

ELECTRONIC PAPER

Haematological effects among silk screening workers exposed to 2-ethoxy ethyl acetate

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14 February 2003**Background:** 2-Ethoxy ethyl acetate (2-EEA) is a solvent with broad industrial and commercial applications. It has been reported to cause hematological toxicity, infertility, and teratogenesis.**Aims:** To investigate the haematological effects in 2-EEA exposed workers.**Methods:** Workers from one silk screening shop (n = 29), using 2-EEA as the major cleaning and printing solvent, were recruited as a high exposure group. Workers with indirect and non-exposure to 2-EEA (n = 56) were recruited as the comparison group. Venous blood was collected for blood routine examination. Air concentration of 2-EEA in this plant was measured by eight hour personal sampling.**Results:** The geometric mean (GM) of air concentration of 2-EEA in the high exposure group was 7.41 ppm (range 1.35–16.5 ppm). The mean exposure of female workers (GM = 9.34 ppm) was significantly higher than that of male workers (GM = 4.87 ppm). The GM of air 2-EEA concentration in the comparison group was 0.07 ppm (range: non-detectable to 3.62 ppm, n = 26). The haemoglobin and haematocrit in the female high 2-EEA exposure workers were significantly lower than those of female workers in the comparison group. No difference was found between male 2-EEA high exposure and comparison group workers. The haemoglobin, haematocrit, and RBC count in the study population had a significant dose-response relation with air 2-EEA levels.**Conclusion:** Results suggest that 2-EEA is a haematological toxicant, which leads to anaemic status in high exposure female workers.

Ethylene glycol ethers (EGEs) and their acetates are solvents with medium to high boiling points and low evaporation rates. 2-Ethoxy ethanol (2-EE) and its ester 2-ethoxy ethyl acetate (2-EEA) are volatile and almost odourless liquids. It has been commercially available for the past four decades and is used primarily as an industrial solvent for coating materials.^{1–12} Data from a hazard survey showed that large amounts of E-series ethylene glycol ethers are imported and used in Taiwan. The annual consumption of 2-EE and 2-EEA is 1200–1800 tons and 5000–8000 tons, respectively.¹³ About 90% are used in the coating industries—that is, in the manufacture of paints, thinner, and inks. 2-EEA is used especially in the silk screening shop as a diluent or detergent.¹³

Overexposure to 2-EE or 2-EEA has been shown to cause toxic effects in animal experiments. Limited subacute and chronic overexposure in humans via inhalation or percutaneous absorption has been reported to result in haematological abnormalities^{1–3} and oligospermia.¹ However, qualitative confirmation of 2-EE or 2-EEA in the content of raw materials and potential confounding effects of other coexisting haematological toxicants such as benzene were not examined in these studies. In addition, the health effects of glycol ethers on female workers were not reported. The objective of this study was to investigate the haematological effects in workers exposed to 2-EEA in a silk screening shop in Taiwan.

MATERIALS AND METHODS

Study population

Workers from one silk screening shop were selected as the study population. All 29 workers (17 males and 12 females) from the printing department with direct exposure to 2-EEA were recruited as the high exposure group. A total of 56 workers (29 males and 27 females) from the photosensitising, design, product compiling, and cutting rooms, and the administration office were recruited as the comparison group (fig 1). All participants were informed and signed consent forms.

Operation processes

This silk screening shop has 15 printing lines. Four are automatic and 11 are manual. Every day the printing workers have to mix the solvents with inks and to clean the printing machine with solvents. The production of automatic printing lines is much higher than that from manual printing lines. Heavy physical work—loading of compiled screen sheet, lifting, and moving—is needed on automatic printing lines. Therefore, automatic printing lines are mainly operated by male workers (15/17 were males), and manual printing lines are mainly operated by female workers (10/12 were females). In automatic printing lines, workers spend 70% of their work time in a control room with fresh air supply. For the manual printing lines, workers stay for eight hours a day at the printing machine. New design samples and small complicated pictures are often tested or printed by the manual printing machine. Manual printing therefore often needs more delicate skills and the screen needs to be cleaned more frequently, leading to high solvent exposures. The main component of the screen cleaning solvent is 2-EEA. The amount of 2-EEA used in this factory is about 1000 kg per month. In addition to 2-EEA, these workers may be exposed to small amounts of methyl isobutyl ketone (MIBK), and toluene. The qualitative confirmation of 2-EEA, toluene, and MIBK in both raw material solvents and in randomly selected air samples were performed by gas chromatography/mass spectrometry by both the Institute of Occupational Safety and Health (IOSH) and another American Industrial Hygiene Association accredited

