Outbreak Reports

An Occupational Trichloromethane-Induced Hepatotoxicity Outbreak — Shenzhen City, Guangdong Province, China, October 2024

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Summary

What is already known about this topic?

Trichloromethane (chloroform), a volatile halogenated solvent, is widely used in printing and industrial operations. Occupational exposure occurs predominantly through inhalation. Chronic exposure can induce hepatotoxicity, but early symptoms are non-specific, frequently resulting in underdiagnosis and severe adverse health outcomes.

What is added by this report?

This study identified 43 cases of occupational trichloromethane-induced liver injury. The trichloromethane content in both solvents analyzed (57.65% and 66.59%) exceeded the regulatory limit of 20%. Furthermore, the peak airborne trichloromethane concentration in the printing workshop reached 110.3 mg/m^3 — 5.5-fold the occupational exposure limit. Solvent exposure was established as the primary risk factor.

What are the implications for public health practice?

This incident highlights effective occupational health response strategies through coordinated occupational health examinations, solvent composition verification, environmental monitoring, and corporate guidance. It also underscores the need for environmental agencies to incorporate trichloromethane-specific exposure limits into VOC regulations. Enterprises should strengthen management of their Environmental, Health and Safety (EHS) departments.

ABSTRACT

Introduction: To investigate an occupational trichloromethane-induced hepatotoxicity incident at a Shenzhen printing enterprise, identify its root causes, evaluate intervention effectiveness, and provide evidence for occupational health regulation and corporate solvent management.

Methods: Routine occupational health examinations in October 2024 identified 34 workers with elevated alanine aminotransferase (ALT) levels. This finding, combined with four hospital-reported cases of abnormal liver function, triggered a comprehensive multisectoral investigation. Thirty-nine solvents and nine air samples were collected for gas chromatography-mass spectrometry (GC-MS) analysis. A case-control study was conducted (18 cases *vs.* 49 job-matched controls), and multisectoral coordination was implemented throughout the response.

Results: Forty-three cases of occupational liver injury were confirmed (83.7% asymptomatic; 10 requiring medical intervention). Both "eco-friendly adhesive-tape cleaner" (57.65% trichloromethane) and "adhesive-tape cleaning restorer" (66.59% trichloromethane) exceeded the 20% concentration limit mandated by GB 38508-2020. The peak airborne trichloromethane concentration in the printing workshop reached 110.3 mg/m^3 (5.5-fold above the GBZ 2.1-2019 occupational exposure limit). Solvent exposure was the primary risk factor [cleaner: odds ratio (*OR*)=32, 95% confidence interval (*CI*): 13.89–73.46; restorer: *OR*=23, 95% *CI*: 18.23–56.93]. No new cases emerged following intervention implementation.

Conclusion: The incident originated from the enterprise's solvent reformulation to meet environmental standards without addressing occupational health risks. Occupational health examinations and multisectoral coordination were pivotal for containment. We recommend: 1) including trichloromethane in priority volatile organic compound (VOC) control lists; 2) strengthening corporate solvent verification; 3) enforcing ventilation management.

On October 29, 2024, routine occupational health

surveillance at a Shenzhen printing facility revealed elevated alanine aminotransferase (ALT) levels in 34 of 269 employees, prompting an immediate investigation by the local public health authority (LPHA). Subsequently, on November 11, area hospitals reported four consecutive cases of abnormal ALT levels among company workers, including the index case (Li), which heightened suspicion of an occupational etiology. Comprehensive screening of 171 high-risk employees on November 12 — integrating epidemiological data, occupational exposure histories (particularly trichloromethane use), clinical presentations, and laboratory findings — confirmed occupational hepatotoxicity resulting from excessive trichloromethane exposure.

Investigation and Findings

The company employs 350 production staff across two air-conditioned floors (2nd and 3rd), with ventilation systems reportedly functioning adequately. The index case, Li, a 25-year-old offset printer, presented on October 16 with vomiting and influenza-like symptoms, with an ALT level of 1,696 U/L. However, initial clinical evaluation revealed no objective evidence linking his symptoms to occupational exposures, and the attending physician did not prioritize further occupational history investigation. Li's ALT declined to 259 U/L by October 23, leading to discharge on October 25. A company-arranged occupational health examination on October 29 recorded ALT at 256 U/L. Upon returning to work, his ALT surged to 535 U/L by November 12, necessitating rehospitalization until November 25 (ALT: 262 U/L). This pattern — decreasing ALT during hospitalization and rising levels post-discharge — demonstrates temporal consistency between occupational exposure and disease progression.

