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Chlorinated Hydrocarbons

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A Preliminary Report
OF THE
Dermatological and Systemic Effects of Exposure to Hexachloro-Naphthalene and Chloro-Diphenyl

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A PRELIMINARY REPORT OF THE DERMATOLOGICAL AND SYSTEMIC EFFECTS OF EXPOSURE TO

Hexachloro-Naphthalene
and
Chloro-Diphenyl

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Introduction

The demand in industry for electric insulation with fire-resistant and water-proof qualities has led to the use of increasing quantities of chlorinated naphthalenes and chloro-diphenyl. While the dermatological effects of other closely related organic chlorine substitution compounds have been studied, there is little mention in the literature of hexachloro-naphthalene and chloro-diphenyl. As early as 1918 Wauer (1) described a condition which he termed "Pernakrankheit," resulting from exposure to perchloro-naphthalene. Teleky (2) found that the gravity of the injuries and the clinical symptoms would appear to depend, in direct proportion, on the halogen content of the chlorinated derivatives. In 1929, J. Nicolas and J. Lacassagen (3) reported a man suffering from chlor-acne of the greater part of the body. These investigators were able to distinguish it from ordinary acne as a result of the localization of the former.

At the last meeting of the American Public Health Association at Milwaukee, Louis Schwartz (4) reported the occurrence of "an acne-like condition of the exposed parts and sometimes of the covered parts, if the fumes penetrate the clothing, of workers exposed to the volatile fumes of these substances." In his paper he stated that patch tests with these substances give negative results.

Chemical and Physical Properties

Chlorinated naphthalene and chloro-diphenyl are organic substitution products. Under trade names they are sold to industry either in the solid or liquid form, combined with other plasticizers such as resins, waxes, and pitch compounds.

The base of the products encountered in this investigation was hexachloro-naphthalene with chloro-diphenyl present in amounts not over ten per cent. The addition of the latter to the synthetic wax tends to lower the melting point of the compound. Synthetic dyes, added in quantities of less than one per cent, give the desired color to the different products.

The compounds have a faint aromatic odor, are insoluble in water and are unaffected by dilute acid and alkaline solutions. They are, however, soluble in organic solvents, such as carbon tetrachloride, naphtha, benzol, acetylene tetrachloride, acetone, gasoline, etc. The melting and boiling points of these compounds are dependent on the nature and amount of the different ingredients present and vary between 140°-275° F. and 500°-752° F., respectively. In their fluid or molten state the waxes have a very low viscosity and readily impregnate textile fabrics. Some of the chlorinated products contract only slightly during solidification, have a low coefficient of expansion as compared with natural waxes, and are non-inflammable.

Plant Process

The fabric covering of wire and cable in the plant studied was impregnated by passing the wire to be insulated through the melted wax or by immersion of the material in a solution of the wax. In the former method the operating temperature of the wax was maintained at 270° F. at which temperature volatilization and condensation of the wax occurred. In the latter method impregnation was effected by passing the wire through a solution of the wax, in either toluene or a mixture of carbon tetrachloride and ethylene dichloride, at room temperature.

Medical Findings

Little mention is made in the literature concerning the systemic effect as a result of exposure to hexachloro-naphthalene and chlorodiphenyl. That the dermatitis resulting from exposure to these chlorinated derivatives can be produced by skin contact with them, may best be illustrated in the presentation of Case Number 26 (See P. 12). What role the effect of the absorption, ingestion, and inhalation of these compounds has, in combination or separately, deserves more detailed study. Whether they may be considered as etiological factors to the production of acute yellow atrophy of the liver has not been determined.

