

Occupational exposure

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9C.1. Introduction

Reports of illness associated with exposure to chlorinated organic chemicals of the type discussed in this book date back to the latter part of the 19th century (Herxheimer, 1899) and the early part of the 20th century (Bettmann, 1901; Wauer, 1918; Lehmann, 1905).

Extensive outbreaks following exposure to chlorinated naphthalenes occurred during World War I, but it was not until the middle of the 20th century that occupational illness from exposure to the other compounds has become a problem. Review of the available literature suggests a clinical syndrome that is produced by the halogenated biphenyls, naphthalenes, dibenzodioxins and dibenzofurans. It is presently not known whether halogenated terphenyls may cause similar problems. Some of the signs and symptoms observed following exposure to toxic levels of these compounds have been noted frequently (Table 9C.1). In all instances, the skin lesion, *chloracne*, was usually one of the first signs noted. Signs and symptoms such as weight loss, general malaise, nausea, loss of appetite, impairment of liver function, hepatic porphyria (porphyria cutanea tarda) (see Chapters 7, 8) and sensory neuropathy were less frequently reported. Other effects were occasionally associated with some outbreaks of occupational illness, but their significance is not well understood. Not all of the observed signs have been reported for all of the chemicals under discussion. Chloracne, weight loss and impaired liver function have been most frequently associated with exposure to toxic levels of these chemicals.

As outlined in Chapter 7, 2,4,5-trichlorophenol and all chemicals made from it may be contaminated with 2,3,7,8-tetrachlorodibenzodioxin. Pentachlorophenol

Kimbrough (ed.) Halogenated biphenyls, terphenyls, naphthalenes, dibenzodioxins and related products

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TABLE 9C.1

Symptoms and signs reported after occupational exposure.

System	Lesion	Chemical	Reference ^a
General	bloodshot eyes, lassitude, headache, abdominal pain, impotence, weight loss, insomnia, alopecia, disturbance in taste	chlorinated naphthalenes technical pentachlorophenol 2,3,7,8-tetrachlorodibenzo-dioxin chlorinated biphenyls	Good and Pensky, 1943 Baader and Bauer, 1951; Behrbohm, 1959 Jirasek et al., 1974 Jones and Alden, 1936
Skin ^b	chloracne, puritus	2,3,7,8-TCDD chlorinated biphenyls chlorinated naphthalenes tech. pentachlorophenol other tech. chlorinated phenols	Kimming and Schulz, 1957 Jones and Alden, 1936 Good and Pensky, 1943 Behrbohm, 1959 Stingily, 1940; Dugois and Colomb, 1956
Liver	acute yellow atrophy, hepatocellular necrosis, mild fibrosis, fatty change, abnormal liver function, porphyria cutanea tarda	chlorinated naphthalenes (tetra-, penta-, hexa-) 2,3,7,8-TCDD tech. pentachlorophenol polychlorinated biphenyls (abnormal liver function tests)	Collier, 1943 Bauer et al., 1961; Weiberg et al., 1964; Goldmann, 1972; Jirasek et al., 1974 Truhant et al., 1952; Gordon, 1956 Ouw et al., 1976
Digestive tract	anorexia, vomiting, hemorrhage	chlorinated naphthalenes 2,3,7,8-tetrachlorodibenzo-dioxin	Good and Pensky, 1943; Dwyer, 1946 Hofmann, 1957; Goldmann, 1972
Peripheral nervous system	sensory neuropathy, peripheral neuritis	2,3,7,8-tetrachlorodibenzo-dioxin	Goldmann, 1972; Jirasek et al., 1974
Respiratory system	bronchitis, reduced vital capacity	technical pentachlorophenol polychlorinated biphenyls	Baader and Bauer, 1951 Warsaw et al., 1979

a. The symptoms and signs listed were observed by a number of other authors. The references listed serve merely as examples.

b. ^bExacerbation was reported in blacks for chlorinated naphthalenes by Cotter (1944).

may be contaminated with more highly chlorinated dibenzodioxins, dibenzofurans and hexachlorobenzene. The polychlorinated biphenyls contain trace amounts of chlorinated dibenzofurans and chlorinated naphthalenes. Whether chlorinated naphthalenes are contaminated with chlorinated dibenzodioxins and chlorinated dibenzofurans has not been established. In fact, little is known about the complete composition of the technical products that have caused outbreaks of occupational illness in the past.

