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E. 研究発表

1.論文発表

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F. 知的所有権の取得状況

なし

表１：TCDD及び類縁化合物の消化管吸収

物質	動物（性）	用量		投与媒体	吸収率(%)	文献
		μmol/kg	μg/kg			
2,3,7,8-TCDD	SD rat (M)	0.16	50	acetone:corn oil (1:7)	70	Piper et al. 1973
2,3,7,8-TCDD	SD rat (M/F)	0.003	1	acetone:corn oil (1:25)	84 (66-93)	Rose et al. 1976
2,3,7,8-TCDD	Hartley guinea pig (F)	0.005	1.45	acetone:corn oil (1:45)	50	Nolan et al 1979
2,3,7,8-TCDD	Golden Syrian hamster (M)	2	650	olive oil	74	Olson et al 1980
2,3,7,8-TCDD	Human (M)	0.000003	0.001	olive oil	87	Poiger and Schlatter 1986
1.2,3,7,8-PCDD	SD rat (M/F)	0.03	9.2	olive oil	NR (19-71)	Wacker et al 1986
OCDD	Fischer 344 rat (M)	0.11	50	DCB:Emulphor (1:1)	12	Virnbaum and Couture 1988
		1.1	500	DCB:Emulphor (1:1)	15	
		1.1	500	corn oil	2	
		11	5000	corn oil	5	

なお、2,3,7,8-TCDDを約20ng/ratをエタノール、土壌中懸濁（10-15時間および8日間）および活性炭懸濁液に溶解或いは吸着させて投与したところ、肝への分布量はそれぞれ投与量の36.7%, 24.1%, 16%, および0.07%以下であったPoiger and Schlatter (1980)。

また、ラットに3-1450ng/kgのTCDDをTimes Beach soilに混和し投与したところ吸収率は43±4%であった(Shu et al 1988)。

表２：2,3,7,8-置換PCDDsとPCDFsのヒト肝臓及び脂肪中の濃度

	脂肪含量あたりの濃度			湿重量あたりの濃度(ppt)	
	脂肪	肝臓	肝臓/脂肪	肝臓a	肝臓/脂肪
TeCDD	8.0	16.4	2.05	1.1	0.14
PeCDD	16.4	20.1	1.22	1.4	0.09
HxCDD	94.7	166.8	1.76	11.7	0.12
HpCDD	106.7	1002.4	9.39	70.2	0.66
OCDD	373.2	4416.2	11.83	309.1	0.83
TeCDF	2.5	5.5	2.20	0.4	0.15
PeCDF	35.2	173.7	4.93	12.2	0.35
HxCDF	41.5	389.5	9.38	27.3	0.66
HpCDF	14.2	218.9	15.42	15.3	1.08
OCDF	4.0	29.7	7.43	2.1	0.52

Thoma et al 1990
ミュンヘン地区の２８人の平均値
a: 肝臓の脂肪を7.02%として計算
TeCDD: tetrachlorodibenzodioxin, PeCDD: Pentachlorodibenzodioxin
HeCDD: hexachlorodibenzodioxin, HpCDD: heptachlorodibenzodioxin
OCDD: octachlorodibenzodioxin, TeCDF: tetrachlorodibenzofuran
PeCDF: pentachlorodibenzofuran, HxCDF: hexachlorodibenzofuran
HpCDF: heptachlorodibenzofuran, OCDF: octachlorodibenzofuran

