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Review

Dioxins: An overview

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Abstract

This review article summarizes what is known about human health following exposure to dioxins. It is meant primarily for health professionals but was also written with the general public in mind. The need for such an article became apparent to the authors following media inquiries at the time the then Ukraine presidential candidate Victor Yushchenko was deliberately poisoned with the most toxic dioxin, tetrachlorodibenzodioxin or TCDD.

Keywords: Dioxins; Poisoning; Yushchenko; Agent orange; TCDD

Dioxins have been featured in the news recently following a poisoning incident in Europe (British Broadcasting Corp. (BBC), 2004; Chivers, 2004; Fackelmann, 2004). Because physicians are not usually taught much about dioxins, this article attempts to provide an overview for practicing physicians. Dioxins are unwanted contaminants almost exclusively produced by industrial processes, including incineration (Olie, 1980; Environmental Protection Agency (EPA), 2004), chlorine bleaching of paper and pulp, and the manufacture of some pesticides, herbicides, and fungicides (Gilpin et al., 2003). Small amounts are synthesized for scientific research. Dioxins and dioxin-like chemicals form a large group of compounds which are structurally related, are environmentally and biologically persistent, induce a common spectrum of responses, and have a common mechanism of action (Van den Berg et al., 1998). This group includes polychlorinated dibenzo-*p*-dioxins (PCDDs), dibenzofurans (PCDFs), biphenyls (PCBs), and related compounds. Dioxins did not exist prior to industrialization except in very small amounts due to natural combustion and geological processes (Czuczwa et al., 1984; Schecter et al., 1988; Ferrario and Byrne, 2000). Today they are found in all humans, with higher levels commonly found in persons living in more industrialized countries (Schecter and Gasiewicz, 2003). These compounds are of concern to both public health workers and clinicians because of the many types of illnesses, both overt and subclinical, they may cause (World Health Organization (WHO), 1997; Centers for Disease Control (CDC), 1998, 2004; Institute of Medicine (IOM), 2001, 2005; Schecter and Gasiewicz, 2003; EPA, 2004).

Dioxins consist of two benzene rings connected by two oxygen atoms and contain four to eight chlorines, for a total of up to 75 compounds or congeners. Fig. 1 shows the chemical structures of a dioxin, a PCDF, and a PCB. The toxic dioxins and PCDFs have chlorines on the 2, 3, 7, and 8 positions. PCDDs, PCDFs, and some PCBs have been assigned dioxin toxic equivalency factors (TEFs) based upon their relative potency compared to the most toxic dioxin, 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD), which is assigned a TEF of 1 (Van den Berg et al., 1998). Some of the less potent dioxin-like PCBs have TEF values of only 0.0001; however, they may still be of concern as they are present in much larger amounts than dioxins. Unlike the measured dioxin levels, TEFs may change over

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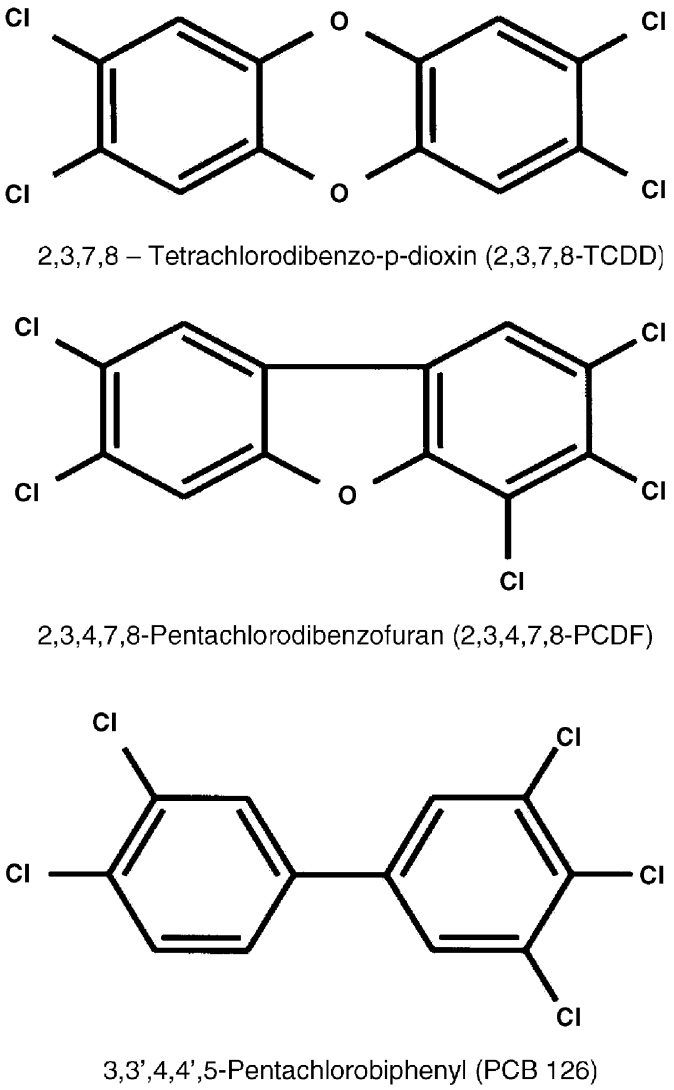

Fig. 1. Chemical structure of a selected dioxin, dibenzofuran, and PCB.

