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SEVERE, ACUTE CHLORACNE, A MASS INTOXICATION
DUE TO 2,3,6,7-TETRACHLORODIBENZODIOXIN

by

Paul J. Goldmann *

1. Previous Events

In 1953, acute and very severe cases of the disease chloracne were observed after an unpredicted chemical reaction in a particular production unit of the Baden Aniline and Soda Factory (BASF). Neither before, nor after have any further cases of chloracne occurred after this one-time mass intoxication.

During alkalic hydrolysis of 1,2,4,5-tetrachlorobenzol into 2,4,5-trichlorophenol, there occurred an unknown reaction in the autoclave unit. Thereby, as it was later assumed, severely toxic "chlorinated hydrocarbons" were formed.

Out of the total number of 55 patients who developed typical chloracne, three cases were of special importance:

1. A dermatitis in a female animal nurse who was contaminated only by the contact with test animals.

* "Schwerste akute Chloracne, eine Massenintoxikation durch 2,3,6,7-Tetrachlorodibenzodioxin.", Der Hausarzt 24: 149 - 152, 1973. GERMAN.
A lecture on the occasion of "Medichem", the 1. International Symposium of the Factory Physicians of the Chemical Industry, April 27 - 29, 1972, at BASF, Ludwigshafen, W. Germany.

2. A fatality due to pancreas-necrosis in a person who in 1958 only briefly visited the autoclave unit illustrated [Fig. 11].
3. The skin symptoms of a 14 year old son of one of the employees due to contact with a scarf and a towel in his home, although the scarf and the towel had been laundered repeatedly.

The anamnesis of the work situation and the disease, later animal experiments, and the analyses indicate that it was not the vapors formed during the reaction which caused the disease, but a residual sublimate from the inappropriate reaction still remaining in the unit. up to 1958 and 1969 [see Fig. 4].

Of the 55 persons afflicted, only 42 cases were, for various reasons, found relevant after the evaluation of the case histories. In about half of the 42 cases, there were, besides skin symptoms, at times very serious, resorptive toxic effects.

2. Casuistry.

When evaluating the 42 actual cases of health disturbances caused by the poisoning, a polymorphic picture of a chloracne disease accompanied by multiple organ-symptoms developed.

The sketch [Fig. 2] is intended to elucidate this polypathy. It is, however, only possible to illustrate approximately the size of the sectors, because of the simultaneous and concurrent organ symptoms. In figure 3, particularly 4 cases of hepatitis, one case of toxic pleuritis, and the above mentioned lethal case of pancreas-necrosis appear striking. Wildhirt in Kassel has published 8 cases from our and his own patient material: he assumes that the intoxication

in 1953 was the indirect cause of a later viral hepatitis in 2 more persons. With only 2 further cases, the liver damages do not stand in the forefront according to our review (see Table I).

In the adjacent table, the overlapping and combined symptomatics in respect to the resorptive disturbances are displayed for the 14 most severe cases [see Table II].

Tables 2 and 3 emphasize once more the clinical forms of the most severe intoxications and for 3 patients also the later causes of death. In all the cases, there were, simultaneously, chronic, relapsing skin alterations or abscesses, lasting for years.

3. Causative Toxin

Ever since Herxheimer as the first in 1899 described chloracne, there have been various opinions on the nature of the triggering cause. In 1968, it was assumed in Japan that rice, contaminated by chlorine, was the cause of about 1000 cases of this disease, accompanied by alterations of the internal organs.

In respect to the poisoning cases mentioned at the BASF in 1953, we succeeded after the most diversified active measures in isolating a by-product of the technical conversion process [Fig. 4], which turned out to be 2,3,6,7-tetrachlorodiphenylene dioxide = 2,3,6,7-tetrachlorodibenzodioxin [diagram A].

During animal tests in the medical-biological research laboratory of the BASF, 10γ/kg was always lethal to rabbits; 3 γ/kg allowed for survival, but still caused liver damages.

The relation of the toxicity of hexachloronaphthalene - which as

the purported causative agent gave rise to the term perna-disease - to that of tetrachlorodibenzodioxin is 10,000:1, that is, the latter is 10,000 times more effective in tests on animals.

Chloracne is not a skin disease in the sense of Item 46 of the 7th Ordinance on Occupational Diseases, but corresponds rather to Item 9 on the list, that is, it is caused by the inhalation of toxic substances into the organism. In the connection with our own observations on this disease, we have given it a definition of its own: damage to the health due to aromatic hydrocarbons and due to *chlorinated aryl oxides*.

4. Differential Diagnosis

In addition to a photo-sensitive melano-dermatitis, benzanthron causes a chloracne-like reaction accompanied by pimples and inflammation of the sebaceous glands [Fig. 5]. At the BASF, there have been 62 cases observed of a similar dermatitis since 1955. Benzanthron has the following structure [see diagram B].

5. Therapy

The most important is a treatment of the vital resorptive disturbances. Visually checked results only after local treatment must always be considered as insufficient.

Since the 30th German Dermatologist Conference, the treatment of *Aene vulgaris* and chloracne with Vitamin A-acid has been much discussed. Vitamin A, administered in subtoxic doses against psoriasis and all kinds of hyperkeratoses had failed. In low doses, as a 0.05 - 0.3% solution or ointment applied locally, it functions against peeling.

It interferes with the keratinization and the proliferation of the cells. As demonstrated by aid of autoradiography [Plewig], the Vitamin A-acid has no point of attack against the sebaceous follicles.

Summary

A clinical-causative report on the medical consequences of an unpredicted industrial reaction in 1953. During a search for the toxic cause of skin alterations in a total of 42 persons of which 14 cases in addition showed damages to the internal organs and disturbances of the nervous system, 2,3,6,7-tetrachlorodibenzodioxin proved to be the decisive chloracne-provoking agent.

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[See the original.]

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Figure 1: The autoclave unit.

Figure 2: Diagram of the occurrence of organ alterations accompanying chloracne. The polymorbidity and pathology of our chloracne patients can also be illustrated in another form [Fig. 3].

