From Risk Assessment to documentation of allergic contact dermatitis among automobile workers in molding manufacture

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Running head: Using the basic steps of risk assessment to determine the sources that caused the allergic contact dermatitis among automobile workers in molding manufacture

Number of tables and figures: 3 tables and 3 figures
Abstract

Problem: A 38 year-old male engineer, who is working with molding manufacture, came to the occupational medical clinical of National Taiwan University Hospital (NTUH), because of reddish swelling, peeling and dry fissuring over skin of his bilateral hands for two weeks. According to the history, the patient developed such a problem after working in the Department of Model-making. The symptom was aggravated after machine maintenance. The purpose of this study was to determine the chemicals that caused autoworkers’ dermatitis and estimate the dose-response relationship in molding manufacture.

Method: The occupational hygiene group of the NTUH went to the workplace to conduct a walkthrough for hazard recognition and exposure assessment. Skin patch test of the automobile worker was performed to identify possible chemicals for dermatitis. The dermal exposure assessment was conducted by glove breakthrough test and the air sampling was collected by canister at the workplace. All the samples were analyzed by the gas chromatography with mass spectrometry (GC-MS).

Results: We found that the molding manufacture resulted exposure to 24 kinds of chemicals, including epoxy resins and tri-propylene glycol methyl ether (TPGME). The epoxy resin was found inside the gloves after 3 minutes persistent contact, but the air concentration of TPGME was below the detection limit. The air concentrations of other chemicals, which were present in the workplace, were all below one tenth of TWA-STEL. Skin patch test showed the worker was hypersensitive to epoxy resin, TPGME and fragrance. The exposure dose of epoxy resins were estimated 0.06-0.79 mg/day for 265 days during the normal operation and 0.23-3.67 mg/day for 10 days during the sub-normal operation. The cumulative doses of epoxy resin were estimated 18.2-246.0 mg for the whole operation before signs of dermatitis appealed.

Conclusion: Improvement of the workplace and replace the use of glove by that made of nitrile was recommended. And the symptom improved. We conclude that the allergic contact dermatitis was probably caused by exposure to epoxy resin.

Key word: allergic contact dermatitis, epoxy resin, TPGME, risk assessment, photopolymerization, automobile workers
**Introduction**

On March 15, 2000, a 38 year-old man came to the occupational medical clinical of National Taiwan University Hospital (NTUH), because of reddish swelling, peeling and dry fissuring over skin of his bilateral hands for two weeks. The patient worked in the automobile factory for 5 years and didn’t develop such a problem until being transferred to the department of model making. The symptom was aggravated due to the machine maintenance more frequently in recent. In the clinical of NTUH, questionnaire and interview were performed to ascertain the individual habits and the past history related to dermatitis, such as occupational history, allergic to drug, allergic disease and cutaneous disease.

According to the description of operations from the patient, there were two chemicals used mainly in the molding manufacturing process. Stereo-Lithography 5510, shortly called SL 5510, was the commercial resin manufactured by the Ciba-Geigy Corporation. The other chemical was tripropylene glycol methyl ether (TPGME), which removed the excess resins from the surface of molds before completing the process. Small parts of ethanol were used for cleaning equipments and tools.

In the past studies, there were many cases reported allergic contact dermatitis from exposures of epoxy resins\(^1\text{--}^5\) or epoxy resin compounds\(^6\text{--}^9\). The main reported
sufferers of occupational dermatitis were from construction, painting and electronics industries\textsuperscript{1, 3, 5, 6, 7, 10} but there were no case finding in the automobile workers. Besides epoxy resins, other substances such as dichromate, nickel, cobalt, fragrance mix, thiuram mix, eugenol, p-phenylenediamine, balsam of Peru, p-aminodiphenylamine, ammoniated mercury, colophony, formaldehyde and thimerosal also were important allergens to cause the patients with allergic contact dermatitis\textsuperscript{4}. However, the skin contact is not the only rout to cause workers’ dermatitis, occupational airborne chemicals might be the other sources of allergic contact dermatitis\textsuperscript{11}. Most of dermal exposure studies focused on the description of the symptom in patients and the qualitative analysis of exposed chemicals\textsuperscript{1-10} and rare studies were performed to determine the exposure doses before the sign appear\textsuperscript{12, 13}.

