Adapted from Furst et al. (1990) and Theelen (1991).

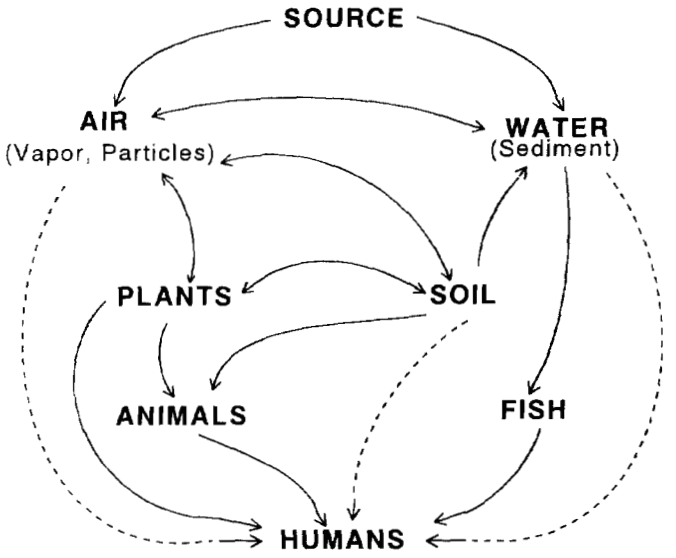


Figure 3. Major potential pathways of transmission of polychlorinated dibenzo-*p*-dioxins and polychlorinated dibenzofurans from emission sources to humans. Broken lines are pathways of lesser importance.

A large portion of the air-borne PCDD and PCDF is adsorbed to particles. The fraction of the particles in dry deposition initially deposited and retained on the plants is related to particle size, leaf area and roughness, plant biomass, and plant density (Martin, 1964; Witherspoon and Taylor, 1970). Removal or reduction in concentration of intercepted particles on plants is accomplished by weathering (wind action, precipitation wash-off), growth dilution, and grazing by animals. It has been estimated that as much as 5% of the annual deposition at a site can be retained on forage plants at harvest (Fries and Paustenbach, 1990). Retention of wet deposition on plants has not been characterized, but the fraction retained is not expected to be great because most precipitation falls through the plant canopy, or is lost as stemflow (Steiner et al., 1983; Parkin and Codling, 1990).

Fate in Soil and Plant Uptake

More than 95% of the aerially deposited contaminants in terrestrial environments ultimately reach soil (Fries and Paustenbach, 1990). The major potential dissipation and transport processes from soil are leaching, photodegradation, volatilization, biodegradation, and erosion. The PCDD and PCDF are strongly adsorbed to soil organic matter and leaching generally is not an important transport or dissipation process (Jackson et al., 1985; Paustenbach et al., 1992). The presence of co-contaminants that enhance the water solubility or oils that serve as carriers have led to leaching in some instances (Freeman and Schroy, 1989; Kapila et al., 1989). Microbial degradation is an important dissipation process for many compounds, but no soil organisms that degrade PCDD and PCDF chlorinated in the 2,3,7,8- positions have been identified (Paustenbach et al., 1992). Photodegradation may lead to minor losses of compounds at the soil surface (Crosby and Wong, 1977).

Volatilization occurs at the soil-air interface, and it will affect soil concentrations to the depths that compounds can be transported to the soil surface in the vapor phase through the unsaturated zone (Jury et al., 1983; Freeman and Schroy, 1989). The rate of volatilization is directly related to vapor pressure, which within a class of compounds such as the PCDD is inversely related to the degree of chlorination (Shui et al., 1988). Because vapor pressure is also related to temperature, large diurnal and seasonal fluctuations in volatilization losses are expected (Freeman and Schroy, 1989). Ultimately, concentrations in surface soil will be in equilibrium with concentrations in ambient air under conditions of continuing contamination from non-point sources.