表３：ダイオキシン類の日本人の血液、脂肪及び肝臓中の濃度

	脂肪含量あたりの濃度(pg/g lipid)								
	血液	脂肪	肝臓	脳	筋肉	脂肪/血液	肝臓/血液	脳/血液	筋肉/血液
2,3,7,8-TeCDD	2.6	3.5	2.2	0.36	4.6	1.35	0.85	0.14	1.77
1,2,3,7,8-PeCDD	13	17.0	13.0	1.50	17.0	1.31	1.00	0.12	1.31
1,2,3,4,7,8-HeCDD	11	7.0	20.0	0.18	5.7	0.64	1.82	0.02	0.52
1,2,3,6,7,8-HeCDD	63	96.0	150.0	2.10	80.0	1.52	2.38	0.03	1.27
1,2,3,7,8,9-HeCDD	-	17.0	33.0	0.71	17.0				
1,2,3,4,6,7,8-HpCDD	100	78.0	760.0	4.70	79.0	0.78	7.60	0.05	0.79
OCDF	2000	2500.0	19000.0	15.00	1200.0	1.25	9.50	0.01	0.60
2,3,7,8-TeCDF	5.2	2.3	10.0	0.90	5.7	0.44	1.92	0.17	1.10
1,2,3,7,8-PeCDF	2	0.6	6.6	1.10	2.1	0.29	3.30	0.55	1.05
2,3,4,7,8-PeCDF	46	42.0	220.0	6.60	35.0	0.91	4.78	0.14	0.76
1,2,3,4,7,8-HxCDF	32	13.0	290.0	6.00	12.0	0.41	9.06	0.19	0.38
1,2,3,6,7,8-HxCDF	34	12.0	340.0	1.60	8.7	0.35	10.00	0.05	0.26
1,2,3,7,8,9-HxCDF	-	-	-	-	1.8				
2,3,4,6,7,8-HxCDF	-	-	-	-	2.8				
1,2,3,4,6,7,8-HpCDF	8.2	5.1	89.0	0.66	6.1	0.62	10.85	0.08	0.74
1,2,3,4,7,8,9-HpCDF	-	0.4	10.0	0.05	-				
OCDF	-	1.2	10	1.30	27				
3,3',4,4'-TeCB	15	6.6	17	8.90	45	0.44	1.13	0.59	3.00
3,3',4,4',5-PeCB	79	180	310	40.00	200	2.28	3.92	0.51	2.53
3,3',4,4',5,5'-HxCB	47	130	66	18.00	130	2.77	1.40	0.38	2.77
Total TEQ	59	76	270	11.00	68	1.29	4.58	0.19	1.15

８人の通常の日本人（19-82 才）の平均値

Iida et al (1999)

表４：TCDD 投与後３日目の組織中分布（Fischer 雄ラット、３ケ月令）

組織	経口投与		静脈内投与		気管内投与	
	pmol/g	%	pmol/g	%	pmol/g	%
肝臓	6.523	(24.406)	10.216	(36.894)	8.987	(32.876)
脂肪組織	2.082	(26.239)	1.830	(20.840)	1.348	(14.907)
皮膚	0.448	(7.361)	0.294	(4.597)	0.281	(4.269)
筋肉	0.039	(1.788)	0.057	(2.474)	0.029	(1.252)
血液	0.025	(0.205)	0.031	(0.243)	0.023	(0.172)
腎臓	0.160	(0.110)	0.142	(0.097)	0.113	(0.077)
副腎	0.705	(0.012)	0.686	(0.012)	0.507	(0.008)
胸腺	0.918	(0.046)	0.569	(0.028)	0.435	(0.023)
脳	0.045	(0.029)	0.030	(0.019)	0.024	(0.015)
脾臓	0.143	(0.028)	0.359	(0.071)	0.086	(0.018)
精巣	0.046	(0.042)	0.034	(0.030)	0.027	(0.024)
肺	0.393	(0.130)	0.612	(0.205)	0.238	(0.081)
心臓	0.103	(0.028)	0.081	(0.021)	0.062	(0.016)
胃	0.261	(0.108)	0.224	(0.082)	0.171	(0.057)
小腸	0.250	(0.111)	0.421	(0.290)	0.298	(0.228)
大腸	0.317	(0.133)	0.307	(0.118)	0.242	(0.087)
小腸内容物	0.210	(0.288)	0.418	(0.540)	0.296	(0.376)
大腸内容物	2.164	(1.877)	3.473	(1.937)	2.672	(1.362)
糞		(32.175)		(22.222)		(26.260)
尿		(1.401)		(2.169)		(1.338)
回収率		(96.382)		(92.820)		(83.436)

