

CRITICALLY ACUTE CHLORACNE CAUSED BY
TRICHLOROPHENOL DECOMPOSITION PRODUCTS

1. Synopsis of the medical literature

Since the first description of chloracne by *Herxheimer* 1899 [6] the causes of the disease have not ceased being discussed. In 1918 *Wauer* [24], industrial counselor, had described the perna sickness in a short paper. In 1927/28 *Teleky* [21] gave detailed reports on the subject, so did *Fuss* [3] (1936) at two conventions of dermatologists. *Schmidt* and *Boslet* [17] reported again (see *Fuss* [3]) on seven persons of the Ludwigshafen area who had been afflicted for twenty years with chloracne. In 1955 a comprehensive monograph on chloracne written by *W. Braun* [2] was published. In 1966 *Londono* [13] published five case studies on occupational acne contracted by peasants in Bogota, Colombia. The disease was caused by a combination of herbicides. The responsible ingredients apparently were the butyl and the methyl ester of the 2,4-dichlorophenoxyacetic acid and the dioxin in the 2,4,5-trichlorophenoxyacetic acid. However, *Londono* was not sure about this. Even today there is no information about these compounds that would explain why they could cause acne. It was noteworthy that these cases were blamed on herbicides from different industrial producers. Trichlorophenol has been produced for years all over the world without any injuries.

In several articles *K. M. Schulz* [18] has investigated experimentally chloracne and he has determined the degrees of toxicity for the various substances, information which is indispensable in determining the etiology and the clinical treatment of chloracne. Finally, in 1969, at the annual convention for occupational medicine in Saarbrücken, *Weber* [22] read his report on 46 workers in an electrical appliance factory.

During a conference of factory doctors Oetzel [14] (1955) reported the experiences he had collected while doing investigation for the BASF after an unknown decomposition had occurred during the production of trichlorophenol at the BASF in 1953. 42 employees feel severely ill as a result of this decomposition. Hofmann [9] reported on this in 1957.

For some time these diseases in southwestern Germany have been repeatedly referred to, but until now no one had published an analytical summary.

Since the case reporting was particularly clear and since the toxicity of certain herbicides is as pressing a question today as it was in the past, the following sections will describe the outcome of the observations made at the time and they will investigate the responsible noxa in greater depth.

2. The accident in the factory of the BASF Company in Ludwigshafen on the Rhine

2.1. Description of the accident

The accident happened on November 17, 1953 in the factory of the BASF. An unforeseen decomposition occurred during the alkaline hydrolysis of 1,2,4,5-tetrachlorobenzene with 2,4,5,-trichlorophenol. On a commercial scale, the hydrolysis is conducted under pressure at a temperature of roughly 180°Celsius and in the presence of an alkaline methanol sodium hydroxide solution. The temperature and the pressure increased explosively in the autoclave. Previously unknown chlorinated hydrocarbons developed. Presumably their toxicity was very high.

The four floors were only accessible from the staircase and they were interconnected by window and conduits. From the second story two autoclaves extended through the floor into the room of the first story. The supply pipes go from this room, through a hole in the wall which has been sealed with sheet metal, into the other production rooms.

Large amounts of gas and steam were generated by the decomposition. The vapors were released through the safety valves and they spread all over the autoclave room, i.e., all the rooms on the four stories. By way of the staircase they entered upper rooms in the other parts of the factory. After a few minutes the vapors had more or less dissipated or formed hard deposits on instruments, walls, windows, doors, etc. and it became possible to enter the rooms.

Due to exposure to these substances 42 workers had the typical symptoms of chloracne or the perna disease. In some cases serious resorptive toxic effects developed.

The walled, fireproof autoclave section in the northeast corner of the plant was four stories high (see Figure 1).

2.2. Sanitation measures carried out by the factory

Since there had been one and then repeated incidences of chloracne, all the walls and the staircase were whitewashed several times over the following weeks and years. In compliance with the regulations the workers always wore protective clothing and Van-der-Grinten masks as protection against the gases. The walls and the instruments were sprayed several times with a chlorinated lime solution. Six painters wearing gas protection outfits painted the instruments and the walls red with a rust solvent and ferric oxide. The floors were covered with a coat of ACRONAL. Firemen later sprayed the floor with a silicon solution to further clean it. Roofers lined all the upper floors with OPPANOL. Six masons applied a second coat of OPPANOL-sheeting on all the rooms and polished it. All the rooms had to be cleaned several times with water. The autoclaves were filled with water and the carbonated products of the decomposition were drained out through an opening in the underside. Four times the autoclaves were filled with dilute sodium hydroxide and the alkaline solution was agitated inside.