The cases of chloracne which Herxheimer reported (1899) occurred in a room where caustic potash was produced by the electrolysis of potassium chloride. The chlorine was reacted with calcium to give calcium chloride. Herxheimer initially assumed that nascent chlorine had caused the dermatitis. Crow (1970a) pointed out that, although many authors clung to the nascent chlorine theory, the cause was halogenated hydrocarbons which originated from the tar lining in the absorption towers, or the anodes of tar, bitumen and charcoal that were used in the electrolytic manufacture of hydrochloric acid and similar substances. These tars were the sources of the cyclic compounds which became halogenated. Thus far, it has not been unequivocally shown whether specific isomers in the mixtures of chlorinated naphthalenes and biphenyls are the acnegenic agents and also cause some of the systemic toxic effects. Most chlorinated biphenyl mixtures are contaminated with 2,3,7,8-tetrachlorodibenzofuran which may contribute to their toxicity. Certainly the contaminants in 2,4,5-trichlorophenol and related products are the agents responsible for chloracne (Kimming and Schulz, 1957). Most likely the contaminant hexachlorodibenzodioxin in pentachlorophenol causes chloracne.

9C.2. Chloracne

Depending on the severity of the exposure and the susceptibility of the individual workers, some will develop an occupational disease commonly referred to as chloracne after having had exposure to the halogenated cyclic compounds mentioned above for several weeks or months. Following exposure to high concentrations of 2,3,7,8-tetrachlorodibenzodioxins, the onset may be more rapid. Even after a single exposure to 2,3,7,8-tetrachlorodibenzodioxins, the onset of chloracne may be delayed for several weeks, but if the exposure is severe, it may appear in as little as 2-3 days. One, or repeated short-term, exposure to 2,3,7,8-tetrachlorodibenzodioxin usually occurs during the production of 2,4,5-trichlorophenol when the reaction overheats, resulting in the increased production of the unwanted contaminant 2,3,7,8-tetrachlorodibenzodioxin. This exothermic reaction may give rise to explosions (Nilnes, 1971).

The clinical features of chloracne, regardless of the type of chemical that caused it, have been most consistent. The most distinctive cutaneous lesion is the chloracne cyst (Crow, 1970b). This lesion is skin-colored and measures from 1 to 10 mm in diameter with a central opening. The other dominant lesion is the comedo (Figs. 9C.1, 9C.2). Usually these lesions start over the maxillary bone, then involve the



Fig. 9C.1. Only mild chloracne over maxillary bone is noted.

entire face, the neck and ears. Often the nose and nasolabial folds are not as extensively involved. In males, the genitalia may be involved. Furthermore, lesions may be present on the back, arms and legs, and other areas of the body, particularly where garments are in close contact with the skin. Depending on the severity, the skin contains only a few lesions (Fig. 9C.1) or the lesions are so close together that they give the skin a rough, grayish-brown appearance. The comedones and cysts can become secondarily infected and large pustules may form. Cysts may rupture and cause foreign body granulomata.

The chloracne-type skin lesion may be preceded by a faint rash which, in some cases, itches severely. In areas exposed to the sunlight, a photosensitivity-type reaction may occur and conjunctivitis with swelling of the eyelids and the rest of the facial skin may precede the development of chloracne. Since the workers are often exposed to the chloracnegenic agent, such as TCDD, as well as other chemicals, such as 2,4,5-trichlorophenol, it is not entirely clear whether the early rash is produced by the TCDD or due to the irritating effect of the 2,4,5-trichlorophenol or other substances.

Once chloracne has developed, it may remain active for many years, and particularly when secondary infections occur, deep-pitted scars may remain as a residual effect. These scars can be quite disfiguring (Fig. 9C.3). No specific treatment is available and most palliative means have not been very effective. Treatment in the



Fig. 9C.2.

past has included pustules. It has also been effective.

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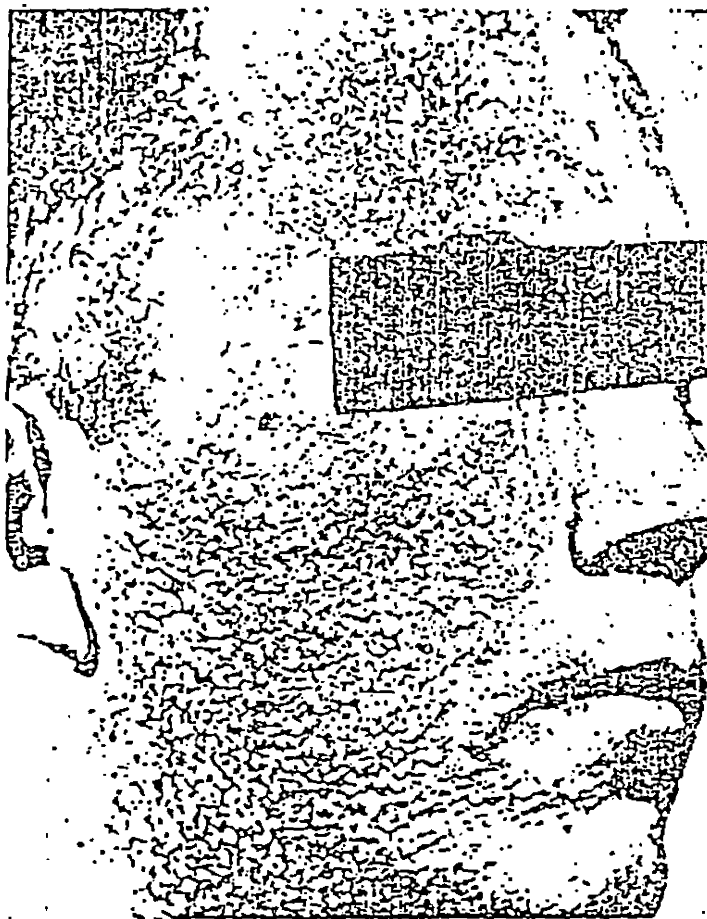


