HETA 99-0035-2757
LDS Hospital/Intermountain Health Care
Salt Lake City, Utah

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PREFACE

The Hazard Evaluations and Technical Assistance Branch (HETAB) of the National Institute for Occupational Safety and Health (NIOSH) conducts field investigations of possible health hazards in the workplace. These investigations are conducted under the authority of Section 20(a)(6) of the Occupational Safety and Health Act of 1970, 29 U.S.C. 669(a)(6) which authorizes the Secretary of Health and Human Services, following a written request from any employer or authorized representative of employees, to determine whether any substance normally found in the place of employment has potentially toxic effects in such concentrations as used or found.

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ACKNOWLEDGMENTS AND AVAILABILITY OF REPORT

This report was prepared by Eric J. Esswein, CIH, MSPH and A. Yvonne Boudreau, MD, MSPH of HETAB, Division of Surveillance, Hazard Evaluations and Field Studies (DSHEFS). Field assistance and consultation were provided by E. Brigitte Gottschall, MD, and Karin Pacheco, MD of the National Jewish Medical and Research Center, Denver, Colorado. Analytical support was provided by Ardith Grote, ARDB, NIOSH and Mark Swanson, Mayo Clinic, Rochester, Minnesota. Desktop publishing was performed by Pat Lovell. Review and preparation for printing were performed by Penny Arthur.

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Health Hazard Evaluation Report 99-0035-2757
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November 1999

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SUMMARY

On November 18, 1998, the National Institute for Occupational Safety and Health (NIOSH) received a request for a health hazard evaluation (HHE) from the Occupational Health Nurse at the Latter Day Saints/Intermountain Health Care hospital in Salt Lake City, Utah. The HHE request stated that several nurses and nurses' aides working in the bone marrow transplant unit (BMT) had experienced allergic symptoms. These included two reports of anaphylaxis and several reports of less severe symptoms, such as shortness of breath, rashes, and itching. The health effects reported by the health care workers were thought to be associated with an activity specific to the BMT: the infusing of patients with a solution containing stem cells and dimethyl sulfoxide (DMSO).

The NIOSH investigation consisted of concurrent medical and industrial hygiene evaluations on December 7, 1998, and an additional medical evaluation on February 18-19, 1999. The medical evaluation included a questionnaire, private interviews with employees, and review of medical records. The industrial hygiene evaluation consisted of air, surface, and bulk dust sampling to evaluate the presence of DMSO and latex proteins in the BMT.

None of the volatile chemicals known to be present in the stem cell infusion solutions, including DMSO, were detected in the air during the administration of stem cells into a patient. Natural rubber latex was not detected in air samples. A medical records review revealed rashes and respiratory symptoms to be the most commonly reported symptoms among affected employees.

Since no direct dermal contact with DMSO occurs, and no chemicals could be measured in the breathing zone of the staff nurse or in the ambient environment of the room where the infusion occurred, it is unlikely that skin and respiratory symptoms are caused by exposures from the administration of stem cells. Medical questionnaires (from 64 workers) revealed that 22% of employees reported some type of chest symptom and 50% reported skin symptoms including rashes (47%) and hives (13%). Hay fever was reported by 59% of the employees and 22% reported a physician diagnosis of asthma. Pre-existing atopy and asthma in the employees who worked in the BMT could explain the upper respiratory symptoms reported by staff in the BMT. Skin symptoms (especially hand rash) are common in the nursing profession due to frequent washing and drying of the hands and the use of gloves as a part of universal precautions.

This evaluation did not find occupational exposure to DMSO or other volatile chemicals in the stem cell infusion solution. Natural rubber latex was not detected in air samples, but latex gloves and other latex products were present in the BMT. A survey of the work environment and work practices in the BMT could not explain the reasons for the upper respiratory symptoms that employees associated with infusing patients with stem cells. Pre-existing allergy in BMT staff may explain some upper respiratory symptoms. Frequent hand washing and the use of gloves as barrier protection could explain the skin symptoms of hand rash.