TABLE I. NUMBER AND PERCENTAGE OF PERSONS SHOWING CHLOR-ACNE ACCORDING TO DEGREE OF SEVERITY

Degree of Severity	Number of Persons		Per cent of Persons	
	Male	Female	Male	Female
Negative	21	2	17.6	25.0
Doubtful	--	2	----	25.0
Mild	41	2	34.4	25.0
Slight	30	2	25.2	25.0
Moderate	7	--	5.9	----
Advanced	19	--	16.0	----
Totals	118	8	99.1	100.0

Physical Examination—A partial physical examination was made on one hundred and one persons, who were exposed to either the solid, liquid, or vapor state of the wax. Of this number seventy-eight per cent were found to be affected with the dermatitis. A second group with well defined dermatoses was selected for complete physical examination in an attempt to determine the presence of any systemic effect. In the latter group were twenty-three men (two of whom were controls) and two women. Table I shows the occurrence and degree of severity of the dermatitis in both groups. Any correlation of the incidence of the dermatitis according to operations in the plant studied was found to be impractical, as a result of frequent transfer of the workers from one operation to another. Those persons having the greatest exposure con-

stituted only twenty-six per cent of the total group examined and may account for the relatively low percentage of those having a moderate or advanced dermatitis.

In the group of twenty-five selected for complete physical examinations only those persons with a well defined dermatitis were chosen. An attempt was made to obtain those individuals with long exposure and those with exposure of shorter durations. The average length of exposure of this group was 24.3 months. Table II shows their age distribution and it will be noted that eighty-seven per cent of the total group examined were under forty years of age.

TABLE II. PERCENTAGE DISTRIBUTION BY AGE OF THE GROUP GIVEN COMPLETE PHYSICAL EXAMINATIONS

Age Group (Years)	Exposed				Controls			
	Male		Female		Male		Female	
	Number	Per cent	Number	Per cent	Number	Per cent	Number	Per cent
Under 20	1	4.8	----	----	----	----	----	----
20—29	11	52.4	2	100	----	----	----	----
30—39	6	28.6	----	----	1	50	----	----
40—49	3	14.3	----	----	1	50	----	----
Totals	21	100.1	2	100	2	100	----	----

The length of exposure before the appearance of the dermatitis, which factor was found to be somewhat dependent on the severity of the exposure, is shown in Table III. In only one person, who was in direct contact with the vapors of the hot wax, did the chlor-acne appear before two months exposure. Fifteen months were required for the earliest manifestation of the dermatitis in two other cases, each of whom had a more remote exposure, while the average length of exposure for the entire group was approximately 5.9 months.

TABLE III. NUMBER AND PERCENTAGE OF PERSONS SHOWING THEIR LENGTH OF EXPOSURE BEFORE FIRST APPEARANCE OF THE DERMATITIS

Months of Exposure	Male		Female	
	Number	Per cent	Number	Per cent
1	1	4.8	--	--
2	5	23.8	1	50
3—6	6	28.6	--	--
7—12	5	23.8	--	--
Over 12	2	9.5	--	--
Undetermined	2	9.5	1	50
Totals	21	100.0	2	100

A complete history, which included chief complaints, objective symptoms, previous illnesses, family, personal, and occupational histories, was obtained from each individual. Particular attention was given, in obtaining the history, to the individual's susceptibility to skin diseases. A preexisting acne vulgaris was present in one person, who noted as a result of his exposure, an accentuation of his symptoms. Symptoms referable to the skin were usually given as chief complaints.

Table IV gives the percentage frequency of objective symptoms as compared with the degree of involvement. Pruritis, remissions, and progressiveness of the dermatitis, were the objective symptoms most frequently elicited. Sensory disturbance of the skin was present in only one individual. A small area on the anterior thigh of this worker showed a loss of heat and cold sensations. Two men, included in the group given a partial physical examination, complained of the rancid odor associated with sebaceous secretions.