Every pipe [not on xerox] had been thoroughly washed several

times with different cleaners, benzol had been boiled in the autoclaves and the instruments had been washed six times with carbon tetrachloride; but even these involved cleaning measures which later turned out to be insufficient.

Production in these rooms was resumed after a second grand scale cleansing operation. Over two years, the autoclaves were emptied 300 times without there being any signs of poisoning, but in 1958 a mechanic who had worked in and around the autoclave fell sick, although the chemical reaction in question had not been conducted in the autoclave since 1953 and the BASF had taken the product off its manufacture list.

While mechanics worked in the autoclave room after the November 17, 1953 exothermic decomposition, nothing was known about the gravity of the diseases that had been caused by the faulty reaction. Only on the occasion of a visit of a patient at the dermatological hospital of Ludwigshafen on December 3, 1953 did the medical staff learn about the gravity of the diseases.

2.3. Experiments on animals

After the first less serious dermatoses were known, an experiment on animals was conducted in the autoclave room in collaboration with the Institute for Professional Hygiene and Pharmacology of the BASF.

All the animals survived this experiment without any signs of sickness. It was therefore thought safe to assume that there could be no toxic substances left in the room. For the time being there was no reason to discontinue the repair work in the autoclave room. On December 4, 1953 however three cases of disease in fellow workers who had not been in the autoclave room at the time of the decomposition suggested that at least these last diseases could not have been caused by vapours present *at the time* of the decomposition, but by a sublimate which was left in the room *even after* the decomposition. Two of these three cases were case F. (5 years of chloracne and blepharoconjunctivitis and patient O. (toxic polyneuritis).

18 days after the catastrophic reaction another experiment was conducted. For three days animals were exposed to the interior of the autoclave. During the first days no visible changes could be observed. It was only on the fifth day after the experiment that two of the animals which had been left in the autoclave died of necrosis of the liver (see *Hofmann* [9]). These findings are typical of lesions caused by chlorinated naphthalenes or diphenyls as the case may be. However at this point in time all six employees were already sick.

3. Clinical Observations

All in all we made 42 case studies after the above described faulty reaction and the intoxication had occurred. We could determine three symptoms; they are characteristic of intoxication, in spite of the fact that they overlap and appear in combinations (see Figure 3).

3.1. Cases exhibiting only skin alterations

In 21 cases only an initial dermatitis developed. The inner organs and the central nervous system were not affected. No attempt will be made to describe all of these cases in detail. We will however take six persons of this group and summarize their cases which are of interest to us for very different reasons.

3.1.1. Case A.

Case A. had never entered the autoclave room in which the accident had occurred. Occasionally, however, he had sat in the dining room next to fellow workers; he was wearing workclothes and there was no particularly close physical contact. He developed acne on the face and on the forearms. All test results, including a liver test, were negative.

3.1.2. Case B.

The son of a severely intoxicated man suffered from the facia

skin alterations typical of chloracne, although he had never been in the plant. The only cause for his disease was contact in the home environment, a demonstration of the extraordinary toxicity of the decomposition products. (The father had a severe toxic dermatitis fere universalis. As a result of the accident he contracted a toxic polyneuritis accompanied by sensory and motor paresis of the forearms and the lower leg, flash pains as well as detectable dysfunctions of the auditory, olfactory and the gustatory organs). After the father had entered the hospital the son had slept in his father's bed, he had used handkerchiefs already used by his father and at the onset of the winter colds. he had worn several of his father's scarves, one of which had already been washed three times.

3.1.3. Case C.

Case C. was afflicted with a great variety of diseases apart from minor blushes in the face and digestive trouble: alcoholism with anacid gastritis, refractory to histamine treatments, sinusitis max. chron., laryngitis, bronchiecstasis, cholecystitis, hypothyreosis with myxedema and apoplexia. However, none of the aforementioned diseases was a consequence of the intoxication. Case C and later Case N demonstrate once again that *post hoc* does not always mean *propter hoc*.

3.1.4. Case D.

The only important aspect of Case D is that extensive and tenacious skin alterations caused by acne vermiculata and cornedosa did cause 2 [illegible] years of work disablement. There were no further internal damages.

3.1.5. Case E.

Tenacious abscesses which could reach the size of chicken eggs kept developing. On the penis and scrotum as well as other sites

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comedones and sebaceous cysts could still be found after 18 years.