LPHA established standardized case definitions and initiated systematic case identification. Employees with medical consultations in the preceding three months were instructed to voluntarily report health information, while the company was directed to submit a current employee roster for cross-referencing. Using this roster, LPHA systematically screened employee medical records in the electronic health records system during the designated three-month observation window (July 16–October 16, 2024). Case inclusion criteria required biochemical evidence of abnormal liver function or unexplained fatigue, nausea, abdominal distension, or hepatic quadrant pain. Cases with confirmed diagnoses of viral hepatitis, drug-induced liver injury, hepatocellular carcinoma, or other pre-existing hepatobiliary disorders were excluded. LPHA investigators conducted individual case verification through clinical documentation (symptomatology, hepatic panel results, diagnostic conclusions), occupational records (employment duration, departmental assignments), and demographic data (age, gender, medical history).[*]

The incident investigation identified 43 cases, comprising 36 asymptomatic individuals (83.7%) and seven symptomatic cases presenting with nausea and dark-yellow urine. Ten patients required medical care (nine hospitalized; one outpatient). Attack rates demonstrated significant variation by department and position (P<0.05), with the highest rates observed among printing personnel, while no significant differences emerged by gender, age, or floor assignment (P>0.05).

Based on the spatiotemporal clustering of cases (predominantly concentrated in printing departments) and documented occupational exposure histories, the preliminary hypothesis suggested an association with occupational exposure to VOCs. The on-site investigation revealed the following key findings: 1) Production Workshop: The printing department occupies 1,200 m^2 and follows a sequential process flow including paper feeding, cutting, silk-screen printing, printing, laminating, hot-stamping, die-cutting, slotting, inspection, forming, gluing, and hand assembly. 2) Ventilation System: The workshop employs a supply and exhaust ventilation system. Each printing unit features a suction trough and updraft external hood with side supply ducts. Exhaust gases are centrally collected and directed to rooftop purification systems. Notably, no activated carbon adsorption units were installed at ventilation terminals. 3) Printing Operations and Chemical Solvent Use: Each printing machine operates with four workers who utilize eco-friendly adhesive-tape cleaners and rubber-tape cleaning restorers. Elevated solvent exposure frequency among printing workers correlated significantly with higher liver abnormality rates compared to non-

[*] Referring to the time when the index case, Li, sought medical treatment, the search period was set as three months in accordance with the diagnostic criteria for chronic hepatic poisoning in Diagnostic standard for occupational toxic hepatopathy (GBZ 59-2024) (*1*). Abnormal liver function was established through clinician consensus guided by evidence-based hepatology protocols.

exposed workers, revealing a clear dose-response relationship. Personal protective equipment includes disposable masks, rubber gloves, and earplugs, though some workers demonstrated improper usage. 4) Chemical Solvent Exposure Assessment: Company procurement records revealed that in April 2024, responding to regulatory mandates from environmental protection authorities to reduce VOC emissions, the company required suppliers to reformulate eco-friendly adhesive-tape cleaners and rubber-tape cleaning restorers. However, the company failed to conduct validation analyses of volatile constituents in the modified formulations, and suppliers did not submit detailed product composition analysis reports. 5) Occupational Hazard Surveillance: Historical occupational hazard evaluations encompassed two monitoring periods (June–July 2023 and June–August 2024), during which 22 VOCs were systematically analyzed: 15 samples from second-floor workshops in 2023 (including eco-friendly adhesive-tape cleaners) and seven samples from third-floor workshops in 2024 focusing solely on occupational hazards including benzene, toluene, and n-hexane (excluding eco-friendly adhesive-tape cleaners and rubber-tape cleaning restorers). Gas chromatography-mass spectrometry (GC-MS) analysis identified constituents including benzene (0.11%), n-hexane (5.67%), toluene (0.68%), ethyl acetate, acetaldehyde, vinyl acetate, methyl acetate, methanol, cyclohexane, and isopropanol. All quantified concentrations remained below national occupational exposure limits (OELs), and trichloromethane was undetectable across all samples. 6) Occupational Health Surveillance: Pre-intervention medical records (January 2022–September 2024) indicated that 504 employees completed standardized occupational health examinations. Two workers were identified with auditory contraindications for noise exposure, with no confirmed occupational disease cases detected during this monitoring period. Beginning October 29, 2024, the company progressively conducted occupational health examinations for employees, with no new cases emerging following intervention implementation.