TCDD はそれぞれ 1nmol (0.32μg)/kg 投与した。

Diliberto et al (1996)

表５：TCDDの排泄半減期

動物種	半減期	備考	文献
ハムスター(Syrian	14.95日		Olson et al (1980b)
ラット (SD)	♂：12日，♀：14日		Fries and Marrow (1975)
ラット (SD)	♂：17日		Piper et al (1973)
モルモット	94日		Olson (1986)
サル	391日	低用量の慢性暴露	Bowman et al (1989b)
サル	約1年		NcNulty et al (1982)
ヒト	5.8年	男性志願者	Poiger and Schlatter
ヒト	8.7年	ベトナム参戦兵士	Michalek et al (1996)
ヒト	7.2年	殺虫剤工場労働者	Flesch-Janys et al (1996)
ヒト	8.2年	セベソ住人	Needham et al (1994)

表６：TCDD及び類縁化合物の主要蓄積臓器からの消失

化学物質	動物種（性）	用量	組織	半減期（日）	注	文献
TCDD	Wistar rat (F)	0.3ug/kg sc	肝臓	11.5	10-49日	Abraham et al 1988
			肝臓	16.9	49-91日	
			肝臓	13.6	10-91日	
			脂肪	24.5	14-91日	
TCDD	Wistar rat (M)	1.0ug/kg sc	肝臓	37.1	20週	Lakshmanan et al 1986
			脂肪	53.2		
TCDD	SD-rat (M)	餌中7 or 20ppb 42日	肝臓	11		Fries and Marrow 1975
TCDD	SD-rat (F)	餌中7 or 20ppb 42日	肝臓	13		
TCDD	C57BL/6J mice (M)	0.5ug/kg ip	肝臓	8.5		Birunbaum 1986
			脂肪	10.3		
			皮膚	16		
TCDD	C57BL/6J mice (F)	0.5ug/kg ip	肝臓	7.1		
			脂肪	7.6		
			皮膚	14.9		
TCDD	DBA/2J mice (M)	0.5ug/kg ip	肝臓	12.4		Birunbaum 1986
			脂肪	13.3		
			皮膚	13.2		
TCDD	DBA/2J mice (F)	0.5ug/kg ip	肝臓	11.9		
			脂肪	11.8		
			皮膚	12.8		
TCDD	rhesus monkey (F)	餌中25ppt	脂肪	391		Bowman et al 1989
OCDD	Fischer 344 rat (M)	50ug/kg iv	肝臓	84		Birunbaum and Couture 1988
			脂肪	38		
			皮膚	3	第1相	
				69	第2相	

表７：TCDD及び類縁化合物のマーモセット肝臓及び脂肪組織からの消失定数と半減期

化学物質名	肝臓		脂肪組織	
	Ke (1/週)	半減期(週)	Ke (1/週)	半減期(週)
TCDD	0.0841 ± 0.0109	8.3	0.0658 ± 0.0072	10.5
1,2,3,7,8-PeCDD	0.0649 ± 0.0101	10.7	0.0490 ± 0.0057	14.2
1,2,3,4,7,8-H6CDD	0.0702 ± 0.0059	9.9	0.0411 ± 0.0083	16.9
1,2,3,6,7,8-H6CDD	0.0558 ± 0.0046	12.4	0.0373 ± 0.0073	18.6
1,2,3,7,8,9-H6CDD	0.0767 ± 0.0078	9.0	0.0525 ± 0.0089	13.2
1,2,3,4,6,7,8-HpCDD	0.0518 ± 0.0081	13.4	0.0372 ± 0.0060	18.6
OCDD	0.0089 ± 0.0084	78.0	0.0122 ± 0.0093	101.0

Neubert et al 1990

CDD/CDF混合物を単回皮下投与した。CDFについてのデータは割愛した。

表８：母乳中塩素化ダイオキシン類の濃度(平均値 ng/kg milk fat)