- Key:
- a) only the skin
 - b) skin and parenchym. organs (liver, spleen, kidneys)
 - c) myocardium
 - d) air ducts
 - e) connective tissues, Meibom's glands, cornea
 - f) and Central Nervous System

Figure 3: Mass intoxication due to trichlorophenolic by-products on Nov. 17, 1953.

- Key:
- a) 42 cases total with dermatitis
 - b) 21 cases with initial dermatitis
 - c) 13 cases with dermatitis and damages to the internal organs.
 - d) 7 cases with dermatitis and damages to the central nervous system, that is, toxic polyneuritis, dissem. encephalomyelitis, and peripheral damages to the auditory, olfactory and gustatory organs.
 - e) 4 cases of hepatitis
 - f) 1 case of toxic nephrosis
 - g) 5 cases of tracheo-bronchitis incl. 1 with haemorrhagic pleuritis.
 - h) 3 other internal disturbances
 - i) 1 lethal case due to pancreas-necrosis.

Figure 4: Active measures taken after the intoxication by trichloro-phenol-processing by-products.

- Key:
- a) Accident occurred, Nov. 17, 1953.
 - b) Attempts to clean up the site of the accident.
 - c) The locality of the accident finally closed.
 - d) Decision to tear down the site.
 - e) The destruction completed, Jan. 16, 1969.
 - f) a) test on animals
 - in order to control the clean-up action;
 - in order to find the active agent.
 - b) chemical tests in order to discover the active agent,
 - g) Active agent identified.

Figure 5: Chloracne-like skin alterations due to benzanthron.

Diagram A: 2,3,6,7-tetrachlorodibenzodioxin

Diagram B: Benzanthron

Table 1. Review of the chloracne patients with damages to the internal organs and the central nervous system at the BASF, 1953.

Column 1) Current no.

- 2) Age (in years)
- 3) Onset of disease after exposure
 - a) Tag(e) = day(s); WO = week(s)
- 4) Hospital treatment for
 - a) Mon = months; Wo = weeks
- 5) Incapacity to work lasting
 - a) months
- 6) Periods of treatment
- 7) Dermatitis
- 8) Fever
- 9) Fatigue
- 10) Dyspepsia
- 11) Conjunctivitis; blepharitis
- 12) Gingivitis; stomatitis
- 13) Heart ailment
- 14) Bronchitis
- 15) Pleuritis
- 16) Liver damages
- 17) Nephritis
- 18) Pancreatitis
- 19) Spleen ailments
- 20) Headaches
- 21) Pains in arms and legs
- 22) Polyneuritis
- 23) Encaphalo-myelitis
- 24) Hyporeflexis
- 25) Hyperalgesia
- 26) Anosmia
- 27) Auditory disturbances.

Table 2. Damages to internal organs accompanying chloracne in 7 patients.

1. Myocarditis, hepatitis, tracheo-bronchitis, nephroses, complete recovery. Independently of the accident, in 1964, rheumatic mitralstenosis and death (hepatitis, thrombophlebitis, pulmonary embolism).
2. Severe haemorrhagic pleuritis 11 months after the intoxication. Recovery. Five years later, schizophrenia and suicide.
3. Exposed only in 1958. Six months later, pancreas-necrosis and death.
4. Laryngo-tracheitis.
5. Hepatitis, splenitis.
6. Hepatitis, laryngitis.
7. Dyspepsia.

Table 3. Predominantly damages to the neurological organs due to chloracne in 7 other patients.

1. Toxic polyneuritis (hyporeflexis, hyperalgesia, hypotony of the muscles).
2. Fatigue in the legs, tracheobronchitis, independent of the accident 10 years after the intoxication: subarachnoidal bleeding.
3. Peripheral paresis of *nervus olfactorius*, anosmia, relapsing gingivitis and stomatitis. Five years after intoxication: *ulcus duodeni*, relapsing after 10 years.
4. Disseminating encephalitis with spastic semi-lateral syndrome, chronic conjunctivitis and blepharitis.
5. Toxic polyneuritis: sensible and motoric pareses of the lower arm and leg. Disturbances in the auditory, olfactory and gustatory organs. Filial chloracne.

(continued)

(Table 3, continued)

6. Polyneuritis with rheumatic discomfort in the legs.

After 5 months, hepatitis.

7. Medium severe, combined middle- and interior-ear
auditory difficulties. Hepatitis.

18.112 # 91

Bernard A. Schwetz, D.V.M., Ph.D.

cc Rowe Gehring

← (Michalski)

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SEVERE ACUTE CHLORACNE, A MASS INTOXICATION BY 2,3,6,7-TETRACHLORODIBENZODIOXIN

by Paul J. Goldmann

Dermatologist
Der Hautarzt, 24, No. 4, p. 149-152, (1973)

CASE HISTORY.

In 1953 at the BASF acute pronounced forms of disease were observed after an unpredicted reaction in a certain part of the plant. Never before nor later further cases of chloracne have occurred after this single mass affliction.

On alkaline hydrolysis of 1,2,4,5-tetrachloro benzene to 2,4,5-trichloro-phenol in an autoclave room this unknown decomposition took place. It was assumed that very toxic "chloro hydrocarbons" were formed in this reaction.

Of the total of 55 persons showing the typical picture of chloracne, three cases were of importance:

1. A dermatitis of an animal keeper which was caused only through contact with experimental animals.
2. A fatality still in 1958 due to pancreas necrosis after a brief stay in the autoclave room shown in the picture.
3. Skin disease of a 14 years old son of an employee through a scarf and towel in household milieu although scarf and towel have been washed several times.

