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Review

Effects of Dioxins in Environmental Pollution on Development of Tooth Disorders

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Abstract

Despite legal regulations limiting emissions of persistent organic pollutants (POPs), including dioxins, to the environment, they still constitute a significant component of environmental contamination. They are released in large amounts during various processes of combustion in industry, the management of refuse materials and also as a result of situations that are partially beyond our control, like fires, explosions and damage in chemical industries. Observations originating from various studies prove that exposure to dioxins results in multiple toxic effects on humans and experimental animals. Among the various disorders caused by dioxins are abnormalities in dentition. The effects of dioxin may last long after exposure.

Keywords: dioxins, teeth

Introduction

In recent decades a certain amount of attention has focused on the group of persistent organic compounds (persistent organic pollutants- POPs) that cause environmental pollution as well as human health problems. POPs include polichlorine biphenyls (PCBs), polichlorine dibenzofuranes (PCDFs) and dibenzoparadioxines (PCDDs). Dibenzoparadioxines constitute a group of compounds causing long-lasting and high toxic biological effects [1, 2]. They consist of 200 isomers that can create congeners. Their mechanisms of action are mediated usually through the aryl hydrocarbon receptor (AhR).

2,3,7,8-tetrachlorinedibenzo-*p*-dioxin (TCDD) (Fig. 1) is the toxicity reference standard used for measurement of toxicity of other dioxins. For the purposes of objective assessment and comparison of various compounds, the concept of toxic equivalency was introduced in mid-1980. Each PCDD has his own, determined individual relative effect potency (REP) for elicit toxic effects relative to the reference compound (2,3,7,8-tetrachlorinedibenzo-*p*-dioxin). Total Toxic Equivalent (TEQ) presents an estimated value of 2,3,7,8-tetrachlorinedibenzo-*p*-dioxin (TCDD)-like activity of the mixture by the sum of the products of the concentration of each compound multiplied by the toxic equivalent factors (TEF) value [3]. TEQ and TEF were established and then systematically re-evaluated by WHO to uniformity at the international level and to provide recommendations for particular countries.

Biological consequences of POPs are related to their particular long-lasting accumulation, which leads to disturbing various homeostatic mechanisms. Despite restrictive

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obligations according to the Stockholm Convention for POP limitation and elimination [4], their emission is still significant, which is related to industry, common use of synthetic materials, and the occurrence of such unpredictable conditions as fires, ecological catastrophes and military activities. These compounds are released into the environment as side effects of defective technological processes, with chlorine use (e.g. production of paper, textiles, pesticides, paints, hygienic products) as well as a result of organic compound combusting (e.g. uncontrolled community waste utilization) [5]. A significant source of POPs is exhausted gases (from impaired motor engines), oils and leaks from poorly protected dumping sites. There is also a risk of their use in various forms of terrorism [2], as they are difficult to detect due to the lack of taste and smell, as well as good solubility in fats.

Environmental pollution results from contamination of air, soil and water with the dioxins which represent various biological activities. Dioxins can be suspended in smoke and ash. For example, concentrations of these compounds in the ground of city's agglomeration is about 10-20 ng TEQ/kg [6]. Recycling (25%), fires (16%), legally burned industrial wastes (18%) and communal wastes (14%) are the highest sources of dioxin emissions (Fig. 2).

This study is a review of actual data concerning the effects of dioxins on human organisms in general and oral health in particular, as well as the result of experimental studies with these compounds.

Review of Available Data Based on Various Clinical and Experimental Studies

The main way for dioxins to penetrate the human body include ingestion of contaminated food with a high concentration of animal fat, inhalation of contaminated air or penetration through the skin. Dioxin infiltration is facilitated by their particular fat affinity. About 90% of accumulated dioxins derive from food. The length of the food chain in animals plays a significant role in the degree of dioxins intake from food and their accumulation. The content of fat in animals is also important. It was found that dioxins are highly cumulated in fat tissue of organisms, which are the last stage in the food chain. One study showed that dioxins are accumulated in human and animal fat tissues, and their elimination depends on life expectancy and the rate of metabolic processes [1]. In humans this period is about 9 years [7].

Elimination of these compounds depends on the number of chlorine atoms present in dioxin's congeners. A significant amount of dioxin is removed from the body with

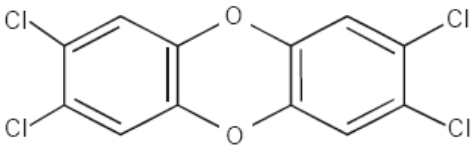

Fig. 1. Chemical structure of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD).

milk during lactation [8-10]. As presented by some authors, this may result in an overdose (even 50-70 times higher) of dioxin concentration in mother's milk [11]. The data obtained from experiments on female rats presented a decrease of dioxin concentration during lactation [12].

Researchers have tried to establish maximum daily doses of dioxins for humans. Occupational exposure, ecological catastrophes and experimental research on animals were taken into consideration. But results differ and are unequivocal, at least as a result of different sensitivity to dioxins of various animal species. European scientists propose acceptable daily doses much higher than US researchers do [13]. The maximum daily tolerated dose for a human on the basis of WHO norms from 1988 is about 1pg-TEQ (toxic equivalent)/kg/day [3].