Keywords: SIC 8062 (General Medical and Surgical Hospitals) Dimethyl Sulfoxide, DMSO, Bone Marrow Transplant Unit, Hospitals, Health Care, Nurses

Highlights of the NIOSH Health Hazard Evaluation

Evaluation of Symptoms at LDS Hospital

The occupational health nurse at the LDS Hospital asked NIOSH to find out why some nurses and nurses' aides had allergic symptoms while working on the Bone Marrow Transplant Unit. These employees were concerned that their symptoms might be related to DMSO (dimethyl sulfoxide), a preservative used for stem cell infusions in patients.

What NIOSH Did

We gathered surface dust and air samples to test for DMSO and latex.
We talked to employees on the Bone Marrow Transplant Unit.
We looked at the medical records of employees who had symptoms at work.
We handed out a questionnaire to employees on the Bone Marrow Transplant Unit.

What NIOSH Found

There was no latex or DMSO detected in the air or surface samples.
Employees who had symptoms did not have skin contact with DMSO.
Some employees wear latex gloves while working.
Many of the employees who reported symptoms had hay fever.

What the LDS Hospital Can Do

Encourage employees to report all symptoms.
Send employees with symptoms for a medical evaluation of their symptoms as soon as possible.
Reduce exposure to latex as much as possible.
Place used stem cell IV bags in an airtight trash bag to reduce odors.

What LDS Employees Can Do

Report all symptoms to the appropriate personnel.
Have your symptoms checked by a qualified medical professional as soon as possible after they occur.
When using gloves, wear non-latex gloves whenever possible.

CDC
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What To Do For More Information:
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NIOSH

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INTRODUCTION

On November 18, 1998, the National Institute for Occupational Safety and Health (NIOSH) received a request for a health hazard evaluation (HHE) from the Occupational Health Nurse at the Latter Day Saints (LDS)/Intermountain Health Care (IHC) hospital in Salt Lake City, Utah. The HHE request stated that several nurses and nurses' aides working in the bone marrow transplant unit (BMT) had experienced allergic symptoms. These included two reports of anaphylaxis and several reports of less severe symptoms, such as shortness of breath, rashes, and itching. The health effects reported by the health care workers were thought to be associated with an activity specific to the BMT: the infusing of patients with a solution containing stem cells and dimethyl sulfoxide (DMSO).

NIOSH representatives conducted two site visits to the hospital. The first was on December 7, 1998, and included employee interviews and collection of air and surface samples for evaluation. The second site visit took place on February 18-19, 1999, and consisted of the administration of a medical questionnaire to employees. An interim report, containing the results of the environmental sampling, was sent to the hospital in January, 1999.

BACKGROUND

Several types of bone marrow transplants are available for patients. The LDS/IHC hospital provides autologous pluripotent stem cell transplants in which the patient is the source of the stem cells for his/her transplant. Blood, which contains stem cells, is drawn from the patient from a central venous line. Stem cells are removed from the patient's blood and the blood is then reinfused into the patient. The stem cells are then cryopreserved (frozen). Cryopreservation is a process used to preserve materials such as previously collected bone marrow, peripheral blood stem cells, and umbilical cord blood by freezing the cells for storage. DMSO is a cryoprotective solvent that is known to protect blood cells and other tissues from damage due to freezing. DMSO is added to the stem cells when they are prepared at the University of Utah Hospital. Other additives include a saline solution called "Hank's Buffered Salt Solution" (HBSS), heparin, and albumin.

Before a patient receives an infusion of preserved stem cells, the cells are thawed by placing the infusion bag into a bath of warm, sterile water. Generally, two nurses are present during this process; one nurse thaws the bag of cells and the other administers the cell-containing solution. Both nurses wear gloves during this procedure. If more than one bag of cells is to be administered to a patient, the bags are serially thawed as the administration of the cells proceeds. The intravenous (IV) infusion occurs within a closed system, so the DMSO/stem cell solution cannot volatilize directly into the ambient environment (the patient's room) while the infusion occurs.

Employee accounts of the onset of their symptoms and concurrent work activities led the requesters to suspect that DMSO exposure was the causative agent. Employees also reported that odors (believed to be due to the presence of DMSO) are detectable shortly after the infusion process begins. This DMSO odor was thought to be released from the patient through respiration or perspiration. Patients receiving the infusions had not reported any unusual symptoms during the procedure.