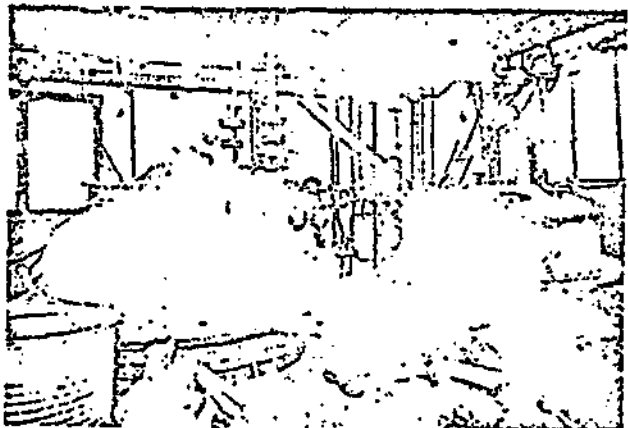


Fig.1. The autoclave room.

Work and disease anamnesis, subsequent experiments with animals and analysis indicated that the diseases were not caused by some vapours formed during the decomposition but by a sublimate remaining in the room after the faulty reaction even still in 1958 and 1969.

Of 55 persons afflicted, after evaluation of the case histories, for various reasons only 42 cases were relevant. For more than half of the 42 cases besides skin changes partially also very serious resorptive poisoning effects were observed.

2. KASUISTRY.

In our 42 essential observations of disturbances of health due to intoxication, a polymorphous disease picture of a chloracne with multiple organ attack was found.

The diagram explains the polypathy. Due to the simultaneous organ symptomatic the size of the sectors can be illustrated only approximately. In fig.3 the three hepatides are especially noted, also toxic pleuritis and the fatal pancreas necrosis mentioned. Wildhirt in Kassel has published 8 cases of hepatitis from his and our case histories. He assumes that the intoxication in 1953 was responsible as direct cause of a later virus hepatitis of two persons. In two further cases the liver damage was not predominant in our summary (see table 1).

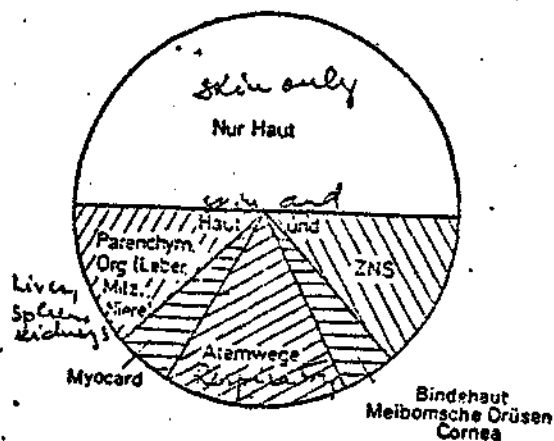


Fig.2. Diagram of the organ changes in case of chloracne. The polymorbidity and pathology of our chloracne cases can be expressed still in another form.

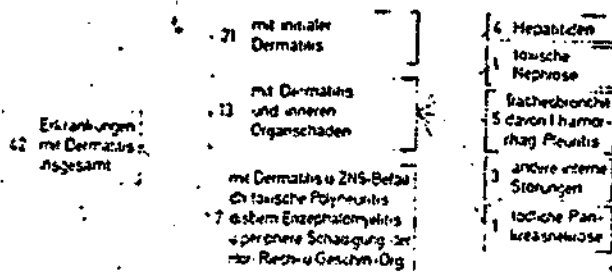


Fig.3. Mass intoxication through decomposition products of trichlorobenzene on Nov.17, 1953.

other internal disturbances
fatal pancreas necrosis

(42 dermatitis total; 21 initial dermatitis; 13 dermatitis and damage of internal organs; 27 dermatitis and ZNS, i.e. toxic polyneuritis, encephalomyelitis and peripheral damage of hearing smelling and taste organs;

Table 1. Summary of chloracne with internal and ZNS-damage 1953 at the BASF.

Lfd. Nr.	Alter (Jahre)	Krankheitsbeginn nach Exposition	Krankenhausbehandlung	Arbeitsunfähigkeit	Heilkuren	Dermatitis	Temperatur	Müdigkeit	Dyspepsie	Conjunctivitis Blepharitis	Gingivitis Stomatitis	Herz	Bronchitis	Pleuritis	Leberschäden	Nephritis	Pankreatitis	Milz	Kopfschmerzen	Schmerzen an Armen und Beinen	Polyneuritis	Encephalomyelitis	Hyporeflexia	Hyperalgesie
1	20	1 Tag	7 Mon.	18 Mon.	3	+																		
2	19	4 Tage	3 Mon.	9 Mon.	3	+	++																	
3	57	4 Tage		6 Mon.	2	+																		
4	47	1 Tag		7 Mon.	2	+																		
5	33	10 Tage		17 Mon.	1	+																		
6	43	2 Tage	5 Wo.	24 Mon.	2	+																		
7	47	2 Wo.	4 Mon.	6 Mon.	2	+																		
8	10	4 Tage	2 Mon.	24 Mon.	1	+																		
9	24	3 Tage		14 Mon.	1	+																		
10	30	4 Tage		21 Mon.	1	+																		
11	20	4 Tage	0 Mon.	9 Mon.	2	+																		
12	51	6 Tage		19 Mon.	1	+																		
13	26	6 Tage		19 Mon.	4	+																		
14	22	1 Tag		21 Mon.	2	+																		
				210 Mon.		14	4	3	2	3	2	1	0	1	0	1	1	1	5	0	1	1	1	1

Eye

Begin of illness after exposure

Hospital treatment

Incapable to work

Healing cures

Tiredness

Heart

liver damage

spleen

Head aches

Pain in arms and legs

The next table shows the overlapping and combined symptomatic of the respective disturbances of the 14 most serious cases (see table 1).

Table 2 once more lists the clinical forms of the most serious intoxications, in 3 cases also the causes of later death. In all cases simultaneous chronic recurring skin changes up to abscessing for years were observed.

Table 2. Chloracne damage of internal organs of 7 patients.

