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REPORT - PATIENTS FROM MONSANTO
CHEMICAL COMPANY, NITRO, W. VA.

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REPORT

Patients from Monsanto Chemical Company, Nitro, West Virginia

It was our privilege to study in some detail the Messrs McClanahan, Willard, Steele and Hurley referred to us by the Monsanto Chemical Company, Nitro, West Virginia. A report of our findings and opinion is submitted herewith.

The incident to which the symptoms and findings of the patients have been related, occurred on March 2, 1949. In one of three autoclaves in Building 41, the safety valve and pipe connections blew out and the contents were scattered throughout the interior of the

building as well as over the surrounding terrain and structures. The chemicals employed in this autoclave operation were tetrachlorobenzene, sodium hydroxide and methanol. According to the history supplied by two of the operators who are included in this study, the temperature and pressure within the autoclave rose very rapidly and exceeded greatly the reaction conditions usually associated with this operation. The material which was ejected from the autoclave covered the interior of the building. It was described variably, as a fine black powder and a thick, sticky, dark brown substance. Employees who developed symptoms were first exposed to this material within a few hours after the accident and up to three and one-half months following the accident. According to the plant chemists the residue has, to date, been unidentified. Theoretically it is probable that the material is a polymer of an halogenated phenol compound.

From reports of the men and data submitted to us concerning

examinations made by Dr. Schwarz, it is inferred that a total of

seventy-seven persons employed at the plant have developed cutaneous and other symptoms probably as a result of this accident since March 8, 1949. In addition a man who had purchased a truck which was in

the vicinity of Building 4) at the time of the accident and his child, both of whom had ridden in the vehicle, developed cutaneous symptoms. Of the total number, four employees with multiple symptoms and in many instances of the disease were studied by us.

The following is the history of exposure and development of illness of each of the four employees studied, as it was supplied by the patients themselves.

Ira McClanahan - age 32, occupation: steamfitter

Less than one hour after the explosion the patient received a

work order to enter Building 4) to attempt to repair the damage and in the process became covered with the dark residue which coated the interior of the building. His exposure on the first day was approximately for three hours and during this time he experienced a burning sensation of the eyes, nose and throat which was attributed to the remaining residue. On the following day he again worked in the same building and was then transferred to another part of the plant.

Several hours after his initial exposure the patient developed a severe headache and nausea. Later in the evening of the same day there was considerable vomiting and vertigo. The severe headache persisted for eight days and has since recurred at occasional intervals.

Six days following the explosion the patient developed a severe

pruritis, erythema and swelling of the face which was most marked over the eyelids, nose and lips. During the next few days inflamed nodules and pustules were noted on the face, forearms, shoulders, neck and trunk. The patient dates the initial appearance of comedones, and cysts from about this time too. The latter two types of skin lesions were observed by the patient, to increase in number, rather slowly, and involve the face, scalp, neck, upper and lower extremities and trunk. It was noted by the patient and another medical consultant that the appearance of acneiform lesions during the first 2-3 months of the illness, was accompanied by marked hyperpigmentation. When the cutaneous eruption first appeared, the patient noted a tendency to fatigue easily and weakness.

One month following the initial exposure the patient developed an aching type of pain in the region of the thighs, calves and popliteal areas. The pain was aggravated by exertion and resulted in a temporary inability to walk even short distances. The pain lasted for about six weeks. It has recurred occasionally and may last from several hours to a few days. At present the patient complains of a weak feeling, fatigue upon exposure to moderate exertion, insomnia and "nervousness."

Previous dermatologic therapy has included superficial X-ray, numerous detergents, lotio alba, peeling lotions containing resorcinol, penicillin, and baciguent ointment.

✓ Paul M. Willard - age 36, occupation: chief operator Bldg. 41

This employee entered Bldg. 41 several hours after the explosion. He is uncertain as to whether his first contact occurred at

the beginning of the next shift following the incident or during the second shift of the following day. In any case when he returned to assume his normal duties as chief operator, it was impossible to avoid becoming covered with the explosion residue.

