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AN ACNEFORM DERMATERGOSIS

JACK W. JONES, M.D.

AND

HERBERT S. ALDEN, M.D.

ATLANTA, GA.

It is only within comparatively recent times that the dermatologist has interested himself in dermatoses associated with or caused by the daily work. With the advent of a more clearly defined appraisal of the words eczema and dermatitis and the more general use of the patch test, dermatologists have necessarily inquired more and more deeply into the innumerable chemical contacts that occur in the day by day lives of their patients. As well as being conversant with dermatology, the dermatologist must have a working knowledge of the manufacture and content of the many new and old compounds that are handled and applied by large numbers of persons. Hence, more and more dermatologists are becoming industrially minded, and it is dawning on them that the solution of some of their industrial difficulties may aid them in a clearer conception of the dermatoses that are encountered in their every-day practice.

Dermatergoses of the acneform type occurring in persons working with chemicals have been repeatedly reported in Europe and discussed as industrial "chlor-acne."¹ This term "chlor-acne" was first used by Herxheimer² in 1899 to describe an eruption composed of comedones and small sebaceous pustules that occurred on the arms and faces of workers manufacturing chlorine gas electrolytically, using carbon electrodes. It was natural to assume that the chlorine was the causative agent. Bettman³ had observed in March 1897 two patients whose skins were diffusely pigmented, dark, rough and dry, in whom were observed small tenacious comedones associated with numerous small follicular abscesses. Subsequently he reported twenty-one additional cases with similar symptoms in workmen who were engaged in cleaning out an acid tower used in the manufacture of hydrochloric acid. At no time did these men come in contact with free chlorine, but numerous loose

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1. White, Prosser: The Dermatergoses, ed. 4, New York, Paul B. Hoeber, Inc., 1934.

2. Herxheimer: München. med. Wchnschr. 46:278, 1899.

3. Bettman: Deutsche med. Wchnschr. 27:437, 1901.

derivatives of coal tar were present. Herxheimer later absolved the chlorine but considered the trouble to be due to various chlorobenzenes.

From time to time other reports of the occurrence of "chlor-acne" have been made in the European journals, each author continuing the error of Herxheimer in assuming that the cause of the condition was chlorine. Some of these reports have been indefinite as to the chemical conditions under which the men worked, except that they were exposed to chlorine gas. However, some authors have suspected various chlorobenzene derivatives, such as hexa-chlorobenzene, hexa-chlorethylene, para-nitrobenzene, perchloronaphthalene ("perna") and probably others.⁴ Chlorinated naphthalene was first indicted by Wauer⁵ in 1918 as a cause of acneform eruptions of the skin, the condition being called *Periakrankheit*. His observations were confirmed by Koelsch⁶ and recently by Teleky.⁷ The latter reported an exhaustive study of a large number of cases occurring in workers engaged in the manufacture of perchloronaphthalene, in which the workers were exposed to fumes of the molten mass and also to the sublimated dusts. In approximately one-half of the workers exposed there developed comedones of a particularly heavy and tenacious type with resultant sebaceous abscesses, containing heavy yellow pus and serum. Considerable improvement resulted when the chlorine content of the mass was decreased from 30 per cent to 8 per cent, and Teleky believed that the disease was due directly to the halogen content of the substance. He mentioned the similarity of the disease to *tearacne* (tar acne) but carried the analogy no further. Individual predisposition appeared to alter receptivity.

Some authors have leaned to the view that the acneform eruption is due to direct external contact with the chemicals (notably Bettman, Hallopeau, Jacquet, Fumouze, Teleky and Koelsch⁸). Others (Lehmann, Herxheimer, Jacobi, Roth and Kobert⁹) considered it to be a

4. Occupation and Health: Encyclopedia of Hygiene, Pathology and Social Welfare, International Labour Office, Boston, World Peace Foundation, 1925, brochures 34 and 285.

5. Wauer, cited in Occupation and Health: Encyclopedia of Hygiene, Pathology and Social Welfare, International Labour Office, Boston, World Peace Foundation, 1925, brochure 34.

6. Koelsch, F., in Ullmann, K.; Oppenheim, M., and Rille, J. H.: Injuries to the Skin, Leipzig, Leopold Voss, 1926, vol. 2, p. 303.