- | | |
|---|---|
| 1. Myokarditis, Hepatitis, Tracheobronchitis, Nephrose, Restitutio ad integrum. Unfallunabhängig 1964 rheumatische Mitralklappenstenose und Exitus. (Hepatitis, Thrombophlebitis, Lungenembolie). | |
| 2. Schwere hämorrhagische Pleuritis 11 Monate nach Intoxikation. Restitutio. 5 Jahre danach Schizophrenie und Suicid. | 2. Severe hemorrhaging pleuritis 11 month after intoxication. Restitutio. 5 years thereafter schizophrenia and suicide. |
| 3. Exposition erst 1958. 6 Monate später Pankreasnekrose und Exitus. | |
| 4. Laryngotracheitis. | |
| 5. Hepatitis, Splenitis. | |
| 6. Hepatitis, Laryngitis. | |
| 7. Dyspepsie. | 3. Exposure only in 1958. Six months later pancreas necrosis and exitus. |

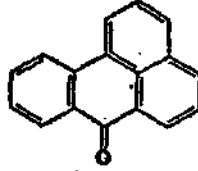
Table 3. Predominantly neurologic organ damage by chloracne of 7 further patients.

1. Toxic polyneuritis (hyporeflexia, hyperalgesia, hypotonia of muscles).
2. Tiredness of legs, tracheobronchitis, independent of the accident 10 years after intoxication subarachnoidal bleeding.
3. Peripheral paresis of N. olfactorius, anosmia, recurring gingivitis and stomatitis. 5 years after intoxication Ulcus duodendi, recurring after 10 years.
4. Disseminated encephalitis with spastic half side syndrom, chronic conjunctivitis and blepharitis.
5. Toxic polyneurosis: sensible and motoric pareses of lower arms and lower legs: Disturbances of hearing, smelling and taste organs. Filius chloracne.
6. Polyneuritis with rheumatic complaints of extremities. After 5 months hepatitis.
7. Moderate combined middle and internal ear loss of hearing. Hepatitis.

3. TOXIN WHICH CAUSED THE DISEASE.

Since the first description of chloracne by Hexheimer in 1899 there have been various thoughts about the nature of the cause. In 1963 in Japan chlorinated rice was presumed as the cause of over 1000 cases with changes in the internal organs.

For the described poisoning in 1953 at BASF it was possible to isolate from the technical conversion process a byproduct which was found to be 2,3,6,7-tetrachloro diphenyldioxide = 2,3,6,7-tetrachloro dibenzo dioxin.



*

In experiments with animals at the medical-biological laboratories of the BASF 10 μ /kg was always fatal for rabbits; 3 μ /kg dosis was survived but still caused liver damage.

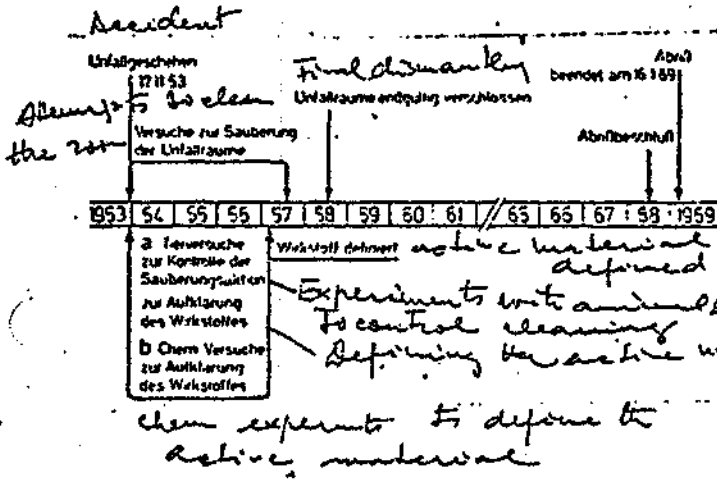


Fig.4. Plant measures after intoxication with decomposition products of trichlorophenol.



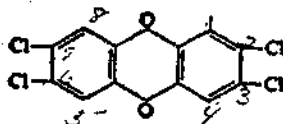
Fig.5. Chloracne-like skin changes through benzantrhon.

The ratio of toxicity of hexachloro naphthalene which apparently as causal agent has given the name to the Perna disease, and tetrachloro dibenzo dioxin is 10,000 : 1, i.e. the latter is 10,000 times more toxic in animal experiments.

The chloracne is not a skin disease according to No. 46 of the 7th Occupational Disease Ordinance but it corresponds to the No.9 of the list, and is caused predominantly through breathing of toxic substances into the body. In association with our disease observations our own designation was derived: Damage of health through aromatic hydrocarbons and through chlorinated alkyl oxides.

4. DIFFERENTIAL DIAGNOSIS.

Besides a pathologic melanodermitis, benzanthrone causes comedone formations and inflammation of sebaceous glands which are very similar to chloracne. At BASF 62 cases of similar dermatitis have been observed since 1955. Benzanthrone has the following structure:



5. THERAPY.

A treatment of vital resorptive disturbances was in the foreground. The visually controllable successes of local treatments are always necessary.

Since the 30th German Dermatology Conference the vitamin A acid has become known in the treatment of Acne vulgaris and chloracne. Vitamin A subtoxically dosed against psoriasis and all hyperkeratoses has failed. When applied at low dosage, 0.05-0.3% solution or cream applied locally, acts as peeling agent. It acts upon the keratinisation and proliferation of the cells. As shown by autoradiographic studies (Plewig), vitamin A acid has no point of attack at the sebaceous glands.

SUMMARY.

Clinical-causistic report about the consequences of an accident of an unpredicted reaction in 1953. In the study of the toxic cause for the skin changes of total of 42 patients of which damage of internal organs and disturbances of health of nervous system occurred in 14 cases, 2,3,6,7-tetrachloro dibenzo dioxin was found to be the cause which presumably represents the decisive chloracnogen due to its comparatively excessive toxicity.

