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Exposure to Benzene-Contaminated Toluene and Bone Marrow Disorders—A Retrospective Exposure Assessment

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Introduction

This case study demonstrates the importance of retrospective exposure assessment by occupational hygienists in the identification of occupational disease.

Two workers (aged 47 and 49 years) employed in the printing trade were diagnosed by their hematologists with bone marrow disorders—specifically, chronic myelogenous leukemia (CML) and thrombocytopenia. The workers contacted an occupational health clinic to investigate the work-relatedness of their conditions. Because of the nature of the chemicals used and work activities, the following issues required investigation:

- evidence of benzene contamination of toluene,
- benzene exposure and chronic myelogenous leukemia, and
- benzene exposure and thrombocytopenia.

The occupational hygienist had no access to the workplace. She relied upon the workers to provide information about the types and quantities of chemicals used, controls in place to prevent exposures, and detailed descriptions of work practices. After discussion with the workers, retrospective exposure profiles were developed to assist the occupational health clinic's physician in determining the work-relatedness of their conditions.

Method

Interview

The occupational hygienist in the clinic did not have access to the workplace. Therefore, exposure profiles relied heavily on information provided by the workers. The interview lasted 3 to 4 hours and discussed exposures in the workplace. Workers were asked to list jobs performed and the dates these jobs were held. For the physical process and materials used, the workers were asked to:

- describe the process (and nearby processes);
- list any materials used, and the amounts (i.e., the consumption rates); and
- describe:
  - the methods used (e.g., spraying, heating, etc.),
  - the physical state of the material,
  - its appearance,
  - its odor,
  - the containers in which it was found,
  - the contents of the labels on containers, etc.

The occupational hygienist then reviewed activities such as:

- cleanup,
- breakdown functions,
- periodic maintenance work,
- occasional and seasonal functions, and
- overtime.

Questions were asked about anecdotal evidence of exposures such as:

- housekeeping conditions,
- storage practices,
- hygiene facilities and practices,
- location and strength of emission sources,
- integrity and extent of control measures in the workplace,
- use and type of protective equipment,
- extent of perceived inhalation and dermal exposures,
- symptoms,
- odors, and
- the perceived prevalence of symptoms or diseases among fellow workers.

Documentation

The workers brought to the clinic all documentation relevant to the assessment of their exposure. Information included:

- MSDSs;
- hygiene reports;
- Ministry of Labour documentation, visits, or other reports;
- engineering process control reports;
- drawings; and
- Joint Health & Safety Committee minutes.

Any product information from company sales literature can also be valuable information.

Exposure Evaluation

The results of the exposure evaluation were compared with any available hygiene reports and literature reports concerning similar processes. This type of information can be found in the NIOSHTIC database. Especially useful in this regard are the health hazard evaluations performed by the National Institute for Occupational Safety and Health (NIOSH).

There was extensive consideration of all possible routes of exposure. This included an evaluation of all possible physical states of the substances of concern. This is especially important when the substance may be present in the workplace air in more than one state, such as a liquid which could be present in vapor form and also as a liquid condensed on particulate suspended in the air.

Occasionally it is necessary to contact suppliers to determine what substances were used 10 to 15 years ago or more. Abundant information can be obtained in conversations with knowledgeable chemists or salespersons with long-standing experience in a field of supplying certain commercial substances.

Employment History

The two workers had been employed by the same employer for 26 and 29 years, respectively. The company manufactures flexible packaging, and the main processes involve printing, coating, laminating, and bag making. During their employment with this company, these workers worked primarily in batch preparation—specifically, at the coating machines and in the mixing room—alternating between the two areas. Currently the worker with thrombocytopenia works mainly at the coating machines and the worker with CML works in the slitting department.

Task Descriptions and Exposures

Coating Machines

The process involves laminating two pieces of film together and applying a coating. The solvents most frequently used in this process are toluene, methylethylketone (MEK), and a variety of alcohols. These solvents were used frequently to remove coatings from the workers' hands. Gloves were made available to workers in the late 1980s.

Workers maintained coating levels in the following manner:

- Toluene-based coatings (in a gel form) were stored in a 45-gallon drum.
- Workers shoveled gel from one drum into another, which was heated to 120° to 140°F.
- Workers poured heated liquid coating into a supply drum.
- Later the process was changed so that toluene was fed into the coating machine using a pump; however, workers often had to revert to the three-drum process.

Workers were also required to clean the coating machines.