Contaminants are transported from soil to aerial parts of plants primarily by two mechanisms: root uptake and translocation within the plants, and volatilization from the soil surface and deposition on plants. The relative significance of the two processes depends on the solubility of the compound (Ryan et al., 1988). Water-soluble compounds are the most likely to be taken up by roots and translocated to aerial plant parts, whereas transfer of semivolatile lipophilic compounds such as PCDD and PCDF is expected to be by volatilization and deposition. This expectation has been confirmed in studies in which no TCDD was detected in plants when suitable vapor barriers were provided (McCrady et al., 1990; Bacci et al., 1992). Lack of absorption and translocation was also found after foliar application of TCDD (Isensee and Jones, 1971). The only exceptions involve several members of the cucumber family (*curubitaceae*) that do take up and translocate PCDD and PCDF to the fruit (Hulster et al., 1994).

Little vapor transfer of the highly chlorinated congeners from soil is expected because vapor pressure of a homologous series of compounds decreases with increasing chlorination. In agreement with this expectation, concentrations of the hepta and octa congeners of PCDD and PCDF in hay were not related to concentrations in soil, and the hay residues were attributed to current aerial deposition (Hulster and Marschner, 1993). The important implications of the volatilization-deposition mechanism are that only the concentrations of contaminants near the soil surface are important in determining plant contamination, and that seeds used for feed will be less contaminated than roughages.

Animal Uptake and Disposition

Exposure Pathways

Consumption of contaminated feed and soil is the only important pathway of animal exposure to

lipophilic environmental contaminants. Balance data from a lactating cow demonstrated that exposure by inhalation and water are negligible sources of PCDD and PCDF (McLachlan et al., 1989). The relative importance of feed and soil depends on the animal types and management systems. The intake of roughages is the most important factor determining animal exposure because feeds derived from seeds are expected to contain much lower concentrations of persistent lipophilic compounds. Thus, ruminants are expected to be more vulnerable to PCDD and PCDF exposure than poultry and swine.

The use of pasture is of particular importance because soil ingestion is added to consumption of contaminated plants as a pathway of animal exposure. Comprehensive summaries of measurements of soil ingestion by cattle and sheep in a number of geographical areas and under a variety of conditions are available (Fries and Paustenbach, 1990; Fries, 1991). Generally, soil ingestion is related inversely to availability of forage when pasture is the sole source of feed and is reduced markedly when supplemental feed is provided. It has been demonstrated that volatilization from soil and deposition on plants is the important pathway of animal exposure when forage is abundant (Willett et al., 1993). It may be inferred, however, that soil may be more important when grazing is sparse because soil ingestion was as great as 18% of the diet of beef cattle on an arid range late in the grazing season (Mayland et al., 1975).

The soil ingestion pathway is not limited to grazing animals. Cattle confined to unpaved lots consume small amounts of soil that can lead to product residues (Fries et al., 1982a). Although most poultry and pork production is conducted in confined operations, the soil ingestion pathway of exposure may be important when these species have access to contaminated soil (Fries et al., 1982b; Chang et al., 1989).

Bioavailability

The PCDD and PCDF contaminants can be associated with a variety of matrices such as plant material, soil, fly ash, and sewage sludge that may affect bioavailability. Net absorption was 75 to 80% when TCDD was administered to rats in corn oil (Rose et al., 1976) but was only 50 to 55% when TCDD was contained in normal rat and cow diets (Fries and Marrow, 1975; Jones et al., 1989). Reviews of the available literature indicated that uptake of TCDD from normal soils is approximately 40%, as low as 30% from fly ash, and less than 20% in soils from some industrial sites (Fries and Paustenbach, 1990; Fries, 1991).

Pharmacokinetics

Pharmacokinetic data on PCDD and PCDF in farm animals are limited, but the data are consistent with findings of studies of other persistent halogenated hydrocarbons. Concentrations of halogenated hydrocarbons in milk fat usually attain steady state within 40 to 60 d of continuous feeding (Fries, 1977). The maximum bioconcentration factor (**BCF**, concentration in milk fat/concentration in diet) for halogenated hydrocarbons is approximately 5.0 (Fries, 1991). Lower BCF are obtained when a compound is metabolizable, or when absorption is decreased in compounds with high degrees of chlorination.