TABLE IV. NUMBER AND PERCENTAGE OF PERSONS[1] HAVING SYMPTOMS INDICATED, AS COMPARED WITH THE DEGREE OF INVOLVEMENT

Symptoms	Degree of Involvement					
	Advanced		Moderate		Slight	
	Number	Per cent	Number	Per cent	Number	Per cent
Remissions	12	92.3	2	100	7	87.5
Pruritis of Skin	12	92.3	2	100	6	75.0
Progressive Dermatitis	5	38.5	1	50	5	62.5
Lassitude	4	30.8	1	50	3	37.5
Burning of Skin	3	23.1	--	--	3	37.5
Pustular Stage Painful	5	38.5	--	--	--	----
Constipation	2	15.4	--	--	1	12.5
Polyuria	--	----	1	50	1	12.5
Insomnia	1	7.7	--	--	--	----
Abdominal Pain	--	----	1	50	--	----
Diarrhea	--	----	--	--	1	12.5
Headache	1	7.7	--	--	--	----
Sensory Skin Disturbance	--	----	1	50	--	----

[1] Two male controls had none of the above symptoms.
Two females, with slight dermatitis, are included.

Evaluation of symptoms referable to other systems and regions, as a result of additional exposure of the group to organic solvent vapors (toluene or a mixture of carbon tetrachloride and ethylene dichloride), is difficult.

Each person given a complete physical examination was at work on the day of the examination. Data was obtained on present and greatest weight and showed practically no variation. Five minute oral temperatures were found to be normal. Examination of the head and neck was

essentially negative in the entire group except for the presence of cervicle adenopathies in a few cases. In one individual a small pedunculated tumor, which developed following trauma to a papule, was found in the region of the right temple. The tumor was spherical in shape, about the size of a large pea, and was attached to the skin by a pedicle. Its surface, devoid of hair, was marked with indefinite convolutions. The tumor was reddish in appearance and showed signs of inflammation of one of its lobulations, the result of an injury produced by scratching.

Physical examination of the chest was essentially negative in the entire group. The pulse and respiratory rates, obtained with the individual at rest, and blood pressures, recorded with a standard mercury syphgnomanometer, were found to be within normal limits.

Observations were made particularly for evidence of tenderness or muscular rigidity over the region of the liver during abdominal examination. This condition was found to be present in one individual, whose liver margin could not be palpated. Other clinical and laboratory findings in this case failed to indicate additional evidence of liver damage.

TABLE V. NUMBER AND PERCENTAGE OF PERSONS HAVING CHLOR-ACNE ON THE INDICATED BODY SURFACES

Body Surfaces	Number of Persons	Per cent of Persons
FACE	22	95.5
Cheeks	19	82.5
Forehead	19	82.5
Angle of the Jaw	11	47.7
Cheek Prominence	6	26.0
All above Surfaces	5	21.7
NECK	18	78.1
Posterior	16	69.4
Anterior	12	52.1
Both Surfaces	10	43.4
ARMS	19	82.5
Extensor	19	82.5
Flexor	--	----
FOREARMS	15	65.1
Extensor	14	60.8
Flexor	2	8.7
Both Surfaces	1	4.3
CHEST	12	52.1
Upper Sternum	10	43.4
Pectoral Region	4	17.4
Both Surfaces	2	8.7
ABDOMEN	9	39.1
Recti	9	39.1
Flanks	--	----
BACK	18	78.1
Scapulae	18	78.1
Thoracic	2	8.7
Lumbar	2	8.7
All above Surfaces	1	4.3
BUTTOCK	6	26.0
THIGHS	16	69.4
Extensor	12	52.1
Flexor	8	34.7
Both Surfaces	4	17.4
LEGS	7	30.4
Extensor	7	30.4
Flexor	--	----

Examination of the skin was made with the subject stripped and exposed to an excellent source of light. Of the entire group, thirteen, or fifty-six per cent, were found to be in the advanced stage of the dermatitis, while the remainder had it to a less marked degree. Four distinct lesions of the chlor-acne were noted, all of which were present at the same time in the moderate and advanced cases. However, in the early stages, comedones and small papules made their appearance, while at later stages, pustules and sebaceous cysts of the skin occurred. Healing, following the pustular stage, usually occurred in a similar manner as the same process in acne vulgaris. At this stage dried serum was found over the pustules which had been traumatized. As healing progressed, slight scaling of the skin was noted over the site of the pustule. The scales were usually very small and dry in character. Tendency to increased oiliness of the skin was not evident. Pitting of the skin was found in fourteen persons, or 60.8 per cent of the group, and the site most frequently affected was the posterior lateral neck. In these cases there was evidence of depigmentation in the cicatricial tissue.