	The Netherlands[a] N=35	Canada[b] N=96	USA[c] N=42	Germany[d] N=526	Siberia[e] N=23	United Kingdom[e] N=57	South Vietnam (1973)[f] N=7	Cambodia[c] N=8
2,3,7,8-TCDD	3.8	2.3	3.3	3.2	2.7	5.6	131.0	0.49
1,2,3,7,8-PeCDD	10.6	4.8	6.7	10.1	3.3	13.0	ND	1.6
1,2,3,4,7,8-HxCDD	1.3	34.5[f]	4.9	8.4	1.8	62.0[f]	70.0[f]	0.6
1,2,3,6,7,8-HxCDD	49.1		30.5	35.8	5.6			3.4
1,2,3,7,8,9-HxCDD	6.5	5.4	5.2	8.4	1.2	8.3		1.1
1,2,3,4,7,8,9-HpCDD	54.3	40.5	42.0	14.2	8.1	10.5	99.0	11.0
OCDD	297.5	131.7	233.0	207.9	50.2	287.0	494.0	59.0
Total TEQ for CDDs only[g]	15.6	9.34	11.5	13.9	5.3	20.1	139.5	20.0

[a]Pluim et al. 1994a
[b]Dewailly et al. 1991
[c]Schecter et al. 1991a
[d]Fürst et al. 1994
[e]Duarte-Davidson et al. 1992
[f]For unseparated congeners
[g]See Section 2.5 for additional information

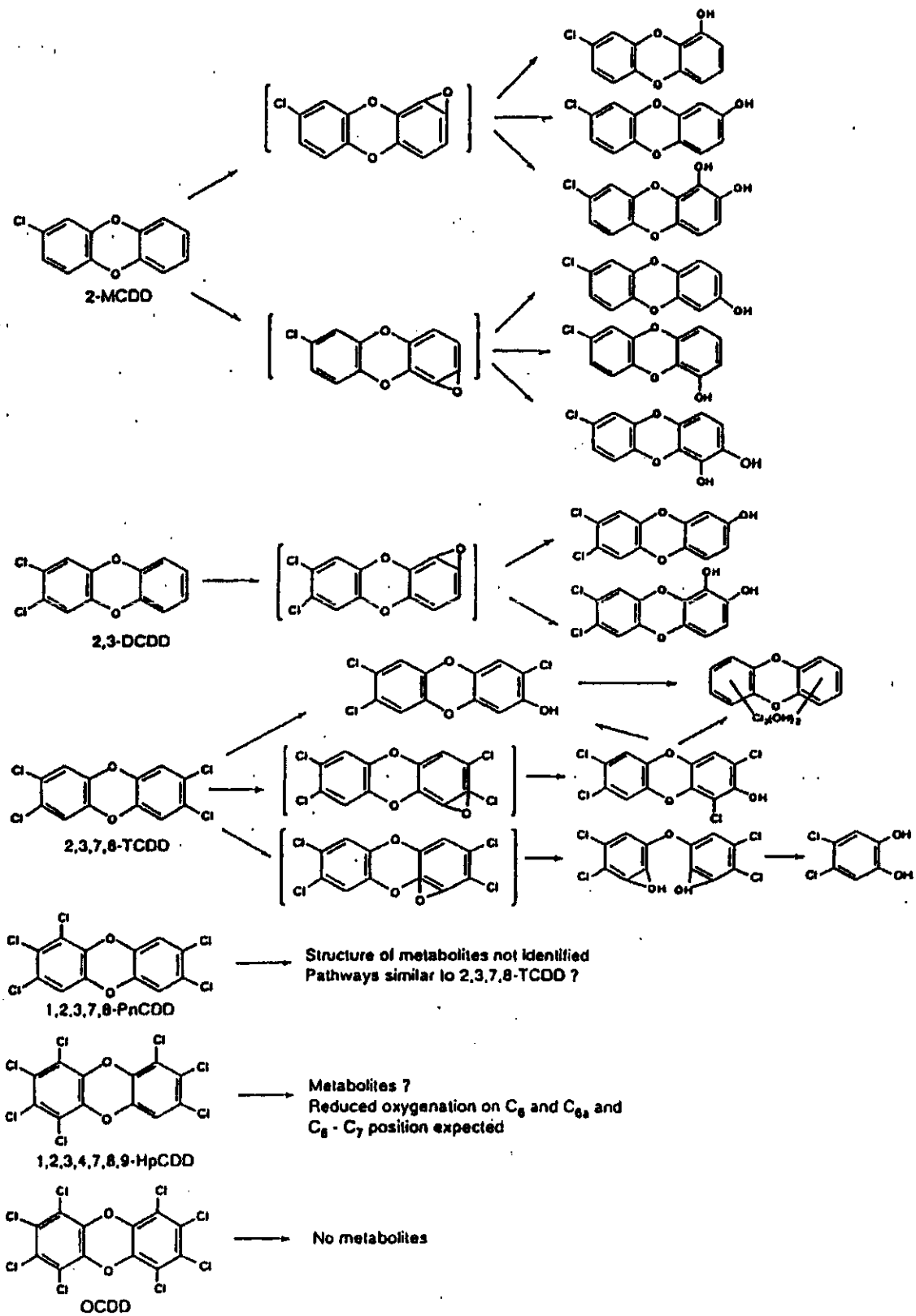
ND = not detected; TEQ = toxicity equivalency

