LESIONS OF THE SKIN IN PROCESS WORKERS CAUSED BY CONTACT WITH BUTYL TIN COMPOUNDS

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(RECEIVED FOR PUBLICATION NOVEMBER 29, 1957)

The industrial production of alkyl tin derivatives has increased rapidly in recent years, but little is known about the hazards to man which may exist in the handling of these substances. Interest in the matter has been sharpened by the catastrophic results of a therapeutic trial of one of the group, diethyl tin di-iodide, in the treatment of furunculosis. The compound was given orally and caused the death of 102 persons, cerebral oedema being found at necropsy (*British Medical Journal*, 1958). Many of those who survived were left with paraplegia or other permanent neurological damage.

As far as experimental work on animals is concerned, interstitial oedema of the white matter of the brain and cord was found by Magee, Stoner, and Barnes (1957) in rats poisoned by certain triethyl tin compounds. Stoner, Barnes, and Duff (1955) studied the toxicity of a number of alkyl tin derivatives for several species, and advised caution in the handling of organo-tin compounds, particularly of the ethyl series, because of the effect these substances had upon the central nervous system.

Barnes and Stoner (1958) showed that repeated application of dibutyl tin dichloride to the skin of the rat damaged not only the skin but also the biliary tract, proving that the compound was being absorbed percutaneously.

Present Investigation

This paper gives an account of the skin lesions seen among process and laboratory workers engaged in the manufacture of dibutyl and tributyl tin compounds.

Processing of Organo-tin Compounds.—Of the alkyl tin compounds made at Pure Chemicals Ltd., dibutyl and tributyl tin derivatives, with tetrabutyl tin, constitute the greater part and are alone considered here. Dibutyl tins are chiefly used as

“stabilizers” in plastics and as polymerizers in silicone manufacture. Tributyl tins have been found effective against certain fungi (van der Kerk and Luijten, 1954) and are used as fungicides in paper making, paint manufacture, and in the preservation of timber.

The butyl tins are produced by a Grignard reaction from stannic chloride, magnesium, and a butyl compound in ethereal solution. The butyl tin salts may be either crystalline, or liquids of varying volatility, and nearly all are insoluble in water. In the course of manufacture men are occupied in manhandling carboys and flasks of reagents, intermediate and final products, and in the supervision of distillations, reaction vessels, and drying ovens.

Circumstances of Skin Contamination.—Chemical burns are most often found among those handling either dibutyl tin dichloride or tributyl tin chloride, especially the first which is an intermediate product in the preparation of dibutyl tin oxide, and is used in alcoholic solution. This solution is colourless, as is the liquid tributyl tin chloride, and, except when hot, it may fall unnoticed on the skin or clothes since the irritant effect of butyl tin derivatives is not apparent for at least an hour, and sometimes as much as eight hours.

The typical acute organo-tin burn only develops when the compound has been allowed to lie on the skin for more than a few minutes; it is found most often upon the face, hands, and wrists and is usually small. More extensive facial lesions have occurred as a result of splashing during sampling and general handling, but these have been less severe because the affected man has immediately washed.

Extensive and severe burns of the hand sometimes result either from working with gloves which have developed leaks or from failing to wear them.

Maintenance engineers and electricians may kneel or lie against a surface which is wet with one of the compounds and so develop burns of the knees and hip or arm. Such accidents are exceptional, the disregarded small splash being responsible for the great majority of typical lesions.

A more diffuse type of injury which heals less quickly than the acute burn is produced by prolonged contact with clothes moistened by vapour or by liquid spilt on the outside of vessels which are then manhandled. This type of injury is most commonly found where the clothes are in close contact with the skin of the ventral aspect of the body. Similar eruptions are found on the calves, level with the top of the protective Wellington boots issued to workers.

The Skin Lesions.—Only two kinds of eruption have been observed, the acute local burn and the subacute, more diffuse dermatosis already described.

Sensitization of the skin, with the development of eczematous types of eruption, has not been observed, even among men known to have become sensitized to other chemicals.

Acute Lesion.—The following is a description of burns produced experimentally on the skin of a group of five volunteers, none of whom had any connexion with the factory, or any previous exposure to organo-tin compounds. The experimental lesions were similar in each subject and were indistinguishable in appearance from the accidental burns found among workmen.