METHODS

On December 7, 1998, NIOSH representatives performed a site visit at the LDH/IHC Hospital. An opening meeting was held with hospital administrative and employee representatives. Following a discussion of the work practices used in the BMT unit, the symptoms that were reported, and the types of medical devices and pharmaceuticals used during BMT procedures, a walkthrough of the BMT was performed. Medical

records for employees who had reported symptoms were obtained and reviewed, and several employees were interviewed.

During our site visit, a patient received an infusion of two bags of stem cells. NIOSH personnel observed the procedure (with the patient's permission), during which qualitative and quantitative air sampling was conducted. Thermal desorption (TD) tubes and standard coconut-shell charcoal solid sorbent tubes (100mg [milligrams]/50mg) were used to collect air samples to evaluate for the presence of DMSO and other volatile chemical compounds which might be released into the air during infusion of the stem cell solution.

Exposures to the nurse administering the stem cells were measured using two types of air sampling tubes placed in her personal breathing zone (PBZ). A TD tube was used to collect air to be analyzed for a qualitative scan of volatile organic compounds, and a charcoal tube was used to collect a sample for quantitative determination of any chemicals identified on the TD tube. Two area air samples were collected at a room return air grill, located near the head of the patient's bed. To determine the presence of chemicals offgassing from the two used infusion bags (which still contained a small amount of liquid, including cells and DMSO), the bags were placed in a clean, one-liter glass Fleaker™, and a TD tube (attached to an SKC® pocket pump outside the flask) was placed into the flask. The TD tubes were analyzed by NIOSH by means of gas chromatography and mass spectrometry (GC/MS) using a Perkin-Elmer ATD 400 thermal desorption system. Each sampling train was calibrated to flow rate of 100 milliliters per minute (mL/min).

Natural rubber latex (NRL) gloves were worn by some employees in the hospital, and because NRL is a sensitizer which can cause symptoms similar to those reported by the health care workers in the unit, sampling for NRL proteins was conducted. Three area air samples were collected for airborne NRL proteins. A sampler obtained from the Mayo Clinic was used to sample at 6.1 liters per second (L/sec). The samplers were calibrated (with filters in-line) at the hospital to confirm the sampling flow rate. Samples were collected using bilaminate (glass fiber and polytetrafluroethylene [PTFE]) membrane filters. One eight-hour sample was collected in the patient's room while infusion took place, and two sequential eight-hour samples were collected in the hallway area outside the patient rooms, and adjacent to the nursing station.

Surface dust samples were collected from the upper (plenum side) surfaces of ceiling tiles in the BMT area, from the upper surface of a ceiling tile above the nurse's station, and from the desk top at the nurse's station (to evaluate the potential for skin contact with NRL-containing dust). Ceiling tiles adjacent to return air grilles were chosen. Surface samples were collected using micro-vacuuming techniques according to ASTM method D 5755-95[1] with several modifications. The area to be sampled was demarcated into a 100 square centimeter (cm^2) area. Dust was collected using 37-millimeter sampling cassettes connected with Tygon® tubing to a personal sampling pump operating at a flow rate of 5 L/min. A 1.5-inch piece of tygon tubing was connected to the face of the cassette to act as a nozzle. The nozzle was cut to a 45° angle. The area was sampled by vacuuming up and down, then back and forth, for a period of two minutes or until no visible dust remained within the sampling area. After the sample was collected, the cassette was inverted and the sampling pump was shut off. The nozzle was capped with a plug, and the sampler was packaged to prevent separation of the nozzle from the cassette and sealed upright in a plastic bag. All samples were sent to the Mayo Clinic for analysis by an inhibition assay using IgE antibodies from latex sensitive individuals.[2]

NIOSH representatives returned to the LDH/IHC Hospital on February 18-19, 1999. A list of employees who worked on the BMT was obtained from hospital administrative representatives, and NIOSH representatives privately interviewed these employees using a medical questionnaire designed to assess allergic symptoms. Employees who were not working during those two days were

mailed a questionnaire and asked to fill it out and return it in a postage-paid envelope that was provided.