Although the patient described the using of SL 5510 and TPGME, we were not sure that there were other allergic chemical exposures during his working period. The objectives of this study were to determine the chemical that caused the autoworker’s dermatitis and to estimate the dose-response relationship in molding manufacture.

**Materials and Methods**

**Walkthrough**

One occupational hygiene group of NTUH went to the workplace and conducted a walkthrough for hazard recognition. The process was called photopolymerization and operated in the two workrooms. The first was called Stereo Lithgraphy Apparatus
(SLA) room where a SLA 5000 machine and a supercomputer were set up and responded with 3-dimensions data input and solidification of resins. The later was called rapid prototyping room including a TPGME washing machine, a clear water trough, a sanding machine and a UV-curing unit.

In the normal operation, when the 3-dimention data of one mold was input by the supercomputer, the resin was converted to a solid polymer upon exposure to lasers under the trough full of SL 5510. Then the worker with VINYL gloves took out the solid polymers in the plate and moved them to the TPGME washing machine to wash the surface resins of molds lasting for 30 minutes. After cleaning with water during 3-5 minutes in the trough, the solid polymers were exposed to UV energy in the UV-curing unit. Finally, the supports in the backside of molds were clean away and the process was finished.

However, when the SLA 5000 machine was maintained or the molds was failed, the worker needed to flex fingers under SL 5510 levels to clean the residual polymers in the plate during 15-20 minutes per time. The cleaning operation of residuals increased the SL 5510 exposures to the worker rapidly, especially in the fingertips. Even carrying on gloves, the SL 5510 still penetrated through and stayed at the skin of palms. The worker just washed his hands with soaps and clear water after the process completed.
Skin patch test

Skin patch test of the worker was performed in the dermatology department of NTUH on 22 March 2000. The patient was tested with VINYL gloves, SL 5510 (1% pet. and 5% pet.), TPGME (2% and 5%), fragrance mix (8% pet.) and 15 kinds of potential allergic substances such as potassium dichromate (0.5% pet.), p-phenylenediamine dihydrochloride (1% pet.), thiuram mix (1% pet.), neomycin sulphate (20% pet.), cobalt chloride (1% pet.), benzocaine (5% pet.), nickel sulphate (5% pet.), quinoline mix (15% pet.), colophony (20% pet.), mercapto mix (2% pet.), balsam of Peru (25% pet.), p-tertiary butylphenol formaldehyde resin (1% pet.), formaldehyde (1% aq), ammoniated mercury (1% pet.) and thimerosal (0.1% pet.) to identify possible sources for dermatitis.

Penetrative test of gloves

The glove breakthrough test was conducted to determine the potential exposure doses of SL 5510 during the working period. The VINYL gloves were soaked in the SL 5510 trough during 3 minutes, and 1 milliliter of ethanol with high polarity was injected to the middle finger to mix the penetrated resins uniformly. After 1 minute, the mixed solution stayed at the first section of the middle finger was extracted and analyzed in a gas chromatograph (HP 5890 Series II Plus; Hewlett-Packard, U.S.A.) with an HP 7673 auto-sampler, a splitless injector, a capillary column (DB-WAX,
30m, 0.53 mm ID, 1.0 μm film thickness, J&W Scientific, Inc., California) and a
flame ionization detector (GC-FID). Stock solutions were prepared by dilution with 4
fold of SL 5510 in ethanol at 0.29 g/mL. The SL 5510 standards were prepared from
the stocks at 0, 0.0125, 0.025, 0.075, 0.1, and 0.5 μL to get the linear relationship
between the concentrations and the amounts on GC-FID for 0-0.146 mg/mL. The
calibration equation of SL 5510 concentrations was

\[
\text{Area counts*seconds} = (-1186) + 2147372 \times \text{SL 5510 value (mg/ml)}, \quad (1)
\]

\[R^2 = 0.9999\]