3.1.6. Case F.

Apart from a severe pyretic skin inflammation which left this person incapable of being gainfully employed for five years, case F is remarkable for a chronic conjunctivitis and blepharitis. Since the Meibomian glands which lubricate the margin of the eyelid are related to the sebaceous glands in the skin with respect to the history of their development, their dysfunction had to be considered as another symptom of the chloracne.

3.2. Cases with dermatitis and lesions of internal organs

At this point we would like to express our most sincere gratitude to all the authorities in various special fields and their predecessors. In this and in the following groups of cases we have made use of the medical findings they have reported. This article could not have been written had it not been for their expert knowledge and several authoritative opinions rendered mostly by university affiliated hospitals.

3.2.1. Case G.

In 1954 W. Schmidt introduced this case to the convention of dermatologists in Mannheim. The mechanic G had worked for 3 days in the autoclave room. He was 20 years old at the time. On the second day of work he had headaches and pains in the small of the back as well as inflammatory swellings and hard infiltrations of the skin of the face and the ears. The hospitalization took seven months.

The wings of the nose were fissured and looked as if they had been scorched. The pilous skin of the head had turned dirt-colored and it was infiltrated with leathery cells. There was a substantial loss of hair. Continuing suppurations could not be

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completely controlled by antibiotics and autovaccines. ESR 60:85; liver tests at first negative; a later Takata test result was 70%. There were temporary lesions of the myocardium and a temporary bronchitis. This already impressive case included, furthermore, a nonspecific epididymitis, arthritis and finally a damaged liver. The anacidity of the gastric juices was at first taken to be a temporary consequence of the liver damages. Innumerable blackheads were the foci from which abscesses the size of a finger tip kept originating.

Several detailed clinical reports no longer regarded achylia as a consequence of the occupational accident, since experience has shown that predisposition is of decisive importance. A sinusitis maxillaris was also unrelated to the accident.

It is possible that the severe bronchitis was caused by the intoxication, but this cannot be maintained with certainty. In 1955 [illegible] and 1960 the patient received treatment in a sanatorium. In 1959 he was hospitalized for a questionable cirrhosis of the liver. A laparoscopy performed in 1959 showed hepatic and perisplenic processes although there were hardly any macroscopic changes in the liver. Histology: mild subacute hepatitis with focal hyaline degeneration, hypertrophy of involuted groups of cells and slight adipositas of liver cells with deposits the size of medium-sized drops. There were no cirrhotic transformation processes.

G.'s general state of health was at its best during his recuperative stay on Sylt. The company paid for this vacation.

G. was incapable of perspiring and he felt as if his skin were boiling.

Subacute hepatitis of a moderate degree was confirmed by laparoscopy and by splenoportography. It was accompanied by pronounced tent-or-rope shaped adhesions extending all over the epigastrium. Occasionally the findings were contradictory and the interpretations different. The diabetic sugar test was repeatedly positive; the value of the blood sugar was always normal and there was a questionable nephric diabetes. Electrocardiogram

1963: P-pulmonal, slight disturbances in the expansion of an excitation; incomplete right bundle branch block. Phonocardiogram: a doubled second tone with a perisystolic crescendo noise and a short diastolic decrescendo noise. A mitral stenosis was probable. In 1963 it was to be decided if a commissurotomy should be recommended. Mitral stenosis reached the second degree.

Specialist discussed the possibility of a toxic mitral stenosis, but this had to be excluded after a comparison of the X-rays. It turned out to be a mitral valvulopathy caused by rheumatism. Therefore, it could not later be recognized as an occupational disease. A slight albuminuria and a glycosuria without accompanying diabetes mellitus indicated residual damages following toxic nephrosis caused by "chlorinated naphthalenes".

After the 1964 hospitalization a coronary insufficiency was diagnosed. Therefore, even though penicillin had been used as a preventive measure, a tonsillectomy was performed during which tibial edemas and pulmonary hemorrhages developed: Hgb 17.8g; streptolysin titer 1280 E., SGOT 509-984; SG'PT 900-500. Thorax X-ray: shadows in the lower left section and laterally in the middle section due to the effusion. Bilateral auxocardia; hemorrhagic transudate; 750 cm³ punctate; thrombophlebitis in the left tibia. Hemoptysis contraindicated anticoagulants and caused pulmonary edema, apnea, ventricular fibrillation and cardiac arrest. The autopsy confirmed the clinical findings: a high degree of mitral stenosis which was acutely decompensated since it was accompanied by an initial hepatitis; a pulmonary embolism with infarct pneumonia and a phlebothrombosis in the left lower leg.