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Priority
 #16

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Accid. Pois (Chloracene)
Accid. (Chloracene)
Phys. (Chloracene)

Severe acute chloracene, a mass intoxication due to
Schwerste akute Chloracene, eine Massenintoxikation

durch 2, 3, 6, 7-Tetrachlordibenzodioxin*
 2, 3, 6, 7-tetrachlorodibenzodioxin
 Paul J. Goldmann

Ärztliche Abteilung der Badischen Anilin- u. Soda-Fabrik AG, Ludwigshafen a. Rh.
 (Leitender Werkarzt: Priv.-Doz. Dr. A. M. Thies)

Eingegangen am 20. Mai 1972

I. Vorgeschichte

1953 sind in der BASF nach einer unvorhergesehenen chemischen Reaktion in einem bestimmten Betriebseteil akute ausgeprägteste Erkrankungsformen der Chloracene beobachtet worden. Niemals früher oder später sind weitere Chloracenefälle nach dieser einmaligen Massenerkrankung hier wieder aufgetreten.

Bei einer alkalischen Hydrolyse von 1,2,4,5-Tetrachlorbenzol zu 2,4,5-Trichlorphenol kam es in einem Autoclavenraum zu der unbekanntem Zersetzung. Dabei entstanden, wie man annahm, sehr toxische „Chlorkohlenwasserstoffe“.

Aus einer Gesamtanzahl von 55 Erkrankten mit dem typischen Bild der Chloracene waren zunächst 3 Fälle von Bedeutung:

1. Eine Dermatitis einer Tierpflegerin, die nur durch den Kontakt mit Versuchstieren verursacht war.
2. Ein Todesfall infolge Pankreasnekrose nach kurzfristigem Aufenthalt in dem abgebildeten Autoclavenraum noch 1958.
3. Die Hauterkrankung eines 14jährigen Sohnes eines Beschäftigten durch Schal und Handtuch im

* Vortrag anlässlich „Medichem“, I. Internationales Symposium der Werkärzte der chemischen Industrie vom 27. bis 29. 4. 1972 in Ludwigshafen, BASF.

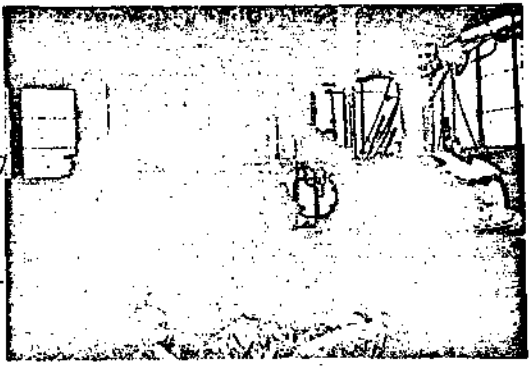


Abb. 1. Der Autoclavenraum

häuslichen Milieu, obwohl Schal und Handtuch mehrmals gewaschen worden waren.

Arbeits- und Krankheitsanamnese, spätere Tierversuche und Analysen deuteten darauf hin, daß nicht irgendwelche während der Zersetzung entstandenen Dämpfe die Erkrankungen hervorgerufen hatten, sondern ein im Raum auch noch 1958 und 1969 nach der Fehlreaktion zurückgebliebenes Sublimat.

Der Hautarzt, 24: 149-152, 1973

ICINE FOR PURPOSES OF STUDY OR RESEARCH IN LIEU OF LENDING THE ORIGINAL.

ENGLISH ABSTRACT ATTACHED FOR "KEY WORDS"

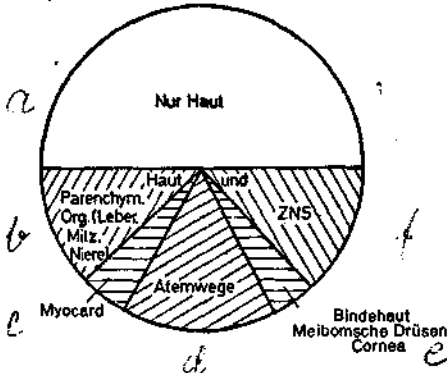


Abb. 2. Schema der vorgekommenen Organveränderungen bei Chloracne. Die Polymorbidität und Pathologie unserer Chloracneerkrankungen lassen sich noch in einer anderen Form verdeutlichen

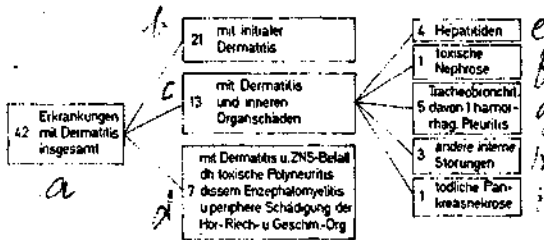


Abb. 3. Massenvergiftung durch Trichlorphenolzerstellungsprodukte am 17. 11. 1963

Von den betroffenen 55 Personen waren nach Auswertung der Krankengeschichten aus den verschiedensten Gründen nur 42 relevant. Bei der Hälfte der 42 Fälle kam es neben den Hautveränderungen außerdem zu z. T. sehr ernstesten resorptiven Giftwirkungen.

2. Kasuistik

Bei unseren wesentlichen 42 Beobachtungen von gesundheitlichen Störungen infolge der Intoxikation stellte sich ein polymorphes Krankheitsbild einer Chloracne mit multiplen Organbefall heraus.

Die Skizze soll diese Polyopathie verdeutlichen. Dabei kann wegen der gleichzeitigen und nebeneinander bestehenden Organsymptomatik die Sektorgröße nur annähernd dargestellt werden. In Abb. 3 fallen insbesondere 4 Hepatitiden auf, eine toxische Pleuritis und die erwähnte letale Pankreasnekrose. Wildhirt in Kasel hat 8 Fälle von Hepatitis aus unserem und seinem Krankengut veröffentlicht. Er nimmt an, daß die Intoxikation von 1953 als mittelbare Ursache noch bei 2 Personen für eine spätere Virushepatitis verantwortlich waren. Bei weiteren 2 Fällen standen in unserer Übersicht (s. Tabelle 1) die Leberschäden nicht im Vordergrund.

In der nächsten Tabelle ist die überschneidende und miteinander kombinierte Symptomatik der resorptiven Störungen der 14 schwersten Fälle festgehalten (s. Tabelle 1).