Working at the coating machines involved exposure—via inhalation as well as skin contact and skin absorption—primarily to toluene and its benzene contaminant and to MEK and alcohols. Personal protective equipment was not worn regularly, and the workers stated that there was lack of enforcement by the company.

Exposure to toluene and thus its benzene contaminant occurred during shoveling of the toluene-based gel from the 45-gallon drum to a heating drum and during pouring into the supply drum. Spills were common, occurring on average about once per week. The gel was cleaned up by scraping. Spilled solvent was left to evaporate.

The workers estimated that one 45-gallon drum lasted about 1.5 hours; therefore, during an 8-hour shift they directly handled about 240 gallons of toluene. They often worked 12-hour shifts, which would have resulted in the handling of about 360 gallons of toluene. Overtime (double shifts) was common.

Regular cleaning involved draining the coating from the machine by removing the level control. The coating was pumped into a holding drum and the level control placed back into the machine. Toluene was manually poured into the machine and all of the machine parts were cleaned using rags while the toluene circulated throughout. No gloves were worn. The duration of cleaning ranged from 2 to 3 hours, about once or twice per week. The workers indicated that they were often overcome by a feeling of drunkenness after the cleaning. The literature indicates that acute exposures to toluene over 200 ppm have caused symptoms similar to drunkenness (giddiness), numbness, and mild nausea.[1]

The workers stated that breaks in the system, in which a fault in the paper caused it to break and splash the coating, were common. The spilled coating was cleaned with toluene, and they indicated that this could take several hours to complete.

The workers stated that in the 1960s the coating machines had virtually no local exhaust. In the late 1970s local exhaust was introduced in the form of a slot hood. The situation improved somewhat, but the workers indicated the exposure to toluene vapors persisted. Also, workers sometimes ate in the area.

Mixing Room

The dimensions of the mixing room were approximately 30 × 50 ft. Here, the workers mixed solvent-based laminants, silicones, various waxes, primers, lacquers, and solvent-based inks. They were also required to melt various solid resins in hot toluene or various vinyls in hot MEK (130° to 160°F) in large mixers.

Mixers with a capacity of 3600 lbs. were filled by workers (via a piping system) with 1200 to 1400 lbs. of toluene heated to 130° to 160°F. Solid toluene-based resins (referred to by the workers as gel lacquer) were manually added to the funnel that fed the mixer. The workers indicated that they were instructed to shovel only one drum of gel lacquer at a time, at which time another worker would be substituted. However, when first starting this job, workers often emptied as many drums of gel lacquer as they could withstand and often, upon leaving the area, had difficulty standing as a result of excessive exposures.

Toluene vapors rose up the mixer stack and accumulated around the funnel located directly in the workers' breathing zones. The fact that the toluene was heated indicates an increased likelihood of vapor being released into the workplace and thus an increased inhalation hazard. After the batch was completed, the workers often experienced feelings of being "stoned." After the toluene vapor left the heated environment of the mixer, it condensed and the droplets accumulated on the workers' faces and nostrils. The literature states that acute exposures to toluene over 500 ppm have caused mental confusion and lack of coordination.[1]

Every shift the mixing room floor was washed with either toluene or MEK. Exposures to these substances in the winter were especially high since all the doors and windows were closed. Personal protective equipment was not used regularly.

Local exhaust ventilation at the mixer was not always used. Local exhaust, when engaged, had the effect of increasing evaporation of the solvent in the batch, which resulted in undesirable viscosity changes. With the local exhaust engaged, more solvent had to be added by the workers to make up for the loss. Therefore, in most cases the exhaust was not turned on when making batches, thus retaining solvent and eliminating the need for viscosity adjustment. As a result of not engaging the exhaust, time and solvents were saved; however, the potential exposure to toluene vapor increased.

The empty coating drums were cleaned using 5 to 10 gallons of toluene. The drum was tilted on its side and washed with ungloved hands. The workers would bend over so that their heads were well inside the drum. Gloves, respirators, goggles, and aprons were not used. Personal protective equipment for this process was introduced in the late

1980s. Today plastic disposable liners are used.

A Theory Gone Wrong

When workers sustained cuts on the job, it was common practice to clean cuts with toluene or MEK. Since workers were applying these solvents directly to open wounds, this practice most definitely allowed for skin absorption, which is of special concern since it is known that toluene was often contaminated with benzene. There was a theory circulating in the workplace that the solvents would destroy any bacteria that may have accumulated in the cut, and this was an appropriate antiseptic. It was also common practice to use steel wool to remove certain coatings from the hands, followed by washing the hands with toluene, further increasing the risk for skin absorption of benzene-contaminated toluene.