Fig. 9C.2. A worker with acute extensive chloracne.

past has included Vitamin A acid, UV light, X-ray, lancing and expressing of pustules. However, the best treatment is prevention, although, dermabrasion has also been effective (Crow, 1970a).

The manufacture of these chlorinated hydrocarbons and the coating of wires and condensers with insulating materials and other industrial processes should be done in enclosed systems. Protective clothing provided by and laundered by the company should be handed out fresh daily. Shower baths after work should be compulsory and supervised. Sufficient shower facilities should be available so that workers are not delayed. Schwartz and Peck (1943) suggested synthetic wetting agents instead of soap as cleanser. They also recommended monthly skin examinations and liver function tests. In the United States, recommendations for a lower polychlorinated biphenyl standard were made by the National Institute of Occupational Health in 1977 (NIOSH, 1977) which suggests proper hygiene procedures to avoid dermal contact and recommends that occupational exposure be controlled so that no worker is exposed to PCBs at a concentration greater than $1.0 \mu\text{g}/\text{m}^3$ of air deter-

mined as a time-weighted average (NIOSH, 1977a). The existing standards for occupational exposure to PCBs in different countries have been summarized by the International Labour Office (1970). They range from 0.5 mg/m³ to 1.0 mg/m³ in many countries.

It is particularly important that no potentially contaminated clothes are taken home since chloracne has been transmitted by this vehicle to other members of the family.

A skin lesion exactly like chloracne can be produced on rabbit ears or hairless mice and the muzzle of rhesus monkeys. In cattle and horses, a microscopically slightly different skin lesion which is also called hyperkeratosis or X-disease develops following exposure to compounds that produce chloracne in humans. In cattle and horses, the skin lesion is usually accompanied by hair loss in the affected areas and the epidermis is covered by a thick layer of keratin (Kimbrough, 1974; Kimbrough et al., 1977). Prior to the ability to detect chloracnegenic compounds by chemical analysis, the rabbit ear test was utilized to screen technical products for their presence (Adams et al., 1941) (see also Chapter 5).

In rabbits, monkeys and men, the microscopic appearance of the skin lesion varies, depending on the interval between last exposure and the time the biopsy was obtained. Microscopic examination of human skin biopsies from chloracne cases or tissue sections from rabbit ears with hyperkeratosis show markedly dilated hair follicles that are filled with keratin. Eventually the entire follicular appendage becomes transformed into a sac of keratin (Figs. 9C.4 and 9C.5). The sebaceous glands involute partially or completely. The epithelial cells lining the follicles and adjacent to them proliferate. Acanthosis is present and the individual prickle cells become enlarged. Polymorphonuclear leukocytes aggregate around hair follicles. This is followed by intrafollicular collections of leukocytes, microvesicles and abscesses within the follicular wall. Subsequently the follicular wall is destroyed and an abscess may develop. According to Shelley and Kligman (1957), who induced chloracne experimentally in 31 male adults with chlorinated naphthalenes, the sebaceous glands returned gradually months after the last application. Eventually, the epithelium lining the keratin-filled follicles atrophies.

Although on casual examination, chloracne resembles juvenile acne, the distribution of chloracne is quite different as is frequently the age of onset. Juvenile acne is characterized by papular eruptions due to inflammation with the accumulation of secretion of the sebaceous glands. Hyperkeratosis and atrophy of sebaceous glands does not occur in juvenile acne.

In a few instances in which workers developed chloracne following exposure to 2,3,7,8-tetrachlorodibenzodioxin, hypertrichosis and hyperpigmentation was pronounced (Jirasek et al., 1976; Bleiberg et al., 1964).

For many years, it was believed that chloracne was due to external contact and not the result of systemic exposure to the acnegenic agents. However, this belief is refuted by two episodes of accidental poisoning following ingestion of the acnegenic compounds. In one episode, 'Yusho' rice bran oil became contaminated with a