A predilection of the dermatitis for the extensor surfaces was especially evident on the arms and forearms, and to a lesser extent, on the thighs and legs in the group given complete physical examinations. Table V shows the percentage frequency of the chlor-acne for various regions of the body. When the dermatitis occurred on the face and neck it terminated at the hair line and in no instance was the scalp involved. Gross involvement of the sebaceous glands of the nose was absent, a tendency to diminution in the intensity being apparent at the mid-line of the face. In a few cases comedones were present on the dorsal surfaces of the hands and feet.

In the group examined differences of complexion apparently had little effect on the susceptibility. The influence of age and sex on the individual's susceptibility was not determined, for the greater number of those examined were between the ages of twenty and thirty years, and only two women were found working in the plant who had definite exposure.

Laboratory Findings—Appreciable changes were not evident in the erythrocyte and haemoglobin determinations. The total average leucocyte count was unchanged except for a slight increase in the group having an advanced chlor-acne. In this group the average leucocyte count was 11,130 cells per cubic millimeter, without a corresponding average increase in the polymorphonuclear leucocytes.

Routine examination showed albumin in the urine of three persons, who were twenty-five years of age or less, as the only evidence of renal pathology.

The icterus index and Van den Bergh determinations were made with a Klett colorimeter and the results are given in Table VI. Coincident with the time the first tests were made, all operations of the plant were stopped, so that those persons (10 in the exposed group and 2 controls) showing an icterus index greater than the upper normal limit, were permitted a week's rest at home. At the end of this period, a second determination was made, and in practically every case the icterus index had returned to normal.

Figure 1—Case Number 4.

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TABLE VI. RESULTS OF ICTERUS INDEX AND VAN DEN BERGH DETERMINATIONS

Case	First Determination		Second Determination [1]	
	Icterus Index	Van den Bergh—mgs. bilirubin per 100 c.c.	Icterus Index	Van den Bergh—mgs. bilirubin per 100 c.c.
1	6.1	0.35	5.2	----
2 [2]	----	----	----	----
3	6.8	0.34	5.2	----
4	5.1	----	----	----
5	6.6	0.33	5.0	----
6	5.4	----	----	----
7	7.5	0.37	6.8	0.34
8	6.5	0.32	5.0	----
9	5.2	----	----	----
10	5.0	----	----	----
11	5.3	----	----	----
12	7.3	0.36	7.5	0.38
13	5.6	----	----	----
14	5.4	----	----	----
15	5.1	----	----	----
16	6.4	0.32	4.5	----
17 (Control)	9.2	0.46	5.5	----
18 (Control)	6.6	0.33	3.9	----
19 [3]	9.4	0.47	----	----
20	5.5	----	----	----
21	10.0	0.50	4.8	----
22	4.6	----	----	----
23	6.2	0.31	----	----
24	4.6	----	----	----
25	5.6	----	----	----

[1] Second determination made after an interval of seven days.
[2] Determinations not made.
[3] Second determination not made.

Figures 1, 2, and 3, and a brief summary of the clinical and laboratory findings of three advanced cases are presented to show the nature of the dermatitis encountered in this study.

Case Number 4—White male; complexion brunette; aged 26 years.

Chief Complaint—"Pimples."

Analysis of Chief Complaint—First noted the dermatitis about twelve months following first exposure. Eruption first noted on cheeks and then gradually spreading to forehead and neck. The dermatitis next made its appearance on the arms and anterior chest. Pruritis present particularly during hot weather. Notices remissions of two or three days. Notes persistence of papules for a period of six months. Burning sensation not present. States that the pustules are painful.