Summary: the mechanic G. who was 20 years old at the time, had a typical case of chloracne with perpetually recidivating finger-tip-sized abscesses. Furthermore, he suffered from temporary lesions of the heart muscle and the liver, bronchitis, residual damages due to toxic nephrosis. After a latency period of ten years, a rheumatic mitral stenosis developed. Hepatitis accompanied by thrombophlebitis of the lower leg and a pulmonary embolism, led to G.'s death at the age of 30. The mitral stenosis

which had developed after a long latency period and the new hepatitis could not be recognized as consequences of the accident.

3.2.2. Case H.

A trained mason (19 years old at the time of the accident) who had "vegetative dystonia" even before the intoxication had spent two hours walling up a hole in the autoclave enclosure. Because of follicular dermatitis of the cheeks he was disabled for 3/4 year, subsequently he spent six weeks in a spa for convalescence. During the third week of treatment, roughly one year after the intoxication, a rise in temperature was recorded. X-ray thoracography showed extensive shadows in the lower left section and extensive ulceration of the left phrenic-costal pleura. Shadows stretching up to the third right frontal rib, indicated further deterioration. ESR 28:54; Hgb 78%; Leuko 16,000. The left apical field and the left upper field were both diffusely clouded. Hence, the lung findings indicated not fully developed, but an on-going process. The differential diagnosis indicated either a specific pleural problem or a tumor.

A severe hemorrhagic pleurisy brought about a hospitalization. Temperature: 38.5°C.

The results of a pleural puncture were: 900 ccm of pure hemorrhagic effusion; specific weight 1023 g; the smear revealed massive Ery. eosinophilia. Experiments on animals and cultures gave only negative results. The eosinophilia would suggest some form of lymphogranulomatosis, but the histology and the final outcome of the diseases exclude such a hypothesis.

Later the assumption of a pleural tumor had to be excluded. A tonsillectomy was found necessary because the tonsils were suspected to be foci. The pleural effusion dissipated, leaving only a cup-shaped turbidity in the left side of the lung, while the diaphragm joined at the angle formed by the ribs on the left. Since there was no specific etiology nor any toxic foci, it would be hard to dispute the causal relation to the accident.

overcome. Two treatments in a sanatorium brought about a cure.

In 1959 H. suffered an acute psychosis with insomnia, hearing of voices, ringing in the ears, suicidal attitude and physical discomforts like burning sensations in the back. A TAXILAN (perazine) treatment was administered and a guardian was appointed.

Clear schizophrenic mental condition with increasing listlessness pronounced affective changes, and finally hospitalization on the grounds of schizophrenia. Suicide by hanging.

Summary: The disease began with a banal dermatitis of the cheek. Eleven months after the carbonated halogen poisoning, which H. had overcome, he suffered a severe *hemorrhagic pleurisy*, a consequence of the poisoning. Subsequently he recovered completely. *The schizophrenia and the suicide, 5-1/2 years later, were not related to the intoxication.*

The question of whether the schizophrenia which brought about his tragic end was causally related to his occupational disease is answered negatively in detailed medical reports.

3.2.3. Case I.

In 1958 a 57 year old employee and a colleague of his did some installation work on the autoclave agitator in the same part of the plant where 5-1/2 years earlier an accidental reaction had occurred. In order to lift a cover and put in a new seal he had to turn the screw away with a blowpipe. During the replacement of the agitating mechanism a ball bearing was heated. This led to the development of vapors. In compliance with the regulations he was wearing protective clothing consisting of a rubber outfit and a gas mask, but he had taken off the mask several times to wipe the sweat off his face. Four days later: burning facial skin, follicular dermatitis, headaches and hearing problems. The liver test was negative. One month later he was hospitalized on ground of a stenocardia. Six months later

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he had to stay in bed to be treated for pancreatitis. The size of the liver had increased: 1-2QF. Temperature: 38.2°C; BSR 35:56 to 82:104; diastasis: 256 to 512 WE. Later a firm tumor in the left epigastral area caused great pain, growing to the size of a child's head. Leuko 18,000, an anacidity which was refractory to histamine treatment, obstinate constipation. 1959: reduced E and A2, somnolence, chills, maximum temperature 41.9°C, Leuko 21,000. Exitus.

The autopsy showed that the necroses were numerous after the pancreatitis and there were perforations the size of a bean in both stomach and bulbus duodeni. Macroscopy could not determine if calculi had grown in the stomach and the duodenum or if a penetration of the pancreas into the stomach and the duodenum had occurred. Furthermore, there had been a widespread formation of abscesses on the lower surface of the liver, general cachexia and chloracne on the stem of the liver.