Abbreviations: 2-EEA, 2-ethoxy ethyl acetate; EGE, ethylene glycol ether; GM, geometric mean; GSD, geometric standard deviation; MCH, mean corpuscular haemoglobin; MCHC, mean corpuscular haemoglobin concentration; MCV, mean corpuscular volume; MIBK, methyl isobutyl ketone; PEL, permissible exposure limit; RBC, red blood cells; TWA, time weighted average; WBC, white blood cells

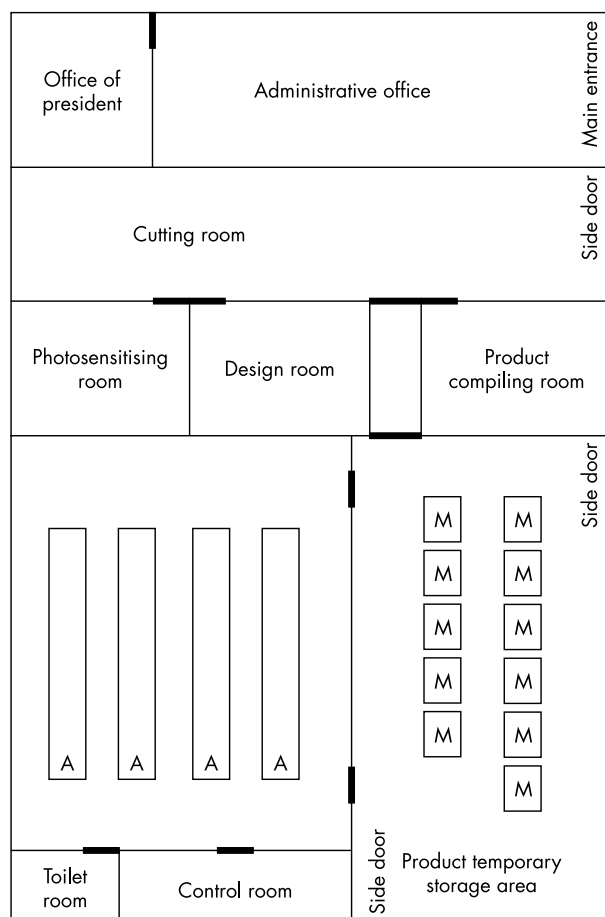


Figure 1 Layout of the silk screening shop in this study. A, automatic printing lines; M, manual printing lines. High exposure areas include the automatic and manual printing lines. Low and indirect exposure areas include the photosensitising, design, product compiling, and cutting rooms. The non-exposure administrative office is isolated from the high and low exposure areas. Doors are normally closed during work hours.

laboratory in Taiwan. No benzene was detected in either raw materials or air samples by these two laboratories.

Data collection

Questionnaires were used to collect personal characteristics, personal habits (for example, alcohol drinking and smoking), reproductive history, disease and drug history, detailed occupational history, and related symptoms. About 10 ml blood was collected from each worker for haematological and biochemical examinations. Haematological parameters examined were: haemoglobin, packed cell volume, white blood cells (WBC), red blood cells (RBC), neutrophils, lymphocytes, platelets, mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH), and mean corpuscular haemoglobin concentration (MCHC).

Forty four randomly selected blood samples were split and sent to a second hospital for analysis of haemoglobin, to confirm the quality control procedures. The haemoglobin results from two reference clinic laboratories showed close correlation (slope = 0.9633, $R^2 = 0.904$, $p < 0.01$, $n = 44$). The mean difference in haemoglobin values between the two laboratories was 0.14 mmol/l, as shown in fig 2.