Tributyl tin monochloride was painted, undiluted and cold, on the skin of the back of the hand. There was no visible reaction till two to three hours later when some reddening and swelling of the mouths of the hair follicles could be seen, and the skin began to itch. Over the next eight hours the follicular inflammation became more intense, but the skin between the follicles was only very slightly affected, and there was only a minor degree of oedema. The pruritus was confined to the tested area and persisted for two or three days, but there was no pain. On the second day, minute pustules formed over some of the follicular openings, in the greatest numbers where the skin was most hirsute. The pustules remained very small and discrete until they dried up on the third or fourth day. The surface of the burn remained dry throughout. On the fifth day resolution was well advanced and after a week faint punctate erythema, with a little perifollicular scaling, was all that remained. The hair in the affected area did not subsequently fall out; on the contrary, in subjects who had been repeatedly tested with a number of compounds at the same skin site, the hair growth was unmistakably more

vigorous there than at the corresponding point of the opposite limb.

Pus taken from a tiny pustule in one case presented no unusual appearances and no organisms were observed.

More extensive accidental burns are sometimes painful, but the degree of pain is never very great, itching being the principal symptom in every case. Healing is always rapid, and is usually complete within a week or 10 days.

Subacute Lesion.—The skin of the lower abdomen, thighs, groins, and perineum is particularly affected, more or less symmetrically. The chief complaint is of pruritus (the organo-tin worker can sometimes be recognized by his habit of absent-mindedly scratching one or other thigh as he works), which may be worse after a hot bath.

No obvious exudation takes place, but the complaint is made that the affected skin is slightly sticky so that the clothes, even when clean, tend to adhere to it.

On examination a faint erythematous eruption with well-marked demarcation from normal skin is seen. Hairy areas are most inflamed. The skin is abnormally friable and scratch marks are usually present. There is neither pustulation nor the characteristic folliculitis of the acute burn, the suffusion of the entire area being quite even. Removal of the patient from contact with organo-tins leads to rapid healing.

Butyl-tin derivatives have been prepared at Pure Chemicals Ltd. for over three years, but until a few months ago no workman had ever reported this type of skin disorder, and only one man has lost any working time on account of it. Protective aprons had not been worn, and it was found on enquiry that every man on the plant suffered in some degree from the condition. None of them was concerned about it, accepting an itch as something to be expected in a chemical works. Only one man later asked for treatment. The general view was that the skin gradually became "hardened", so that the more experienced men had less trouble than the newcomers to the plant.

Accidents Involving the Eyes.—These are rare, since protective goggles are issued and their value is appreciated by process men. In the course of a year, the writer saw only one instance of splashing of the face during sampling from a carboy. The worker was not wearing goggles and both eyes were affected. Lachrymation and intense suffusion of the conjunctivae appeared within minutes, despite immediate lavage, and persisted for four days. At the end of a week there was still some erythema of the surrounding skin, but the eyes appeared normal.

TABLE 1
DETAILS OF ACCIDENTAL BURNS REPORTED IN A SAMPLE GROUP OF 15 MEN

Case No.	1	2	3	4	5	6	7
Site of burn	L. cheek	Hands	R. ankle	Legs	Eyelids, cheeks approx. 2×2	L. leg	Brow, L. cheek, lower jaw
Size of lesions (in in.) ..	$\frac{1}{2} \times 1$	5×4	3×2	2×2 2×1 3		2×1	5×2, 4×3, 1×1 4
Time taken to heal (in days)	4	*	3		4	3	
Job	Dibutyl tin dichloride distillation	Maintenance	Dibutyl tin dichloride distillation	Tributyl tin oxide still	Cleaning carboys (fume)	Tributyl tin oxide still	Tributyl tin chloride distillation

*Case 2 did not report for follow-up examination.

Incidence of Accidental Burns.—Because most burns are small, almost painless, and resolve rapidly, they are not usually reported. Carelessness on the part of the workman is responsible for the majority of accidents, and this consideration doubtless predisposes a man to remain silent about his injury. As a rule, therefore, only the more extensive lesions come to light.

For the purposes of this survey, a group of 15 men who were engaged in the most hazardous jobs was asked to report every burn, however trivial, sustained during one normal working month. Unfortunately some of these people known to have had burns failed to report them. Table 1, therefore, is incomplete, and the true incidence of burns is somewhat higher than one per man per eight-week period.

Prophylaxis and Treatment.—Protective clothing, including long-sleeved polyvinyl chloride gloves, goggles, Wellington boots, and, where indicated, respirators, provides an effective defence against most accidents. Polyvinyl chloride aprons have been issued since the existence of the subacute type of eruption was recognized. The gloves are replaced at intervals because there is some uncertainty about the stability of polyvinyl chloride which is continually in contact with organo-tin compounds. Men are urged to wash well whenever they are splashed with these compounds, as this undoubtedly prevents the development of lesions.