Fig. 9C.3



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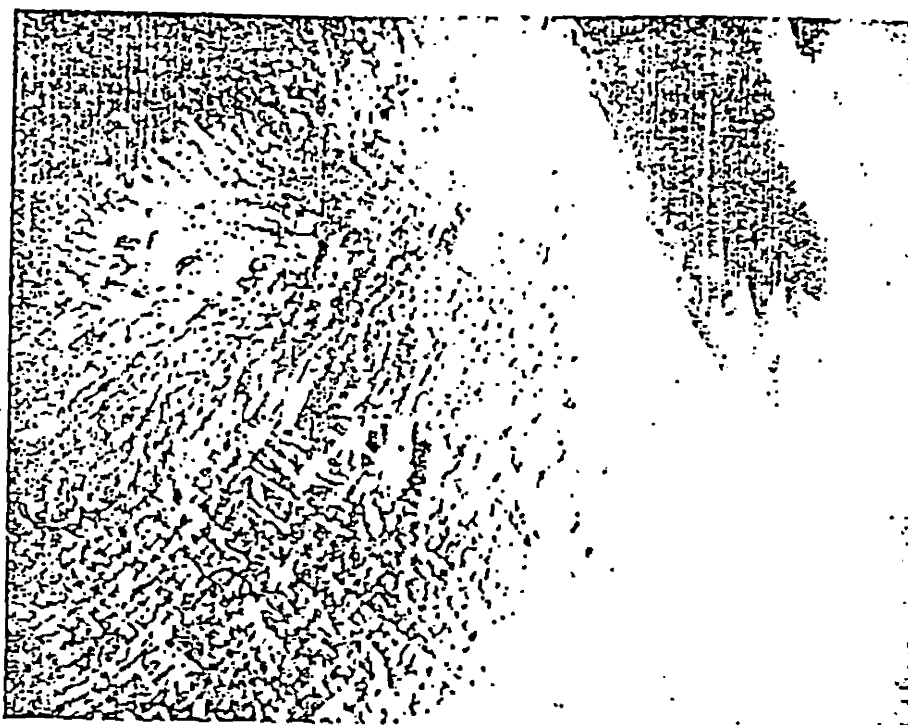


Fig. 9C.3. Residual scars subsequent to chloracne.

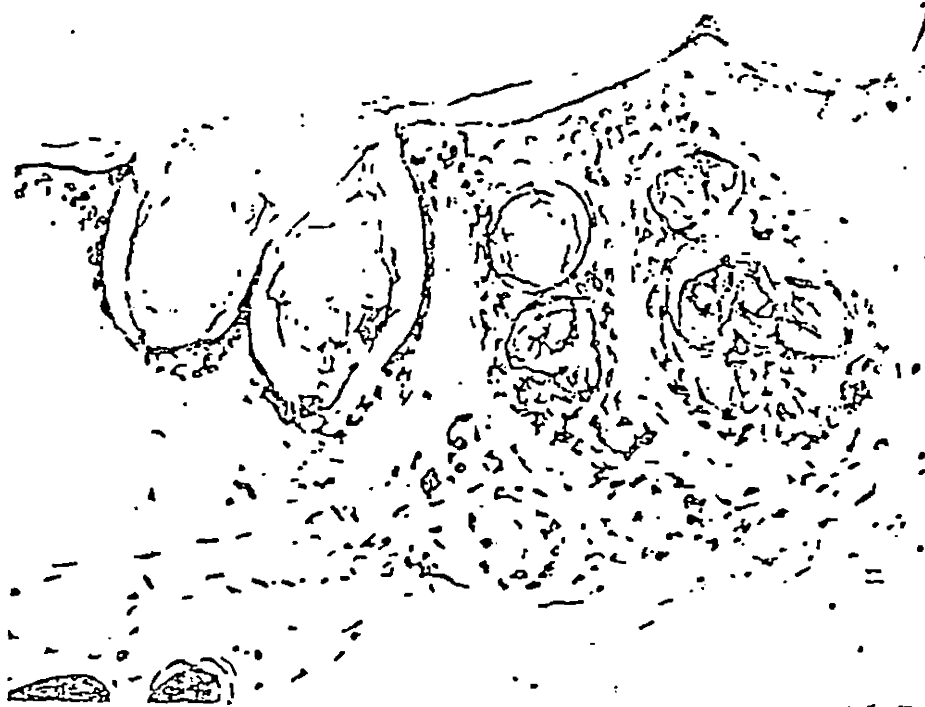


Fig. 9C.4. Follicular appendage of the skin from a normal rabbit ear.