Environmental monitoring

The air concentration of 2-EEA in this silk screening shop was investigated by personal sampling. 3M 3500 passive samplers were used for eight hour sampling.¹⁴ Eight hour time weighted

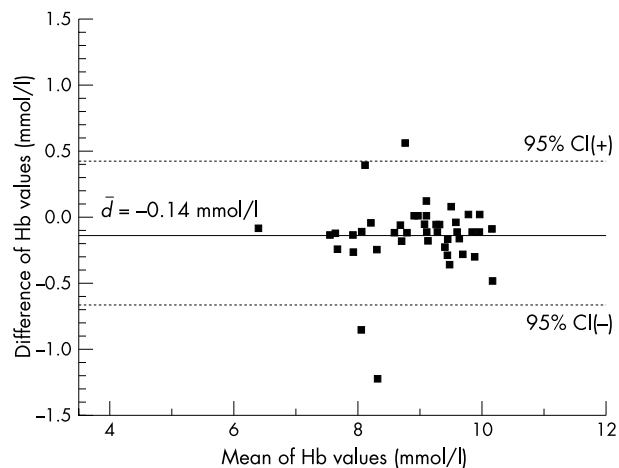


Figure 2 Haemoglobin value difference versus mean haemoglobin values for two reference clinic laboratories ($n = 44$). Solid lines indicate the mean concentration (-0.14 mmol/l) and 95% CI of limits of agreement (LOA) (-0.68 to 0.39 mmol/l); 95% CI of bias: (-0.22 to -0.06 mmol/l); 95% CI of lower LOA: (-0.77 to -0.58 mmol/l); 95% CI of upper LOA: (0.25 to 0.53 mmol/l).

average (TWA) samples were collected for 29 high exposed workers in the printing department and 26 randomly selected workers in the photosensitising, design, product compiling, and cutting rooms, and administrative office. Twelve evenly distributed eight hour fixed point samples were collected in the four rooms (three samples for each room), and five samples were collected in the administrative office. The passive badge was then desorbed in 1.5 ml of mixed solvent of 95:5 (v/v) dichloromethane and methanol. After 40 minutes of shaking, the desorbed 2-EEA was analysed using a gas chromatograph (Hewlett-Packard 5890 Series II, CA, USA) equipped with an HP 7673A autosampler and a flame ionisation detector. Limit of quantitation of 2-EEA was 1.82 μg . The mean (SD) recovery of 2-EEA at three concentrations was 99.6% (1.30, $n = 21$).

Statistical analysis

Geometric mean (GM) and geometric standard deviation (GSD) were used to express the distribution of air 2-EEA concentrations. Student's t test and the χ^2 test were used to compare the difference between the exposed and comparison groups. A test for equality of variance was performed for Student's t test, and adjusted variance and degree of freedom were applied if the variances were not equal. Non-parametric statistics, the Mann-Whitney test, and Fisher's exact test were used in comparison of haematological parameters stratified by gender due to small sample size. Multiple linear regression was also used to evaluate the dose-response relation between air 2-EEA concentrations and haematological outcomes adjusted for potential confounders.

RESULTS

Environmental monitoring data

The geometric mean (GM) air concentration of 2-EEA in the printing department (high exposure group) was 7.41 ppm (GSD = 1.62, range: 1.35–16.5 ppm, $n = 29$), which was over the current permissible exposure limit (PEL, 5 ppm) of 2-EEA in Taiwan, as shown in table 1. The air 2-EEA concentration (GM) in the comparison group was 0.07 ppm (GSD = 5.84, range: non-detectable (ND) to 3.62 ppm, $n = 26$). No 2-EEA was detected in the 17 fixed point samples obtained from the photosensitising, design, product compiling, and cutting rooms, as well as the administrative office.

Stratified by gender, the female workers were exposed to higher concentration of 2-EEA than male workers. This result

Table 1 Air concentration of 2-EEA in the silk screening shop stratified by gender in the high exposure and comparison group

	High exposure group			Comparison group
	Male	Female	Total	Total
n	17	12	29	26
GM (GSD) (ppm)	4.87 (1.74)	9.34 (1.54)	7.41 (1.62)	0.07 (5.84)*
Range (ppm)	1.35–8.69	4.1–16.5	1.35–16.5	ND–3.62

ND, non-detectable.

*Half the limit of quantitation (0.05 ppm) was used for ND samples.

implied that screen cleaning work using 2-EEA as cleaning solvent may expose workers to high concentrations of 2-EEA. It was also noticed that the exposure level in manual printing lines was higher than that in automatic printing lines.

Distribution of characteristics among study subjects

Table 2 shows the distribution of characteristics among study subjects. There were no differences between the high exposure and comparison groups in the distribution of age, gender, duration of work, marital status, personal habits, and smoking status. However, the distribution of education was significantly different between these two groups. The comparison

group workers had higher education than the high exposure group. Since the criteria for haematological abnormalities are varied between genders, the analysis in this study was stratified by gender.