表９：日本人の母乳中ダイオキシン類濃度
油症患者２名(U, W)と一般人４人から母乳をそれぞれ 1988 年および 1989 年採取した母乳について測定した。

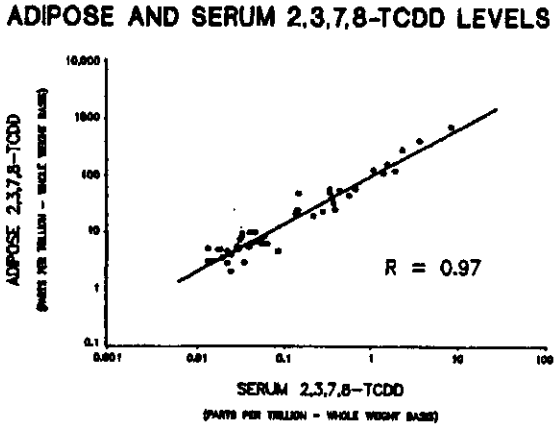
		Concentration, ppb (Whole basis)					
				Control			
		Yusho U	Yusho W	Average	S.D.	Ratio	
	TEF(WHO)	Fat 3.10%	Fat 1.69%	Fat 2.76%		U/Cont	W/Cont
2,3,7,8-Tetra-CDD	1	0.0006	0.0004	0.0004	0.0001	1.58	1.13
1,2,3,7,8-Penta-CDD	1	0.0015	0.0004	0.0007	0.0002	2.23	0.67
1,2,3,4,7,8-Hexa-CDD	0.1	nd	0.0001	0.0001	0.0000	–	0.50
1,2,3,6,7,8-Hexa-CDD	0.1	0.0064	0.0021	0.0018	0.0004	3.66	1.17
1,2,3,7,8,9-Hexa-CDD	0.1	nd	0.0002	0.0002	0.0001	–	0.87
1,2,3,4,6,7,8-Hepta-CDD	0.01	nd	0.0003	0.0007	0.0003	–	0.52
Octa-CDD	0.0001	0.0018	0.0026	0.0043	0.0033	0.41	0.60
Total PCDDs		0.0103	0.0061	0.0075	0.0036	1.36	0.81
2,3,7,8-Tetra-CDF	0.1	0.0015	0.0023	0.0009	0.0005	1.57	2.44
2,3,4,7,8-Penta-CDF	0.5	0.1009	0.0188	0.0178	0.0068	5.66	1.05
1,2,3,7,8-Penta-CDF	0.05	0.0012	0.0028	0.0012	0.0007	1.07	2.37
1,2,3,4,7,8-Hexa-CDF	0.1	0.0117	0.0043	0.0028	0.0010	4.18	1.54
1,2,3,6,7,8-Hexa-CDF	0.1	0.0026	0.0018	0.0008	0.0003	3.12	2.08
1,2,3,7,8,9-Hexa-CDF	0.1	nd	0.0001	0.0001	0.0000	–	1.00
2,3,4,6,7,8-Hexa-CDF	0.1	nd	0.0003	0.0013	0.0015	–	0.27
1,2,3,4,6,7,8-Hepta-CDF	0.01	0.0009	0.0004	0.0005	–	1.67	0.78
1,2,3,4,7,8,9-Hepta-CDF	0.01	nd	nd	–	–	–	–
Octa-CDF	0.0001	nd	nd	0.0002	0.0000	–	–