EVALUATION CRITERIA

As a guide to the evaluation of the hazards posed by workplace exposures, NIOSH field staff employ environmental evaluation criteria for the assessment of a number of chemical and physical agents. These criteria are intended to suggest levels of exposure to which most workers may be exposed up to 10 hours per day, 40 hours per week for a working lifetime without experiencing adverse health effects. It is, however, important to note that not all workers will be protected from adverse health effects even though their exposures are maintained below these levels. A small percentage may experience adverse health effects because of individual susceptibility, a pre-existing medical condition, and/or a hypersensitivity (allergy). In addition, some hazardous substances may act in combination with other workplace exposures, the general environment, or with medications or personal habits of the worker to produce health effects even if the occupational exposures are controlled at the level set by the criterion. These combined effects are often not considered in the evaluation criteria. Also, some substances are absorbed by direct contact with the skin and mucous membranes, thus potentially increasing the overall exposure. Finally, evaluation criteria may change over the years as new information on the toxic effects of an agent becomes available.

The primary sources of environmental evaluation criteria for the workplace are: NIOSH Recommended Exposure Limits (RELs),[3] the American Conference of Governmental Industrial Hygienists' (ACGIH®) Threshold Limit Values (TLVs®),[4] and the U.S. Department of Labor, Occupational Safety and Health Administration (OSHA) Permissible Exposure Limits (PELs).[5] Employers are encouraged to follow the OSHA limits, the NIOSH RELs, the ACGIH TLVs, or whichever is the most protective criterion.

A time-weighted average (TWA) exposure refers to the average airborne concentration of a substance during a normal 8- to 10-hour workday. Some substances have recommended short-term exposure limits (STEL) or ceiling values which are intended to supplement the TWA where there are recognized toxic effects from higher exposures over the short-term.

OSHA requires an employer to provide to employees a place of employment that is free from recognized hazards that are causing or are likely to cause death or serious physical harm.[6] Thus, employers should understand that not all hazardous chemicals have specific OSHA exposure limits, such as PELs and STELs. An employer is still required by OSHA to protect their employees from hazards, even in the absence of a specific OSHA PEL.

Dimethyl Sulfoxide (DMSO)

No OSHA, NIOSH, or ACGIH occupational health exposure limits exist for DMSO. DMSO was discovered in 1866 by a Russian scientist, Alexander Saytzeff.[7] The solvent is inexpensively obtained as a wood pulp by-product and was first produced on an industrial scale for use as a commercial solvent during the 1950's. In the early 1960's, research began into its potential medical properties and applications. Beneficial effects attributed to DMSO include anti-inflammatory effects,[8,9] reduction of pain by blocking C-fibers,[10] reduction of trauma-induced pathology to the brain and the spinal cord,[11,12,13] and softening of collagen in diseases such as scleroderma.[14,15] DMSO was noted to be radioprotective and cryoprotective and has been used to preserve red and white blood cells, bone marrow and bone marrow stem cells, spermatozoa, and entire organs prior to transplantation.[16] DMSO is water soluble and osmotically active (it can readily cross biological membranes). Because of this, it has been used to facilitate the transport of substances (molecular weights of 3000 or more) across membranes.[17,18] DMSO also has histamine releasing effects.[19,20] In 1965, the US Food and

Drug Administration (FDA) suspended all medical research involving DMSO because a fatality in Ireland was associated with exposure to this compound.

Currently, DMSO is approved by the FDA only for use as a cryopreservative of organs for transplant (in a 5-10% solution), and for treatment of interstitial cystitis, a bladder disease. The main use for DMSO in the United States is the treatment of acute inflammation due to trauma in dogs and horses. This is typically achieved with a 90% DMSO solution. A 99% solution of DMSO has been marketed for many years as an industrial degreasing solvent. In addition, varying concentrations of DMSO are widely used in medical research laboratories as a general solvent in chromatography and filtration techniques.