Table 3. Balance data for polychlorinated dibenzo-*p*-dioxins in a midlactation dairy cow[a]

Congener	Feces, %	Milk, %	Other[b], %
2,3,7,8-	75	35	−10
1,2,3,7,8-	51	33	16
1,2,3,4,7,8-	55	17	28
1,2,3,6,7,8-	41	14	45
1,2,3,7,8,9-	76	18	6
1,2,3,4,6,7,9-	44	1	55
1,2,3,4,6,7,8-	57	3	40
1,2,3,4,6,7,8,9-	80	4	16

[a]From McLachlan et al. (1989).
[b]Determined by difference and includes storage, metabolism, and analytical errors.

The BCF of 3.7 for TCDD in a 21-d study is consistent with the maximum expected BCF (Jensen and Hummel, 1982). A study in which contaminated pentachlorophenol was fed for 70 d yielded BCF of 5.7, .6, and .1 for 1,2,3,6,7,8-HxCCD, 1,2,3,4,6,7,8-HpCCD, and OCDD, respectively (Firestone et al., 1979). A recent short-term dosing study has confirmed and extended the observations on the decline in accumulation with increased chlorination. Absorption ranged from approximately 30% for TCDD to 1.6% for 1,2,3,4,6,7,8-HpCCD (Olling et al., 1991). Half-lives for the decline in milk fat concentrations of PCDD and PCDF ranged from approximately 60 to 100 d during early lactation in cows that had been dosed during the nonlactation period (Tuinstra et al., 1992). These values are consistent with the range of biological half-lives of other halogenated hydrocarbons in lactating cattle (Fries, 1977).

The comparative behavior of congeners is illustrated by the balance data for a cow in mid-lactation exposed to normal background contamination (Table 3). The largest fraction of the intake of most congeners is excreted in feces, suggesting a low rate of absorption for the compounds. A small part of the fecal concentration represents excretion, but excretion by this route is small if the long half-life of TCDD in humans is applicable to nonlactating cattle. As is true of other homologous series of halogenated compounds, excretion in milk is inversely related to the degree of chlorination. Approximately 30% of the tetra- and penta-CDD in the diet were excreted in milk, a value