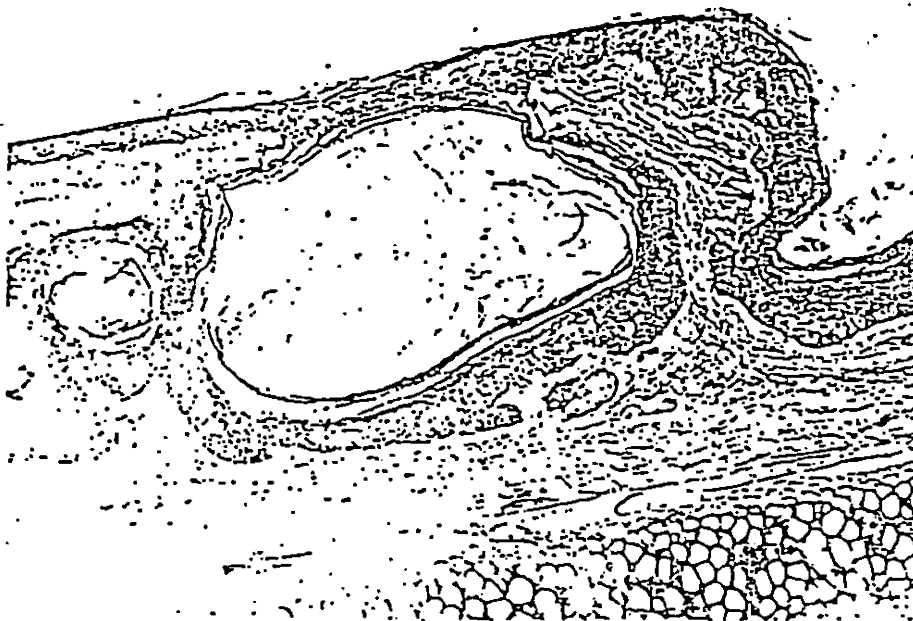


Fig. 9C.5. Follicular appendage from a rabbit ear affected by a chloracneogenic agent.

mixture of chlorinated biphenyls, quarterphenyls and dibenzofurans (Rappe et al., 1977; Miyata et al., 1978), and resulted in illness which included chloracne (Chapter 9B.1).

In 1945, six people fried vegetables in a fat-like substance thought to have been hexachloronaphthalene which they found in the bomb ruins of Berlin in Germany (Hertzberg, 1947) and subsequently developed chloracne. Similar skin lesions can also be produced in primates by oral exposure to chlorinated biphenyls or chlorinated dibenzodioxins (Barsotti and Allen, 1975; Allen et al., 1977). In rabbits, depending on the dose, application of acneogenic agents on the ear may either only result in local hyperkeratosis or at higher doses also produce a toxic effect on the liver (Kimbrough, 1977). Thus, local dermal application of these compounds, particularly the 2,3,7,8-tetrachlorodibenzodioxin may also lead to systemic disease. More recently, occupational exposure to 3,4-dichloroaniline and some herbicides made from it, such as propaflil (*N*-(3,4-dichlorophenyl)propanamide) have also produced chloracne. In these instances, the toxic contaminant is tetrachloroazobenzene or tetrachloroazoxybenzene (Morse et al., 1979). These compounds are not as stable as the chemicals discussed in this book, and hence may be less of a problem.

9C.3. Presence of halogenated aromatics in human tissues and body fluids

Of all the chemicals discussed, only the chlorinated biphenyls have been measured with any frequency in human tissues. Chlorinated dibenzofurans were found in patients suffering from Yusho (Chapter 9B1) and in one instance, tissue was analyzed for 2,3,7,8-tetrachlorodibenzodioxin from a resident living in the Seveso area in Italy (Chapter 9B2). Brominated biphenyls are not as prevalent in human tissues as chlorinated biphenyls and are primarily found in the population of the state of Michigan, U.S.A. (Chapter 9A). Since the chlorinated biphenyls are lipophilic, the highest concentration is found in adipose tissue, although proportionally lower concentrations are present in other organs as well as blood. The different chlorinated biphenyl isomers are metabolized at different rates (Chapter 4) resulting in shifts in the gas-chromatographic pattern. The ratio of polychlorinated biphenyls between adipose tissue, other organs and blood varies somewhat, depending on whether exposure is current or took place in the past and whether the blood specimen was fasting. Pregnancy, weight loss and kidney disease may also affect this ratio. In order to determine the body burden of these compounds, adipose tissue would be the most suitable specimen for most of the halogenated aromatic compounds. Although appropriate for individual cases, it is usually not feasible to obtain adipose tissue samples in large population studies. In spite of the limited value of blood levels as an indicator of body burden, they can give some idea of the levels of exposure. A person with a polychlorinated biphenyl blood level of 10 ppb ($\mu\text{g/l}$) might at the most have adipose tissue levels of a few ppm (mg/kg) or less, while those with blood levels of 100 ppb ($\mu\text{g/l}$) might have adipose levels anywhere from 20 to 50 ppm (mg/kg). Since the chlorinated dibenzodioxins and chlorinated dibenzofurans, particularly the 2,3,7,8-tetra- isomer, are so extremely toxic, illness would be expected to be present at lower concentrations than for chlorinated bi-

TABLE 9C.2

Partial list of chemical companies where explosions or sudden accidental release of large quantities of TCDD has occurred during the production of 2,4,5-trichlorophenol and related products.^a

Name of company	Place	Year	Reference
Montanto	Nitro, W.Va., U.S.A.	1949	IARC, 1978
Badische Anilin und Soda Fabrik	Ludwigshafen, Rhein, G.F.R.	1953	Hofmann, 1957
Philips Duphar Ltd.	Amsterdam district, Harlem, The Netherlands	1963	Dalderup, 1974a, 1974b
	Grenoble, France	1966	Dugois and Colomb, 1956
Coalite and Chemical Products Ltd.	Bolsover, U.K.	1968	May, 1973
	Hamburg, G.F.R.	1954	Schulz, 1957; Kimming and Schulz, 1957
JCMESA	Seveso, Italy	1976	Hay, 1979

a. Additional companies are listed by Hay (1979).

diphenyls. The chloracne was usually found in electricians engaged in stripping (the coated cables). The halowax which was stripped off was impregnated in asbestos which was wrapped around the wires as insulation.

