Epidemiological Investigations on Health Effects in Toner-Manufacturing Workers

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Adverse health effects can occur in occupational engagements in various industries, and there have been several reports on the contamination of work environments by long-term exposure to chemicals such as heavy metals and organic solvents. Dust has long caused serious health problems at workplaces such as coal mines, tunnel construction, arc welding, metal grinding, foundries, and quarries.

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1. Introduction

Adverse health effects can occur in occupational engagements in various industries, and there have been several reports on the contamination of work environments by long-term exposure to chemicals such as heavy metals and organic solvents [1][2]. Dust has long caused serious health problems at workplaces such as coal mines, tunnel construction, arc welding, metal grinding, foundries, and quarries.

A toner particle is a particulate material sized 5–10 μm in diameter and used in photocopiers and laser printers to form printed images and text on paper. The toner particle is not nano-sized, and industrial nanomaterials are used as the constituent components. Industrial nano-substances include coloring agents such as carbon black (dispersed in the resin, which is the main component of toner), with nano-titanium dioxide and nano-amorphous silica as external additives.

Since the first reported case of siderosilicosis due to toner exposure in 1994, there have been additional case reports of sarcoidosis, allergic rhinitis, and asthma associated with toner exposure [3][4][5][6][7]. These reports raised concerns about the health effects associated with toner exposure and copier and printer use. A recent study found that many studies have shown that the use of laser printing devices (LPDs), such as printers and copiers, contributes to the emission of particles into the indoor environment and may increase indoor air pollution [8][9][10]. However, despite more than 20 years of mixed results on this issue, the substantial relationship between the physico-chemical properties of LPD-emitting particles and the possible health effects of particle exposure in workplaces is still being debated. However, from the industrial hygiene standpoint, toner particles' production method has changed since the 1990s, and the working environment has also changed. Therefore, the potential health effects of PM emitted from office equipment in laser printer users must be evaluated separately.

2. Work Environment Evaluation

Exposure concentrations in the work environment in five papers are shown in **Table 1**. Dust concentration measurements in toner handling workplaces were evaluated through individual exposure measurements and workplace dust concentration measurements. As mentioned in the Terunuma paper [11][12], there were differences in individual exposure concentrations among work categories by toner operation, with significantly higher concentrations in the machine recycling and toner manufacturing work categories than in the other work categories. This trend is similar to that observed in the Kitamura paper [13], where results of individual exposure measurements showed that the average dust concentration over the 10-year observation period ranged from 0.109 to 0.215 mg/m^3 for toner manufacturing, 0.038 to 0.575 mg/m^3 for toner research and development, and 0.044 to 0.323 mg/m^3 for engineering. This is also similar to the Ikegami paper [14] (by work category, “production and maintenance”) which found a tendency for the average TWA8 h to be higher than that of “research and development”. However, each of the papers’ reports calculated 8-h weighted average concentrations of personal dust exposure and compared them to the ACGIH definition of allowable concentrations of 3.0 mg/m^3 for “non-water soluble or insoluble substances that cannot be classified”. Still, no circumstances were found where the work was performed above this standard over the 10-year observation period. In addition, occupational health measures such as wearing protective equipment and installing local exhaust ventilation systems were implemented in almost all workplaces.

Table 1. Exposure concentrations in the work environment in five papers.

Authors	Published Year	Journal	Overall Average Personal Toner Exposure
Ikegami et al. [14]	2016	Industrial Health	TWA 8h <0.24 (mg/m^3): R&D of toner or machine development group <0.08 (mg/m^3): production and maintenance group
Kitamura et al. [13]	2019	J UOEH	Mean dust concentration <0.215(mg/m^3) in toner manufacturing group <0.575(mg/m^3) in R&D of toner group <0.323(mg/m^3) in engineering group
Hasegawa et al. [15]	2018	Int J Occup Med and Env Health	TWA 8h <0.30 (mg/m^3) in customer service group, toner manufacturing group, and toner development group
Yanagi et al. [16]	2021	J UOEH	arithmetical mean <0.054(mg/m^3) in Laser printer quality assurance group, and laser printer mechanism group
Terunuma et al. [11][12]	2019	Atmosphere	A total of 0.989 (0.786) mg/m3 for toner and copy machine recycling, 0.203 (0.441) mg/m3 for toner manufacturing, 0.034 (0.030) mg/m3 for tonerdevelopment, 0.019 (0.063) mg/m3 for toner and copy machine
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Authors	Published Year	Journal	Overall Average Personal Toner Exposure
			development, and 0.020 (0.060) mg/m3 for customer service.