Table 1
World Health Organization (WHO) dioxin toxic equivalency factors (TEFs)

		WHO TEF
Dioxins	2,3,7,8-Tetra-CDD	1
	1,2,3,7,8-Penta-CDD	1
	1,2,3,4,7,8-Hexa-CDD	0.1
	1,2,3,6,7,8-Hexa-CDD	0.1
	1,2,3,7,8,9-Hexa-CDD	0.1
	1,2,3,4,6,7,8-Hepta-CDD	0.01
	OCDD	0.0001
Dibenzofurans	2,3,7,8-Tetra-CDF	0.1
	1,2,3,7,8-Penta-CDF	0.05
	2,3,4,7,8-Penta-CDF	0.5
	1,2,3,4,7,8-Hexa-CDF	0.1
	1,2,3,6,7,8-Hexa-CDF	0.1
	1,2,3,7,8,9-Hexa-CDF	0.1
	2,3,4,6,7,8-Hexa-CDF	0.1
	1,2,3,4,6,7,8-Hepta-CDF	0.01
	1,2,3,4,7,8,9-Hepta-CDF	0.01
	OCDF	0.0001
Coplanar PCBs	3,3′,4,4′-TCB (77)	0.0001
	3,4,4′,5-TCB (81)	0.0001
	3,3′,4,4′,5-PeCB (126)	0.1
	3,3′,4,4′,5,5′-HxCB (169)	0.01
Mono-*ortho*-PCBs	2,3,3′,4,4′-PeCB (105)	0.0001
	2,3,4,4′,5-PeCB (114)	0.0005
	2,3′,4,4′,5-PeCB (118)	0.0001
	2′,3,4,4′,5-PeCB (123)	0.0001
	2,3,3′,4,4′,5-HxCB (156)	0.0005
	2,3,3′,4,4′,5′-HxCB (157)	0.0005
	2,3′,4,4′,5,5′-HxCB (167)	0.00001
	2,3,3′,4,4′,5,5′-HpCB (189)	0.0001

time as new data become available; they are order-of-magnitude consensus estimates based on all the available data.

The total dioxin toxic equivalency (TEQ) value expresses the toxicity as if the mixture were pure TCDD. The TEQ concept was first developed in New York by the State Health Department in a series of experiments in response to the need for reentry criteria of an office building contaminated by a mixture of PCBs, PCDFs, and dioxins following an electrical transformer fire (Eadon et al., 1986). The TEQ approach and current values (Table 1) have been adopted internationally as the most appropriate way to estimate the potential health risk of mixtures of dioxins (Van den Berg et al., 1998).

The gold standard since the 1980s for diagnosis of dioxin exposure has been congener-specific high-resolution gas chromatography high-resolution mass spectrometry (HRGC-HRMS), a method first used for detection of TCDD in the 1970s for human milk and for fish exposed to dioxin-contaminated Agent Orange in Vietnam (Baughman and Meselson, 1973). Later, in the 1980s, HRGC-HRMS was used to identify dioxin and PCDF congeners in adipose tissue, human milk, and blood; all human and tissues studied to date by this methods have measurable dioxins and PCDFs (Schecter and Tiernan, 1985; Ryan et al., 1987; Schecter and Ryan, 1992). This method is now used by most dioxin laboratories worldwide, including the CDC, the US Air Force, and the WHO for dioxin exposure assessment (Michalek et al., 1990; Fingerhut et al., 1991; WHO, 1996). In addition, bioassays and immunoassays are also sometimes employed as less expensive and relatively rapid screening methods for determination of total TEQ in environmental and biological samples (Ziccardi et al., 2000). However, HRGC-HRMS remains the only way to measure specific dioxin congener levels (Rappe et al., 1979; Schecter and Tiernan, 1985; Schecter et al., 1985). There are a relatively small number of laboratories worldwide which have been certified by the WHO for the analysis of dioxins in blood (WHO, 2000).

The most toxic dioxin, TCDD (Fig. 1), became well known as a contaminant of Agent Orange herbicide used in the Vietnam war (IOM, 2005). Dioxins were found in Times Beach, Missouri (Kimbrough et al., 1977), in Love