Air sampling and analysis

We conducted air sampling with a canister to determine the potential allergic
chemicals in the workplace. With the standard sampling method from U.S.
Environmental Protection Agency\textsuperscript{14}, the canister was set up in the rapid prototyping
room for 15 minutes during the working period and 100 mL air samples from the
canister were analyzed in a gas chromatograph (HP 6890; Hewlett-Packard, U.S.A.)
with an ENTECH 7016CA autosampler, an ENTECH 7100 preconcentrator, a
capillary column (DB-502.2, 60m, 0.25 mm ID, 1.4 μm film thickness, J&W
Scientific, Inc., California) and a mass selective detector (MS, HP 5973;
Hewlett-Packard, U.S.A.).
Result

Hazard identification

We observed two chemicals mainly used in molding manufacture and collected the chemicals information from the material safety data sheet (MSDS) at the workplace. SL 5510 is a mixture of six chemicals, including acrylate ester (10-30%), cycloaliphatic epoxy resin (30-60%), aliphatic glycidyl ether (10-30%), diacrylate esters (0-10%), photoinitiator (0-10%) and acrylic ester (0-10%). Epoxy resin is the primary composition of SL 5510 and had been proven a resource of occupational dermatitis\textsuperscript{1-5}. TPGME is an industrial solvent with low viscosity, completely miscible in water and the vapor pressure at 25\textdegree C is 0.02 mmHg. TPGME could cause transient irritation to eyes but injury corneal unlikely. The prolonged or repeated exposure to TPGME was not likely to cause significant skin irritation.

Dose-response assessment

As showed in Figure 1, the results of skin patch tests after 4 days revealed that the worker displayed a strong 3+ reaction to 8% of fragrance mixture, 2+ reactions to 1% and 5% of SL 5510 and 2+ reactions to 2% and 5% of TPGME. The VINYL gloves and other 15 kinds of potential allergic substances represented negative responses to the patient. The response of the patient to fragrance mix was greater than SL 5510 and TPGME.
We reviewed related papers and international standards to assess the dose-response relationship of epoxy resins and TPGME, neither the U.S. Occupational Safety and Health Administration (OSHA) nor the American Conference of Governmental Industrial Hygienists (ACGIH) had established occupational exposure limits or Threshold Limit Values (TLVs) for the two chemicals.

**Exposure assessment**

The results of breakthrough tests on gloves revealed two major peaks in the Figure 2-1, and the retention time of them were 4.79-minute and 26.12-minute respectively. The peak presented in the 4.79-minute was the ethanol and the peak in the 26.12-minute might be the SL 5510. For making sure our doubt, we added 0.5 µL of SL 5510 from the workplace to the ethanol vial. As the Figure 2-2 showed, the peak rose in the 26.12 minute and proved that the substance was SL 5510. The area counts*seconds of SL 5510 in Figure 2-1 was 34812.3 and translated to 0.0168 mg/mL with using the calibration equation (1). With adding 1 mL ethanol to the inner of VINYL gloves, the penetrated does of SL 5510 was 16.8 µg. Because of the does from soaking in the SL 5510 during 3 minutes, the penetrated rate of SL 5510 to VINYL gloves was 5.6 µg/min.

As showed in Figure 3, there were 16 kinds of occupational airborne chemicals surrounding the rapid prototyping room, including acetaldehyde, ethanol, isopropyl
alcohol, acetone, methyl acetate, 2-butanone, benzene, 3-methyl-2-butane, toluene, n-butyl acetate, ethylbenzene, m/p-xylene, o-xylene, styrene, cyclohexanone and 1,2,4-trimethyl-benzene. We found TPGME in the workplace below the detection limit of GC-MS and the concentrations of these chemicals presented below one tenth of the threshold limit value short-term exposure limit (TLV-STEL) in Table 1. However, because some chemicals such as acetaldehyde, n-butyl acetate and m/p-xylene had concentrations more than the odor thresholds, there were strange odors in the workplace.