Summary: The first time patient I. had been exposed to the products of the trichlorophenol decomposition was in 1958, 5 years after the accident had occurred. He was so unprotected from the exposure that he developed an acute skin disease with skin alterations which were typical of the perna disease. It was a sign of the gravity of the primary exposure that these alterations spread to other parts of the body and were still present at the patient's death, 9 months after the contact with the toxin. The patient died of a pancreatitis which the autopsy confirmed. Apart from numerous necroses of adipose tissue, there was a double pea-sized perforation in the middle of the stomach and a duodenal ulcer with penetration into the pancreas. The point of perforation covered the pancreas thus establishing a direct communication between both.

Oettel and colleagues of his had conducted experiments on animals which showed that one single administration of the toxin (5 micrograms kg body weight) was sufficient to cause necrosis of the liver and after weeks or months, brought about the death of the animals. Furthermore, it is known specifically that

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the products of a trichlorophenol decomposition affect the lipase metabolism which is related physiologically to the pancreas. These considerations lead to the conclusion that *the necrosis of the pancreas* was most probably a late consequence of the poisoning caused 9 months earlier by the products of the trichlorophenol decomposition. The trade union paid an appropriate indemnity for the necrosis of the pancreas.

3.2.4. Case J.

Case J. was an elderly employee with a chronic interstitial cirrhosis of the liver in his medical history. An exposure to the toxic products caused only laryngitis and tracheitis. After an operation on the upper jaws the trade union withdrew the temporary pension of 20% it had been paying for the sinusitis.

3.2.5. Case K.

In 1953, Case K. had taken a dirty chain hoist from the autoclave room and had worked on it. After that skin eruptions occurred. Lab results: (1954) Takata 30; Gros [illegible]; Wuhrmann [illegible]; electrophoresis: alpha-, beta- and gamma-globulin very high; BSR on March 22, 1954: 22:44. The patient complained of fatigue and dyspepsia. He was disabled until August, 1955. In 1954 he was treated for a hepatolienal syndrome, *hepatitis and splenitis*, jaundice, fully compensated cirrhosis of the liver, hyperacidic gastroduodenitis and dysfunction of the auditory nerve on the left side. The liver test was finally negative. A liver test made in 1966 was also negative.

Summary: In K.'s case the intoxication led to dermatitis and, additionally, to a *hepatitis and splenitis* with complete disablement and 100% compensation for a 1-1/2 year period, then one more year of a 49% decrease in income, reduced later to 20%. Two and one-half years after the accident liver dysfunction could no longer be detected.

3.2.6 Case L.

In 1953 L. had spent a very short time loosening screws on the cover of a manhole. Two days later L displayed dermatitis. Takata 1955: 60%; thymol ++.

Summary: L. had lesions of the liver cells and laryngitis. He received compensation for complete disablement. The laryngitis corresponded to a 10% decrease in income. According to experts, in 1967 the liver dysfunction was still responsible for a 20% decrease in earning capacity. The following were not classified as recognized occupational diseases: pneumonectasis, gastritis affecting the esophagus, vegetative dystonia and hardness of hearing on the right side.

3.2.7. Case M.

Eight months after the accident, the 43 year old employee M. suffered an *acute sinusitis maxillaris* on the left side accompanied by a purulent rhinitis. In 1963, the sinusitis maxillaris on the left side chronically recurred. This recidivation could not be considered a consequence of the intoxication. The same holds for the 1963 angiosteosis of the tibialis anterior and posterior arteries. In 1966, there occurred a trophic decalcification of the right wrist. Like M. Sudcek's disease exhibited a wrist sclerosis syndrome and pronounced sclerosis of the blood vessels.

3.3 Cases with dermatitis and lesions of the central nervous system

3.3.1. Case N.

In 1954 Schmidt introduced this case to dermatologists from southwest Germany who had convened in Mannheim. The clinical findings were as follows:- four days after exposure: dermatitis of the thighs, the legs and the feet. There were no dysfunction of the bladder or the rectum. After seven weeks all neurological

symptoms had disappeared. At the end of September, 1954 a toxic polyneuritis started developing.

Summary: In N.'s case there was a neurasthenic syndrome and skin alterations caused by chloracne on the legs, the buttocks and the penis. His case is impressive because, in addition, there were dysfunctions symptomatic of a *toxic polyneuritis* with hyporeflexia, hypotonia of the muscular system and hyperalgesia in the saddle block region. The changes in the central nervous system were evaluated to cause a 30% decrease in earning capacity. For years the results of repeated liver check-ups were negative. A vegetative dystonia and a fixation neurosis were not at all connected with the accident.

