

PCDDs are in progress. The carcinogenic potentials of PCDFs have not been studied.

2,3,7,8-TCDD is teratogenic in mice and hamsters. The threshold teratogenic dose in mice was estimated to be 0.1 mcg per day (Smith et al, 1976). 2,3,7,8-TCDD has been shown to be fetotoxic in a wide variety of species, including primates. HCDD was teratogenic in rats at a dose of 100 mcg/kg per day (IARC, 1977). There is as yet no data on the fetotoxic potentials of PCDFs in animals.

The toxic effects of 2,3,7,8-TCDD in man are summarized in Table 7. The toxic effects most consistently observed in occupational studies are chloracne, liver dysfunction, neuropsychiatric disturbances, and abnormalities in porphyrin metabolism. Table 8 summarizes the findings of the morbidity studies of workers exposed to 2,3,7,8-TCDD to date. The few follow-up studies which have been done show resolution of gross liver dysfunction and porphyrin abnormalities following removal from exposure. (Pazderova-Vijlupkova et al, 1981; Suskind, 1984).

Several of the occupational exposures occurred as the result of uncontrolled exothermic reactions during the production of trichlorophenol. A similar process accident at Seveso, Italy in 1976 resulted in widespread community exposure to 2,3,7,8-TCDD. Health effects included chloracne, primarily in children, and peripheral neuropathy in a small percent of those exposed (Pocchiari et al, 1979).

The epidemiologic studies on the carcinogenicity of TCDD are summarized in Table 9. While individual occupational mortality studies reveal no excess of cancer, the pooled data suggest an excess of soft tissue sarcoma (Honchar and Halperin, 1981).

Table 7. Toxic Effects of 2,3,7,8-Tetrachlorodibenzo-p-dioxin in Man.^a

Effects

DERMATOLOGICAL

Chloracne

Porphyria cutanea tarda

Hyperpigmentation and
hirsutism

INTERNAL

Liver damage^b

Elevated serum hepatic
enzyme levels

Disorders of fat metabolism

Disorders of carbohydrate
metabolism

Cardiovascular disorders

Urinary tract disorders

Respiratory disorders

Pancreatic disorders

NEUROLOGICAL

Polyneuropathies
(peripheral neuritis)

Lower extremity weakness

Sensory impairments
(sight, hearing, smell,
taste)

PSYCHIATRIC

Neurasthenic or depressive
syndromes

^aSource: Huff, Moore, Saracci, and Tomatis, 1980

^bMild fibrosis, fatty changes, hemofuscin deposition and parenchymal-cell degeneration were observed in a few cases.

TABLE 8. REPORTED OCCUPATIONAL EXPOSURES IN CHLORINATED PHENOLS RESULTING IN HUMAN ILLNESS^a

Year, Place, and chemical(s)	Type of exposure and no. of cases	Effects on the skin	Neurological effects	Effects on the liver and serum lipids	Other effects	References
1936 Michigan Tetrachlorophenol 2-(2-chlorophenyl) phenol	Production 21	Chloracne, hyperkeratosis			Fatigue, weight loss	Butler, 193
1936 Mississippi Tetrachlorophenol	Wood treat- ment 300-400	Chloracne, facial erythema, vesicula- tion, ulceration, hyperkeratosis, hyperpigmentation			Fatigue, colored urine, urinary problems, venous thrombosis	Anonymous, 1936; Sting 1940
1949 West Virginia Trichlorophenol 2,4,5-T	Explosion 117 Production 111	Chloracne, facial erythema, hyper- pigmentation, melanosis	Nervousness, irritability, insomnia, personality change, de- pression, headache, vertigo, pain and weakness lower extrem- ities, paresis, peripheral neuro- pathy, abnormal nerve biopsy (loss of myelin)	Hepatomegaly, ab- normal liver function, toxic hepatitis, elevat- ed triglycerides and cholesterol	Fatigue, weight loss, weakness, decreased libido, impotence, intol- erance to cold, increased sus- ceptibility to infection (es- pecially respir- atory)	Ashe and Suskind, 19 1950; Susk: 1953; Susk: 1977
1949 Germany Trichlorophenol Tetrachlorophenol Pentachlorophenol	Production, Industrial Laboratory 17	Chloracne, hyperpigment- ation, scarring	Lower extremity pain and weak- ness, paresis without atrophy, paresthesia, polyneuritis	Abnormal liver function, cirrhosis	Fatigue, severe bronchitis, de- creased libido, impotence, bursi- tis, myocardial damage	Baader and Bauer, 195