We used the individual exposure information from walkthrough and the results of breakthrough tests on gloves to estimate the exposure doses of SL 5510 resin in the molding manufacture. The worker’s exposure information included the working history of the process, the frequency of operation per day during the period, the procedure and the duration of each unit operation, the use of personal protective equipments (mainly gloves) and the probability of contacting the SL 5510 during each operation. We assumed the penetrated rates of SL 5510 resin in other VINYL glove fingers were equal to the middle finger with 5.6 µg/min and were proportional to the working duration. Because the surface areas of all fingers were 10 fold to the middle finger and the first sections of them were the frequently contact areas of the worker,
which were 25% surface areas of all fingers, we estimated the contacting doses of SL 5510 in the fingers with 14-56 µg per minute.

The exposure doses of each unit operation were calculated by multiplying working duration with the penetrated rate and the contact probability. The probability of contacting SL 5510 was from workers’ memories. As showed in Table 2, each unit operation presented the potential exposure doses of SL 5510 in fingers under the normal operation. The cumulative exposure doses of the worker were 0.21-1.32 mg per day. During the sub-normal operation, the frequencies of the process were 2-3 times as showed in Table 3 and the cumulative exposure doses were 0.76-6.12 mg per day. From the start of working in the molding manufacture, the worker had operated the machine under normal condition for 265 days and under sub-normal condition for 10 days. Because the percentages of epoxy resin in SL 5510 were 30-60, the exposure doses of epoxy resin were estimated 0.06-0.79 mg/day for 265 days during the normal operation and 0.23-3.67 mg/day for 10 days during the sub-normal operation. The cumulative exposure doses of epoxy resin on the worker were estimated 18.2-246.0 mg for the whole operated duration before signs of dermatitis appealed. Discussion

The symptom of allergic contact dermatitis on the worker was improved after using the gloves made of nitrile to replace the VINYL gloves and avoiding the contact to SL 5510. The local ventilation of the workplace was conducted to remove the
strange odor in the rapid prototyping room. After 3 months, the patient was recovery. As stated in the case history, the patient had no allergic dermatitis on his hand before transferring to the mold manufacturing. He also had no habit with using fragrance mixture in the past. We conclude that the allergic contact dermatitis of the patient was probably caused by exposure to epoxy resin.

Epoxy resin and epoxy resin compounds had been reported as the source of occupational allergic contact dermatitis in previous studies\(^1\text{-}^{10}\). The main patients were from the construction, painting and electronics industries\(^1,\text{ }3,\text{ }5,\text{ }6,\text{ }7,\text{ }10\). This is the first study reported the allergic contact dermatitis case from exposures to epoxy resin in the automobile workers. The polymerization of epoxy resin in the molding manufacture was not a new technology and had been used in the application of coatings, paints and varnishes with the durable characteristics from 1950s\(^5\). However, the use of lasers as the energy source is a more recent innovation.

As the trend of molding manufacture was inclined to use the polymerization with lasers, the health hazard of epoxy resin to exposed workers must be concern. Though there were MSDSs in the workplace, many cases were reported to contact the epoxy resin without the perceptions of warning to carry on adequate gloves\(^6,\text{ }15\). The legal requirement by government to enforce employees with gloves during working period
was the only effective method to avoid the occupational allergic contact dermatitis from epoxy resin\textsuperscript{5}.

This is the first study to estimate the dose-response relationship between the exposure doses of epoxy resin and the occupational contact dermatitis. Our study had designed and performed through the four steps of risk assessment (hazard identification, dose-response assessment, exposure assessment and risk characterization) to collect information and determine the potential sources of occupational dermatitis among the automobile worker systematically. The polymerization of epoxy resin with laser was a new introduced technology in our study and only one engineer was responded to operate the machine and the supercomputer. With clear starting running schedule, operating process, the patient’s habits and disease history, we estimated the cumulative doses of epoxy resin with 18.2-246.0 mg before the symptom of occupational dermatitis appeal. Despite of one case reported in the study, we revealed the complete process of risk assessment to document the allergic contact dermatitis in the occupation.