Haematological effects

Table 3 shows the means of haematological parameters stratified by gender. There were significantly lower values of haemoglobin and haematocrit in high exposure female workers than in comparison female workers; however, there were no significant differences among male workers. There were no differences in the red blood cell, white blood cell, and platelet counts in female workers.

The cut points of male abnormal values for haemoglobin, haematocrit, red blood cell count, white blood cell count, and platelets were set at 8.385 mmol/l, 0.40, $4.5 \times 10^{12}/l$, $5 \times 10^9/l$, and $150 \times 10^9/l$, respectively, based on the diagnostic criteria of abnormalities usually used in clinic. The cut points of female abnormal values for haemoglobin, haematocrit, red blood cell count, white blood cell count, and platelets were set at 7.453 mmol/l, 0.40, $4.0 \times 10^{12}/l$, $5 \times 10^9/l$, and $150 \times 10^9/l$, respectively. Comparisons were made for the distribution of abnormal values among male and female workers (table 4). The proportions of abnormal values in all parameters were not significantly different between high exposure and comparison groups for both male and female workers.

Dose-response relation between 2-EEA exposure and haematological effect

Table 5 shows the multiple regression models of haematological parameters on air 2-EEA concentrations in 36 workers. Haemoglobin, haematocrit, and red blood cell count were significantly associated with air 2-EEA concentrations, after adjustment for the potential confounders. The higher the concentration of 2-EEA, the lower the haemoglobin, haematocrit, and red blood cell count. However, the white blood cell count and platelets were not significantly associated with air

Table 2 Distribution of characteristics in 2-EEA high exposure and comparison groups

Variables	High exposure n=29	Comparison group n=56	p value*
Age (y)**	23.07 ±5.90	25.71 ±5.75	0.38
<20	9 (31.0%)	9 (15.8%)	
20–30	17 (58.6%)	37 (64.9%)	
30–40	3 (10.3%)	10 (17.5%)	
>40	0 (0%)	1 (1.8%)	
Duration of work (y)	3.55±3.02	4.55±3.43	0.21
<2 mth	3 (10.4%)	5 (8.8%)	
2 mth–1 y	5 (17.2%)	5 (8.8%)	
1–5 y	10 (34.5%)	25 (43.9%)	
>5 y	11 (37.9%)	22 (38.5%)	
BMI (kg/m ²)	20.49±2.65	20.62±2.90	0.85
Sex (male)	17 (58.6)	31 (54.4)	0.70
Married	10 (34.5)	24 (42.1)	0.56
Smoker	10 (34.5)	14 (24.6)	0.42
Alcohol (non-drinker)	16 (55.2)	30 (52.6)	0.53
Coffee (non-drinker)	11 (38.0)	16 (28.2)	0.10
Tea (non-drinker)	8 (27.8)	9 (15.8)	0.34

*By Student's *t* test for continuous variables or χ^2 test for categorical variables.

**Mean ± standard error.

Table 3 Comparison of haematological parameters between 2-EEA high and low exposure workers, stratified by gender

Items	Male			Female		
	High exposure n=17	Comparison group n=29	p value*	High exposure n=12	Comparison group n=27	p value*
Hb (mmol/l)	9.51 ±0.60	9.76 ±0.67	0.20	8.12 ±0.47	8.55 ±0.61	0.03
Haematocrit	0.46 ±0.025	0.47 ±0.03	0.08	0.40 ±0.03	0.42 ±0.03	0.02
RBC ($10^{12}/l$)	5.11 ±0.38	5.33 ±0.56	0.16	4.42 ±0.57	4.62 ±0.65	0.36
WBC ($10^9/l$)	6.51 ±1.73	6.19 ±1.34	0.49	6.69 ±1.24	6.61 ±1.77	0.89
Neutrophils ($10^9/l$)	3.82 ±1.20	3.70 ±1.08	0.71	4.24 ±1.14	4.18 ±1.62	0.91
Lymphocytes ($10^9/l$)	2.42 ±0.72	2.25 ±0.45	0.32	2.19 ±0.28	2.19 ±0.37	0.97
Platelets ($10^9/l$)	254.1 ±76.7	271.5 ±64.5	0.41	239.4 ±65.9	261.8 ±56.0	0.28
MCV (fl)	90.13 ±7.99	89.34 ±7.52	0.74	90.70 ±8.33	91.78 ±7.16	0.68
MCH (fmol)	1.90 ±0.19	1.87 ±0.20	0.68	1.89 ±0.20	1.90 ±0.16	0.86
MCHC	0.33 ±0.009	0.33 ±0.01	0.68	0.33 ±0.01	0.33 ±0.01	0.57

*Mann-Whitney test.