7. Teleky: *Klin. Wchenschr.* 6:845 (April 30); 897 (May 7) 1927; 7:214 (Jan. 29) 1928.

8. Bettman; Hallopeau; Jacquet; Fumouze; Teleky, and Koelsch, cited in Occupation and Health: Encyclopedia of Hygiene, Pathology and Social Welfare, International Labour Office, Boston, World Peace Foundation, 1925, brochure 285.

9. Lehmann; Herxheimer; Jacobi; Roth, and Kobert, cited in Occupation and Health: Encyclopedia of Hygiene, Pathology and Social Welfare, International Labour Office, Boston, World Peace Foundation, 1925, brochure 285.

dermatitis due to the absorption of chemical compounds by the lungs or gastro-intestinal tract, with elimination by way of the sebaceous glands. The majority of writers on the subject, particularly Prosser White,¹ have seemed to feel that chlorine as such has little to do with the formation of the comedones and cysts, and they have repeatedly referred to tar and products of the distillation of tar as the prime causative factors. Prosser White rebuked authors for using the term "chlor-acne" at all and expressed the belief that the process is one of the manifold cutaneous reactions produced by tar and its derivatives.

Recently we have had the opportunity to study, with the full cooperation of the manufacturers, an outbreak of acneform eruption occurring in a group of workers engaged in the manufacture of chlorinated di-phenyl. This study has brought out some points in the production of this unusual dermatosis that we feel are important in solving its exact cause. The following case is typically illustrative of the disease as it occurred in the men working in this plant.

REPORT OF A CASE

History.—O. D., a Negro aged 26, began work in the distillation of chlorinated di-phenyl in April 1930 and worked regularly until the latter part of the year 1933. About May of 1933, he noticed the appearance of blackheads on his face, neck, arms and legs. These areas itched slightly. In a short time blackheads began to appear on the chest, back and lower part of the abdomen, around the navel and on the scrotum and penis. Many of these blackheads swelled and became infected, discharging thick pus. The areas healed with difficulty and often left scars. The condition seemed to be progressive until November 1933. When seen in December 1933 the patient complained of lassitude, loss of appetite and loss of libido and said that his cutaneous condition seemed to be improving.

Physical Examination.—On examination he seemed in good general health. His complaint of lassitude was not borne out by anything more than the usual temperament of the Negro toward work. On the forehead, extending within the hair line, and on the cheeks, chin, nose and neck were numerous small, very black, tenacious comedones, their distribution best described as being "peppered" within the skin. Many of the comedones surmounted firm shotlike cysts, which in some areas contained viscid yellow pus. The pustular elements were more noticeable on the neck. Similar shotlike comedones and cysts had appeared on the shoulders, midportion of the back and chest, with an occasional large cyst. A peculiar peppering of the skin with tenacious carbon-colored comedones was apparent around the umbilicus and lower portion of the abdomen. The scrotum and penis were involved in a similar process, the former being given more to the formation of cysts. The outer surfaces of the forearms and anterior thighs showed similar but fewer comedones. The whole eruption was acneform but differed from acne particularly in the lack of a seborrheic appearance of the skin and in the peculiarly deep black of the comedones as well as the general peppered distribution in areas not usually involved in acne vulgaris. A general physical examination had revealed nothing of importance.

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Treatment.—He was instructed to scrub his skin thoroughly before and after his hours of work, to wear fresh clothing each day during work and to use a lotion made up as follows: zinc sulfate 4 Gm., potassium sulfurata 4 Gm. and distilled water to make 125 cc. On recommendation he later reported for weekly doses of roentgen radiation according to the usual manner of treating acne vulgaris.

Microscopic Examination.—A portion of the skin of the chest was removed for microscopic study (fig. 1). The chief feature of the sections was noted in the hair follicles and sebaceous glands, in which there were cystic dilatation,