Testing results for 39 chemical solvents potentially encountered by workers are presented in Table 1. Trichloromethane constituted 57.65% and 66.59% of the eco-friendly adhesive-tape cleaner and rubber-tape cleaning restorer, respectively. Both formulations exceeded the 20% trichloromethane concentration limit for organic solvent-based cleaners specified in GB/T 38508-2020 Limits of volatile organic compounds in cleaning agents (*2*). Their headspace VOC peak area percentages exceeded 84%. A total of 9 air samples collected from distinct production workshop locations revealed trichloromethane in three samples (5.65, 110.3, and 52.96 mg/m^3; Table 2). According to GBZ 2.1-2019 Occupational exposure limits for hazardous agents in the Workplace (*3*), the permissible time-weighted average (TWA) concentration for trichloromethane is 20 mg/m^3. The latter two samples exceeded this limit by 5.5-fold and 2.6-fold, respectively.

We identified exposure to eco-friendly adhesive-tape cleaners, rubber-tape cleaning restorers, smoking, alcohol consumption, and employment duration >6 months (defined by the six-month interval between solvent reformulation in April 2024 and the October 2024 investigation) as potential risk factors for the incident. A case-control study was conducted through structured questionnaire surveys and face-to-face interviews with workers. The case group comprised 18 workers with liver function abnormalities identified from printing-related positions [abnormal liver function was defined according to the diagnostic criteria for chronic hepatotoxicity in Diagnostic standard for occupational toxic hepatopathy (*1*)]. The

TABLE 1. Analysis results of volatile components in chemical solvents.

Chemical solvents name	Total volatile organic components peak area percentage (%) in headair	Trichloromethane (%)	Dichloromethane (%)	Methyl methacrylate (%)
Eco-friendly adhesive-tape cleaners	85.25	57.65	6.09	0
Rubber-tape cleaning restorers	84.5	66.59	10.33	0
Water-based semi-dull oil	25.91	0.51	0	0
UV low-odor abrasion-resistant reverse-gloss oil	24.39	0	0	9.15
UV low-odor reverse-gloss oil	39.59	0	0	0.36
Other chemical solvents	The above 3 substances were not detected. Main components include methanol, ethyl acetate, butyl methacrylate, cyclohexane, etc.			

Abbreviation: UV=ultra-violet.

TABLE 2. Detection results of air samples from different locations. (mg/m^3)

Detection location	Trichloromethane	Tetrachloroethylene	Carbon tetrachloride	Methanol	1,2-dichloroethane	Trichloroethylene	Methyl acetate	Dichloromethane
Six-color offset machine 3# operating position in printing department	5.65	<1.00	<1.00	<1.00	<0.13	<0.89	<1.00	<0.13
Seven-color offset machine 4# operating position in printing department	110.30	<1.00	<1.00	<1.00	<0.13	<0.89	<1.00	<0.13
Operating position in laminating department	52.96	<1.00	<1.00	<1.00	<0.13	<0.89	<1.00	<0.13
Other locations	<1.00	<1.00	<1.00	<1.00	<0.13	<0.89	<1.00	<0.13

control group comprised 49 workers with normal liver function from printing-related positions. Univariate analysis demonstrated that exposure to both the cleaner and restorer was significant risk factors (P<0.05), as shown in Table 3. Multivariable log-binomial regression analysis confirmed exposure to the cleaner [odds ratio (OR)=32, 95% confidence interval (CI): 13.89, 73.46] and restorer (OR=23, 95% CI: 18.23, 56.93) as independent risk factors.