Tabelle 2 hebt noch einmal die klinischen Formen der schwersten Intoxikationen hervor, bei 3 Erkrankungen auch die späteren Todesursachen. In allen Fällen waren gleichzeitig chronisch rezidivierende Hautver-

Lfd. Nr.	Alter (Jahre)	Krankheitsbeginn nach Exposition	Krankenhausbehandlung	Arbeitsunfähigkeit	Heilkuren	Dermatitis	Temperatur	Müdigkeit	Dyspepsie	Conjunctivitis Blepharitis	Gingivitis Stomatitis	Herz	Bronchitis	Pleuritis	Leberschäden	Nephritis	Pankreatitis	Milz	Kopfschmerzen	Schmerzen an Armen und Beinen	Polynouritis	Encephalomyelitis	Hyporeflexie	Hyperalgesie	Anosmie	Hörstörung	
1	20	1 Tag	7 Mon.	18 Mon.	3	+																					
2	19	4 Tage	3 Mon.	9 Mon.	3	+																					
3	57	4 Tage	6 Mon.	7 Mon.	2	+																					
4	47	1 Tag	7 Mon.	6 Mon.	2	+																					
5	38	10 Tage	5 Wo.	17 Mon.	2	+																					
6	43	2 Tage	4 Mon.	24 Mon.	2	+																					
7	47	2 Wo.	2 Mon.	24 Mon.	2	+																					
8	19	4 Tage	2 Mon.	14 Mon.	1	+																					
9	24	3 Tage	14 Mon.	21 Mon.	1	+																					
10	30	4 Tage	9 Mon.	21 Mon.	1	+																					
11	28	4 Tage	9 Mon.	19 Mon.	2	+																					
12	54	6 Tage	19 Mon.	19 Mon.	2	+																					
13	26	6 Tage	6 Mon.	19 Mon.	4	+																					
14	22	1 Tag	6 Mon.	24 Mon.	2	+																					
					216 Mon.	14	4	3	3	3	2	1	6	1	6	1	1	1	1	5	6	1	1	1	1	1	2

Tabelle 1. Übersicht der Chloracne-Erkrankungen mit internen und ZNS-Schäden 1963 in der BASF

Tabelle 2. Interne Organschäden der Chloracne bei 7 Patienten

1. Myokarditis, Hepatitis, Tracheobronchitis, Nephrose, Restitutio ad integrum. Unfallunabhängig 1904 rheumatische Mitralklappenstenose und Exitus. (Hepatitis, Thrombophlebitis, Lungenembolie).
2. Schwere hämorrhagische Pleuritis 11 Monate nach Intoxikation. Restitutio. 5 Jahre danach Schizophrenie und Suizid.
3. Exposition erst 1958. 6 Monate später Pankreasnekrose und Exitus.
4. Laryngotracheitis.
5. Hepatitis, Splenitis.
6. Hepatitis, Laryngitis.
7. Dyspepsie.

Tabelle 3. Vorwiegend neurologische Organschäden der Chloracne bei weiteren 7 Patienten

1. Toxische Polyneuritis (Hyporeflexie, Hyperalgesie, Hypotonie der Muskulatur).
2. Müdigkeit der Beine, Tracheobronchitis, unabhängig vom Unfall 10 Jahre nach Intoxikation Subarachnoidalblutung.
3. Periphere Parese des N. olfactorius, Anosmie, rezidivierende Gingivitis und Stomatitis. 5 Jahre nach Intoxikation Ulcus duodeni, 10 Jahre rezidivierend.
4. Disseminierte Enzephalitis mit spastischem Halbseitensyndrom, chronische Conjunctivitis und Blepharitis.
5. Toxische Polyneuritis: Sensible und motorische Parosen der Unterarme und Unterschenkel. Störungen der Hör-, Riech- und Geschmacksorgane. Filiius Chloracne.
6. Polyneuritis mit rheumatischen Beschwerden der Extremitäten. Nach 5 Monaten Hepatitis.
7. Mäßige kombinierte Mittel- und Innenohrschwerhörigkeit. Hepatitis.

änderungen bis zu jahrelangen Abszodierungen vorhanden.

3. Ursächliches Toxin

Über die Natur der auslösenden Ursache hatte man seit der Erstbeschreibung der Chloracne durch Herzheimer 1899 verschiedene Vorstellungen. In Japan vermutete man 1968 chlorierten Reis als Ursache bei über 1000 Erkrankungen mit Veränderungen der inneren Organe.

Für die dargestellten Vergiftungen 1953 in der BASF gelang es nach den verschiedensten betrieblichen Maßnahmen aus dem technischen Umwandlungsprozeß ein Nebenprodukt zu isolieren, welches sich als 2,3,6,7-Tetrachlordiphenylendioxin = 2,3,6,7-Tetrachlordibenzodioxin herausstellte.

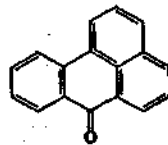


Diagram A

In Tierversuchen der medizinisch-biologischen Forschungslaboratorien der BASF wirkten 10 γ /kg bei Kaninchen immer tödlich; 3 γ /kg wurden überlebt, waren aber noch lebensschädigend.

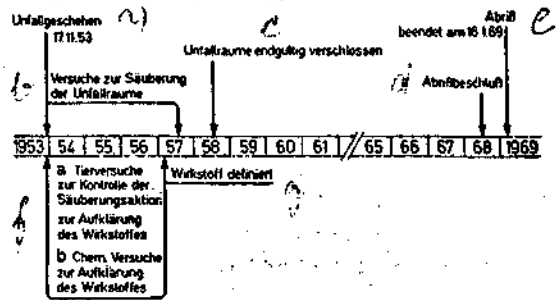


Abb. 4. Betriebliche Maßnahmen nach Intoxikation durch Trichlorphenol-Zersetzungsprodukte



Abb. 5. Chloracne-ähnliche Hautveränderungen durch Benzanthron

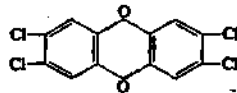
Das Verhältnis der Toxizität von Hexachlor-naphthalin, welches als angeblich kausales Agens der Perna-Krankheit den Namen gegeben hat, gegenüber Tetrachlordibenzodioxin ist 10000:1, d. h. letzteres ist im Tierversuch 10000mal wirksamer.