Summary of the Symptoms and Treatment in Sixteen Cases of Acneiform Eruption

Case	Age	Race	Type of Skin	Type of Eruption	Time of Exposure	Special Treatment
1H	22	White	Seborrheic; previous acne	Diffuse comedones; few cysts	6 months	Incision; roentgenotherapy
2B	28	White	Average	Diffuse comedones; few cysts	5 months	None
3S	32	White	Seborrheic	Diffuse comedones; large cysts and pustules	Throughout	Incision; drainage
4W	36	White	Average dry	Diffuse comedones; large cysts and abscesses	10 months	None
5F	28	White	Average	Diffuse comedones; few cysts on face and neck	Throughout	None
6S	30	White	Seborrheic; previous acne	Diffuse comedones; deep abscesses on neck; severe cysts	10 months	Incision; drainage
7B	20	Negro	Seborrheic	Erythematous diffuse comedones; few small cysts	8 months	None
8B	19	Negro	Average	Few scattered comedones; occasional cyst	5 months	None
9D*	26	Negro	Seborrheic	Diffuse comedones; cysts; small abscesses	Throughout	Roentgenotherapy
10C	37	White	Average	Scattered comedones; occasional abscess	9 months	None
11G	56	White	Dry	Scattered comedones; occasional abscess	Throughout	Roentgenotherapy
12P	20	White	Seborrheic	Few comedones; occasional cyst	2 months	None
13H	37	White	Average	Occasional comedone	Throughout	None
14B	23	Negro	Average	Very few comedones	12 months	None
15F	22	White	Seborrheic	Scattered comedones	Throughout	Roentgenotherapy
16P	20	Negro	Seborrheic	Diffuse comedones; few cysts back and face	?	Roentgenotherapy

* This case is reported in detail.

destruction of the hair, marked thinning and atrophy of the epithelium of the follicles and a heavy plug of keratinized material which partly filled the cystic cavity. In some areas there was a superficial plug at the surface opening; others showed the surface open and the plug deeply situated. There was no purulent exudate. There were a zone of moderately dense connective tissue surrounding the enlarged follicles, slight edema and infiltration by lymphocytes but no leukocytes. Slight edematous changes were noted in the occasional sebaceous glands present, but they were strikingly few. The sweat glands were normal.



Fig. 1.—Section of skin from the chest, showing histologic changes in the formation of an acneform eruption.

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Of the twenty-four men working in the manufacture of chlorinated di-phenyl within the period from the late summer of 1932 to October, 1933, twenty-three were reported to have had an acneform eruption on the face and body. Of the twenty-three, sixteen were examined. These men presented eruptions of acneform character similar in type and distribution to that in the case referred to but varying in severity (table). In many patients numerous small sebaceous abscesses developed, particularly around the collar line, which exuded heavy, tenacious pus.



Fig. 2.—Characteristic appearance and location of an acneform eruption.

and the remaining ulcers were indolent, leaving in their wake much scarring. In two of the cases, particularly, many large abscesses developed on the neck and back.

Until very recent times di-phenyl and chlorinated di-phenyl were only laboratory curiosities, and their commercial manufacture was unknown. In the experimental stage of manufacture the apparatus was necessarily crude, and experimenters and workers were exposed for long periods to fumes and dusts containing much chlorine, both free and combined. In the early experiments, as well as in the early manufacture in large

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quantities, the di-phenyl was made by heating benzene derived from crude coal tar. When heated in a suitable medium benzene (C_6H_6) becomes di-phenyl ($C_{12}H_{10}$). This substance is then chlorinated at various saturation points, by exposing it under suitable conditions to free chlorine gas. Distillation of the resulting chlorinated di-phenyl¹⁰ results in a purified commercial product (fig. 3). The commercial benzene always has a small quantity of impurities, but some of the cruder commercial benzenes contain relatively large quantities of these impurities, such as xylene, toluene and paraffin. On the heating of the