In addition to the chemicals involved in the explosion, this patient had been working with aniline, carbon disulfide, hydrogen sulfide, sulfuric acid and sulfur in the same building.

Symptoms were first noted by this patient about six weeks following his first exposure. He noted a papular eruption in the popliteal fossa of the right leg which was followed by an aching type of pain in the calf of this leg. The rash and the pain according to the patient spread to the other leg within a few days. At this time (six weeks following the explosion) the patient was recommended for ultraviolet light therapy for a mild eruption of the face, neck and lower extremities. However it was not until mid-August that the patient became aware of a severe comedonal, cystic, nodular and pustular eruption on face, neck, back, abdomen and penis. During the period of six weeks prior to the present study the cutaneous eruption has become more severe.

Following the first episode of pain in the calves, the patient experienced repeated bouts of such pain which increased in intensity with time. During first part of July 1949 the aching was so intense that he was unable to walk and he entered a hospital where he remained for 16 days. He was treated with intravenous injections and within one week his pains subsided. Six weeks prior to the beginning of the present study he was again admitted to a hospital for severe pain in chest, back and

neck which was accompanied by difficulty in breathing. He was treated again with intravenous injections. Since his last hospitalization there has been no recurrences of thoracic or cervical pain. He does have an occasional dull ache in the right popliteal fossa. He complains of insomnia and nervousness.

Jesse G. Steele - age 38, occupation: pipefitter.

The patient worked in Building 41 during the last week in June 1949. During the second week of July 1949, the patient was assigned to work with pipes and fittings which were originally part of the autoclave installation involved in the March 8, 1949 explosion. His work required him to burn and buff flanges returned from salvage.

About the second week in July he noticed an eruption on his upper lip, pain in the back, lower extremities and chest. At this time he developed an infected throat which was treated with penicillin and sulfonamides and was off from work for two weeks. It was at this time that he first observed that a skin eruption had developed on his face, buttocks, back, shoulders and neck.

Following a two week layoff he returned to work in early August feeling weak and lightheaded. It was recommended by his employer that he not continue working because of his skin condition. The skin eruption has become gradually more severe during the past 2 months.

During the mid-July episode he also developed RUQ tenderness. X-ray studies of the stomach and gallbladder were read as negative. The tenderness has persisted to the present.

The patient complains of insomnia, nervousness and a weight loss of 15 lb. since July 1949.

Two years ago the patient developed urticaria while working in Building 54. When he finished work in that building, the rash disappeared.

There is no knowledge of the nature of the substances to which he was exposed. One of the patient had an attack of jaundice with fever which lasted for about six weeks.

Jonathan A. Harper, age 36, occupation: operator, Bldg. 41.

The patient was working in another building during the day of the accident. However he did visit the building a few hours after the

explosion. Six weeks later he was again assigned to work in Building 41, this time to wash down the involved autoclave prior to inspection.

He wore a respirator, goggles, gloves, and coveralls on this occasion. Two weeks following this assignment he noticed the development of numerous comedones and cysts on his face and neck. In June 1949 he developed an erythema and edema of the face which involved the eyelids particularly. The comedones and cysts have become more extensive and involve the upper and lower extremities, abdomen, as well as the face. Previous dermatologic therapy consisted of fractional superficial X-ray therapy, peeling lotions and expression of cysts.

About six weeks following the assignment in the autoclave the patient developed severe aching pains in the right hip, right and left feet. He was hospitalized for 10 days during June for his pains in the lower extremities. With the onset of lower extremity symptoms the patient became irritable, developed fatigue with slight exertion and insomnia. Following his discharge from the hospital the patient became

emotionally disturbed, found himself unwilling to talk to people and tried frequently. This emotional upset lasted for 3 weeks.

The patient has been unable to work since the beginning of August.

Six weeks prior to his admission for study here, he developed lobar pneumonia, was hospitalized for six days and was treated with penicillin.