3.3.2. Case O.

This 24 year old employee assisted once at a dismantling about six weeks after the faulty reaction. He was wearing appropriate protective clothing. He suffered mild nondisfiguring skin alterations and, most of all, nervous dysfunctions with fatigued legs and irritation of the upper air passages. Fourteen years after the intoxication a subarachnoid hemorrhage occurred. The appraisal determined that this bleeding was independent of the accident, since in 1953 there had been only functional disorders.

3.3.3. Case P.

An initial dermatitis on the face, ears, throat, neck, breast and back was later aggravated by the formation of abscesses. A temporary anosmia caused by a peripheral toxic lesion of the nervous olfactorius lasted one year. A pyretic stomatitis and gingivitis recidivated. An organic psychosyndrome with neurosis was diagnosed. Five years after the intoxication a duodenal ulcer had formed, it recurred for 10 years.

3.3.4. Case Q.

The first skin alterations occurred four days after the accident. Q. undertook two cures in 1954. On January 15, 1954 an X-ray of the lumbar region showed a degeneration of lumbar disk 5 with spondylosis deformans of the adjacent vertebrae.

In 1955 gastritis could be diagnosed by X-ray. In addition to chloracne, the medical record included a chronic inflammation of the conjunctiva and the incibomian glands as well as trophic disorders of finger-and toenails of the hands and the left foot. The strength of the left leg was diminished. The proprioceptive reflexes were livelier on the left side. The clonus in the left foot was always active. The Babinski sign was weakly positive on the left side. The muscles of the left leg were atrophied. (Decrease in circumference of 3 cm for the left upper leg and 1 cm for the left lower leg as compared with the equivalent measurements of the right side).

Thus this was a case of toxically disseminated encephalomyelitis with mild hyperesthesia and hypalgesia extending distally from the left upper leg. Furthermore, there was a spondylosis (left 5) and an osteochondrosis (semilunar lunate). Trophic disorders were observed in the left leg and the left foot with a clonus on that foot. The sensation of vibration in the left leg was remedied.

In 1959 the diagnosis showed a pronounced spastic syndrome on the left side of the body particularly involving the left leg, as well as neurasthenic symptoms which were suggestive of a toxic lesion of the central nervous system.

Summary: Apart from the skin alterations, which in the case of seborrhea led to cheloids on breast and throat, Q. had *chronic conjunctivitis* and *blepharitis* as well as a *toxic disseminated encephalomyelitis with a spastic hemisindrome on the left side*. Because of these neurological disorders, S. (sic) receives to this day a 35% annuity from his trade union. In 1971, a hydrops of the right knee joint and a bilateral Dupuytren's contracture occurred, both consequences of the accident.

3.3.5. Case R.

R. spent a short time working in the autoclave room. After seven weeks R. suffered from *facial paresis* with *ageusia* of the *left side*; both were *unrelated to the accident*. The rest of the findings were of no importance.

4. Discussion

The medical literature (see [1,2,3, etc.]) has described the characteristic groups in which the various diseases connected with acute chloracne fall. Since 1953, the BASF has witnessed the important and typical disorders as they appeared in the form of severe skin damages, disorders of the liver, lesions of other inner organs and changes in the nervous system.

To 3.1. In 21 cases there was an *initial facial dermatitis* particularly affecting the lobules of the auricle and the cheeks. There were irritations of the conjunctiva with acne slowly developing predominantly in the face but also on the neck, the shoulder, the trunk, and all over the body, even on the penis and the scrotum. The visible symptoms were comedones, retention cysts, nodules, pustules, furuncles and the formation of abscesses. Almost all cases had these symptoms, although to varying degrees. Two cases additionally exhibited a tenacious *chronic conjunctivitis and blepharitis*.

To 3.2. Fourteen cases had disorders of *internal organs* in addition to the skin symptoms. There were *four cases of hepatic damage*. A characteristic microscopic finding of the biopsy was the storage of an iron-free gray pigment. Furthermore, there were temporary *lesions of the heart muscle* and *toxic nephrosis*. Inflammations of the upper air passages with *laryngitis, tracheitis and bronchitis* were diagnosed in five cases, one of which was complicated by a severe *hemorrhagic pleurisy*, another one by a tenacious pyretic *gingivitis and stomatitis*. A number of cases were generally sensitive to infections as a consequence of the diseases, sometimes this was shown as a significant decrease in

blood serum gamma globulin. One case died of a typical pancreatitis.