Die Chloracne ist keine Hauterkrankung nach Ziffer 46 der 7. Berufskrankheitenverordnung, sondern sie entspricht der Nr. 9 der Liste, verursacht überwiegend durch Einatmen toxischer Substanzen in den Organismus. Im Zusammenhang mit unseren Krankheitsbeobachtungen wurde dafür eigens eine Ziffer geschaffen: Gesundheitschädigung durch aromatische Kohlenwasserstoffe und durch chlorierte Aryloxyde.

4. Differentialdiagnose

Neben einer photoallergischen Melanodermis verursacht Benzanthron der Chloracne sehr ähnliche

Comedonenbildungen und Talgdrüsenentzündungen. In der BASF sind seit 1955 62 Fälle ähnlicher Dermatitiden zur Beobachtung gelangt. Benzanthron weist folgende Struktur auf:



Diagramm

5. Therapie

Im Vordergrund stand eine Behandlung vitaler resorptiver Störungen. Die visuell kontrollierbaren Erfolge einer Lokalbehandlung gelten immer noch als dürftig.

Seit dem 30. Deutschen Dermatologentag hat die Vitamin A-Säure in der Behandlung der Acne vulgaris und Chloracne von sich reden gemacht. Vitamin A, subtoxisch dosiert gegen Psoriasis und alle Hyperkeratosen, hatte versagt. Niedrig dosiert, als 0,05—0,3% Lösung oder Creme nur lokal appliziert, wirkt es als Schälmittel. Es greift in die Keratinisation und Proliferation der Zelle ein. An den Talgdrüsen selbst hat

die Vitamin-A-Säure, wie autoradiographische Untersuchungen (Plewig) beweisen, keinen Angriffspunkt.

Zusammenfassung. Klinisch-kasuistischer Bericht über die Unfallfolgen einer betrieblich unvorhergesehenen Reaktion im Jahre 1953. In der Erforschung der toxischen Ursache für die Hautveränderungen bei insgesamt 42 Personen; von denen es außerdem in 14 Fällen zu Schädigungen an inneren Organen und gesundheitlichen Störungen des Nervensystems gekommen war, stellte sich das 2,3,6,7-Tetrachlordibenzodioxin als Ursache heraus, welches wegen seiner vergleichsweise exzessiven Toxizität vermutlich das entscheidende Chloracnegen darstellt.

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Brit. J. Derm. 88, 599 (1970).

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Geschichte der Dermatologie

Probleme der dermatologischen Nomenklatur

II. Teil

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Eingegangen am 14. April 1972

I. Einführung

Die Nomenklatur ist notwendigermaßen ein Kunstprodukt: Begründet vor Jahrhunderten mit oft willkürlichen Wortbildungen, hergeleitet aus der lateinischen wie der griechischen Sprache oder aus Eigennamen, dargestellt nach den grammatischen Prinzipien des Lateinischen, enthält sie viel Hybrides, Ungenaueres oder Unrichtiges. Schon der Aufbau eines Terminus, seine Schreibweise, seine Betonung werfen Fragen auf; sie wurden im I. Teil der Arbeit beantwortet.

Im nun folgenden Teil dringen wir in das einzelne Wort ein und analysieren Ableitung oder Herkunft; noch mehr als anfangs wird jetzt die Problematik offenbar; mit der sich die früheren Dermatologen auseinandersetzen mußten, um einen bezeichnenden, bildhaften Terminus zu fassen; noch mehr als anfangs gilt es, abzuwägen, was man als Tradition oder Herkommen beibehalten und was man kompromislos als falsch ablehnen und erneuern soll.

II. Die exakte Nomenklatur

1. Grammatische Elemente

1.1 Die Arten der Wortbildung

Nach ihrer Bildung lassen sich die Wörter, aus denen sich die dermatologische Nomenklatur zusammensetzt, ordnen in:

1. Wurzelwörter:
λεχηρ (G) lichen; vis (L).
2. abgeleitete Wörter:
πρό-σις (G) ptosis; tuber-culum (L).
3. zusammengesetzte Wörter:
πολύ-μορφος (G) polymorphus; multi-formis (L).

Wurzelwörter sind selten, abgeleitete und zusammengesetzte Wörter häufig.

Während Wurzelwörter stets rein griechische oder rein lateinische Wörter sind, werden abgeleitete und zusammengesetzte Wörter oft hybrid — aus griechischen und lateinischen Elementen — gebildet.

Ableitung (hybrid):

coniunctiv-itis → coniunctivitis
tuber-culo-oides → tuberculooides

Zusammensetzung (hybrid):

δερμ(ι) -i-formis → acniformis
μετά-λευς → metalues

Auch von Namen werden Wörter abgeleitet; sie sind mit wenigen Ausnahmen hybrid:

Ἱπποκράτης-ιός-ος → Hippocraticus
Neisser-ia → Neisseria
Bartholin-itis → Bartholinitis
Paget-ο-ειδής → Pagetoides

Die an den Stamm oder die Wurzel angefügten Bildungselemente, mit denen neue Wörter abgeleitet werden, heißen Suffixa. Man leitet stets ausschließlich vom Wortstamm ab:

Präfix	Stamm	Suffix	Endung
ἀ	τρός	ιός	ος (G) atrophicus
διά	γνος	σι	ος (G) diagnosis
	tuber	cul	um (L) tuberculum
	sana	t	us (L) sanatus

1.2. Das Substantiv

Es werden an dieser Stelle Wurzelwörter und abgeleitete Wörter behandelt; den Zusammensetzungen ist ein besonderer Abschnitt gewidmet.