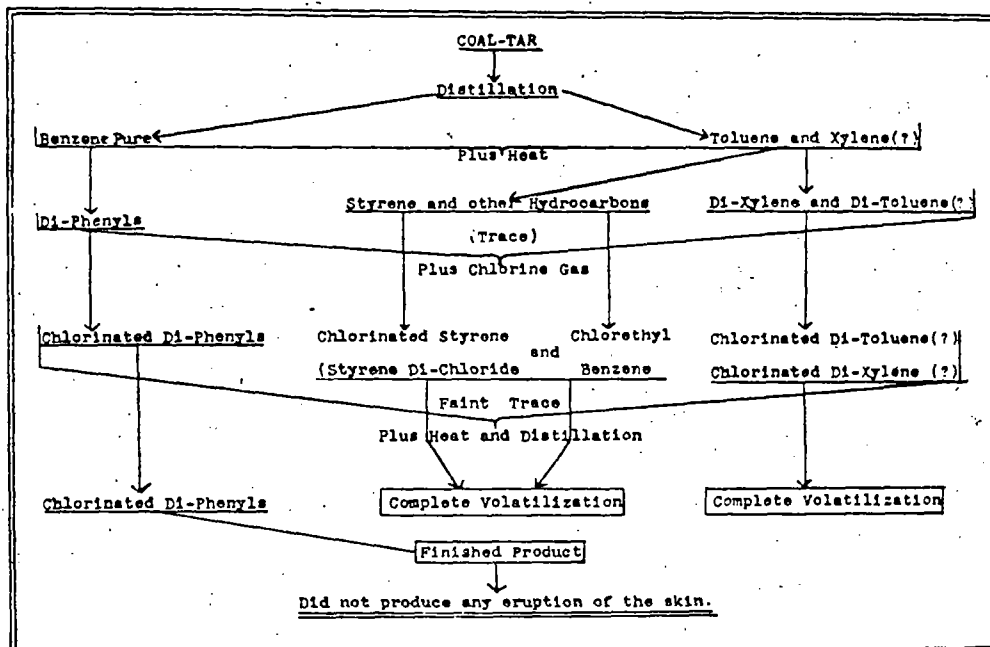


Fig. 3.—Chart illustrating the process of manufacture of chlorinated di-phenyl.

cruder benzenes, the toluenes and xylenes, when present in large quantities, may produce the chemical substance styrene, which has the formula $C_6H_5CH=CH_2$. Styrene when chlorinated (it being inseparable from the di-phenyl) is an unstable compound dropping its chlorine atoms very readily. It is probable that other complex hydrocarbons may be formed from these impurities, which on chlorination become quite as unstable as the styrene. One of these compounds may be chlorethyl benzene ($C_6H_5CH-Cl-CH_3$).

10. Chlorinated di-phenyl consists of a mixture of di-phenyl chlorinated at various saturation points: nona-chloro-di-phenyl ($C_{12}HCl_9-C_6Cl_6$) etc.

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In the experimental stage and in the early manufacture of chlorinated di-phenyl, the men working were exposed for long periods to these chlorinated products. As the demand for the finished product increased, quantitative manufacture was speeded up rapidly, and open stills and heating units were of necessity used until better equipment could be designed and made. But since no physical trouble had developed in the workers previously there was no apparent hazard connected with manufacture. On or about March 1933 the electrical properties of the chlorinated di-phenyl produced in the plant the workmen of which were examined fell below the specifications, and the color of the product deepened. About one month later an acneform eruption was observed on the faces and arms of several of the workers, which became progressively worse, gradually becoming apparent among all the workers engaged in the process at that time. Although one of the men had had a slight acneform eruption on his face in January, little thought was given to it until the eruption appeared in the others. In the summer of 1932, six or eight months previous to the general outbreak of the condition, owing to a difference in price, the crude benzene was purchased from another source, and it was not until the purchase of this particular benzene was discontinued, in October 1933, that the finished product came up to the standard. During the period from March 1933 until October 1933, the eruption continued among the men, and it was present as already described when the men were examined in December of the same year.

The appearance of the eruption coincidentally with the production of a poor grade of chlorinated di-phenyl seemed to indicate a relationship. On due chemical investigation styrene was assumed to be the offending substance causing the low grade of the finished product.

It seems that it may be readily assumed that our problem as to the causative agents of the acneform eruption was connected with the chlorinated products of the impurities present in the crude benzene. However, with the exception of styrene, these products are not known. The problem hence becomes difficult of exact solution, and it is necessary to resort to a reasonable deductive hypothesis.

The exact conditions under which the men contracted their eruption cannot be satisfactorily duplicated experimentally since prolonged mild contact seems to be a deciding factor. Repeated patch tests made on numerous persons with the finished product, chlorinated di-phenyl, and the foreign substances styrene, styrene di-chloride and chloroethylbenzene, have not resulted in an acneform eruption except in one instance. Repeated patch tests made with chloroethylbenzene in the same area produced on the third attempt an erythematous follicular eruption, which persisted only a few days but which was by no means typical.