DMSO can be administered intravenously, orally, or by topical application. Exposure can also occur through inhalation. Regardless of the route of exposure, DMSO is metabolized to dimethyl sulfdioxide ($DMSO_2$), an odorless compound excreted by the kidney, and dimethyl sulfide (DMS), which is excreted by the lungs. DMS is reported to be the chemical responsible for the distinctive breath odor, which is common when DMSO is applied to the skin.[16] Kolb, et al., studied the absorption and elimination of DMSO in animals and man by administering radiolabeled DMSO intravenously and through cutaneous application.[16] After intravenous injection of 2.0 g of 50% DMSO, the elimination half-time was 4 days. Within a week, 80% was eliminated. An almost complete recovery of the injected dose was accomplished by day 18. Following cutaneous application, 10-15% was eliminated within 24 hours, and half of the dose was eliminated by 12.5 days. In summary, over 20 days, 80-90% of the compound given by either route was excreted by the kidneys as $DMSO_2$ and 3-6% was excreted in the breath as DMS.[21,22]

Infusion of autologous bone marrow cryopreserved with DMSO has been associated with mild nausea, vomiting, flushing, abdominal cramping, and headaches in the recipient.[23,24] Cardiovascular abnormalities, such as asymptomatic bradycardia, and hyper- and hypotension, are often reported with autologous bone marrow infusion. Some degree of erythrocyte hemolysis is routinely seen after infusion. Severe life-threatening reactions, however, are rare, and include acute renal failure, cardiac arrest, respiratory depression, and pulmonary edema.[23,25]

There is one report of severe hemolysis mimicking a hemolytic transfusion reaction in a man who was given DMSO as part of an experimental protocol that used DMSO to decrease intracranial pressure.[26] Yellowless, et al., reported liver toxicity in an elderly person receiving intravenous DMSO treatment for arthritis in England.[27] All of the above reactions occurred in the individuals receiving DMSO intravenously, and not in bystanders.

Exposure of human skin to high concentrations of DMSO (70-90%) results in immediate stinging and burning. This is followed by mild erythema and itching, which lasts an hour or two in most individuals. In some people, blistering may occur. This reaction lessens after a few days of continued application.[28] Since this response may occur at first contact, the mechanism is thought to be irritant rather than immunologic.[29]

DMSO can accelerate skin absorption of other materials. It can be used to facilitate the absorption of therapeutic drugs such as corticosteroids, antibiotics, anti-inflammatories and others. However, DMSO can also accelerate the absorption of carcinogens and amyl nitrate. Banthorpe and Lamont found that these undesirable materials dissolved in 30% DMSO were capable of penetrating rubber and surgical gloves.[30] To our knowledge, there is no data in the literature examining the facilitation of natural latex rubber protein absorption with DMSO.

Inhalation of DMSO in animal models produces no serious toxicity.[31] In humans, it may lead to headache, nausea, and vomiting. There are no reports in the literature of adverse effects in bystanders exposed to the metabolite DMS

exhaled by individuals who received DMSO by any route. Ingestion of DMSO can lead to drowsiness, nausea and vomiting. It has also been reported to lead to gastroenteritis and bowel hemorrhage.[32]

In summary, a number of potential benefits have been attributed to DMSO use. Because clinical trials were terminated in the U.S. in 1965, and because blinded trials are difficult to conduct due to the odor on the breath of individuals who receive DMSO, limited information is available regarding DMSO's clinical effectiveness as a therapeutic agent and on its long term safety in humans who receive it regularly via oral, intravenous, or cutaneous application. Case reports of adverse health effects in individuals who receive DMSO in varying concentration on a one-time basis were reviewed above. Of note is that DMSO is frequently used in veterinary medicine and in medical laboratories throughout the U.S. without any reported bystander side effects.

Latex

Natural latex is an intracellular milky fluid produced by the laticifer cells of the tropical rubber tree, *Hevea brasiliensis.* It is manually harvested and, through multiple processes, is converted into natural rubber latex (NRL). This, in turn, is used for the manufacture of commercial latex products, including latex gloves, balloons, and condoms.

Isolated descriptions of reactions to NRL first appeared in the literature nearly 70 years ago.[33,34] Over the last 20 years, however, reports of adverse reactions to NRL have increased, and latex allergy has been recognized as an occupational health hazard.