Results expressed as mean ± standard error.

Table 4 Comparison of abnormal proportion of haematological parameters between 2-EEA high exposure and comparison group workers, stratified by gender

Items	Male			Female		
	High exposure n (%)	Comparison group n (%)	p value*	High exposure n (%)	Comparison group n (%)	p value*
Hb (mmol/l)						
Abnormal**	1 (5.9)	1 (3.4)	0.61	1 (8.3)	1 (3.7)	0.53
Normal	16 (94.1)	28 (96.6)		11 (91.7)	26 (96.3)	
Haematocrit						
Abnormal	1 (5.9)	0 (0)	0.37	2 (16.7)	1 (3.7)	0.22
Normal	16 (94.1)	29 (100)		10 (83.3)	26 (96.3)	
RBC ($10^{12}/l$)						
Abnormal	0 (0)	0 (0)	–	2 (16.7)	2 (7.4)	0.36
Normal	17 (100)	29 (100)		10 (83.3)	25 (92.6)	
WBC ($10^9/l$)						
Abnormal	2 (11.8)	4 (13.8)	0.61	1 (8.3)	2 (7.4)	0.68
Normal	15 (88.2)	25 (86.2)		11 (91.7)	25 (92.6)	
Platelets ($10^9/l$)						
Abnormal	0 (0)	0 (0)	1.00	0 (0)	0 (0)	0.85
Normal	17 (100)	29 (100)		12 (100)	27 (100)	

* χ^2 test.**The cut points of abnormal values for haemoglobin, haematocrit, RBC, WBC, and platelets were set at 8.385 mmol/l, 0.40, $4.5 \times 10^{12}/l$, $5 \times 10^9/l$, and $150 \times 10^9/l$, respectively, for males, and 7.453 mmol/l, 0.40, $4.0 \times 10^{12}/l$, $5 \times 10^9/l$, and $150 \times 10^9/l$, respectively, for females.**Table 5** Regression model of the haematological parameters of air 2-EEA concentration adjusted for potential confounders (n=36)

Dependent variables	Independent variables	Regression coefficient	p value
Hb (mmol/l)	Constant	12.49	–
	Sex	–1.43	<0.0001
	BMI	–0.062	0.31
	Education	0.30	0.05
	Log(air 2-EEA)	–0.95	0.03
Haematocrit	Constant	0.66	–
	Sex	–0.065	<0.0001
	BMI	–0.005	0.08
	Education	0.009	0.16
	Log(air 2-EEA)	–0.053	0.007
RBC ($10^{12}/l$)	Constant	8.08	–
	Sex	–4.23	0.17
	BMI	–0.03	0.68
	Education	–0.13	0.39
	Log(air 2-EEA)	–1.15	0.01
WBC ($10^9/l$)	Constant	4.69	–
	Sex	0.13	0.82
	BMI	0.12	0.33
	Education	0.09	0.75
	Log(air 2-EEA)	0.27	0.75
Platelets ($10^9/l$)	Constant	144.97	–
	Sex	–10.99	0.76
	BMI	10.25	0.19
	Education	–5.55	0.76
	Log(air 2-EEA)	–8.27	0.87

concentration of 2-EEA. This regression data indicates a negative dose-response relation between 2-EEA exposure and red blood cell damage.

DISCUSSION

Although many workers are potentially exposed to 2-EE or 2-EEA, the published articles about haematological toxicity, especially for female exposed workers, are very limited. A case of 2-EE poisoning was reported in Russia.¹⁵ Another case of

aplastic anaemia was reported in a lithographer with potential exposure to dipropylene glycol monomethyl ether, 2-EE, and a range of aliphatic, aromatic, and halogenated hydrocarbons used for offset and ultraviolet cured multicolour printing.⁴ Although dipropylene glycol monomethyl ether and 2-EE were suspected to be the causes of bone marrow injury, no detailed evaluation has been done.