Experimental studies were carried out with the chlorinated naphthalenes which caused outbreaks in different working situations. These mixtures were composed of chlorinated naphthalenes with various percentages of chlorination. Teleky (1927) pointed out that in factories where the substances used contained only 14% chlorine, the incidence of chloracne was much reduced. In one of the companies, the health status of the workers was greatly improved when naphthalenes with only 7-8% of chlorine were substituted for those with higher percentages of chlorine. A number of experimental studies stimulated by the health problems observed in workers exposed to these chlorinated naphthalenes demonstrated that the penta- and hexachloronaphthalenes seemed to be the most toxic. This experimental work also indicated that mixtures of chlorinated naphthalenes with chlorinated diphenyls increased the toxicity of these materials (Von Wedel et al., 1943). During that time, the most extensive studies were done by Bennett et al. (1938). In these studies, the trichloronaphthalenes were less hepatotoxic than the higher chlorinated compounds and the chlorinated diphenyls were considered to be the most toxic of all. However, no chemical analyses for any of these compounds were performed at the time to determine whether any toxic impurities might be present. Similarly, Shelley and Kligman (1957) tested a number of halowaxes for acneogenic potential in humans. The following mixtures of chlorinated naphthalenes were tested:

Mono- and dichloronaphthalenes (Halowax 1000), tri- and tetrachloronaphthalenes (Halowax 1001), penta- and hexachloronaphthalene (Halowax 1014), heptachloronaphthalene (Halowax 1052) and octachloronaphthalene (Halowax 1051). Of these, only the mixture of penta- and hexachloronaphthalene produced chloracne. The other four chlorinated naphthalene mixtures were without effect. However, Mayers and Silverberg (1938) reported a series of patients who had developed chloracne after being exposed to a mixture of tri- and tetrachloronaphthalenes. Again, no chemical analysis of this particular mixture was done. On the other hand, studies in rabbits injected with mixtures of tri- and tetrachloronaphthalene, or tetra- and pentachloronaphthalene or penta- and hexachloronaphthalene only showed liver damage when they were given the penta- and hexachloronaphthalenes, but not when they were given the mixtures of the other chlorinated naphthalenes. Thus, most of the clinical observations as well as the available experimental data seem to indicate that the penta- and hexachloronaphthalenes are the most toxic components of the mixtures of chlorinated naphthalenes.

9C.6. Contaminants (chlorinated dibenzodioxins and chlorinated dibenzofurans)

Chlorinated dibenzodioxins and chlorinated dibenzofurans are contaminants of a number of commercial products (Chapters 1, 2). The only documented episode of substantial exposure of humans to chlorinated dibenzofurans occurred in Japan,

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and these subjects were also exposed to polychlorinated biphenyls (Chapter 9B1). It is known that products such as pentachlorophenol are contaminated with chlorinated dibenzodioxins and chlorinated dibenzofurans, but in the published reports dealing with occupational exposure to technical pentachlorophenol no efforts have been made to distinguish the effects of these trace contaminants from those of pentachlorophenol per se. Through the efforts of Kimming and Schulz (1957), it is known, however, that to a large extent, illness caused by technical 2,4,5-trichlorophenol and all products made from 2,4,5-trichlorophenol is actually caused by TCDD. TCDD is the most toxic isomer of the group of chlorinated dibenzodioxins (Chapter 5).

Occupational exposure to TCDD may occur in the production of 2,4,5-trichlorophenol and all products for which 2,4,5-trichlorophenol is used as starting material. In addition, exposure to commercial products contaminated with TCDD may also result in illness.

Two types of exposures have occurred in these occupational settings. Workers may be exposed daily to TCDD during normal production of 2,4,5-trichlorophenol and its end products. In this type of setting, chloracne developed gradually in some workers after they have been exposed for several weeks or months. In addition, these workers may also show systemic illness.

The other type of occupational illness has a more sudden onset. When 2,4,5-trichlorophenol is produced from tetrachlorobenzene, unless the reaction is carefully controlled, it may overheat and result in an explosion of the reaction vessel. Once the temperature of the reaction exceeds 160°C, increasing amounts of TCDD are also formed. Exposure of workers to TCDD during the explosion and subsequently during clean-up operations has often been quite heavy and has resulted in the onset of chloracne in a week or two, sometimes accompanied by systemic illness. A number of such episodes have been published in the literature and some are listed in Table 9C.2. Clean-up crews and maintenance men are particularly endangered.