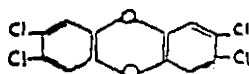
To 3.3. Dermatitis and disorders of the central nervous system, general fatigue and neuromuscular weakness occurred almost regularly. The central nervous system was unequivocally affected in seven cases. Three times it was diagnosed as a peripheral toxic polyneuritis, twice as peripheral toxic damage to the auditory, olfactory and gustatory organs and twice as a toxic disseminated encephalomyelitis with a hemisindrome. Other authors (see [1]) set up a fourth group for vegetative complaints with neurasthenic symptoms, i.e., subjective complaints concerning changes in mood, lack of motivation, sleep disorders, particularly an increased need for sleep, and decrease of libido and potency. Several of our cases developed neurotic personalities and often made inadequate claims for damages. We did not take this group into consideration in our evaluation (Figure 3). Similar complaints were voiced by persons in any of the three groups, whether an internal or neurological disorder could be objectively diagnosed or not.

Since Herzheimer, in 1899, there have been various opinions thought chlorine gas was responsible. According to Braun, the decisive prerequisite was a protracted direct contact with chlorinated organic compounds, mostly belonging to the naphthalene group (see [2]). In 1968, 1000 workers in Japan suffered chloracne and lesions of inner organs caused by chlorinated rice oil [15]. In Weber's observations, chloracne had developed practically only in seborrheic patients. He found out that the responsible substance had to be in the state of a vaporous melted form, in order to cause a perna disease.

In the great majority of studies, highly chlorinated chlorophenols are considered to be responsible for the toxic effect. Kimmig and Schulz [4] have proven that analytically pure tri- and pentachlorophenol cannot produce the expected chloracne symptoms.

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Once experimental test results had been gathered by critically exploring the literature on occupational medicine, and once the circumstances of the 1953 accident at the BASF had been taken into consideration, the suspicion arose that at least in the particular instance perchlorinated naphthalene [21] did not cause the typical perna disease; most probably it cannot be made responsible for any poisonings elsewhere either. The decomposition at the BASF did not produce perchlorinated naphthalene. It is reasonable to assume that the same impurity that caused the intoxication at the BASF was the toxic substance which caused the innumerable chloracne cases that occurred in various other parts of the whole world. After years of experimentation, the isolation of a by-product of the industrial conversion process succeeded [11,8,18]; it turned out to be 2,3,6,7-tetrachlorodibenzodioxine = tetrachlorodiphenylenedioxide



According to present day knowledge, one assumes that the following compounds are responsible for chloracne:

1. Five to six times chlorinated naphthalene, the efficacy of which remains in our opinion unclear.
2. The toxicity of more chlorinated diphenyl oxides which was 100 times higher than that of chlorinated naphthalenes seems to be established with greater certainty. This substance could not have been the toxin liberated at the accident at the BASF.
3. 2,3,6,7-tetrachlorodibenzodioxine. One peroral administration of 20 to 50 micrograms/kg body weight regularly brought about a fatal hepatic necrosis in rabbits; doses of 10 micrograms/kg proved fatal to half of the rabbits. In tests at the Institute for Professional Hygiene and Pharmacology 10 micrograms/kg were always deadly, whereas doses of 3 micrograms/kg caused liver damage without being fatal. The toxicity ratio of hexachloronaphthalene to tetrachlorodibenzodioxine was 1000 to 10,000:1. Thus the latter toxin is 10,000 times more effective in tests

on animals. The pathogenic effect seems to be dependent on the cyclic ether structure.

The chemical compounds of an aromatic halogen hydrocarbon nature that have been described can be absorbed through the skin since they are lipid soluble. *Braun* had described skin resorption in his monograph. Our cases A and B were also caused by skin resorption. For occupational medicine this possibility is of little importance, since the organism mostly absorbs the toxin by inhalation of vapors. All the diseases in question here were occupational diseases which would be catalogued under No. 9 of the list established by the 7th BKVO.

In connection with our observations, a new number was added to the list: to the disorders caused by aromatic halogen hydrocarbons those caused by chlorinated + aryl oxides were added. According to No. 46 of the occupational disease list, the different kinds of chloracne are not skin diseases.

5. Definitive demolition of the building

The safety measures which were taken at the demolition of the autoclave room from Winter 1968 to Spring 1969 had been established in writing beforehand. The destruction work was carried out with the greatest precautions and under careful supervision of the security organ of the BASF. In 1969, the demolition of the autoclave room could be considered completed. There were no injuries in connection with the demolition..