The reported prevalence of NRL sensitization and allergy varies widely. This variation is partly due to different levels of exposure and a variety of methods for estimating NRL sensitization or allergy. The prevalence of latex allergy in the general population is believed to be less than 1%.[35,36,37] People who have a genetic predisposition for allergy ("atopics") may have a 3-7% prevalence of latex allergy.[34,35] Studies in health care workers have shown latex allergy prevalence rates of 2-16.9%.[38,39,40] People at the highest risk for latex allergy are individuals who undergo multiple surgical procedures, such as spina bifida patients. Prevalence rates in the 30-60% range have been reported in this group.[34,41,42]

Routes of exposure to NRL include dermal, mucosal, percutaneous, and inhalation. NRL sensitization is also associated with allergies to certain foods, including banana, avocado, potato, tomato, passion fruit, kiwi fruit, papaya, and chestnut.[43,44]

Several reasons may exist for the increase in reports of latex allergy and other adverse reactions to latex. The use of latex gloves has increased significantly since the introduction of universal precautions to prevent the transmission of human immunodeficiency virus, hepatitis B virus, and other infectious agents. To meet the increased demand for latex gloves, some manufacturers may have produced more allergenic gloves because of changes in raw materials, processing, or manufacturing procedures. Also, physician and public awareness of latex allergy has increased.

Clinical manifestations of latex allergy are typically divided into three categories: irritant contact dermatitis, allergic contact dermatitis (delayed hypersensitivity), and IgE-mediated latex allergy.

The most common reaction to latex products is *irritant contact dermatitis*, a nonallergic, cutaneous response that manifests as dry, crusted lesions on the hand. Irritation is aggravated by sweating and rubbing under the glove, leading to papular and ulcerative lesions. Exposure to other workplace products and chemicals, as well as repeated hand washing and drying, may contribute to this problem.[45]

Allergic contact dermatitis is a Type IV delayed hypersensitivity reaction to chemicals added to natural latex during harvesting, processing, or manufacturing. These additives include thiurams, mercaptobenzothiazoles and carbamates.[46,47] The acute phase of the reaction occurs 1 to 3 days after exposure and is characterized by vesicular skin lesions. Patch testing may help to distinguish allergic contact dermatitis from irritant dermatitis. Typically, patch testing is positive in Type IV, delayed hypersensitivity reactions.

IgE-mediated latex allergy (immediate hypersensitivity) may present as urticaria, rhinoconjunctivitis, asthma or anaphylactic shock.[48] Multiple proteins in latex products may cause sensitization. Anaphylactic reactions have most often been caused by exposure to a surgeon's glove during abdominal or genitourinary surgery, or by other sources of mucosal exposure to latex (e.g., barium enema, dental procedures). There is increasing awareness of the potential for anaphylaxis from exposure to latex in the air.

The prevention of adverse latex reactions depends on the identification of individuals who are allergic so that they can avoid exposure to NRL-containing products. However, diagnostic procedures for latex allergy have only very recently been standardized, partly due to the fact that full characterization of the antigen that causes latex allergy is not complete. More than 20 potential allergenic proteins in NRL have been recognized, the presence and amount of which changes from one latex product to another. Several of these proteins have been characterized only recently and may vary between groups at risk. Prohevein (Hev b 6.01) and hevein (Hev b 6.02) have been shown to be major IgE-binding allergens in health care workers and other adult patients allergic to NRL. Allergy to rubber elongation factor (Hev b 1) and the 23/27 kd NRL allergen (Hev b 3) is a characteristic of children with latex allergy who have spina bifida and of other children requiring multiple operations at an early age.[49]

Skin prick testing (SPT) is used as a diagnostic test in evaluating latex allergy.[50] However, at the present time, no NRL SPT extract has been approved by the FDA. Another test that has been widely used is the measurement of *latex-specific IgE* antibodies in the patient's serum. If there is a discrepancy between a clinical history and medical tests (such as a positive clinical history and negative skin prick test results), further diagnostic procedures may be necessary to establish or refute the diagnosis of latex allergy. In patients with skin symptoms, the *use test* exposes them to latex gloves. If they show a typical allergic response, latex allergy is confirmed.[51]

RESULTS

DMSO and Other Volatile Compounds

Of the four TD tube samples collected on the day of the survey, only two indicated the presence of any significant amounts of volatile organic chemical compounds. The PBZ sample (AO4620) from the health care worker administering the stem cells showed the presence of acetone, isopropyl alcohol, and limonene. DMSO was not detected. The area sample in the patient's room (AO5370) showed minute amounts of acetone and isopropyl alcohol, but no DMSO.