His complaints upon admission consisted of progressive acneiform eruption of face, neck, penis, scrotum, erythema and edema of face, particularly the eyelids, persistent pain from the anterior tibial surface of both lower legs to tips of toes, numbness of both feet, nervousness, insomnia, fatigue.

Three years ago while working in Bldg. 41 the patient developed a scaling, pruritic eruption on his legs, hands, face and was treated effectively by a local physician.

All four patients were seen by several dermatologic consultants who made the diagnosis of chloracne. No definite diagnosis has been suggested for their non-cutaneous symptoms by previous consultants.

Cutaneous findings

In the 16 cases studied the skin lesions followed, more or less, an identical morphologic pattern. The essential lesions are comedones and small yellowish cysts. They involve in each case the skin of the face, neck, shoulders, upper extremities, back, buttocks. In some instances the abdomen, penis, scrotum and thighs are involved. In two cases where the face is heavily laden with cysts the pinnae and lobes of the ears and the upper lids are also included. In only one of the four cases was a mild hyperpigmentation of the exposed areas noted. Scattered among the

comedones and cysts are erythematous papules, nodules, pustules and small abscesses. One of four cases manifested periorbital erythema and edema.

Systemic Findings

The physical examination findings on each of the four men are tabulated below.

	McClanahan	Willard	Steele	Harley
Temperature	98.6	98-99.2	98.2-99.4	97.0-98.2
Pulse	80	80-100	78-100	70-100
Respirations	18-20	15-20	16-22	16-20
Blood Pressure	124/80	120/80	136/70	144/66
Appearance (including skin)	well	well	undernourished	chronically ill
Head	normal	normal	normal	normal
Papillary reaction	"	"	"	"
Funduscopy	"	"	"	narrow tortuous vessels
Nystagmus	none	none	none	none
Nasal septum	Dev. rt.	normal	dev. rt.	dev. left
Ear canals	normal	normal	normal	normal
Ear drums	"	"	"	"
Tongue	"	"	"	"
Mouth	"	"	"	"
Teeth	"	"	"	false
Throat	sl. enlarged tonsils	"	"	normal
Neck	normal	"	"	"
Lymphatics	not enlarged	not enlarged	enlarged	axillae and groin
Vessels	normal	normal	normal	thickened tortuous
Chest	large	"	"	normal
Breasts	normal	"	"	"
Lungs	clear	clear	clear	clear
Heart	normal	normal	normal	normal
Liver	not palpable	palpable	palpable	? palpable
Spleen	"	not palp.	not palp.	not palp.
Kidneys	"	"	"	"
Abdominal wall	McBurney scar	normal	normal	normal
Other abdominal	none	none	"	"
Penis	normal	normal	"	"
Scrotum	"	"	"	"
Inguinal rings	"	"	"	"
Rectal	"	"	"	Left prostatic lobe enlarged

	<u>McClanahan</u>	<u>Willard</u>	<u>Steele</u>	<u>Hurley</u>
Muscle strength	normal	normal	normal	poor
Muscle tone	"	"	"	fair
Deep tendon reflexes	"	"	"	hyperactive in lower extremities
Superficial reflexes	"	"	"	normal
Sense of touch	"	"	"	{ diminution absent sen- sation in all modalities except pos- ition on do- lateral aspect of each foot
Pyramidal signs	negative	negative	negative	negative
Romberg	"	"	"	"
Other:	none	none	nervousness, insomnia	nervousness, insomnia, dependent edema

When these men are in a closed room together, there is a strong odor which suggests a phenolic compound, but cannot be identified with certainty. This odor is definitely not the odor of sweat nor the odor of the rancid fat in their skin lesions. While we have been unable to prove it, we believe these men are excreting a foreign chemical through their skins.