Sanalison

Zusammensetzung
Emulsionen
pyridinium
0,1 g. Vitamin
Indikationen:
Ekzeme im
allergische
Ekzeme, miki
Ekzeme, Ulo
zierte Mykon
akute Lichtde
Kontraindikati
prozesse, Va
Coelierung: M
Handelstform:
20 g DM 4,2
100 g DM 15.

and related products are presented. Zero tolerance for banned pesticides such as aldrin, dieldrin, and chlordane, and for arsenic and organomercurial pesticides at the respective limits of detectability is proposed. With a few exceptions the same tolerance is proposed for grain and flour. The maximum allowable concentrations being proposed are 0.1 ppm for arachlor, barban, buturon, dichlorprop, monolinuron, naled, lindane, and hydrogen phosphide; 0.01 ppm for BHC; 0.2 ppm for linuron, trichlorobenzoic acid, and demeton derivatives; 3 ppm for malathion and pyrethrin; 10 ppm for piperonyl butoxide; and 50 ppm for inorganic bromides.

74-1874. Pokornits, Ya.; Kulikova, Kh. (Dept. General and Communal Hyg., Inst. Hyg. Epidemiol., Prague, Czechoslovakia). Vliyaniye pestitsidnykh preparatov na kachestvo vody vodoyemov. [Effects of pesticides on reservoir water.] *Gig. Sanit.* 39(1): 89-91; 1974. (Russian)

Studies on the effects of pesticides on the organoleptic and biological properties of reservoir water and on general analytical methods are reviewed. Pesticides may contaminate reservoirs by infiltration or washout from treated farm lands, or by being discharged by pesticide manufacturing plants. Pesticides in water can be determined by colorimetry, gas chromatography, and thin-layer chromatography following extraction and concentration by means of activated carbon or by biological methods using algae, phytoplanktons, and fish as indicators. The odor threshold of most of the pesticides in water lies below 1 mg/liter; that of the major organochlorine pesticides varies from 0.13 µg/liter to 22 mg/liter; that of the major organophosphorus pesticides from 0.2 µg/liter to 1 mg/liter. Phenoxyacetic acid derivatives have odor thresholds ranging from 3 µg/liter to 3 mg/liter. The maximum allowable concentration of most of the pesticides, as determined by biological tests, lies below 1 mg/liter, but is as low as about 0.01 mg/liter for such preparations as atrazine, thiometon, and malathion. Bacteria are much more resistant to pesticides than plankton and fish. *Agrobacterium* spp. decomposed dalapon and *Pseudomonas fluorescens* decomposed atrazine.

74-1875. Burkatskaya, Ye. N.; Tsapko, V. G. (Inst. Occup. Hyg. and Occup. Dis., Kiev, USSR). Voprosy gigiyeny truda pri razlichnykh sposobakh primeneniya pestitsidov v sel'skom khozyaystve. [The problems of industrial hygiene in case of different means of use of pesticides in agriculture.] *Gig. Sanit.* 39(3): 19-21; 1974. (17 references) (Russian)

Sanitary hygienic studies on the occupational hazards occurring during different modes of pesticide use and application are presented. Seed dressing should be done in centralized, airtight equipment by the wet method to prevent air pollution by seed dressing agents. Pilots and tractor drivers are exposed to high pesticide

concentrations, noise, vibration, and high temperature. Trichlorfon potentiated the effect of noise in rats. Therefore, aircraft and tractors should be equipped with airtight cockpits and cabins, respectively, as well as with air purifying and air conditioning devices. The application of pesticides of finely dispersed aerosol by a new method is hazardous due to skin resorption and inhalation of such aerosols.

74-1876. Mukhtarova, N. D.; Kulagina, T. P. (Inst. Hyg. Toxicol. Pesticides, Polymers, and Plastic Materials, Kiev, USSR). Kliniko-encefalograficheskiye paralleli pri khronicheskom vozdeystvii na organizm cheloveka nebol'shikh doz etilmerkukhlorida. [Clinico-encephalographic parallels in chronic exposure of the human organism to the effect of small doses of ethylmercury chloride.] *Gig. Tr. Prof. Zabol.* 17(6): 26-30; 1973. (7 references) (Russian)

Comparative clinical and encephalographic investigations are described for 25 subjects in the 20-55 yr age bracket chronically exposed to low oral doses of ethylmercury chloride. Asthenovegetative syndrome in 8 cases, encephalopathy with involvement of the diencephalic region in 5 cases, encephaloradicular polyneuritis in 4 cases, and encephaloradicular polyneuritis with involvement of the diencephalic region in another 8 cases were diagnosed. In one group with predominant lesion of the mesodiencephalic region electroencephalographic examinations revealed the absence of normal EEGs, disruption of the cortical-subcortical links, and pronounced disorganization of the basic rhythm. Another group including cases of asthenovegetative syndrome and encephaloradicular polyneuritis demonstrated moderate diffuse changes in the brain bioelectric activity with certain degree of disorganization of the basic rhythm and predominance of low-amplitude slow waves. Monomorphic nature of the abnormal activity, increased proportion of polyrhythmic EEG, as well as low frequency and amplitude of the basic rhythm were determined. The degree of the nervous system involvement and the intensity of the electrographic changes were related.

74-1877. Goldmann, J. J. (Badische Anilin- u. Soda-Fabrik AG, Acetylchem. Abteilung, Ludwigshafen am Rhein, Germany). Schwerste akute Chlorakne, eine Massenintoxikation durch 2,3,6,7-Tetrachlorodibenzodioxin. [Severe acute chloracne, a mass epidemic caused by 2,3,6,7-tetrachlorodibenzodioxin.] *Hautarzt* 24(4): 149-152; 1973. (3 references) (German)

The clinical picture and the etiology of a severe acute chloracne epidemic are described. The incident involved 55 workers at BASF in 1953 and was caused by inhalation of organochlorine vapors as a result of an unpredictable chemical reaction. The toxic agent was 2,3,6,7-tetrachlorodibenzodioxin in 44 cases, 14 of which had damages to the inner organs and central

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