Past Medical History—Essentially negative.

Family History—Negative.

Occupational History—Negative.

Physical Examination—Apparently healthy adult male. Height 67 inches. Weight 152 pounds (greatest weight 155 pounds). Pulse rate at rest: 78. Respiratory rate: 14. Blood pressure 142/94. Head and Neck: chronic right otitis media; cervicle lymph glands not palpable. Chest: normal shape; percussion normal; breath and voice sounds normal; no rales. Heart: apical impulse, 5th interspace midclavicular line; no murmurs. Abdomen: flat; no areas of tenderness or rigidity; no masses. Skin: comedones; papules; pustules; pitting of the skin especially prominent posterior lateral neck. Lesions especially prominent over cheeks, forehead, and posterior

Figure 2—Case Number 5.

lateral neck. Upper Lip and Nose: clear. Arms: all stages of dermatitis present over extensor surfaces. Forearms: relatively unaffected except for a few comedones over extensor surfaces. Chest and Back: occasional comedo, papule, and pustule, particularly over upper portion of the sternum and over scapulæ. Abdomen: all stages of dermatitis over both recti. Thighs: distribution on extensor surfaces. Buttock: dermatitis present and uniform both sides. Legs: rare comedones over extensor surfaces. Scalp: clear. Hands, Feet, and Nails: negative.

Laboratory Findings—Blood Examination: erythrocytes 4,940,000; leucocytes 9,050; haemoglobin 100. Differential Count: polymorphonuclear leucocytes 66 per cent; small lymphocytes 12 per cent; large lymphocytes 20 per cent; basophiles 0.5 per cent; eosinophiles 1.5 per cent. Icterus Index 5.1. Urinalysis: reaction acid; specific gravity 1.020; albumin negative; sugar negative; microscopic examination, many pus cells in small clumps; no casts; no erythrocytes.

Case Number 5—White male; complexion blonde; aged 24 years.

Chief Complaint—"Pimples."

Analysis of Chief Complaint—Dermatitis developed about three months after first exposure. Eruption first noted on face at the angle of the jaw. Noted gradual extension of the condition over the rest of the face during a period of one month's time. Dermatitis next involved the arms and neck. Pruritis noted at times especially after hot bath or in warm weather. Burning sensation not present. Remissions of two or three days.

Past Medical History—Usual childhood diseases.

Family History—Essentially negative.

Occupational History—Negative.

Physical Examination—Apparently healthy adult male. Height 68 inches. Weight 132 pounds (greatest weight 140 pounds). Pulse rate at rest: 70. Respiratory rate: 16. Blood pressure 140/80. Chest: normal shape; percussion normal; breath and voice sounds normal; no rales. Heart: apical impulse, 5th interspace midclavicular line; no murmurs. Abdomen: flat; no areas of tenderness or rigidity; no masses. Skin: comedones; papules; pustules; pitting of the skin. Face: dermatitis pronounced over the angle of the jaw and cheeks. Neck: posterior lateral neck most markedly involved. Chest and Back: essentially negative. Arms and Forearms: distribution of dermatitis noted over extensor surfaces but less marked on the forearms. Thighs: small patches present anteriorly above the knees. Legs: essentially negative. Hands, Feet, and Nails: negative. Scalp: clear.

Laboratory Findings—Blood Examination: erythrocytes 5,190,000; leucocytes 9,050; haemoglobin 100. Differential Count: polymorphonuclear leucocytes 67 per cent; small lymphocytes 25 per cent; large lymphocytes 4.5 per cent; eosinophiles 3 per cent; basophiles 0.5 per cent. Icterus Index 6.6; Van den Bergh 0.33 mgs. bilirubin per 100 c. c.; icterus index (7 days later) 5.0. Urinalysis: reaction acid; specific gravity 1.015; albumin 3 +; sugar negative; microscopic examination negative.