The clinical pathological findings and Laboratory data are summarized in the following table:

	McClanahan	Willard	Sterle	Hurley
BLOOD COUNTS				
R.B.C.	4.2	4.5	4.2	4.38
Hemo-globin	12.8	13.7	12.8	12.1
W.M.C.	9,750	10,000	115,300	115,150
		110,300	112,350	110,150
Polys	60	65	74	63
Lymphs	35	21	22	26
Monos	2	7	3	7
Eosms	3	7	2	1
Baso.	0	0	0	1
URINARY FINDINGS				
Specific gravity	1.022		1.013	1.014
H ₂ O ₂	5-0	6-0		5-5
Albumin	0	0	0	0
Sugar	0	0	0	0
Microscopic	Rare rbc, occasional wbc, many casts	Rare wbc, many casts	Occas. wbc	4-6 wbc, 1-2 rbc
BLOOD CHEMISTRY				
Total cholesterol	250	(268 (343	(217 (240	290
Cholesterol esters			153	206
Lipids	830	1,110	1850 (975	900
Total protein	7.6	6.64	6.64	6.5
Serum albumin	4.64	4.3	4.3	4.1
Serum globulin	2.96	2.4	2.4	2.4
BUN	7.0	13	13.0	19.0
Sugar	82	80	78	80
Cephalin flocculation	0	0	0	0
Thymol turbidity	4	5	4	4
Bilirubin				
Direct	0.1	0.1	0.2	0.1
Total	0.2	0.5	0.6	0.6
Prothrombin conc %	56	61	54	58
Alkaline phosphatase	4.2	-	4.8	2.8
BSP Retention %	4	4	2	4
BMR	-15	-6	45	-15
Urine inorganic sulphates %	92	96	93	

Chest X-ray - not abnormal for age (all men).

X-ray abdomen - not abnormal for age (all men).

Blood Kahn - negative on all men.

* PSP 90% excretion in 2 hr.; serum globulin 0.85, globulin (a.

globulin 0.95; EKG - left axis deviation, myocardial damage.

** Normal not over 750.

Urinary glucuronate excretion: McC 320 mg./L; W 217 mg./L; S 400 mg./L
(Normal mean 135. Range may be up to 300.)

- Specific gravity very high.

Summary of Pathological Findings

Skin

Although the histochemical and microchemical study of individual skin lesions and of the cysts is still incomplete, the following histopathological descriptions are representative for

1) pilosebaceous apparatus, 2) sebaceous cysts found in the patient's

1) Pilosebaceous apparatus. There is a lymphocytic and histiocytic infiltrate around the sebaceous glands and hair follicles,

which in some instances invades the epidermal wall of the glands and the follicles themselves. Many of the orifices of the follicles and glands are plugged. Similar cellular collections are observed in focal perivascular sites.

The intact sebaceous acini reveal a normal distribution of lipid elements: triglycerides, phospholipid and cholesterol.

There is a suggestion that there may be more free cholesterol than in the normal sebaceous cell.

The comedonal plugs are also seen to contain triglycerides, cholesterol, phospholipids and keratin.

2) Cysts. Within the dermis are moderate sized cystic structures whose walls consist of flattened epidermal cells of the prickle cell type and the contents of which with special stains reveal small amounts of lipid substances: neutral fat and phospholipid; large amounts of combined cholesterol and perhaps free cholesterol and keratin. In some instances the neck of the cysts are visualized with a plugged passageway to the surface of the epidermis.

Some cysts show little, if any, cellular reaction around them, others a moderate amount of focal reaction composed of lymphocytes and histiocytes.

Other Cutaneous Findings

In addition to pilosebaceous pathology, all sections show focal perivascular collections of lymphocytes and histiocytes. In some instances there is destruction of the pilosebaceous apparatus with partial replacement by necrotic material. Some sections reveal thin atrophic type of epidermis around the follicular openings, others reveal an irregular type of acanthosis.

The histopathological findings are characteristic of acne with cyst formation.