We could not duplicate this in other instances. Since styrene, chlorinated styrene, chlorethylbenzene, xylene, toluene and their probable products are for the most part lipid solvents, they will produce death and denudation of the epithelium, and one always obtains a chemical burn in response to a patch test made with the styrene and styrene di-chloride. Small quantities mixed loosely with an inert powder or dissolved in ether produce a mild erythematous reaction but no acneform eruption. Patch tests made with the finished product, chlorinated di-phenyl, at no time produced any erythema or evidence of irritation; hence the chlorinated di-phenyl can be absolutely absolved as an irritating agent. In looking over the consecutive history of the development of the eruption, we found it apparent that the men were in some degree exposed to the chlorinated impurities in the benzene for some time before the eruption actually appeared, and that to duplicate the conditions we should have to make repeated patch tests daily for long periods in the same person, a procedure which is not feasible.

As a group, the workers in the dusts and vapors, which were presumably saturated with chlorinated hydrocarbons, were not cleanly, making little effort to bathe after work, and sweating and rubbing enhanced the liability to deposition of the substances on the skin. Theoretically, the chlorinated hydrocarbons, presumably styrene di-chloride and chlorethylbenzene, deposited on the skin gather around the hair follicles and sebaceous glands and are gradually rubbed in. Being lipid solvents, they dissolve sebum and in the reaction, which is modified by the heat of the body and the water present, give off hydrochloric acid, which causes death or irritation of the cells. This in turn causes an excess of cell growth, inflammation, sebaceous plugging and an acneform eruption (fig. 4). This process repeated over a long period may result in severe sebaceous infection, sebaceous abscess and scarring. One would naturally expect this process to occur in the seborrheic areas as well as where clothing might rub the particles into the skin. Also one would expect the process to enhance an already existing acne vulgaris. This occurred in cases 1 and 6 (table 1), the cases in which there was the worst involvement with sebaceous abscesses.

In the beginning an attempt at prevention of the condition was made by being especially careful that all men engaged in the manufacture of chlorinated di-phenyl should have a thorough bath after working hours and that they should wear freshly laundered clothing before starting work. They were also instructed to apply night and morning veterinary white lotion to the affected parts. Some of the patients having the most numerous cysts and follicular infections were instructed to report for roentgen treatment administered in the manner usually employed in treating acne vulgaris. Following the

change in the type of benzene used and the employment of enclosed distilling apparatus and ventilation fans, there was noted a gradual improvement in the acneform eruption. Those patients receiving roentgen radiation improved much more rapidly, but it cannot be said that this form of treatment gave unusual results. The final treatment, of course, was removal of the patient from the offending chlorinated hydrocarbons, and then cleanliness and relief from any infection. All the men showing evidence of cutaneous disease, so far as is known, are greatly improved, or the condition has entirely cleared except for an occasional comedo and a few scars.

