CHLORINATED DIOXIN, DIBENZOFURAN AND PCB LEVELS IN HUMAN FETAL TISSUE AT 8-18 WEEKS GESTATIONAL AGE, COMPARED WITH PLACENTAL, NEWBORN AND ADULT TISSUE LEVELS

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ABSTRACT: Data on human tissue levels of dioxin, dibenzofuran and PCB congeners are increasing rapidly. However, little data exists on fetal levels of these compounds. This data is potentially of interest because dioxins and their structural analogues are known to affect fetal tissue development. This has been demonstrated in toxicology studies showing increase in rates of spontaneous fetal death in utero abortions, and congenital malformations. Recent data suggests altered hormone levels as well as learning disabilities in the offspring of maternally exposed animals and humans. We present data from gestational age 8 to 18 weeks in 3 pooled specimens of whole fetal tissue. This will be compared with levels in stillborn and adult tissue and with levels considered of possible toxicological relevance based on a review of the published toxicology, epidemiology and clinical literature.

KEY WORDS: Dioxins, Dibenzofurans, PCBs, Human Fetal Tissue

INTRODUCTION: Human fetal tissue was collected from a New York health care facility in an anonymous fashion from tissue which was scheduled to be discarded after medical termination of pregnancies. Each whole fetal tissue, without placenta, was collected and labeled in a separate container. Tissue was frozen and shipped to the analytic laboratory where tissue was combined by gestational time, homogenized and analyzed by high resolution GC-MS as previously described in detail by the laboratory[(1)]. The laboratory had previously established its competency in human tissue analysis in WHO interlaboratory comparison studies.

TABLE I: COMBINED 8-14 WEEK POOLED HUMAN FETAL (N=10) AND STILLBORN LIVER SAMPLES (N=3) (pg/g, lipid)

Congeners	I-TEF	Fetus measured	Fetus TEq	Stillborn Livers* measured	Stillborn Livers* TEq
2,3,7,8-TCDD	1	1.40	1.40	3.03	3.03
1,2,3,7,8-PeCDD	0.5	2.00	1.00	6.63	3.32
1,2,3,4,7,8,-HxCDD	0.1	2.30	0.23	4.13	0.41
1,2,3,6,7,8-HxCDD	0.1	8.90	0.89	5.27	0.53
1,2,3,7,8,9-HxCDD	0.1	1.70	0.17	3.03	0.30
1,2,3,4,6,7,8-HpCDD	0.01	22.90	0.23	16.00	0.16
OCDD	0.001	98.80	0.10	62.33	0.06
2,3,7,8-TCDF	0.1	1.30	0.13	0.87	0.09
2,3,4,7,8-PeCDF	0.5	1.10	0.55	2.40	1.20
1,2,3,7,8,-PeCDF	0.05	nd(0.40)	nd(0.02)	1.23	0.06
1,2,3,4,7,8-HxCDF	0.1	2.20	0.22	4.60	0.46
1,2,3,6,7,8-HxCDF	0.1	1.00	0.10	2.63	0.26
1,2,3,7,8,9-HxCDF	0.1	nd(0.70)	nd(0.08)	nd(0.30)	nd(0.03)
2,3,4,6,7,8-HxCDF	0.1	1.50	0.15	0.57	0.06
1,2,3,4,6,7,8-HpCDF	0.01	3.10	0.03	4.43	0.04
1,2,3,4,7,8,9-HpCDF	0.01	nd(1.70)	nd(0.02)	nd(0.33)	nd(0.00)
OCDF	0.001	nd(6.40)	nd(0.01)	nd(0.50)	nd(0.00)
TOTAL PCDDs		138.00	4.02	100.42	7.81
TOTAL PCDFs		14.80	1.24	17.30	2.18
TOTAL PCDD/Fs		153.00	5.26	117.72	9.99

nd=not detectable, detection limit in ( ), one half of the value used for calculation
Fetal lipid=0.647%, Stillborn lipid=3.7%
*Ref 2

RESULTS: The results are shown in a series of tables for data available at time of submission of this paper. Three additional analyses of whole fetal tissue at various gestational times from 8 to 18 weeks for PCDD/Fs and coplanar PCBs will be completed and presented at Dioxin 95. Table I shows PCDD/F levels and TEQs for the first pooled analysis of whole human tissue presenting measured congeners and also dioxin toxic equivalents. It also compares this with previously obtained stillborn liver data,[2] from south of Vietnam, where human tissue PCDD/F levels are currently about the same as US levels. The lipid percent for the whole fetal tissue is a relatively low 0.647. By way of comparison, Table II shows PCDD/F levels in adult human blood, milk and placental tissue, all from the United States.[3] Congener specific measured levels are shown, as well as calculated dioxin toxic equivalents. For ease of comparison, Table III shows total PCDDs, total PCDFs, and total PCDD/Fs for dioxin toxic equivalents only, for adult blood, milk and adipose tissue, pooled American placentas and the pooled placental data.[4,5] Last, Table IV, after Williams Textbook of

Obstetrics, lists approximate gestational age at which selected fetal malformations can occur. This is for reference only, to point out the potential significance of any agent, including dioxins, viruses, etc., which might affect organogenesis at different fetal time periods.