The sample from the 1-liter glass Fleaker® with the two used infusion bags inside contained many compounds, the most significant of which were isopropanol, dimethyl sulfide, DMSO, cyclohexanone, dimethyl disulfide, toluene, phenol, siloxane compounds, ethanol, acetone methyl mercaptan, and C_{10}-C_{12} branched alkane compounds.

Air and Surface Dust Samples for NRL

The three air and three surface samples for NRL contained no detectable NRL proteins. The limit of detection (LOD) for the air samples was 1 nanogram per cubic meter of air (ng/m^3); the LOD for the surface samples was 200 nanograms per 100 cubic centimeters ($100/cm^3$).

Medical Records Review

Medical records were reviewed for the eight BMT employees who, prior to the NIOSH HHE request, had reported work-related symptoms to the hospital's occupational health nurse. One employee reported two separate episodes. Dates of these symptoms were January and February, 1996; May, 1997; August, 1997; October 3 and 21, 1998; and November 1, 10 and 11, 1998. Symptoms (number of employees affected) included itchy skin (4); rash on arms (4); rash on head, arms, chest, and abdomen (1); rash on neck (1); throat tightness (1); chest tightness (2); difficulty breathing (1); shortness of breath (3); facial flushing (2); red, itchy eyes (1); numbness of tongue or mouth (2); nausea (1); dizziness (1); and weakness (1).

At the time of their symptoms, three of the employees were in the process of administering stem cells to patients. Two had gone into a patient's room where stem cells had been administered earlier in the day but were not currently being administered, and two were working in the BMT but had not gone into a patient's room on the day of their symptoms. Four of these symptomatic employees were seen by a physician at a local allergy and asthma clinic. One received "latex allergy testing" of an undefined nature, which was reported in the medical record to be negative. The other three employees received skin testing with dilutions of DMSO, heparin, Hank's media and a latex solution. In two of these employees, all of these were tests were "negative." In the other employee, "significantly positive" reactions were reported for latex and Hank's media, and a "less positive" reaction was reported for DMSO.

Medical Questionnaires

A total of 84 employees worked on the BMT wing during our evaluation. Forty-two employees filled out the medical questionnaire during our February 18-19 visit. Questionnaires were sent to the remaining 42 employees who were asked to fill out and return them in an enclosed, postage-paid envelope. Twenty-two of these questionnaires were returned. Questionnaire information was analyzed for the 64 (76%) BMT employees who filled out a questionnaire.

The majority (92%) of the employees on the BMT wing are female. Fifty-eight (91%) of the questionnaires returned were from women employees. We do not know the ethnicity of the employees at the LDH/IHC Hospital, but of those who filled out questionnaires, 55 (86%) were white, non-Hispanic; one (2%) was black; four (6%) were American Indian or Alaskan Native, and three (5%) were Asian. Ethnicity information was missing for one individual.

Job titles included 38 (59%) clinical RNs, two (3%) Administrative RNs, three (5%) LPNs, 13 (20%) nursing assistants, five (8%) ward clerks, one (2%) housekeeper and two (3%) "other," unidentified job titles. The majority of questionnaire respondents (26, 41%) had worked at this hospital between 1 and 5 years. Eighteen (28%) had worked there less than one year. Ten (16%) had worked there 6-10 years, three (5%) had worked there 11-20 years and six (9%) had worked there more than 20 years. Thirty-two (50%) worked mainly in the BMT. Of these, 24 reported ever being in a patient's room during the administration of stem cells, and of these, nine reported this occurring less than once per month, eight reported this occurring once per month, and seven reported this event more than once per month.

With respect to symptoms that were reported to have begun only after starting work at this hospital (number of people reporting is in parentheses): 14 people (22%) reported some sort

of chest symptom, including wheezing (2), cough (8), shortness of breath (5), and chest tightness (6); 20 people (31%) reported upper respiratory symptoms, including runny nose (13), post-nasal drip (10), frequent throat clearing (9), and stuffy nose (8); 17 (27%) people reported allergic symptoms, including sneezing (9) and itchy eyes (12); 32 (50%) reported skin symptoms, including rash on hands (30) and hives (8); and 7 reported miscellaneous symptoms, including tingling in fingertips (2), dizziness (5), and confusion (1).