1952 Germany
Trichlorophenol

Production
31

Chloracne,
hyperpigmen-
tation

1953 Germany
Trichlorophenol

Explosion
55

Chloracne

30

1956 France
Trichlorophenol

Production
17

Chloracne

1966 France
Trichlorophenol

Explosion
21

1956 New Jersey
Trichlorophenol

Production
29

Chloracne,
hyperpigmen-
tation, hy-
pertrichosis,
acquired porphy-
ria cutanea tarda

1963 Holland
Trichlorophenol
2,4,5-T

Explosion
106

Chloracne,
facial erythema

Lower extremity pain and weakness, paresthesia, memory and concentration deficits, sleep disturbances, hypsomnolence, abnormal psychological tests (apathy, dulled emotional response)	Toxic hepatitis, abnormal liver biopsy	Fatigue, chronic bronchitis, persistent blepharoconjunctivitis, myocardial damage, intolerance to alcohol	Suskind, 1
Sensory impairment of smell, taste, hearing; tendency to orthostatic collapse, limited paresis, peripheral neuropathy, reading difficulties	Toxic hepatitis	Fatigue, drowsiness, bronchitis, laryngitis, blepharoconjunctivitis, hemorrhagic pleuritis, myocardial damage, increased susceptibility to infection	Goldman,
Peripheral neuropathy	Toxic hepatitis, elevated tryglycerides and cholesterol		Dugois et 1956; Dug et al, 19
Clinical examination normal	Abnormal liver function, abnormal liver biopsies (parenchymal cell degeneration, fluorescence)	Right upper quadrant pain	Bleiberg 1964
No information	Liver function normal	Fatigue	Vos et al

1964 USSR
Trichlorophenol
2,4,5-T

Production
128

Chloracne

1968 England
Trichlorophenol

Explosion
79

Chloracne,
facial
erythema

1965-1968
Czechoslovakia
Trichlorophenol
Pentachlorophenol
2,4,5,-T

Production
80

Chloracne,
hyperpigmenta-
tion, hyper-
trichosis,
scarring, ac-
quired porphyria
cutanea tarda

1969 New Jersey
Trichlorophenol
2,4,5-T
2,4-D

Production
73
Followup of
plant
studied by
Bleiberg
(above)

Chloracne in 48,
hypertrichosis
in 16, hyperpig-
mentation in 30,
no overt por-
phyria cutanea
tarda

1978 England
Trichlorophenol
no longer in
production

Followup of
41 workers
in 1968
explosion
(above)
41

Chloracne

Headache, loss of memory, somnolence, sleeplessness, increased sweating		Fatigue, joint pain, stomach pain	Telegina and Bikbulatova 1970
	Abnormal liver function	Transient glycosuria, mild conjunctivitis	May, 1973; Jensen and Walker, 1966; Jensen et al 1972
Lower extremity weakness and pain, somnolence, headache, insomnia, emotional and psychiatric disorders, peripheral neuropathy (confirmed by abnormal EMG)	Hepatomegaly, abnormal liver function, abnormal liver biopsies (mild steatosis, periportal fibrosis, fluorescence). Elevated triglycerides, phospholipids, and cholesterol	Fatigue, weight loss, abnormal glucose tolerance, no evidence of myocardial or renal damage or of increased eye inflammation or respiratory infection	Jiraskek et al 1964; Pazderova-Vejlupkova et al, 1980; Pazderova-Vejlupkova 1981
Lower extremity weakness, correlation between chloracne and hypomania scale on MMPI	No significant abnormalities	Eye irritation, mild uroporphyrinuria in one worker	Poland et al 1971 (see Bleiberg et al 1964)
	Elevated GGT, elevated triglycerides, elevated urinary D-glucuronic acid		May, 1982

1949 West Virginia Trichlorophenol 2,3,5-T	226 Followup of plant studied by Ashe and Suskind (above)	Chloracne 70-residual 47-by his- tory	Abnormal sensory findings in those with chloracne
1949 West Virginia Trichlorophenol 2,4,5-T	204 Followup of plant studied by Ashe and Suskind and Moses et al (above)	Chloracne in 107 Actinic Elastosis	
32 1976 Seveso Trichlorophenol	No. not given ICMESA workers follow-up five years after explosion		

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Source: Moses et al, 1984

Elevated GGT
in those with
chloracne

Decreased libido,
sexual dysfunction

Moses et al
1984

History of GI
ulcer
Lower pulmonary
function in
exposed smokers

Suskind and
Hertzberg,
1984

Elevated Alk.
Phos.

Elevated urinary
porphyrins

Ghezzi et
al, 1984