The Ikegami paper [14] evaluated the effects of each biomarker (except CRP) between toner-treated and non-toner-treated groups at the three survey points in 2004, 2008, and 2013. No significant differences were found and no interaction effects between biomarkers and each dependent variable were detected. No statistically significant differences were found between the toner-handling and non-toner-handling groups over the 10-year observation period for CRP. In the Hasegawa paper [15], in analyzing the interaction between working with toner and smoking over a 10-year observation period, some years showed significant differences in SP-D concentrations between the toner-handling and non-handling groups in two-way ANOVA, but not in multiple comparisons. A similar trend was also observed in the blood IgE concentration item between the toner-handling and toner-non-handling groups in years in which concentrations were significantly higher in the toner-handling group than in the past smoker or nonsmoker groups. Statistically significant differences were detected for several biomarkers, but all values were very low and varied within the test reference range. In the Kitamura paper [13], among the biological markers measured, IL-4, IL-8, and IFN-γ were excluded from the analysis. Most parameters showed no significant difference between the toner-handling group and the non-handling group during the ten years of investigation. The Yanagi paper [16] showed no statistically significant differences between groups for CRP, IgE, SP-D, and 8-OHdG/Cre throughout the 10-year observation period. However, KL-6 was significantly higher in the toner non-treatment group than in the toner treatment group. In the Terunuma paper [11], measurement of four cytokines (IL-4, IL-6, IL-8, and IFN-γ) was discontinued by 2008 (fifth follow-up) and excluded from the longitudinal analysis. IL-4 and IL-8 showed no significant differences between the toner-handling and non-toner-handling groups in any year up to the fifth year of the study. For IL-6 and IFN-γ, significant differences were observed between the two groups in some years, but these differences were not consistent and did not exceed reference values. Therefore, they concluded that these parameters, such as cytokines, were not clinically significant.

4. Pulmonary Function Test

Pulmonary function tests were performed annually using a spirometry measuring unit that meets the criteria set by the American Thoracic Society. Forced vital capacity (FVC), forced expiratory volume in 1 s (FEV1), and percentile forced expiratory volume in 1 s (FEV1%) were analyzed. In the Ikegami paper [14], the multiple comparisons analysis showed that %VC and FEV1% analysis was adjusted for smoking with a statistical model. Still, there was no respiratory effect due to toner exposure, regardless of smoking status. In the Hasegawa paper [15], individual annual changes were determined from the measured values of FVC, FEV1, and FEV1% for each participant over 10 years to determine a standard curve. The slope was calculated as the annual change (l/year or %/year). As a result, no significant difference was observed in any items when the changes in FVC, FEV1, and FEV1% were analyzed for the toner handling and non-toner-handling groups. Since pulmonary function tests are affected by smoking, no significant differences were observed when participants were analyzed by smoking status (current or former smokers and non-smokers). They also evaluated the relationship between long-term occupational toner handling history and changes in respiratory function. However, no correlation was found for any variable, including long-term occupational toner handling history. The analysis did not find variables influencing annual respiratory

function changes in the Kitamura paper [13]. Annual changes in lung function indices such as vital capacity (VC), forced vital capacity (FVC), and FEV1.0 were used to assess the effects of toner exposure. Multiple regression analysis was performed using the annual change in pulmonary function index as the dependent variable, and the estimated average dust concentration over 10 years and cumulative toner handling years up to 2013 as the independent variables adjusted for age and smoking status in 2004. No significant effect was observed in the estimated average dust concentration and cumulative toner age. The Yanagi paper [16] found no statistically significant difference between baseline and 10-year toner-handling and non-toner-handling groups. They also compared the difference in the annual decline in respiratory function between all participants and his 10-year non-smoker, examining changes in respiratory function over time with and without toner exposure. However, no statistically significant difference was observed between the two groups. A similar analysis was conducted on 55 non-smokers (20 non-users of toner, 35 users of toner) during the 10-year survey, but no statistically significant difference was observed between the two groups. In the Terunuma paper [11], the effect of toner exposure on respiratory function was shown as the difference in annual changes in parameters between the toner-handling group (including subgroups) and the toner-non-handling group. No significant difference was observed when comparing the results of respiratory function tests in the toner-handling and non-toner-handling groups at baseline and in the 10th year. In addition, the annual decrease in respiratory function was compared. This was obtained by subtracting the respiratory function test value at the 10th year from the baseline respiratory function test value, dividing it by 9 years, and comparing the respiratory function of the toner-handling group and the non-toner-handling group. The functional change rate was examined. However, no significant difference was observed. Since smoking affects respiratory function, similar comparisons were performed in non-smokers at year 10, controlling for smoking factors. Still, there were no significant differences between the toner-handling and non-toner-handling groups.

5. Chest Radiography and CT Examination

In chest radiography findings, no significant results attributed to toner-related work were observed with respect to the development of pneumoconiosis, pulmonary fibrosis, and lung cancer throughout the 10-year observation period. In Kitamura's paper [13], toner-handling workers, namely toner manufacturing groups, research and development groups, and technology groups, were compared with non-toner-handling groups. Regarding the detection rate of ILO pneumoconiosis classification of 0/1, no significant relative risk was observed in the toner-handling group. In the Terunuma paper [11], which had the largest number of studies, 11,563 chest radiography examinations were performed during the 10-year follow-up period. No significant findings related to toner exposure were observed even when analyzed separately for each engagement of toner exposure. The chest CT examination is discussed in the Yanagi paper [16]. They also found no findings suggesting granulomatous pneumonia or malignancy in baseline and 10-year chest CT results for workers who did not handle and workers who handled toner.

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