Dioxin concentrations in human tissue depend on diet and lifestyle. Overweight people have higher dioxin concentrations in their bodies related to higher animal fat consumption and higher content of fat tissue. The results of the study showed that total dioxin elimination time after a single dose of 105 g of TCDD for a human is 9.5 years [7].

Dioxin in the human body is transported by lipids in blood serum to the liver and fat tissue (Fig. 3), where it accumulates. In the hepatocyte TCDD they bind to aryl hydrocarbon receptors, forming the complexes which are subsequently transported to the nucleus. These complexes then bind the dioxin response element (XRE) of DNA, which results in stimulation of genes for P 450 and P 448 cytochrome and consequently enhances their production. The formed cytochromes participate in the further metabolic processes of dioxins. Long-lasting accumulation of dioxins in the liver and their interaction with DNA influence metabolism of protein in liver and also in the haematopoietic system [1].

These compounds largely impact the human body, affecting many biological processes and also promoting behavioural disorders [14]. The effects may be signs and symptoms of acute dioxin toxicity or be related to long-lasting exposure

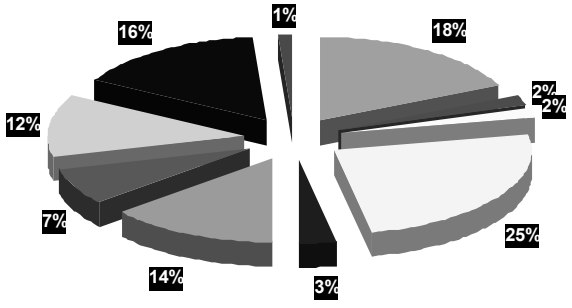

Fig. 2. Dioxin emission sources in percentage [5].
18% - legal industrial waste combustion,
2% - coal combustion in home stoves,
2% - industrial coal combustion,
25% - recycling,
3% - road transport,
14% - legal waste combustion,
7% - illegal industrial waste combustion,
12% - hospital waste combustion,
16% - fires,
1% - others.

to these compounds. They may also be distant results demonstrating many years after initial exposure, even in the next generation.

A good example of acute dioxin toxicity are the two cases described by Geusau et al. [15]. The two patients experienced heavy intoxication with TCDD of unknown origin, probably related to the workplace. After a short period of nonspecific gastrointestinal symptoms, one of these patients developed massive chloracne with multiple painful cysts covering not only the face, but the whole body. These skin lesions were irresponsive to applicated treatment of isotretinoin and, due to deep inflammation, required surgical intervention. Skin symptoms were associated by nausea, vomiting and gastric pain, which subsided after a year. Laboratory parameters revealed normochromic anemia, leukocytosis and elevated levels of blood lipids. Soon after intoxication, amenorrhoea also occurred. The intensity of skin changes corresponded in these with the concentration of the TCDD in blood lipids. The second patients with lower concentration of TCDD revealed only a mild form of chloracne, although the other two persons working the same institute and presenting elevated levels of TCDD in blood lipids did not manifest any gastric or skin symptoms. Becher has reported a higher risk of cancer incidence after long-term exposure to dioxins [16].

Distant results of heavy exposure that demonstrates high heterogeneity were observed in the population of Seveso, Italy, which in 1979 experienced an industrial catastrophe. Among the effects of dioxins are: endocrinological disturbances [17, 18] in the form of alteration in TSH and T_3, T_4 blood level, altered immunity response [19] (particularly to inflammatory factor [1]), and cardio-vascular disorders [1, 20]. A recent study revealed that dioxins may cause oxidizing stress and present cardiotoxicity in the form of connective tissue hypertrophy. Affected lung function and their inflammatory disorders [1, 17, 18] were also observed after exposure.

They are also known for leading to thymus involution developmental growth disorders, infection susceptibility, hyper pigmentation and sexual function disturbances [21].

Significant prevalence of complete cleft of palate [22] and neuromotoric disorders were noticed among the population of children living in an area of high-level dioxin contamination [23]. Cases of chlorine acne (not only in children) were also observed [24].

Some authors report a close relationship between dioxin pollution and infertility, as well as miscarriages [6, 8, 14]. The influence of dioxins on reproductive processes may be related to their xenobiotic nature (hormone alike) through aryl hydrocarbon receptors (AhR). This receptor has suppressive action onto genes, liable for estrogen receptor synthesis [25].

Most observations concerning distant and indirect effects of dioxins are derived from studying rats. Appreciable decreases in body weights among individuals exposed on dioxins were observed. Cahexy was a commonly occurring condition that impaired skeletal development as well as behavioural disorders. Most individuals showed reproductive disorders related to confirmed dysfunction of gonads due to hormonal disturbances [14, 17].