Acute symptoms occurring after such accidents have consisted of headaches, nausea and dizziness. Rarely, severe itching, redness and swelling of the face or other areas of the skin may develop, and swelling of the eyelids with conjunctivitis may also be present. Within two or three weeks chloracne develops and systemic illness, such as weight loss, easy fatigueability and aching muscles, particularly in the lower extremities and chest, may be present. Other complaints often recorded were insomnia, irritability and loss of libido. The liver may become tender and enlarged, and sensory changes, particularly in the lower extremities, have been observed. Total serum lipids may be increased and the prothrombin time may be prolonged. Symptoms may be quite persistent, particularly the severe aches and pains which are manifestations of peripheral neuropathy and the fatigueability (IARC, 1978; Bauer et al., 1961; Bleiberg et al., 1964; May, 1973; Jensen and Walker, 1972; Oliver, 1975). Unfortunately, since chloracne is the most obvious manifestation of TCDD poisoning, the systemic effects have been less well studied

and reported. While in some episodes, chloracne seems to be the only significant health effect (May, 1973) in most episodes, systemic illness was also noted. Unfortunately, a number of these episodes either have not been published at all or have only been insufficiently reported, such as the accident which occurred in Nitro, West Virginia, in 1949 or the health effects observed in the Philips Duphar Co. in the Netherlands. The reports made by Bauer et al. (1961), Schulz (1957), Bleiberg et al. (1964), Oliver (1975), Goldman (1972) and Jirasek et al. (1976) describe systemic effects in more detail. Most of the persons exposed in industrial settings were exposed to a mixture of chemicals, such as 2,4,5-trichlorophenol, TCDD, 2,4,5-trichlorophenoxyacetic acid, and, in the episode reported by Jirasek (1976), also to pentachlorophenol. It is, therefore, not clear whether all effects were solely caused by TCDD. Only the two laboratory workers studied by Oliver (1975) had exposure to pure TCDD.

Systemic illness is usually reported only in workers with chloracne. However, Jirasek et al. (1976) cite 4 workers with systemic illness without chloracne. From the other published reports, it is not clear whether all exposed workers were examined for systemic illness or whether they were selected on the basis of chloracne which may have led to the perhaps erroneous assumption that in humans, illness caused by TCDD must always be accompanied by chloracne.

Jirasek et al. (1976) found that a number of their patients had porphyria cutanea tarda. In addition to the chloracne, hypertrichosis and hyperpigmentation were noted. Abnormal liver function test results (elevated SGOT and SGPT) were obtained for 11 of 80 patients. In more than half of the workers, total cholesterol, total lipids, and phospholipids were elevated. Urinary uroporphyrins were elevated in 23 workers. Thin layer chromatography showed that urinary 8- and 4-carboxyporphyrin were increased. Both liver and urine fluoresced under UV light. A peripheral neuropathy was documented in 17 of these workers. In 4 workers, localized effects on the central nervous system were also observed. In the outbreak reported by Bleiberg et al. (1964), a number of workers had, in addition to chloracne, abnormal excretion of urinary uroporphyrins, hirsutism, and hyperpigmentation. Six years later, in a followup study of the same plant, only one worker had persistent uroporphyrinuria (Poland et al., 1971). In addition, a number of authors (Schulz, 1957; Bauer et al., 1961; Jirasek et al., 1976; Oliver, 1975) observed a neurasthenic syndrome characterized by a lack of drive and vigor, sleep disorders, emotional instability and diminished libido or potency (Kleu and Goltz 1971).

Bauer et al. (1961) studied three groups of workers in Germany who had developed chloracne and/or systemic illness after working in the production of chlorinated phenols. Liver biopsies of three workers showed in one instance a fatty liver with slight fibrosis and an inflammatory reaction, and in two instances, 'perihepatic' changes and a brown pigment which stained partially positive for iron. A liver biopsy from another showed a gray pigment which was not positive for iron.

Among the long-term followup studies reported thus far in workers exposed to

TCDD is one by Thiess and Goldmann (1976). Of the 53 original workers exposed to TCDD in 1953, 22 were still employed by BASF in 1976; 3 workers received partial compensation - 1 for persistent chloracne, 1 for residual paresis of the left leg, and 1 because of deafness. Apart from residual scars, the other 18 workers had no persistent skin lesions in 1976. Causes of death were as follows: 2 - myocardial infarct, 4 - cardiovascular decompensation, 4 - carcinoma of different sites, 1 - mitral stenosis, 2 - suicide, 1 - bleeding of the esophagus. As mentioned, one worker had died earlier (Goldmann et al., 1972). No information was given on the 16 retired workers. This study illustrates how persistent the chloracne may be in some individuals.