Epidemiological studies of haematopoietic effects of 2-EEA in humans have been reported. Cullen *et al* conducted a study of a small group of lithographers occupationally exposed to organic substances used in the press operation that have not been previously associated with haematological disease in humans or animals.⁴ The organic solvents used in this press operation were ultraviolet curing wash solution (predominantly dipropylene glycol monomethyl ether diluted with n-propanol) as well as wash solution for non-ultraviolet curing inks, composed of 10% 2-EE mixed with aromatic and aliphatic hydrocarbons. In addition to the clinical case, evaluation of the seven co-workers revealed normal peripheral blood pictures, but bone marrow specimens showed absolute myeloid hypoplasia plus multifocal areas of stromal injury in three, while the others showed absolute myeloid hypoplasia without multifocal areas of stromal injury. The authors raised serious questions about the insensitivity of studies limited to blood counts. Kim *et al* studied the bone marrow toxicity among a group of shipyard painters exposed to 2-EEA.³ The air concentrations of 2-EEA in the high and low exposure group were 3.03 and 1.76 ppm, respectively. The mean WBCs in the high exposure group were significantly lower than in the control group, and 11% of 57 painters were leucopenic. The RBCs were within normal limits. Bone marrow aspiration was done on the three leucopenic workers; they were shown to have bone marrow hypoplasia. The authors stated the reason leucocytes but not RBCs are affected by 2-EEA in that study might be explained by the experiment done by Nagano and colleagues,¹⁶ in which leucocytes were affected by a lower dose, and RBCs only affected by a higher dose of 2-EEA. A cross sectional study of shipyard painters exposed to a mean (SD) 2-methoxy ethanol (2-ME) level of 0.8 (1.0) ppm and a mean (SD) 2-EE level of 2.6 (4.2) ppm found a higher proportion of anaemia (haemoglobin <8.70 mmol/l (14 g/dl) in the painters than in the non-exposed workers, but the mean values of haemoglobin and other haematological indicators were not different between exposed and non-exposed workers.⁵

Before this study was conducted, monitoring of air concentration of 2-EAA had been performed in the same plant as part of another study.¹⁷ Eight hour personal sampling was performed during working hours. The air 2-EAA concentration (GM) was highest in the automatic printing line (45.51 ppm, n = 8), followed by the manual printing line (38.82 ppm, n = 14), the cutting room (9.98 ppm, n = 2), and the office and design room (2.71 ppm, n = 4). Since the results of that exposure assessment were much higher than the PEL, the enterprise was asked to do their best to reduce workers' exposures. More fresh air was provided for general ventilation in the entire exposure working areas after the exposure survey, and slot ventilation was installed over the coating and heating ovens of each printing line. In addition to the improvement of engineering control, additional fresh air was provided to reduce the mean exposure level in the control room from 20.5 ppm to 4.31 ppm. Four months after the improvement of engineering control, we conducted this follow up exposure assessment and health examination. We did not know whether or not the haematological effects we observed in this study were partially carried over from the previous high exposures. The recovery of haematological effects of 2-EE or 2-EAA in humans is not known. Human case reports depicted that the haematological effect of 2-methoxy ethanol (2-ME), a structurally similar ethylene glycol ether as 2-EAA, could quickly return to normal in 4 weeks to 3 months after cessation of exposure.¹⁸⁻²³ Our recent study also showed that the 2-ME induced haematological effect recovered very quickly as the airborne concentration of 2-ME and its major toxic metabolite MAA (2-methoxy acetic acid) was reduced.^{24, 25} Since the half life of MAA in humans (77-100 hours)²⁶⁻²⁹ is much longer than that of EAA (23-42 hours),^{30, 31} we speculated that the toxic metabolite EAA stayed in humans for a shorter time than MAA, and the 2-EAA induced haematological effect could recover faster than that induced by 2-ME in humans. Qualitative analyses of the bulk samples of raw material solvents and randomly selected air samples showed that 2-EAA was the only haematological toxicant exposed in this workplace. Therefore, we believed that the health outcome we observed in this study occurs mainly as a result of the recent exposure to 2-EAA and not from the carry over of previous high exposures.