When asked about glove use, 59 (92%) employees reported using gloves during their work at this hospital. Of those, 25 wore non-latex gloves, and 34 wore powdered latex or non-powdered latex gloves. Of those who wore either type of latex gloves, 13 reported having symptoms "such as runny nose, sneezing or rash" associated with wearing latex gloves. Four of these reported having had a test for latex allergy and one of those reported testing positive.

Thirty-eight (59%) reported having "hay fever" or seasonal allergies. Of those, 27 reported a family history of hay fever. Eleven others denied having "hay fever" themselves, but reported hay fever in at least one family member. Fifteen (23%) reported having asthma, and 14 of those reported that their asthma had been diagnosed by a physician.

DISCUSSION

Neither air samples collected in the PBZ of the nurse administering the stem cells nor samples collected in the patient's room while the infusion occurred showed the presence of DMSO. The TD tube sample placed in the glass Fleaker® identified the presence of a number of chemicals, but only two of these chemicals (isopropanol and limonene) were detected in the PBZ sample. The small amounts of airborne acetone, isopropyl alcohol, and limonene that were detected could not explain the reported symptoms. NRL was not detected in any air or surface samples.

The presence of isopropanol is explained by the fact that alcohol is ubiquitous in the health care environment where it is used as a topical disinfectant. The source of the limonene in the PBZ sample is less clear, but its presence is not surprising. Limonene is a terpene citrus fruit essential oil which is often used in "green" (environmentally friendly) cleaners and degreasers. Terpenes are also used in the perfume and flavor industry. Any of these sources, or even the presence of citrus fruit, could explain the presence of limonene in the air sample. Limonene was not detected in the area air sample collected in the patient's room nor was it detected in the sample collected in the glass Fleaker.™ This indicates that the infusion of the stem cells was not the source of the limonene.

A number of volatile chemicals detected on the sample in the glass jar suggest that the DMSO may have reacted with the plastic bag.

Review of the medical records for employees who had reported work-related symptoms prior to the NIOSH request showed rashes and respiratory symptoms in these employees. Since there was no direct contact with DMSO among these employees, it is unlikely that their skin symptoms could be related to the administration of that compound. Review of the literature on DMSO (see Evaluation Criteria section) does not show any similar reactions among bystanders present during the administration or application of DMSO, even in high concentrations.

The medical questionnaires revealed respiratory symptoms and skin rashes or hives in a number of employees. They also showed that 49 (77%) of the employees who filled out a questionnaire reported either having hay fever themselves or having a family history of hay fever.

CONCLUSIONS

We cannot conclude that exposure to DMSO or other chemicals was responsible for the symptoms reported by health care workers. Nor is it likely

that dimethyl sulfate (a metabolite of DMSO) is the cause, since similar symptoms have not been reported in patients (who presumably have greater exposure) or in exposed workers at other facilities. Although latex was not detected in the samples we analyzed, the use of latex gloves (especially powdered gloves) by workers with hand dermatitis (which compromises the barrier function of the skin) could contribute to allergic symptoms in some employees.

RECOMMENDATIONS

The following recommendations are based on the results of this investigation and the impressions of the NIOSH investigators.

1. Employees who experience adverse reactions while administering stem cells to patients (or while performing any other work-related task) should not perform that nursing task. If a specific causative exposure is identified, efforts should be directed at reducing that exposure.

2. Used stem cell IV bags should be placed in an airtight trash bag and disposed of as soon as the procedure is completed to reduce objectionable odors from the trash receptacle. While not a health hazard, nuisance odors should be controlled where possible.

3. Employees who experience symptoms, such as rashes, hives, wheezing, or shortness of breath, while at work should report to the appropriate personnel and have these symptoms evaluated as soon as possible after their occurrence. Latex sensitivity should be considered as a cause of such symptoms and employees should be tested for latex allergy by a physician trained in the evaluation of latex allergy.

4. Use of latex gloves should be limited to low-protein, powderless gloves and non-latex gloves should be used whenever possible.

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