Various applications have been used in the treatment of burns, but healing proceeds equally quickly in the treated and the untreated. Itching is relieved to some extent by the use of bland preparations such as oily calamine.

The Causal Agent

The butyl tins produced at Pure Chemicals Ltd. are stable under normal conditions, except that tributyl tin compounds break down slowly to their dibutyl equivalents in the presence of light, and the

salts hydrolyze to the oxide in the presence of alkali.

It was thought at first that the halides alone caused burns, but skin testing, using a number of other dibutyl and tributyl tin derivatives specially prepared so as to be halide-free, disproved this. Table 2 shows the results obtained from testing each compound on the skin of a small group of volunteers. Liquid derivatives, or saturated solutions of crystalline ones in alcohol, were used to paint an area on the back of the hand about the size of a sixpenny-piece. Single applications only were made in each instance. Whenever any reaction occurred at all, the type of lesion was the same, but the amount of follicular inflammation and pustulation varied somewhat, being least in the case of tributyl tin laurate and most marked in that of tributyl tin chloride. The most slowly healing burn was that caused by tributyl tin acetate.

Dibutyl tin oxide is an almost inert substance, insoluble in water, alcohol, or ether, and was rubbed into the skin in powder form.

TABLE 2
ABILITY OF A GROUP OF BUTYL TIN COMPOUNDS TO CAUSE CHEMICAL BURNS IN MAN ON SINGLE APPLICATION

Dibutyl tin dichloride ..	+	Tributyl tin chloride ..	+
Dibutyl tin diacetate ..	—	Tributyl tin acetate ..	+
Dibutyl tin dilaurate ..	—	Tributyl tin laurate ..	+
Dibutyl tin oxide ..	—	Tributyl tin oxide ..	+
Dibutyl tin maleate ..	—	Tetrabutyl tin ..	—

Discussion

The lesions of the skin observed among men handling butyl tin compounds, though of common occurrence, are of minor importance as a source of complaint, and almost of no importance at all as a cause of absenteeism. In these respects, as in their appearance, they are similar to the burns reported among people working with antimony trichloride and trioxide (Schwartz, Tulipan, and Birmingham, 1957). Of greater concern than the burns themselves must be the potential danger of the percutaneous

absorption of butyl tin derivatives, especially in those cases with the subacute and diffuse dermatosis which is so prevalent. It seems that man is at least as sensitive, dermally, to organo-tins applied externally as the animals tested by Barnes and Stoner (1958), but, unlike the animals, none of the men has so far fallen sick with any illness which might be attributed to organo-tin poisoning.

The only general symptoms which have been consistently recorded are sore throat, cough, and retching which sometimes occur several hours after exposure to vapour or fumes. No chronic cough, and no physical or radiological signs have developed in the people who occasionally are exposed in this way. It seems likely that the symptoms are the result of irritation, with the characteristic delay in onset, of the mucous membranes of the pharynx and larynx.

It is concluded that some butyl tins, particularly of the tributyl series, are strong irritants of the human skin, and that the site of action is not on the surface but in the depths of the hair follicles.

It is probable that these substances are to some extent absorbed subcutaneously in man as in animals, and man may be more susceptible to poisoning by organo-tins than laboratory animals. We have no evidence that this is so, but the experimental evidence in animals, coupled with the therapeutic disaster with oral diethyl tin di-iodide referred to above, must be sufficiently disturbing to impel those interested in the commercial exploitation of organo-tins to do everything possible to protect workmen from contact with them. Adequate protective clothing and education of the men are measures of cardinal importance, which together should reduce the incidence of skin lesions and

consequently the risk of systemic poisoning.

Summary

Certain organo-tins, notably of the tributyl series, cause skin lesions.

The lesions are of two types: (1) acute localized burns resulting from splashes falling on the skin, and (2) subacute irritation of large areas of skin of the trunk and thighs, caused by contamination of the clothes by vapour or spillings.

Neither eruption causes any appreciable loss of time at work; both are usually painless and heal without special treatment.

No evidence of any general toxic effects arising from absorption of butyl tin compounds has been found among workmen concerned in the processing of these compounds.

It is considered that, notwithstanding the apparent absence of long-term ill-effects either on factory economy, or on the workers' health, care should be taken to prevent skin contact with butyl tin derivatives.

My thanks are due to members of the management of Pure Chemicals Ltd. for their interest in this survey, for the provision of samples of butyl tin compounds, and for technical advice. I would also like to thank Dr. B. J. Leonard for his assistance with microscopy.

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