Recently, a followup study was also conducted on the workers in Nitro, West Virginia (Zack and Suskind, 1980) in which the acute symptoms initially suffered by the workers were described. Aside from the symptoms and signs already mentioned, 4 of 6 workers who were examined in 1949 and 1950 had an enlarged liver and a delayed prothrombin time at that time. A regression of symptoms and signs was observed in these workers when they were reexamined in 1953. The mortality experience of 121 of these workers who had developed chloracne following the explosion in 1949 was also reported. Among this group of workers, 32 deaths were recorded against 46.41 expected. There were 9 deaths from malignant neoplasms with 9.04 expected. There were 5 lung cancer deaths versus 3.02 expected, 1 skin cancer death with 0.15 expected, and 3 deaths from neoplasms of lymphatic and hematopoietic tissue.

A followup examination of 11 of 23 workers who had first become sick in 1953/1954 following exposure to TCDD were reexamined in 1976 (Krause and Brunsow, 1978). The chloracne had completely disappeared in only 2 workers. Seven of the 11 still complained of epigastric pain, nausea and intolerance of alcohol. Six of the 11 had an enlarged liver which was not present when they were examined in the 1950s and 6 of the 11 had at least one abnormal liver function test. Furthermore, Hardell and Sandström (1979) have reported an increased incidence of mesenchymal tumors in workers who were either exposed to technical 2,4,5-trichlorophenol or 2,4,5-trichlorophenoxyacetic acid. The problem with all of these studies is that the number of cases examined is small. Hardell and Sandström tried to control for that by conducting a case control study where they matched 4 controls to each case by age, sex and locality. However, by excluding all control cases with cancer, they may have biased their study.

Another chlorinated phenol, pentachlorophenol, is used extensively as a wood preservative and fungicide. This product is contaminated with chlorinated dibenzodioxins and chlorinated dibenzofurans, but usually with the hexa-, hepta- and octa-homologs (Chapter 2). Occasionally, workers engaged in the production of pentachlorophenol have also developed chloracne (Baader and Bauer, 1951) and complaints such as neuralgic pain in the lower extremities, persistent bronchitis and eye irritation (Behrbohm, 1959). The bronchitis seems to be more prevalent in workers exposed to technical pentachlorophenol than to the other technical products

discussed in this chapter. Workers dealing with wood preservatives again experience mixed chemical exposure. Other chemicals used in such industries include organic arsenic and tin compounds, copper derivatives and creosotes. Pentachlorophenol per se is an uncoupler of oxidative phosphorylation and, like 2,4-dinitrophenol, increases the metabolic rate, resulting in hyperthermia, profuse sweating and weight loss. A number of fatalities following exposure to pentachlorophenol have been described (Mason, et al., 1965; Bergner et al., 1965). In these cases, absorption of several hundred mg of pentachlorophenol has usually occurred in severe or fatal poisoning and pentachlorophenol blood levels as high as 10–20 ppm ($\mu\text{g/g}$) have been measured soon after exposure. On the other hand, workers in wood-treating plants may reach pentachlorophenol blood and urine concentrations as high as 10–20 ppm without symptoms of toxicity (Casarett et al., 1969). Simultaneous exposure to heat may make workers more susceptible to the toxic effects of pentachlorophenol. Since pentachlorophenol is used extensively, detection of ppb (ng/g) concentrations of pentachlorophenol in blood or urine must be considered to represent background levels which are frequently detected in the general population (Bevenue et al., 1967; Casarett et al., 1969). In some fatal human cases, hepatocellular necrosis was observed (Truhaut et al., 1952; Gordon, 1956). Whether these effects resulted from the simultaneous exposure to toxic contaminants in pentachlorophenol has never been investigated (see also Chapters 2 and 5). Vacuolation of hepatocytes was also noted in livers of infants who were accidentally exposed to technical-grade pentachlorophenol in a nursery (Robson et al., 1969).

9C.7. Chlorinated terphenyls and brominated compounds

Essentially no information is presently available on halogenated terphenyls and only one preliminary study on workers exposed to brominated biphenyls has been conducted (Kay, 1977). In addition, Bahn et al. (1980) examined 35 workers of a total cohort of 86 men who had been engaged in the manufacture of decabromobiphenyl and decabromobiphenyl oxide. A total of 89 control subjects were chosen from steel workers and wire men. Studies of thyroid function revealed four cases of primary hypothyroidism in the 35 exposed workers and in none of the controls. This represented a prevalence of 11.4% which is statistically significantly higher than the background incidence of 2.8% found in males in the United Kingdom. Since the group of subjects studied was small, additional studies will have to be done to determine how prevalent hypothyroidism is following exposure to these types of compounds.

Summary

The occupational diseases caused by halogenated biphenyls, terphenyls, naphthalenes, dibenzodioxins and dibenzofurans were reviewed. Occupational illness has primarily occurred following exposure to 2,3,7,8-tetrachlorodibenzodioxin, chlorin-

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ated biphenyls and chlorinated naphthalenes. The health problems associated with exposure to these compounds include chloracne, liver disease, porphyria cutanea tarda, and neuropathies. Not much is known about the other compounds mentioned.

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