Case Number 26—Infant male; complexion blonde; aged 2½ years.

History Obtained from Mother—Child's father had been working at the plant for about two months when the mother first noticed development of the dermatitis. Mother stated that the child's father returned home in his soiled working clothes and that it was his habit to play and romp with his son, without changing to clean clothing. She also stated that father and son slept together, the father always sleeping in his underwear. The dermatitis made its first appearance on the child's anterior thighs above the knees. She next noticed small patches on the flexor surfaces of the forearms which gradually extended to the extensor surfaces. Finally, the dermatitis

Figure 3—Case Number 26.

developed on the neck and face. Mother stated that she noted child scratching occasionally. She has noticed a diminution in his appetite. Constipation not present. No vomiting. Stools normal in color and consistency. No jaundice. No haematuria. No polyuria. Mother stated that child has been active, sleeps well, and is apparently unchanged except for the anorexia.

Past Medical History—Pertussis at age of six months.

Family History—Father suffering from generalized chlor-acne as result of exposure to hexachloro-naphthalene and chloro-diphenyl. Mother shows dermatitis: cheeks; buttock; and extensor surfaces of thighs. Sister, 11 months old, with chlor-acne in the comedo stage over both cheeks.

Physical Examination—Well developed infant male. Weight 35 pounds. Axillary temperature: 101°. Pulse rate at rest: 140. Respiratory rate: 26. Head and Neck: essentially negative except for acute left otitis media; anterior cervicle lymph glands palpable. Chest: normal shape; breath and voice sounds normal; no rales. Heart: no apparent enlargement; no murmurs. Abdomen: convex; no tenderness or rigidity; liver edge not palpable. Extremities: negative. Skin: comedones; papules; pustules; slight pitting of the skin. Face: comedones and papules abundant over cheeks and forehead. Nose and Upper Lip: relatively unaffected. Neck: anterior and posterior neck involved with occasional pustule. Arms and Forearms: all stages of the dermatitis present particularly on the extensor surfaces. Chest: few comedones over superior portion of the sternum. Back: few comedones and papules over scapulæ. Abdomen: essentially negative. Thighs: dermatitis present on both lateral and anterior surfaces. Legs: occasional comedones over extensor surfaces. Scalp: clear. Hands, Feet, and Nails: negative.

Prevention

The production of industrial dermatoses is partially dependent upon the nature and severity of the exposure and upon individual susceptibility. The relatively high percentage of those individuals affected, following exposure to hexachloro-naphthalene and chloro-diphenyl, in a total group of one hundred and twenty-six persons examined, indicates a need for the adoption of preventive measures where these compounds are used in industry. Prevention of skin contact with these substances would depend somewhat upon the process employed. In those processes where the compounds are heated to a temperature sufficient to cause volatilization and subsequent condensation in air, either closed methods, operating under partial vacuum, or exhaust ventilation should be instituted. In those processes where the compounds are handled in the solid or liquid form, other means of prevention must be adopted. When the operation is such that contamination of the exposed portions of the body and clothing is unavoidable, adequate protective clothing, lockers, and other sanitary facilities, should be provided. Further prevention of skin contact with these substances, for persons handling the finished product in the plant and for the consumers, could be had by application of protective coatings applied to the finished product.

Summary

1. Hexachloro-naphthalene and chloro-diphenyl produce, on contact with the skin of some individuals, an acne-like dermatitis after varying degrees of exposure.

2. From one to fifteen months exposure to varying amounts of hexachloro-naphthalene and chloro-diphenyl on the group examined was required before the onset of the dermatitis.

3. The dermatitis, in the group of twenty-three persons examined, resulting from exposure (average length of exposure approximately 24.3 months) to hexachloro-naphthalene and chloro-diphenyl had a predilection for the face and the extensor surfaces of the body.

4. Systemic effects produced as a result of exposure to hexachloro-naphthalene and chloro-diphenyl should be further studied.

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