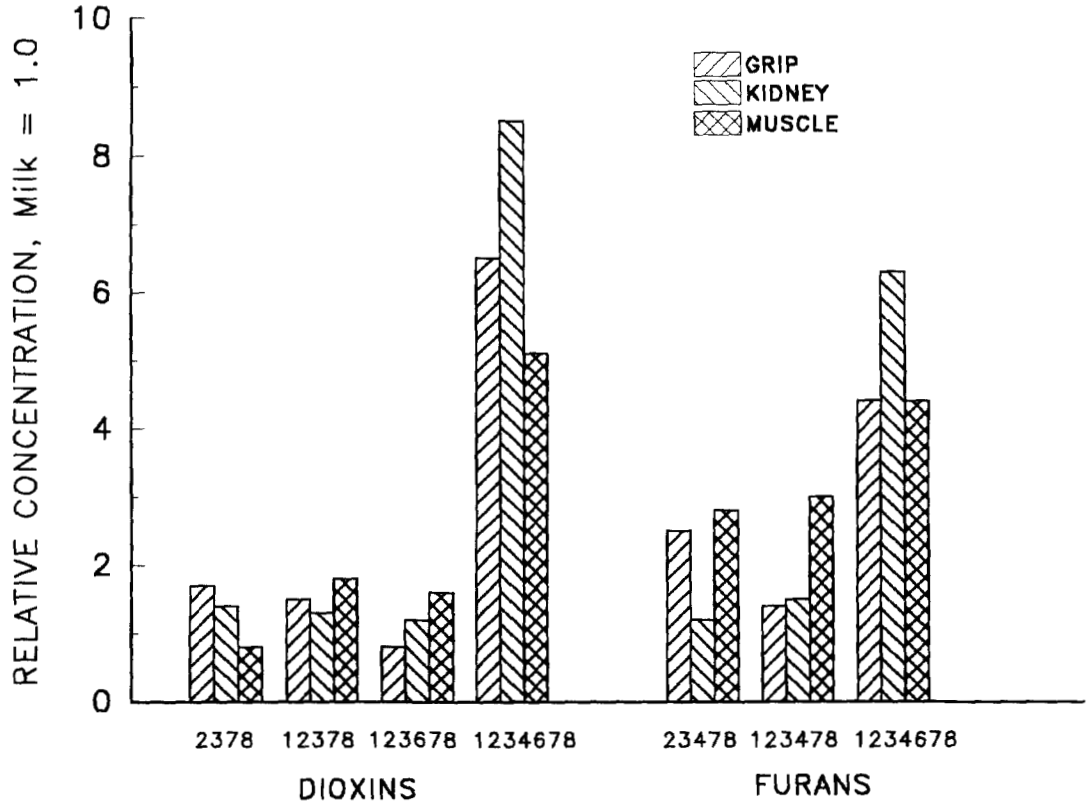


Figure 4. The relative concentrations of polychlorinated dibenzo-*p*-dioxin and polychlorinated dibenzofuran congeners in tissue fats of dairy cows dosed 93 d previously. Data from Olling et al. (1991).

that is typical of chlorinated hydrocarbons such as DDE and dieldrin (Fries, 1977). Transport of hepta- and octa-congeners to milk were negligible, whereas values for hexa-congeners were intermediate.

Accumulation of persistent organics in meat animals has not been studied as extensively as in dairy animals. In addition, interpretation of most work is difficult because studies with meat animals have been too short to reach steady-state concentrations (Fries, 1991). Results of several longer studies, which included repeat tissue samples, indicated that constant concentrations of chlorinated hydrocarbons were reached within 100 to 200 d (Fries, 1991). Modeling of residue accumulation in growing animals suggests that steady-state concentrations can be attained if diets with adequate energy concentrations are available on an ad libitum basis (Fries, 1994). Steady state will not be attained, however, when diets are adequate only for maintenance or restricted growth.

The BCF in subcutaneous fat was 3.5 when TCDD was fed to steers weighing 200 kg for 28 d (Jensen et al., 1981). The half-life during the subsequent elimination phase was 16.5 wk. This decline in concentration probably represented dilution by the increase in fat pool size during growth, but this could not be evaluated because growth data were not presented. Yearling dairy heifers fed dioxin and furan contaminants containing pentachlorophenol for 160 d had BCF that ranged from 2.1 for 1,2,3,6,8,9-CDD to .05 for OCDD (Parker et al., 1980). The rankings of BCF based on body fat were consistent with the rankings of BCF based on milk fat.

The concentrations of lipophilic chemicals in most edible tissues have been found to be approximately equal on a fat basis (Rumsey et al., 1967; Fries and Marrow, 1977; Fries et al., 1978). Data for PCDD and PCDF are limited, but the concentrations in fat of three tissues of lactating cows slaughtered 93 d after dosing were relatively uniform (Figure 4).

There are no pharmacokinetic data on accumulation of dioxins in pork, and data in poultry are limited to a single study of the transfer of PCDD and PCDF to eggs (Petreas et al., 1991). The BCF for the tetra- and penta- PCDD and PCDF in eggs are similar to those for typical persistent halogenated hydrocarbons (Figure 5). The BCF declined with increased chlorination, as was found for cattle.

Discussion

The general population is exposed to low background levels of dioxins and related compounds. The dioxins are carcinogenic and cause a spectrum of adverse effects in animals, and it can be expected that