Total PCDFs		0.1189	0.0308	0.0240	0.0083	4.96	1.28
81 3,4,4'5-Tetra-CB	0.0001	nd	nd	–	–	–	–
77 3,3',4,4'-Tetra-CB	0.0001	0.0041	0.0023	0.0026	0.0004	1.57	0.89
126 3,3',4,4',5-Penta-CB	0.1	0.0056	0.0013	0.0023	0.0008	2.45	0.58
169 3,3',4,4',5,5'-Hexa-CB	0.01	0.0266	0.0045	0.0059	0.0021	4.50	0.77
Total Coplanar PCBs		0.0363	0.0082	0.0100	0.0021	3.64	0.82
105 2,3,3',4,4'-Penta-CB	0.0001	0.0580	0.0589	0.0986	0.0271	0.59	0.60
114 2,3,4,4',5-Penta-CB	0.0005	0.1400	0.0605	0.0545	0.0118	2.57	1.11
118 2,3',4,4',5-Penta-CB	0.0001	0.2435	0.2243	0.3625	0.0961	0.67	0.62
123 2',3,4,4',5-Penta-CB	0.0001	na	na	–	–	–	–
156 2,3,3',4,4',5-Hexa-CB	0.0005	7.5012	1.4594	1.3731	0.4995	5.46	1.06
157 2,3,3',4,4',5'-Hexa-CB	0.0005	2.2126	0.4187	0.4007	0.1468	5.52	1.04
167 2,3',4,4',5,5'-Hexa-CB	0.00001	0.0909	0.0480	0.0593	0.0154	1.53	0.81
189 2,3,3',4,4',5,5'-Hepta-CB	0.0001	0.7473	0.1433	0.1380	0.0493	5.41	1.04
Total Mono-ortho PCBs		10.9935	2.4130	2.4868	0.7107	4.42	0.97
Total PCBs		11.0298	2.4212	2.4967	0.7128	4.42	0.97

三村ら(1999)

図１：塩素化ダイオキシン類のほ乳類での代謝経路



Source: adapted from Van der Berg et al. 1994



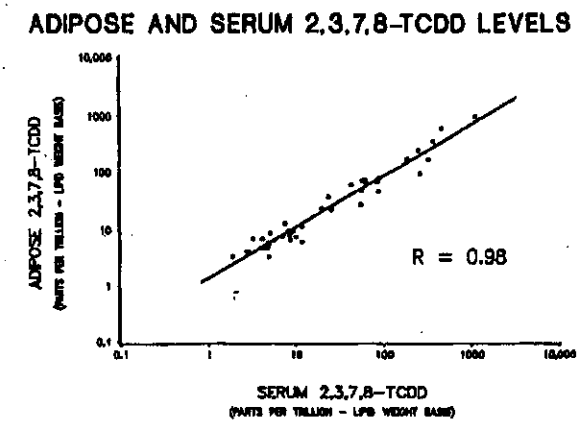


図２：血清中および脂肪中 TCDD 含量の相関
（米国ミズーリ州の住民 50 人の結果。相関係数は湿重量あたりでは 0.97（左図）、脂肪含量あたりでは 0.98 であった（右図）。

Patterson et al (1988)