It was inadequate to use the cumulative doses of epoxy resin in our study as the standards to prevent occupational allergic contact dermatitis. The main reason came from that the allergic contact dermatitis was associated with individual immune responses, which involved an initial contact with the sensitized substance and the
subsequent exposure to the same allergen\textsuperscript{16}. The induction of sensitization to a susceptible subject was initiated under sufficient exposures of chemical allergens to induce the dermal immune response. If the sensitized individual was exposed to the same chemical allergen subsequently, the more vigorous immune response will be provoked at the contact site. We estimated the cumulative exposure doses of epoxy resin among the automobile worker, but we did not calculate the doses that were enough to induce the initial stage of sensitization in the present study.

The other reason was that we might underestimate the exposures of epoxy resin in the automobile worker. We assumed that the penetrated rate of SL 5510 with 14-56 $\mu$g/min was proportional to the working duration to calculate the cumulative doses. However, when the SL 5510 penetrated to the VINYL gloves, the fingers were completely soaked in the SL 5510 trough, especially in the sub-normal operation. In conclusion, we proved that the allergic contact dermatitis among the automobile worker was probably due to the exposure of epoxy resin. With the steps of risk assessment, we presented the complete process to determine and document the occupational dermatitis. It is believed that this will be an effective method to describe the occupational disease in the future.
Reference


Table 1. Chemical concentrations from air sampling in the rapid prototyping room

<table>
<thead>
<tr>
<th>Chemicals</th>
<th>Molecular weight</th>
<th>Concentration (ppmv)</th>
<th>TLV-STE (ppm)</th>
<th>Odor threshold (ppm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetaldehyde*</td>
<td>44</td>
<td>0.1345</td>
<td>100</td>
<td>0.0028-1000</td>
</tr>
<tr>
<td>Ethanol</td>
<td>46</td>
<td>0.4691</td>
<td>1000</td>
<td>0.34-40</td>
</tr>
<tr>
<td>Isopropyl Alcohol</td>
<td>60</td>
<td>0.0145</td>
<td>400</td>
<td>1-610</td>
</tr>
<tr>
<td>Acetone</td>
<td>58</td>
<td>0.1515</td>
<td>750</td>
<td>0.4-800</td>
</tr>
<tr>
<td>Methyl Acetate</td>
<td>74</td>
<td>0.0322</td>
<td>200</td>
<td>180-200</td>
</tr>
<tr>
<td>2-Butanone</td>
<td>72</td>
<td>0.0095</td>
<td>200</td>
<td>0.05-85</td>
</tr>
<tr>
<td>Benzene</td>
<td>78</td>
<td>0.0042</td>
<td>5</td>
<td>0.16-160</td>
</tr>
<tr>
<td>3-Methyl-2-Butanone</td>
<td>86</td>
<td>0.0714</td>
<td>200</td>
<td>1.9-3.1</td>
</tr>
<tr>
<td>Toluene</td>
<td>92</td>
<td>0.0166</td>
<td>100</td>
<td>0.021-69</td>
</tr>
<tr>
<td>n-Butyl Acetate*</td>
<td>116</td>
<td>0.1337</td>
<td>150</td>
<td>0.0063-368</td>
</tr>
<tr>
<td>Ethylbenzene</td>
<td>106</td>
<td>0.0774</td>
<td>100</td>
<td>0.092-2.3</td>
</tr>
<tr>
<td>m/p-Xylene*</td>
<td>106</td>
<td>0.1496</td>
<td>100</td>
<td>0.081-2.1</td>
</tr>
<tr>
<td>o-Xylene</td>
<td>106</td>
<td>0.0329</td>
<td>100</td>
<td>0.18-5.4</td>
</tr>
<tr>
<td>Styrene</td>
<td>104</td>
<td>0.0009</td>
<td>50</td>
<td>0.0047-61</td>
</tr>
<tr>
<td>Cyclohexanone</td>
<td>98</td>
<td>0.0034</td>
<td>25</td>
<td>0.019-219</td>
</tr>
<tr>
<td>1,2,4-trimethyl-Benzene</td>
<td>120</td>
<td>0.0010</td>
<td>25</td>
<td>0.0024-2.4</td>
</tr>
</tbody>
</table>