6. Therapy

All therapies, no matter how involved, will hardly influence the chronic progress of chloracne. The removal of comedones is always recommended and practiced. [Illegible]. Most successful therapies, relatively speaking, were cures (sulfuric and salicylic skin peeling acid), most frequently using Lassar's paste (i.e., naphthol and sulfur). Greater successes have recently

been made with local vitamin A acid treatment [15].

Although the use of climatotherapy was widespread until 1968, it effects no change in the chronic progress of the disease, but it revivifies the patient.

7. Summary

Detailed occupational and case histories are reported in connection with an accident arising from an unforeseen chemical reaction, which occurred in works in 1953.

It was found that 2,3,6,7,-tetrachlordibenzodioxin was the toxic substance responsible for skin changes in a total of 42 serious cases, where 14 persons suffered consequent damage to internal organs and 7 persons experienced disturbances of the nervous system. Appropriate chemical investigations, as well as tests on animals, were undertaken to establish the substance involved.

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Figure 1. The autoclave room [the photo would not xerox].

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Figure 2. Measures carried out by the factory after the intoxication caused by the products of the trichlorophenol decomposition

The accident occurred
on November 17, 1953

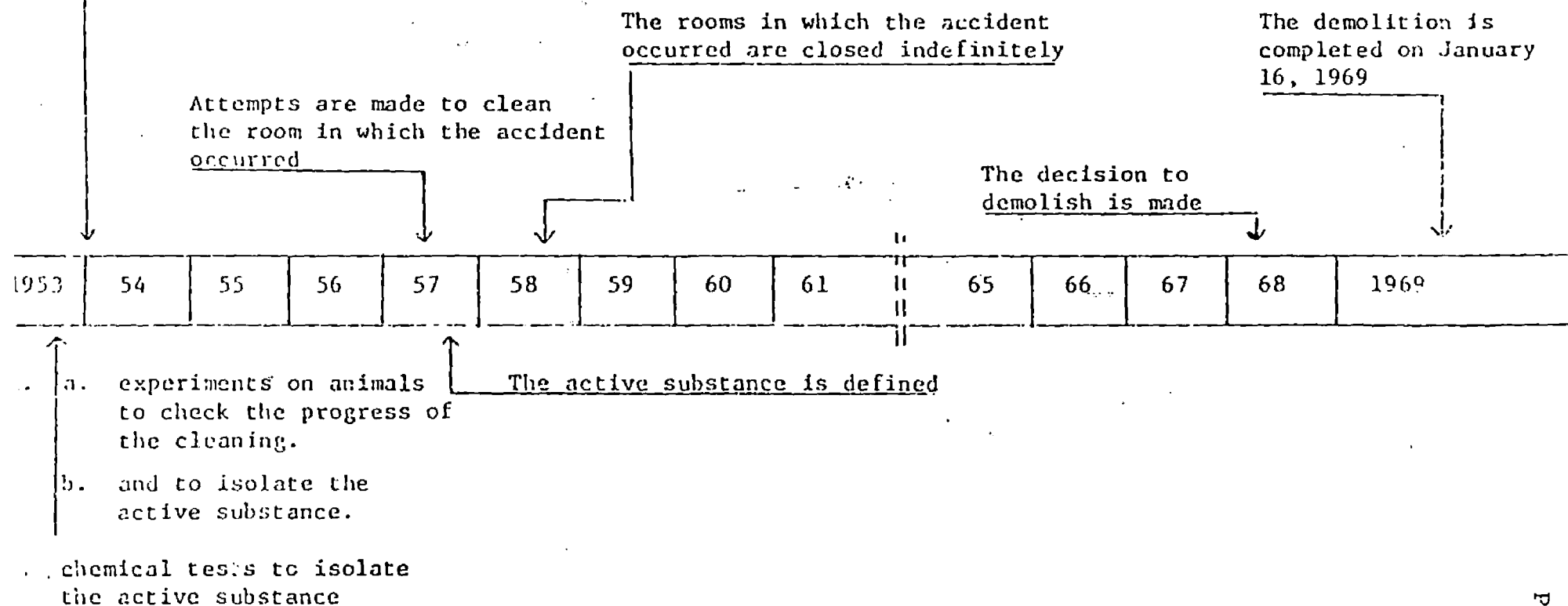


Figure 3. General intoxication caused by the products of a trichlorophenol decomposition on November 17, 1953.