Some specimens were sectioned too superficially and evaluation of their pathologic changes will have to await further sectioning. The comedones and cyst content are to be examined for trichlorophenol when a suitable analytical method becomes available.

Peripheral Nerve Biopsy (Mr. John Hurley)

Stained with PTA, several small subcutaneous nerves are seen cut in cross section and the larger nerve shown in the H + E is also demonstrated. These nerves show marked diffuse increase in collagen throughout their structures with slight increase in cellularity but there is no evidence of inflammatory cell infiltration. Myelin sheaths in these nerves are scanty and appear to be swollen and distorted in many cases. Some of the deeper blood vessels appear to show fibrous thickening of their walls with some narrowing of the lumens. The changes in the nerves are confirmed by Bielschowsky.

stain to demonstrate the neurofibrils. There appears to be a diffuse loss of neurofibrils in many of the nerves and those remaining show

in many cases distortion, atrophy, and localized swelling.

Loyer stain demonstrates diminution in the number of myelin sheaths in these nerves with swelling and distortion as seen with PTA.

Sections of muscle stained with Nissl's method demonstrate only diffuse loss of neurofibrils as seen in some bundles. The stain is not too satisfactory or else neurofibrils have been completely destroyed because in wide areas of the tissue no neurofibrils are seen.

The appearance seen in the nerves throughout these tissues is that of peripheral neuropathy associated with destruction of myelin

sheaths and nerve fibers and replacement by connective tissue which gives the nerve a more cellular appearance. There is no evidence of inflammatory infiltration present.

Muscle Biopsy

Muscle biopsies from Willard, Steele and Hurley were

negative for muscle or small artery pathology.

Hospital Course.

The skin lesions were treated with neutral soap and water scrubs twice daily and the application of lotio alba (without resorcinol) after bathing. The hair was shampooed with neutral soap daily.

Periodically cysts, comedones and pustules were evacuated. Vitamin A, 200,000 daily, were administered to each man. The diet consisted of high protein high vitamin intake. Mild sedatives were given for sleep as needed. Codeine was used for pain in Mr. Hurley.

There was improvement in the skin lesions of all men and

most marked in Mr. McClanahan. There was also marked symptomatic improvement. Mr. Hurley's neuralgia improved but did not disappear during his stay.

Recommended continued therapy was sent to Dr. Nelson as each man was discharged from the hospital.

Summary

It is our opinion that these men are suffering from systemic intoxication from a common agent arising out of their employment.

This intoxication is characterized by acneiform skin lesions, hepatitis, disturbed lipid metabolism, peripheral neuropathy and probably mild central nervous system involvement. From the point of view of the morphologic dermatologist, the type of exposure and the resultant skin lesions may justify the diagnosis of chloracne. There is little, if any, information reported concerning metabolic and systemic disturbances associated with chloracne. In the cases herein reported metabolic and systemic manifestations other than the skin were prominent.

In the cases herein reported metabolic and systemic manifestations other than the skin were prominent.

Their course to date suggests that there will probably be slow improvement in all manifestations with ultimate complete recovery. Three of the men have already recovered from symptoms of peripheral neuropathy. The skins of most of the men have improved, and may be expected to continue to improve rapidly under

hygienic care when free from irritant atmospheres, as was evident during their stay in Cincinnati.

It is not possible for us to predict what their reactions will be to work in a chemical plant. The possibility exists that any irritating environment will cause a flare-up of additional trouble.

Because in spite of an obvious endogenous at dermatitis, there may also be some degree of hypersensitivity to any skin irritant.

It is to be hoped that they will be able to resume work in the near future in atmospheres free of excesses of heat, and free of phenols,

chlorinated and nitrated aromatic compounds and other primary

irritants. Such an experiment should be tried out but only under careful medical supervision. The plant physician should be guided

by their symptomatic picture as to when to send them to work, and

by their skin reactions, after they have gone back to work. If it is possible to employ them to clean outdoor work, they will probably have the least trouble.

Signed:

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Staff Dermatologist

December 5, 1949