The difference in health outcome mainly came from the different exposures between female and male workers in high exposure groups. Ten of the 12 female workers operated the manual printing machines and spent their entire eight hours in a work environment with only poor general ventilation. More delicate skills and more frequent clean ups with solvents were needed in manual lines. Our data showed that the exposure levels in manual lines were higher than in automatic lines. Fifteen of the 17 male workers operated the automatic printing lines with much higher productivity. However, workers in the automatic lines spent 60-80% of their working time in a control room with better fresh air supply. Therefore, the female high exposure group had much higher exposure than the male high exposure group, as shown in table 1.

Our study also indicated a lower mean haemoglobin and haematocrit in the 2-EAA high exposure group than in the low exposure group. However, the RBC, WBC and platelet counts were not shown to be decreased in the high exposure group. The difference was only found in the female workers, but not in male workers. The reason why the haematological effects are only seen in the female workers may be due to high exposure to 2-EAA during cleaning work as shown in table 1 and potential dermal absorption of 2-EAA from skin contact. Cleaning works in this printing shop were usually done by female workers, without wearing protective gloves, leading to dermal contact and absorption of 2-EAA. Male workers, however, were usually assigned to do mixing jobs, for which respirators were provided by the company. Therefore, the haematopoietic effect cannot be seen in male workers. Our findings

were different from those of Kim and colleagues,³ who found that WBC count, but not haemoglobin or haematocrit, was lower in the exposed group than in the comparison group. These two studies had similar mean and range of 2-EAA concentrations in the high exposure group. However, qualitative confirmation of 2-EE or 2-EAA in the content of raw materials and potential confounders of other co-existing haematological toxicants such as benzene were not examined in Kim and colleagues' study. The difference may be due to the selection of a comparison group. The low exposure group, including office workers, was selected as the comparison group in our study, while office workers only were selected as the comparison group in Kim and colleagues' study. Although urinary EAA was not measured in our study, both studies showed a dose-response relation between environmental or biological monitoring data and haematological effects.

In an animal study, Nagano *et al* found that 2-EAA administered orally to mice for five weeks produced leucopenia in peripheral blood in addition to marked testicular atrophy.¹⁶ Nagano *et al* reported that leucocyte counts were affected at a lower dose and RBC counts were affected at a higher dose of 2-EAA. In another animal experiment, 2-EAA applied to rats by skin contact caused a considerable decrease (50-70%) in peripheral white blood cell count, but the red blood cell decrease did not exceed 15-20% and blood haemoglobin showed little variation.³² Yu *et al* found a significant decrease of WBC and platelet counts along with some reduction of haematocrit, haemoglobin, and MCH in rats treated with 2-EE.³³ Ruchaud *et al* also reported that 2-EE and 2-BE should be considered as haemopoietic toxins through their *in vitro* studies of acute exposure.³⁴

The major route of exposure to 2-EAA is inhalation, but skin absorption is often overlooked. Lack of recognition of the potential toxic effects of these chemicals as well as the potential toxic effects from skin absorption are common among the workers.¹³ Recently, low molecular weight E-series glycol ethers (including 2-ME, 2-MEA, 2-EE, and 2-EAA) have been found to have haematological, reproductive, and teratogenic toxicity.^{24, 25} This study showed similar haematological toxicity (specifically erythropoietic) of female workers exposed to 2-EAA. Thus, occupational health education, modification of work practice, and provision for substitutes are urgently needed. Based on the potential toxicity of ethylene glycol ethers, the ACGIH adopted a new 2-EAA threshold limit value of 5 ppm in 1984. The same exposure standard, 5 ppm, has also been adopted in Taiwan, Japan, Norway, Australia, Denmark, France, the Netherlands, Switzerland, Sweden, Russia, Belgium, Hungary, Argentina, Bulgaria, Colombia, Jordan, Korea, New Zealand, Singapore, and Vietnam in recent years.^{1, 13} Taiwan discontinued production of ethylene glycol ethers and their acetates several years ago. However, the imported quantity of 2-EE and 2-EAA in 2001 was still as high as 4258 tons and total quantity of EGEs was 24 060 tons.^{13, 14} Although ethylene glycol ethers have been phased out in the semiconductor manufacturing industry since 1997, they are still widely used in silk screening, detergents, paints, and copper laminate circuit board manufacturing industries in Taiwan. Special attention to ethylene glycol ether induced health hazards is still urgently required in Asian and other developing countries.

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