Literature Review

While there are no measurements of the workers' exposures to toluene or benzene, a combination of literature evidence (including historical reports) and a reconstruction of the workers' job tasks provided convincing evidence of the possibility of regular excessive exposures to benzene along with excessive peaks.

The literature review focused on three issues:

1. evidence of benzene contamination of toluene,
2. benzene exposure and CML, and
3. benzene exposure and thrombocytopenia.

Evidence of Benzene Contamination of Toluene

The *Criteria for a Recommended Standard—Occupational Exposure to Toluene*[2] provided abundant evidence of benzene contamination of toluene. The studies quoted in this document indicated that toluene from the 1940s until the early 1980s was frequently contaminated with benzene, and certain grades of toluene may have contained as much as 25 percent benzene. Because of the benzene content in toluene, conclusions made by early investigators confused the effects of toluene on the hematopoietic system.

Benzene Exposure and CML

The NIOSH document stressed that, although toluene frequently contained benzene in significant quantities, its presence was seldom mentioned and attempts were rarely made to identify the benzene either qualitatively or quantitatively. Thus, in any evaluation of reported myelotoxicity for toluene, the benzene content, if known, is an important factor for consideration.

The chronic form of illness resulting from benzene exposure is related to the localization of benzene in the bone marrow.[3] *Environmental and Occupational Medicine*,[3] states that leukemia in workers exposed occupationally to benzene was first recognized in the 1920s. It reports that additional case reports and case series published from the 1920s to the 1960s repeatedly noted the association between leukemia and exposure to benzene. All types of leukemia—principally myeloid and myelomonocytic, but also acute and chronic lymphocytic leukemia—have been observed in these reports of workers exposed to benzene.

Benzene can cause problems in the synthesis of all blood-forming elements. This can occur in the very early stages of development, even at the stem cell stage, at very low levels of exposure.

In a study by Yin *et al.*[4] of workers employed in a variety of occupations—including painting, printing, and the manufacture of footwear, paint, and other chemicals—among the leukemia subtypes, only acute myelogenous leukemia (AML) incidence was significantly elevated, although nonsignificant excesses were also noted for CML and lymphocytic leukemias.

Benzene Exposure and Thrombocytopenia

Thrombocytopenia refers to a condition resulting from a decrease in platelet count which can occur due to decreased production or increased destruction.[5]

Many studies in the literature pointed to a link between benzene exposure and thrombocytopenia.[6–18] This condition can arise from the hematologic effects of benzene toxicity. One author stated that thrombocytopenia may be more prominent than anemia or leukopenia in benzene-affected workers, and that a major problem of surveillance programs is the lack of specificity of the manifestation of benzene hematotoxicity. It is stressed by the author that each case must be evaluated individually.[9]

Workers' Compensation Board Status

Although the literature indicated studies which concluded there was a link between benzene exposure and leukemia (primarily AML), the Workers' Compensation Board (WCB) initially denied the worker's claim for benzene exposure and CML, citing as one of the reasons inadequate epidemiological evidence to show an association between CML and occupational exposure to benzene. The WCB did recognize, however, that the association between CML and benzene exposure was plausible in view of the increased risks of acute nonlymphoid leukemias found in populations occupationally exposed to benzene and the common origin of the acute nonlymphoid leukemias or AMLs and CML at stem cell levels in the bone marrow. The worker appealed this decision. The decision review specialist considered all of the available evidence and noted that, according to scientific literature, there is evidence to link CML with benzene exposure and the objection to the claim denial was allowed.

The thrombocytopenia WCB claim was denied at the initial stage. The worker has appealed this decision and a review is pending. It is important to note that this worker came forward upon hearing of the case of his co-worker diagnosed with CML.

Conclusion

Based on a retrospective review of the workers' occupational exposures to toluene, historical reports indicating significant benzene contamination of toluene, and a review of the literature on benzene exposure and CML and thrombocytopenia, there was evidence to suggest that the workers' conditions were linked to workplace exposures that occurred via inhalation and dermal absorption during their employment in the printing industry. Since historically there is evidence that toluene often contained benzene as an impurity from the 1940s until the early 1980s, the workers may have been significantly exposed to benzene from the time they began work at this plant until the time that benzene concentrations in toluene were significantly reduced.

These cases stress the importance of the retrospective exposure profile compiled without access to the workplace and in the absence of air monitoring data from previous decades. Based on detailed worker interviews and workplace descriptions, an exposure picture can be created to assist in identifying occupational disease in the workplace.

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