

Contact sensitization to Letterflex urethane photoprepolymer mixture used in printing

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Three printers showed a contact sensitization to the Letterflex® urethane photoprepolymer mixture. The technical chemistry of this new printing procedure is described.

Key words: Letterflex – photoprepolymer – isocyanate – polyurethane – polythiol cross-linking agent – printing.

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An ordinary rubber or metal stamp uses the principle of relief printing, just as ordinary printing with movable lead letters. The elevated parts of such stamps are the ink-bearing parts. In recent years relief printing photopolymer procedures have been developed. A metal sheet is coated on one side with such a polymer. A photographic negative is laid on top of this followed by exposure to UV light. The exposed parts of the polymer become hardened, the unexposed parts of the polymer remain soluble or in some cases removable by a stream of air. After removal of the non-reacted polymer there follows a second exposure to increase the hardness of the exposed parts, which have now become elevated above the level of the removed surround.

In the Nyloprint® procedure an acrylamide derivative polymer has already been applied to a steel plate by the supplier. The plate, in a dry state, is ready for use. Removal of the unexposed parts is achieved

by alcohol spray-washing. The washing fluid is used several times and due to this, comes to contain an increasing amount of unexposed acrylic polymer. The alcohol is recovered from this by distillation and the polymer discarded. Sporadic cases of Nyloprint allergic contact dermatitis have been reported by Magnusson & Mobacken (1972), Tilsley (1975) and Pye & Peachey (1976). The allergen is thought to be an acrylamide derivative. I have also seen some cases in Holland. Tilsley (1975) observed a photo dermatitis with persistent light sensitivity. Beurey et al. (1976) described an irritant contact dermatitis in printers due to tetraethylene glycol diacrylate. Replacement by tetraethylene glycol dimethacrylate made the dermatitis disappear.

In the Letterflex procedure an aluminium precoated sheet is machine-coated with a photopolymer in the printer's workshop just before use. This is done in such a way as to leave a 2-cm uncovered area at the sides of

the sheet. If this sheet is handled cautiously, the printer need not touch the sticky polymer which has just been applied.

After a short pre-exposure to UV light the polymer is covered with the photographic negative and exposed to UV light again. The plate is then removed to a second machine in which the unexposed polymer is blown away by a strong current of air. In the new (English) version of this machine the polymer which is blown off in this manner is extracted by an exhaust located very close to the place where the air blasting takes place, thus shortening transport of the unreacted polymer and, thereby, lessening spillover on to other machine parts. The unreacted polymer is recovered and can be recycled. The plate is blotted by mechanical contact with paper sheet and then re-exposed to UV to increase the strength of the now elevated (letter) parts. Dutch printers have installed many technical and hygienic improvements to various Letterflex machines.

Case Reports

The Letterflex procedure has been in use in the Netherlands in a number of places for some months or years without giving rise to any dermatoses. Recently, however, in various printing works some eight patients have been reported. Three of these patients were seen in our out-patient clinic and their case histories are as follows:

Case 1 – W. N., a 54-year-old printer, during the last 1½ years, had spells of eczema on the dorsal aspects of the hands which spread to the forearms and sometimes also to his face. He had worked with the American Letterflex photoprinting machine from the very beginning. This means that he had worked with the equipment at a stage when the printing people had not yet developed a routine for the use of this machine, and when the exhaust system dur-