*Chemicals had concentrations more than the odor thresholds

TLV-STE: the threshold limit value-short term exposure limit
Table 2. Exposure assessment of SL 5510 during normal operation for 265 days

<table>
<thead>
<tr>
<th>Unit operation</th>
<th>Taking molds from SL 5510 trough</th>
<th>Moving molds to TPGME machine</th>
<th>Taking molds from TPGME to sink</th>
<th>Washing molds with water</th>
<th>Drying molds</th>
<th>Cleaning mold supports away</th>
<th>Moving and placing molds</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration (min)</td>
<td>3</td>
<td>1</td>
<td>2</td>
<td>3-5</td>
<td>3-5</td>
<td>40</td>
<td>2</td>
</tr>
<tr>
<td>PPE use</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Probability of contacting resins</td>
<td>100%</td>
<td>10-20%</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
<td>10-20%</td>
<td>10-20%</td>
</tr>
<tr>
<td>Exposed doses in fingers (µg)</td>
<td>42-168</td>
<td>1.4-11.2</td>
<td>28-112</td>
<td>42-280</td>
<td>42-280</td>
<td>56-448</td>
<td>2.8-22.4</td>
</tr>
</tbody>
</table>

Probability of contacting resins: remembered by the worker
Exposed doses in fingers: assumption that the penetration rate of SL 5510 with 14-56 µg/min was proportional to the working duration
Table 3. Exposure assessment of SL 5510 during sub-normal operation for 10 days

<table>
<thead>
<tr>
<th>Unit operation</th>
<th>Taking molds from SL 5510 trough</th>
<th>Cleaning failure molds in SL 5510 trough</th>
<th>Moving molds to TPGME machine</th>
<th>Taking molds from TPGME to sink</th>
<th>Washing molds with water</th>
<th>Drying molds</th>
<th>Cleaning mold supports away</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration (min)</td>
<td>3</td>
<td>15-20</td>
<td>1</td>
<td>2</td>
<td>3-5</td>
<td>3-5</td>
<td>40</td>
</tr>
<tr>
<td>PPE use</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Probability of contacting resins</td>
<td>100%</td>
<td>100%</td>
<td>10-20%</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
<td>10-20%</td>
</tr>
<tr>
<td>Exposed doses in fingers (µg)</td>
<td>42-168</td>
<td>210-1120</td>
<td>1.4-11.2</td>
<td>28-112</td>
<td>42-280</td>
<td>42-280</td>
<td>56-448</td>
</tr>
</tbody>
</table>

Probability of contacting resins: remembered by the worker
Exposed doses in fingers: assumption that the penetration rate of SL 5510 with 14-56 µg/min was proportional to the working duration
Figure 1. Skin patch tests of the patient after 4 days

Fragrance Mix (8% pet.): +++;
SL 5510 (1% pet.): ++; SL 5510 (5% pet.): ++;
TPGME (2%): ++; TPGME (5%): ++
Figure 2-1. The GC-FID spectrums of breakthrough tests on gloves

Figure 2-2. The GC-FID spectrums of the standard SL 5510 solution
Figure 3. The GC-MS spectrum of air sampling with a canister in the rapid prototyping room

1. Acetaldehyde
2. Ethanol
3. Isopropyl Alcohol
4. Acetone
5. Acetic acid, methyl ester
6. 2-Butanone
7. Benzene;
   2-Butanone, 3-methyl-
8. Toluene
9. Acetic acid, butyl ester
10. Ethylbenzene
11. m/p-Xylene
12. o-Xylene;
   Styrene
13. Cyclohexanone
14. Benzene, 1,2,4-trimethyl-
   *: ISTD