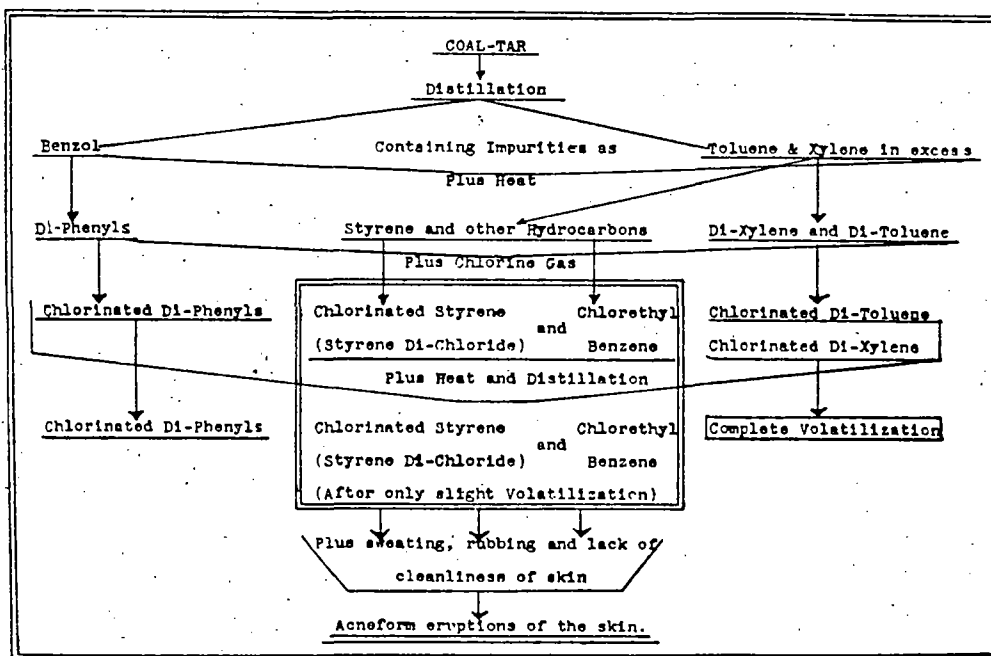


Fig. 4.—Process of manufacture of chlorinated di-phenyl containing impurities which cause an acneform eruption.

When one recalls the cases reported by the European investigators, it is altogether plausible that the chemical process outlined here occurred in most instances. The slow liberation of chlorine in the presence of a lipid solvent (usually chlorinated hydrocarbons) was present in most cases. It is doubtful whether the disease is influenced by the quantity of chlorine present; it is apparently more due to the formation of unstable chlorinated hydrocarbons as well as to the liability of the workers to close contact without a thorough cleansing of the skin and a change from saturated clothing. It is also probable that the disease has little to do with tar itself but more with the products formed by the

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chlorination of tar. Hence, the disease cannot be called "chlor-acne" or "tar acne." That it is not caused by internal absorption is evident when one considers the following facts: First, acute intoxications by chlorine rarely occur, since suffocation and death by pulmonary edema ensue even in the presence of relatively small quantities of chlorine gas in the air. Second, when ingested, chlorine and the chlorinated hydrocarbons are so rapidly oxidized and chlorine so readily combines with sodium that opportunity for acne-like eruptions, such as occur in bromine intoxication, is not possible.

In retrospect, we are intrigued by the hypothesis that these theoretical considerations may have some relation to acne vulgaris. The past quarter of a century has seen an enormous increase in the use of coal for heating homes as well as in industry. The smoke stacks of the cities have belched an ever increasing stream of coal smoke—smoke heavily laden with carbonaceous products containing numerous hydrocarbons. It is well known that coal smoke contains hydrochloric acid. Is it not possible that at least some of the acne vulgaris may have a part of its origin in the constant contacts with the chlorinated hydrocarbons of coal smoke?

SUMMARY

We have recorded herein observations concerning an industrial dermatosis of an acneform type. The type of eruption and the causative factors are analogous to those in the previously reported cases spoken of in the European literature as instances of "chlor-acne," tar acne or *Pernakrankheit*. Although exact duplication of the conditions under which the workers acquired the dermatosis cannot be accomplished by experimental means, reasonable deductions as to the cause of the difficulty can be made. The eruption occurred during the manufacture of chlorinated di-phenyl from benzene. The dermatosis occurred at a time when the benzene used contained excessive quantities of toluene, xylene and paraffin as impurities. The heating and chlorination of these impurities probably resulted in the production of styrene di-chloride and chloroethylbenzene, which, we believe, on contact with the skin produced the acneform eruption by the slow liberation of hydrochloric acid and not by internal absorption of any chemical. While many chlorinated hydrocarbons, as brought out by Prosser White,¹ are lipid substances producing death or irritation of the cells by the liberation of chlorine, this is not true in all instances, since the finished product, chlorinated di-phenyl, did not, either experimentally or actually, produce any cutaneous or sebaceous irritation. Irritation apparently depends on the ease with which chlorine atoms are released from the hydrocarbon base. We believe that these dermatoses should be labeled acneform dermatergoses resulting from certain unstable chlorinated

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hydrocarbons and should not be spoken of as "chlor-acne" or tar acne. The suggestion has been made that some of the acne vulgaris of the skin may be the result of the same type of irritation from soot or coal smoke.

ABSTRACT OF DISCUSSION

DR. OLIVER S. ORMSBY, Chicago: I should like to add an experience I had three months ago that is of interest in this connection. I think that Dr. Jones' paper is extraordinarily interesting and valuable, and the small group of cases I am going to report may add to his troubles rather than solve any of the problems.