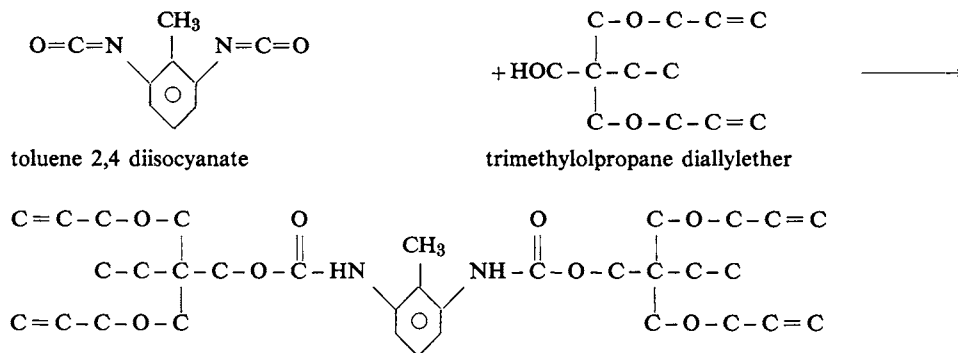
ing light exposure and during the blowing away of the unexposed unreacted polymer was not yet adequate. Contact with the skin occurred more frequently than nowadays. The patient reported that the polymer can be removed with alcohol and if this is not done immediately a brownish skin discoloration results and the polymer loses its stickiness. It can then be removed from the skin only by using pumice-stone or a strongly alkaline solution.

The patient was patch-tested with the substances contained in the European Contact Dermatitis Standard tray (ICDRG 1973; Malten et al. 1976), our own additional standard tray containing among others p. aminoazobenzene, Pellidol®, di-amino-diphenylmethane, urea-formaldehyde resin, glyoxal-urea resin and materials from the patient's working place. He only reacted as follows:

	48 h	72 h
Letterflex polymer 5 %		
in 100 % alcohol	–	+
Letterflex polymer 5 %		
in toluene and ol.olivae		
(equal parts)	–	++
Letterflex polymer		
exposed to UV light		
for 1.8 secs.	+	++

After leaving this type of printing work he recovered uneventfully.

Case 2 – P. G., a 51-year-old printer, developed a vesicular eczema on all the fingers of both hands after having worked with the Letterflex machine (old American type) for only a few months. There were fissures under the nails, possibly due to vigorous cleansing with liberal amounts of alcohol. After he had started to use polyethylene disposable gloves while cleansing the machine parts in contact with the Letterflex polymer his eczema improved, but he recovered completely only after a change of work. He was patch-tested with the European standard tray, our own addi-



Schematically represented by:

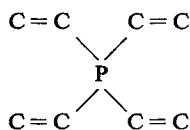
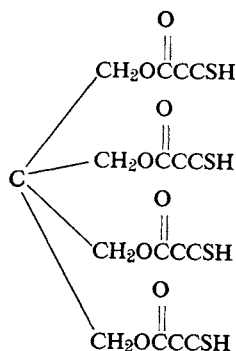


Fig. 1. Chemical structure of the urethane prepolymer.

tional standard tray and a number of epoxy resins and hardeners, unsaturated polyester resins and radical donors, and acrylic resins, with negative results. He also showed negative reactions to materials from his work environment such as the alcohol used, hand cleansers, and (cosmetic) creams he had applied before he came to the outpatient department. However, he reacted to the American and to the English brand of

Letterflex polymer, both dissolved in methylethylketone (10 %), with equally strong reactions (++).

Case 3 – P. v. S., a 41-year-old printer, developed a contact eczema on his fingers and the volar aspect of his right wrist after having worked with the American type of Letterflex machine for half a year. After the start of the eczema he had protected himself by wearing rubber gloves.



Schematically represented by:

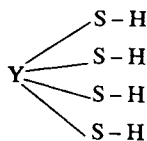


Fig. 2. penta erythritol-tetrakis-3 mercaptopropionate

At first this seemed to have had a beneficial effect; however, the eczema later showed exacerbations. In addition he suffered from rhinitis when he worked in the Letterflex department. He was patch-tested with the European standard tray substances, our additional standard tray and materials from his own work. He reacted to the thiuram-mix. This mix-reaction appeared to be based on a contact hypersensitivity to tetraethyl-thiuram-disulphide possibly present in his yellow rubber gloves to which he also reacted positively.

In addition he reacted to the American Letterflex polymer (10% in methylethylketone) with a ++ reaction (the English polymer being not yet in use at that time). He was also tested intracutaneously with extracts of housedust, human dander, grass pollen, moulds and animal epidermal products with negative results. This agreed with his negative atopic history.

Technical Chemistry

From the patent literature one may obtain details of the chemistry of this Letterflex photopolymer procedure. It appears to be a crosslinking heteropolymerization using a urethane monomer and a polythiol crosslinking agent.