This incident resulted from trichloromethane exposure exceeding national occupational health limits (*3*), which led to occupational hepatotoxicity. The temporal sequence was clearly established, with all cases demonstrating definitive occupational exposure. Strong supporting evidence emerged from clinical presentations, comprehensive on-site hygiene investigations, and laboratory analyses. We identified a consistent dose-response relationship and exposure-disease distribution pattern. Both univariate and multivariate analyses demonstrated a statistically significant association between chemical solvent exposure and case occurrence. The company's transition to eco-friendly adhesive-tape cleaners and rubber-tape cleaning restorers in April 2024 represented a critical risk factor. The high organic volatile content and elevated concentrations of these chemical solvents constituted the primary cause of liver function abnormalities observed across workers in different departments and positions.

Public Health Response

On October 29, 2024, LPHA detected abnormal liver function in multiple workers during routine occupational health surveillance at a printing facility, prompting immediate directives for confirmatory testing, medical referrals, and initiation of a comprehensive field epidemiological investigation. Following hospital reports of four employees (including index case Li) with elevated ALT on November 11, 2024, LPHA implemented the following coordinated response: collection and analysis of chemical and air samples, execution of a matched case-control study to identify exposure pathways, immediate sealing of trichloromethane-containing solvents, mandatory suspension of production operations, and validation requirements for the company's ventilation system performance. On November 12, 2024, additional interventions were deployed, prioritizing liver function screening for 171 high-exposure workers while establishing a comprehensive triage-based medical response system

TABLE 3. Risk factors for occupational liver injury: univariate and multivariable analysistion.

Risk Factor	Univariable Analysis *OR* (95% *CI*)	Multivariable Analysis *OR* (95% *CI*)
Exposure to cleaner	384.0 (32.6−623.0)	32.0 (13.89−73.46)
Exposure to restorer	260.7 (3.9−500.3)	23.0 (18.23−56.93)
Smoking	2.0 (0.6−6.3)	−
Alcohol consumption	1.3 (0.3−4.8)	−
Employment duration >6 months	2.8 (0.9−8.7)	−

Note: "−"means that the variable was not included in the multivariable analysis model because it did not show statistical significance (*P*>0.05) in the univariate analysis.
Abbreviation: *OR*=odds ratio.

focused on occupational liver disease management and psychological support. Concurrently, regulatory authorities in supplier regions were engaged to trace chemical supply chains, and the company received mandates to replace trichloromethane with low-toxicity alternatives.

DISCUSSION

Trichloromethane, a protoplasmic toxin, primarily targets hepatocytes and causes significant liver damage (*4*). Previous investigations have documented multiple incidents of trichloromethane-induced hepatotoxicity in occupational settings (*5*–*6*). This occupational trichloromethane-induced hepatotoxicity incident demonstrates the essential role of routine occupational health examinations as an early warning system. These periodic screenings serve as a frontline defense mechanism, enabling prompt detection of abnormal liver function and providing critical time for local public health authorities to activate emergency response protocols, coordinate medical interventions, and initiate comprehensive epidemiological investigations.

The multisectoral collaboration among local public health authorities, healthcare facilities, and the affected enterprise, combined with systematic information sharing, proved instrumental in effectively controlling the outbreak. Population-based epidemiological analysis successfully identified high-risk occupational positions within the printing department, thereby enabling targeted intervention strategies that maximized resource allocation efficiency.

According to the Comprehensive Management Plan for Volatile Organic Compounds in Key Industries issued by China's Ministry of Ecology and Environment (No. 53, 2019) (*7*), trichloromethane is not classified as a priority-controlled VOC, which resulted in its oversight during the company's solvent substitution process. We strongly recommend including trichloromethane in the priority-controlled VOCs list alongside enhanced regulatory frameworks.

Enterprises must strengthen their environmental, health, and safety (EHS) management systems by implementing rigorous procurement protocols and conducting comprehensive volatile component analyses of all solvents to ensure regulatory compliance.

Several limitations warrant acknowledgment in this investigation. Limited occupational health literacy among workers compromised the reliability of personal protective equipment usage assessments, while questionable accuracy regarding reported work tenure and medical histories undermined overall data credibility. Additionally, our screening was restricted to 171 high-exposure workers, potentially missing cases in other departments. The non-specific clinical presentation of trichloromethane toxicity, combined with high workforce turnover patterns, increased the risk of missed diagnoses. Most critically, our inability to identify the specific causative solvent batch prevented definitive attribution, and we could not exclude potential confounding effects from other chemical components present in the workplace environment.

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