About three months ago in Michigan, I saw a patient, through the courtesy of Dr. Milton G. Butler, who presented an extraordinary acneform eruption. This patient was 18 years old and had been observed by Dr. Butler. The eruption in these various cases consisted of acneform pustules and comedones of variable size and depth, with scars, some of which were keloidal. The eruption occurred on the face and neck, particularly over the posterior portion, and extended well up into the scalp. The trunk, arms, thighs and legs were also involved. Two of the patients presented on the back of the neck deep perifollicular pustular lesions, with keloidal scars, such as are seen in Kaposi's dermatitis papillaris capillitii. Both deep and superficial atrophic scars, such as are seen in deep lesions leaving acne, were present in other portions of the neck, face and trunk. The comedones were prominent in all areas, including the legs. They were of variable size, and many were large and deep. The age of the affected patients varied from 18 to 50 years, the younger ones being more severely affected. The condition was apparently produced by contact with an ingredient in a fungicide produced by a chemical company for destroying fungi in lumber. The particular chemical in this fungicide that apparently was responsible for the eruption was sodium tetrachlor-ortho-phenylphenate, which is a yellow powder. Only those who came in contact with it had the eruption. Those who handled the other ingredients of the fungicide and did not come in contact with this particular chemical had no difficulty. As there were apparently no chlorine, bromine or tar radicals in the formula, it is difficult to determine the active factor in the production of the lesions and also whether the eruption was caused by local action by contact or through absorption and internal effects. The eruption was not concerned in any way with acne, and no patient in whom the eruption developed had had acne previously.

DR. MARION B. SULZBERGER, New York: I think that Dr. Jones has contributed a study that will be very interesting when continued. I had an opportunity of seeing a group of patients with acne of external origin about a year and a half ago. The patients were all employed in a factory making radio condensers. Pitch tar and a type of wax (halowax, a chlorinated naphthalene) were used in these condensers. The acne which developed was like that described by Dr. Jones and also included comedones on the legs, as did that which Dr. Ormsby has mentioned. I saw six patients from this one small factory. They were all in the age of puberty or the early twenties, and the group included persons of both sexes.

I believe the most important point in this study is the possible connection between acneform dermatoses distinctly due to external irritants and true acne vulgaris. It is interesting that many derivatives of tar are closely allied to the estrogenic hormone, that certain components of tar are both estrogenic and acnegenic and that the estrogenic hormone must perhaps be incriminated in the production of acne vulgaris. There can be no doubt that acne is often due to stimulation or

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irritation of the pilosebaceous apparatus and that hormonal as well as external influences can produce this stimulation. In the patient suffering from acne, who has, of course, come in contact with the estrogenic hormone during intra-uterine life and then has had no further contact with this hormone (or the closely related testicular hormone) until he or she begins to form his or her own hormones, one can readily conceive the pathogenesis of acne vulgaris as being based on an excessive stimulation of the hair follicles, a stimulation produced by the sudden new formation of the hormones at puberty. It is as though the follicles, after being sensitized to the hormones during fetal contact and then passing through a period of freedom from contact, react excessively to the new and massive contacts with the products of the gonads at puberty. I have discussed this subject in great detail elsewhere.

DR. H. G. IRVINE, Minneapolis: I wish to comment on one point and to compliment Dr. Jones on an excellent piece of work and his presentation of it. There was a difference between his situation and that which Dr. Tunnaclyff and I encountered (*ARCH. DERMAT. & SYPH.* **33**:306 [Feb] 1936). In his case the manufacturers called on the medical profession to help solve the problem. Our study was undertaken where lay people were in charge. It shows clearly the need of medical advice in the production of various chemical preparations.

DR. JACK W. JONES, Atlanta, Ga.: I am very grateful for the discussion. I did not have time to go into the various preventive measures attempted in controlling the outbreak or the treatment. In most of the cases the condition has finally cleared up.

Regarding Dr. Sulzberger's discussion, we studied this outbreak and the literature rather carefully for a year and a half or two years, and we are convinced that the etiology in this particular group can be ascribed to external irritation and not to any internal complications. Our idea is that the unstable chlorinated hydrocarbons give off chlorine very easily, whereas the chlorine that is fixed in the benzene ring is comparatively stable. When these unstable chlorinated hydrocarbons come into contact with the skin and enter the hair follicles, they are broken down slowly, giving off chlorine to form hydrochloric acid. We feel that this is the primary cause of the trouble.

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