The urethane monomer can be produced by reacting toluene 2,4 diisocyanate with trimethylolpropane diallylether with, for instance, dibutyltin dilaurate serving as catalyst. To this reaction product an antioxidant is added such as 2,6 di-tertiary butyl para-methylphenol to prevent spontaneous vinylic polymerization. This urethane prepolymer contains four olefinic bonds ($-C=C-$). The structure shown in Fig. 1 may therefore be called a "tetra-ene".

During the crosslinking heteropolymerization reaction that follows, one or more of these olefinic bonds may react with $-SH$ groups of the penta erythritol-tetrakis-3-

mercaptopropionate, being mentioned as a polythiol crosslinking agent (Fig. 2). The result of this reaction may be as represented in Fig. 3.

Polymerization can proceed rapidly enough only when an initiator is present in the system. In most instances this is a molecule differing from the prepolymer in that it is more easily activated than the monomer itself. Its activation takes place by the absorption of energy (UV in the case of a photochemical initiator) resulting in the formation of short-lived intermediates. These intermediates have an odd number of electrons and are known as free radicals (symbol: R^* ; see also R in Fig. 3). Free radicals, once formed, initiate polymerization by an addition reaction to the double bond of the monomer. This generates a new radical; the monomer-radical, which may react with another monomer to form a dimer-radical. This process goes on until long chains of covalently bonded atoms are produced. At each addition the unpaired electron of the free radical pairs with one electron of the double bond (the bond in excess) and the second electron of that bond, now being unpaired, serves the new radical function. In the terminal reaction two polymer radicals with unpaired electrons, having opposite spins, react with each other to form the final "dead" macromolecular endproduct (Maltén & Zielhuis 1964).

Benzophenone ($C_6H_5-\overset{\overset{O}{\parallel}}{C}-C_6H_5$) can be used as photopolymerization initiator, giving

rise to two radicals $C_6H_5-\overset{\overset{O^*}{\parallel}}{C}$ and $C_6H_5^*$. Whether this radical polymerization is the only chemical reaction occurring after light exposure is unknown. Reactions of the $-SH$ groups different from the reaction shown in Fig. 3 may be expected.

In order to fix the photopolymer mixture on the aluminium sheet, the sheet has been