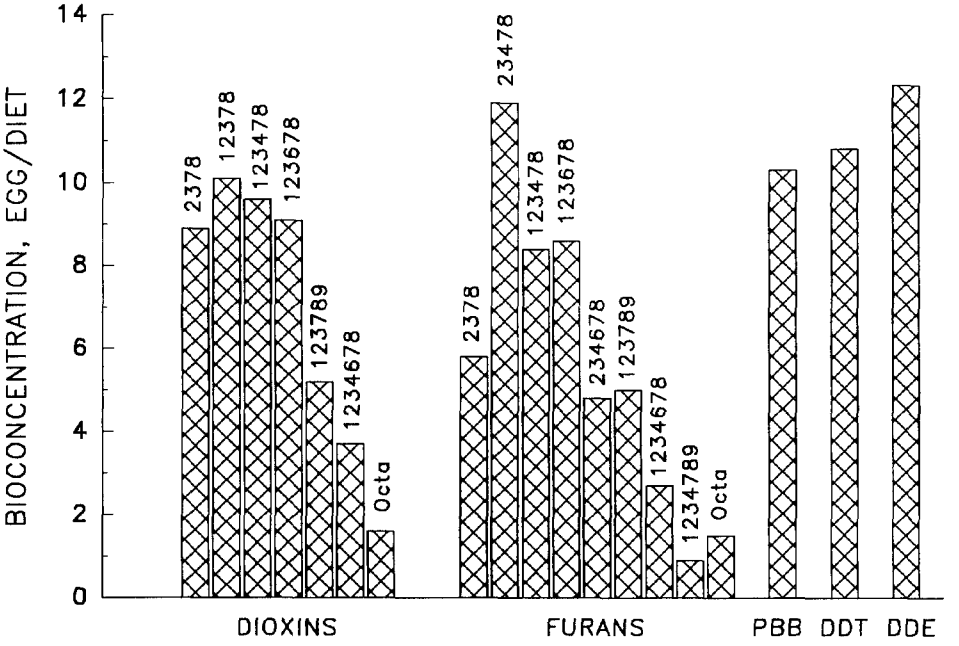


Figure 5. Concentrations of polychlorinated dibenzo-*p*-dioxins, polychlorinated dibenzofurans, and other halogenated hydrocarbons in lipid of eggs relative to concentrations in diets. Dioxin and furan data from Petreas et al. (1991), PBB (polybrominated biphenyl) from Fries et al. (1976), and DDT (1,1,1-trichloro-2,2-bis-(4-chlorophenyl)-ethane) and DDE (1,1-dichloro-2,2-bis-(*p*-chlorophenyl)ethylene) from Cecil et al. (1972).

these effects will be expressed in humans at some level of exposure. Although the dioxins are the most extensively studied class of environmental contaminants, many uncertainties surround the evaluation of the margin of safety between current background exposures and the level of exposure required for expression of adverse effects. A conservative approach to risk assessment suggests that the margin of safety is narrow and that efforts to reduce background human exposures are desirable. This conclusion, however, is controversial and arguments can be made that the conservative approach is not justified. The use of the TEF approach to evaluate the additive effects of congeners has not been fully validated, and the appropriateness of equating single-dose and chronic exposures on the basis of body burdens has not been established. Additionally, use of conservative parameters for individual steps in exposure pathways will, when combined, provide unrealistically high estimates of exposure.

The most likely medium of human exposure is food. The residues in food are inadvertent because dioxins have never been synthesized for industrial uses and, since the phaseout of contaminated products based on chlorophenol, the major sources of dioxins are combustion, waste incineration, and industrial processes that use chlorine. The dioxins emitted from sources are transported aerially and deposited on crops, soils, and water. Because of their lipophilic nature, the dioxins tend to concentrate in fats of animals and animal products in terrestrial environments, and in fish and seafoods in aquatic environments. Research findings are available to confirm the existence of the individual transport mechanisms from sources to food products. The available data suggest that products from animals that have the greatest reliance on roughage and pasture as feed sources will be the most likely medium for food residues.

Evaluation of the quantitative significance of individual pathways and the importance of various food products as exposure sources is hampered by the lack of a comprehensive research and monitoring data base. Dioxin analyses are difficult and labor-intensive, and they require expensive equipment. Thus, limited research resources should be devoted to those areas that will provide the greatest insight into the pathways of human exposure. Statistically based measures of the contributions of various food classes to human exposure and the determination of the basic pharmacokinetic parameters of the various congeners in food animals are important research needs. The similarity of the environmental and metabolic behavior of the dioxins to other halogenated compounds can provide support for inferences that must be drawn from limited data.

Implications

The potential for public concern over exposure to dioxins is high and regulatory actions to reduce emission of dioxins into the environment and food

chains can be expected. Alterations in production practices or recommendations for dietary change do not seem to be realistic because of the diversity and uncertainties of the exposure pathways. Changes in animal production practices to reduce dioxin transmission to animal food products would require increased confinement of animals and greater use of concentrates. These practices are antithetical to the current emphasis on animal welfare and sustainable agriculture.

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