TABLE II: AVERAGE CONCENTRATIONS AND TOXIC EQUIVALENCY OF DIOXINS AND DIBENZOFURANS IN BLOOD, HUMAN MILK AND PLACENTAL TISSUE IN U.S. GENERAL POPULATION (ppt, lipid)

		Blood = Mean value (n=50)		Human Milk* (n=43)		Pooled American ** Placentas (n=14)	
Congener	TEF	Measured	TEq	Measured	TEq	Measured	TEq
2,3,7,8-TCDD	1	3.8	3.8	3.3	3.3	2.4	2.4
1,2,3,7,8-PeCDD	0.5	9.3	4.65	6.7	3.35	4.0	2
1,2,3,4,7,8-HxCDD	0.1	9.8	0.98	6.0	0.6	2.4	0.24
1,2,3,6,7,8-HxCDD	0.1	72.1	7.21	6.2	0.62	15.9	1.59
1,2,3,7,8,9-HxCDD	0.1	11.9	1.19	30.5	3.05	3.2	0.32
1,2,3,4,6,7,8-HpCDD	0.01	118.6	1.186	42.0	0.42	36.2	0.362
OCDD	0.001	793.9	0.7939	233.0	0.233	282.1	0.2821
2,3,7,8-TCDF	0.1	2.3	0.23	2.9	0.29	1.9	0.19
2,3,4,7,8-PeCDF	0.5	8.8	4.4	7.3	3.65	3.6	1.8
1,2,3,7,8-PeCDF	0.05	1.2	0.06	0.5	0.025	<1.0	0.025
1,2,3,4,7,8-HxCDF	0.1	10.6	1.06	5.6	0.56	4.0	0.4
1,2,3,6,7,8-HxCDF	0.1	6.9	0.69	3.2	0.32	2.0	0.2
2,3,4,6,7,8-HxCDF	0.1	2.8	0.28	1.9	0.19	nd (1.0)	0.05
1,2,3,7,8,9-HxCDF	0.1	2.8	0.28	NA	NA	1.7	0.17
1,2,3,4,6,7,8-HpCDF	0.01	19.6	0.196	4.1	0.041	6.3	0.063
1,2,3,4,7,8,9-HpCDF	0.001	3.1	0.0031	4.1	0.0041	<1.0	0.005
OCDF	0.001	9.3	0.0093	4.1	0.0041	<5.0	0.003
Total PCDDs		1019.3	19.8	327.7	11.6	346.2	7.2
Total PCDFs		67.4	7.2	33.7	5.1	23.5	2.9
Total PCDD/Fs		1086.8	27.0	361.4	16.7	369.7	10.1

NA = not available

"<" = half of < value was used to calculate totals and TEq

* = average value of two pooled samples: Binghamton, NY (n=21) and Los Angeles, CA (n=22)

** ERGO analysis

After: Schecter, A. Dioxins and Health. New York, NY: Plenum Publishing Corporation 1994. pp449-486.

TABLE III: TOTAL PCDD/F TOXIC EQUIVALENTS IN U.S. HUMAN BLOOD, MILK 1982 AND 1987 ADIPOSE TISSUE, PLACENTAL AND FETAL TISSUE (ppt, lipid)						
Compound	Blood (n=50)	Milk (n=43)	Adipose '82 (n=827)	Adipose '87 (n=865)	Pooled American Placentas (n=14)	Pooled Fetal Tissue(n=10)
Total PCDDs	19.8	11.6	29.6	21.2	7.2	4.0
Total PCDFs	7.2	5.5	16.5	5.1	2.9	1.2
Total PCDD/Fs	27.0	17.0	46.1	26.3	10.1	5.3

After: Schecter,A. Dioxins and Health. New York, NY: Plenum Publishing Corporation 1994. Adipose data from ref.4 and 5.

TABLE IV: APPROXIMATE PERIOD OF GESTATION DURING WHICH SELECTED FETAL MALFORMATIONS CAN OCCUR	
TIME FROM CONCEPTION	MALFORMATION
Week 3-4	Anencephaly, meningomyelocele, cyclopia, sirenomelia
Week 5	Transposition of great vessels, cleft lip, limb reduction defects
Week 6-8	Diaphragmatic hernia, rectal atresia, ventricular septal defect, syndactyly
Week 7	Congenital heart disease, limb reduction defects
Week 8	Congenital heart disease
Week 9	Cleft Palate
Week 10	Omphalocele
Week 12	Hypospadias

After: Williams Obstetrics, 17th Ed; Eds: Pritchard, MacDonald, Gant; Appleton-Century Crofts, Norwalk, Conn., 1985

DISCUSSION: We present measured dioxin and dibenzofuran levels in whole human fetal tissue. We calculate that, if the fetus' weighed from 0.001 to 0.1 kg, on average, at 8 and 14 weeks, respectively, published average values, the TEQ would be 5.2 ng/kg lipid and 0.00034 to 0.0034 ng total body burden. These findings demonstrate the existence, at the

levels measured, for these congeners in fetal tissue for these time periods in American fetal tissue and transplacental transfer from mother to fetus. The levels are lower than in adult tissue on a lipid basis, and still lower on a per kilogram basis, considering the low lipid content of the tissue. The levels in fetal tissue will be further characterized at Dioxin 95 by presentation of additional data from three more analyses at three time periods of importance on organogenesis between 8 and 18 weeks gestational age. These levels will be compared with dosing levels from dioxin, dibenzofuran and PCB reproductive and developmental literature.

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