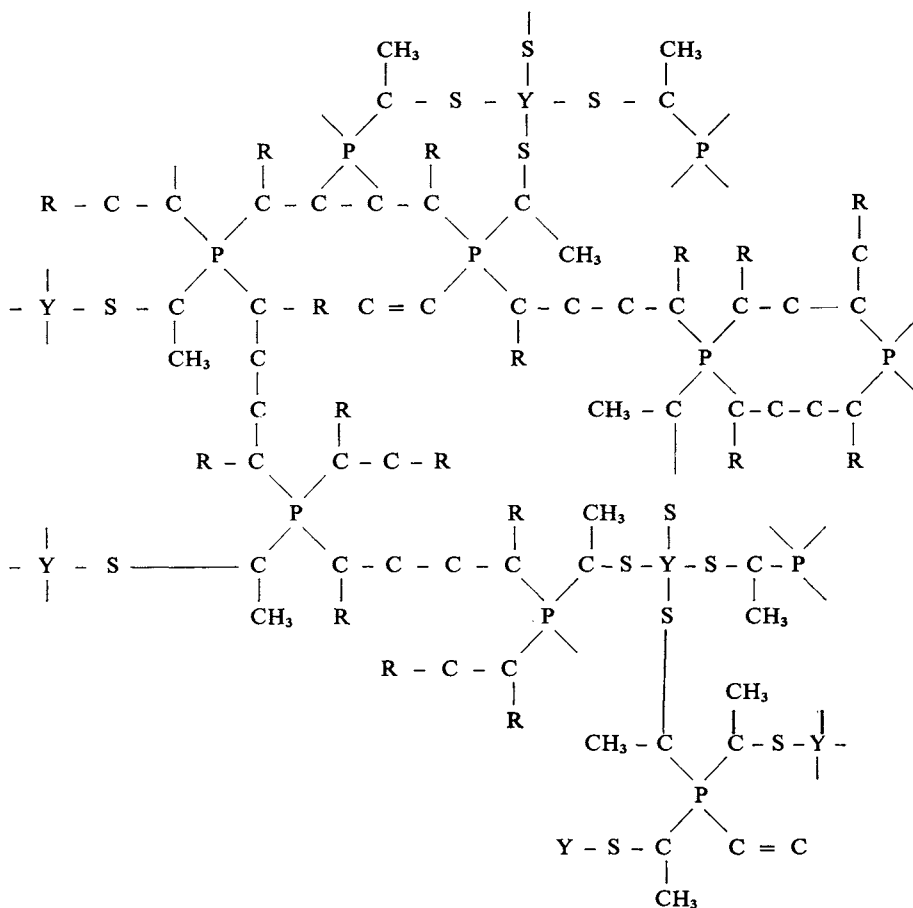


Fig. 3. The Letterflex photopolymer endproduct may be similar to the above.

processed in advance by the supplier as follows: the aluminium oxide surface layer of the sheet is replaced by aluminium acid salts such as chromates, fluorides and similar chemical groups. Then the sheet is coated with a layer of a copolymer of vinyl chloride and vinyl acetate, etc. Organic dyes are mixed in this vinyl coating to improve the definition of the image, for instance Irgacet Orange and Irgacet Yellow 2GL from Ciba Geigy Ltd. The firm was able to reveal (in confidence) the chemical structure of these dyes; they do not seem to have played a role in sensitizing our patients.

Discussion

In the old printing trade lead, acacia gum, certain azodyes, tricresyl phosphate, solvents and photographic developers were hazardous to the operatives' general or dermatological health (Foussereau & Benezra 1970). In offset printing dichromates, cobalt salts, rubber additive chemicals from the printing cylinders and certain photographic developers are present as contact sensitizers (Spruit & Malten 1975).

In the Nyloprint process it appeared to be the acrylamide derivative photopolymer

which caused contact sensitizations (Pye & Peachey 1976, Magnusson & Mobacken 1972, Tilsley 1975).

In the Letterflex procedure it seems to be the photopolymer mixture which produces contact sensitization. This photopolymer is composed, for the greater part, of a mixture of a urethane prepolymer, containing several olefinic bonds, and a polythiol. Two per cent of the mixture is made up of stabilizers to increase the shelf-life time, and UV sensitizers which act as catalysts in the presence of UV light. The manufacturer had the whole composition tested in regard to topical irritant effects on rabbit skin and delayed sensitizing capacity in guinea pigs; nine sensitizing injections with the total unirradiated composition gave no sensitization. Nevertheless the photopolymer mixture appears to contact sensitize humans. The discrepancy between the pre-use animal test and the apparent sensitizing capacity in humans may be due to one or several of the following factors:

- a) species-specific differences concerning the ability to become sensitized
- b) too low a concentration of the sensitizer in the injected mixture
- c) possible production of greater amounts of the real hapten only after UV irradiation of the photopolymer
- d) simple injection method used in animal experiments instead of the combined method of injection with Freund's adjuvant and topical application to induce sensitization (Magnusson & Kligman 1970).

In order to devise preventive measures and for purposes of re-employment it is necessary to pinpoint the exact allergen in the photopolymer mixture. The hapten may be one or more of the admixed auxiliary substances, the penta erythritol-tetrakis-3 mercaptopropionate or the toluene 2,4 diisocyanate or its reaction product with trimethylol propane diallylether. Up to the

present time contact sensitization to isocyanates has rarely been reported, most of the skin ailments being irritant in character. Acute and chronic irritation of mucous membranes, especially of the eyes and the respiratory tract (even simulating allergic asthma) have been reported since the mid-1950s (compare the third patient described above). A recent survey on the occupational health and skin problems in the processing of polyurethanes has been published by Hansen & Roth (1976). They consider MDI (4,4'-diisocyanatodiphenylmethane) and PA-PI (polymethylene-polyphenyl- 3,5,5 trimethylcyclohexylisocyanate) even as a potent contact sensitizer. Hjorth (1975) described trimethyl hexamethylene diisocyanate as a contact sensitizer.