The influence of dioxins on humans, especially on oral health, was evaluated in the study performed by Alaluusua [26]. The author analyzed oral health in the population of Seveso (Italy). The region was contaminated in the past by dioxins, mainly TCDD, released during the explosion of a reactor with triclorophenol. The catastrophe took place 25 years before the study was performed. Dioxins were spread over 18 km^2. 93% of examined participants in this study were 5 years old at the time of the explosion. The oral examination performed 25 years later showed developmental disorders, including neonatal teeth, hypodontia, impaired development of crowns and roots, and numerous defects of enamel in permanent dentition. It was also observed that the most susceptible to environmental pollution with TCDD was the enamel of children aged 5 to 7 years [26].

Experimental studies performed on rats confirmed these observations, revealing that dioxins cause various changes in the morphology and structure of the teeth in these animals [27]. The examination of teeth showed commonly

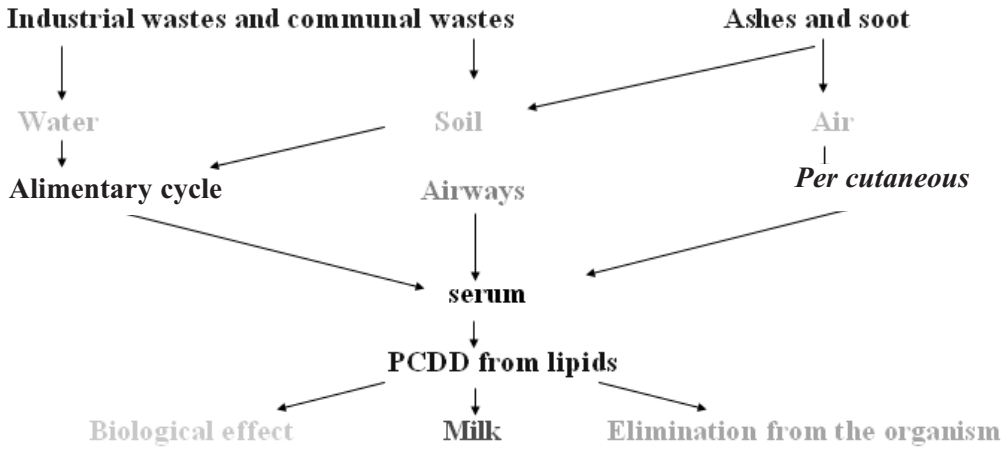

Fig. 3. Sources of natural environmental contamination [1].

Table 1. Toxicity of dioxins (TCDD) to different animal species' teeth [28].

Animal species	Defect
rat	Aberrant shape and reduced size
rat	Arrest of third molar development
rat	Arrested root development
rat	Disturbed dentin formation
rat	Enamel colour defect
rat	Increased eruption rate
rat	Pulpal perforation
rat	Reduced mesio-distal dimension
mouse	Disturbed morphogenesis, formation and mineralization of tooth
Rhesus monkey	Hypodontia
Rhesus monkey	Hypomineralization
Rhesus monkey	Squamous metaplasia of ameloblasts
Rainbow trout	Anodontia

existing perforations on the incisal edge of anterior teeth, reaching the pulp chamber and grey and mottled discoloration. Histological analysis showed a decrease in the dentine thickness, which caused the enlargement of the pulp chamber. The pulp chambers were also very irregular in their shapes. The enamel was hypoplastic, pigmented and poorly mineralized. It was also proved that TCDD accelerates eruption of the incisors in mice [28, 29].

TCDD disturbs normal amelogenesis and dentinogenesis and promotes the formation of various morphological abnormalities such as a thin layer of the dentine and enamel, which leads to pathological attrition and consecutive pulp chamber perforations. It may also disturb maturation of the enamel matrix and inhibit development of the crowns and roots [30].

There is also evidence that dioxins cause an accumulation of iron, which results in characteristic brown and yellowish discoloration of the teeth, especially in precocious incisors [30].

It has been also proved that dioxins influence hormonal systems leading to hormonal disorders. The affection of parathyroids results in calcium and phosphate disturbances which eventually may impair mineralization of the hard dental tissues of the teeth. A reduction in the diameter of the skull in exposed rats was also observed [27].

Some researchers assessing permanent dentition in exposed animals (Table 1) showed that exposure during the perinatal period caused consecutive developmental disorders such as significant acceleration in incisor eruption, delays in molar eruption and common absence of third molars. Yasuda [31] made similar observations concerning premature teeth eruption, impaired mineralization and hypodontia in rhesus monkeys.

It was also proved that exposure to TCDD caused increased caries susceptibility in rats fed a cariogenic diet. The lesions were present mainly in second and third molars.

A study performed in Japanese children whose mothers worked in the chemical industry and were exposed to dioxins (PCBs) showed increased susceptibility to caries and brittleness of hard dental tissues. The prevalence of developmental disorders such as confluent teeth was also more common in these children [32].

Conclusion

It is evident on the basis of various studies that environmental exposure to dioxins may result in multiorgan functional and morphological disorders, including multiple teeth disorders, especially if the exposure takes place in developmental stage of life. The effects of exposure can also manifest themselves over a long period of time.

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