Ten eczematous controls were negative to 10% of the polymer mixture in MEK as well as to 5% in alcohol.

Postscript (12 January 1977)

The manufacturer of the Letterflex photopolymer did not react adequately to several demands made during a more than 6-month period (July-Dec 1976) to cooperate in solving this occupational problem. He did not procure the separate components of the Letterflex mixture we had demanded. French investigators Calas et al. (1977), however, were able to analyze the composition of the mixture. With the guinea pig maximization test (Magnusson & Kligman 1970) they were able to show that the Letterflex prepolymer mixture can sensitize.

Their testing with the separate components revealed the polythiol (penta erythritol-tetrakis-3 mercaptopropionate) as the allergenic agent. This appeared to be a strong sensitizer in the guinea pig maximization test. The manufacturer should label his product with an adequate warning against contact sensitization to this substance. He should advice local cleansing

with ethanol and subsequent washing off any spillage on the skin with ordinary soap and an excess of lukewarm water.

T. Fischer (1976) in a personal communication to me reported that in 1974–1975 in Sweden he saw six patients with contact sensitization to the Letterflex prepolymer mixture. Five of them gave a positive reaction to the tetra(mercaptopropionyl-oxi-) neopentane (= penta erythritol-tetrakis-3-mercaptopropionate) component present in the Letterflex mixture.

References

- Beurey, J., Mougeolle, J. M. & Weber, M. (1976) Accidents cutanés des résins acryliques dans l'imprimerie. *Annales Dermatologie et Syphilologie* 103, 423.
- Callas, E., Castelain, P. Y., Raulot, Lapointe, H., Ducos, P., Cavalier, C., Duprat, P. & Poitou, P. (1977) Allergic contact dermatitis to a photopolymerizable resin used in printing. *Contact Dermatitis*. (In press).
- Fischer, T. (1976) Personal communication. Derm. Department, University Hospital, Uppsala, Sweden.
- Foussereau, J. & Benezra, C. (1970) *Les eczémas allergiques professionnels*. Paris: Masson et Cie.
- Grace & Co., W. R. Applications for patents in the Netherlands number 7206252: Procedure to produce a laminate and 7403490: Procedure to produce a polymer printing plate.
- Hansen, I. & Roth, A. (1976) *Arbeitsmedizinische Gesichtspunkte bei der Verarbeitung von Polyurethanen*. Berlin, German Democratic Republic: Verlag Tribune.
- Hjorth, N. (1975) Dermatitis from trimethyl hexamethylene diisocyanate. *Contact Dermatitis* 1, 59.
- International Contact Dermatitis Research Group (1973) Routine patch test series (1974). *British Journal of Dermatology* 89, 437.
- Magnusson, B. & Kligman, A. M. (1970) *Allergic Contact Dermatitis in the Guinea Pig*. Springfield: Charles C. Thomas.
- Magnusson, B. & Mobacken, H. (1972) Allergic contact dermatitis from acrylic printing plate in a printing plant. *Berufsdermatosen* 20, 138–142.
- Malten, K. E. & Zielhuis, R. L. (1964) *Industrial Toxicology and Dermatology in the Production and Processing of Plastics*. Amsterdam, The Netherlands: Elsevier.
- Malten, K. E., Nater, J. P. & van Ketel, W. G. (1976) *Patch Testing Guidelines*. Nijmegen, The Netherlands: Dekker & v. d. Vegt.
- Pye, R. J. & Peachey, R. D. G. (1976) Contact dermatitis due to Nyloprint. *Contact Dermatitis* 2, 144–146.
- Spruit, D. & Malten, K. E. (1975) Occupational cobalt and chromium dermatitis in an offset printing factory. *Dermatologica* 151, 34–42.
- Tilsley, D. A. (1975) Contact and photodermatitis from Nyloprint. *Contact Dermatitis* 1, 334–335.