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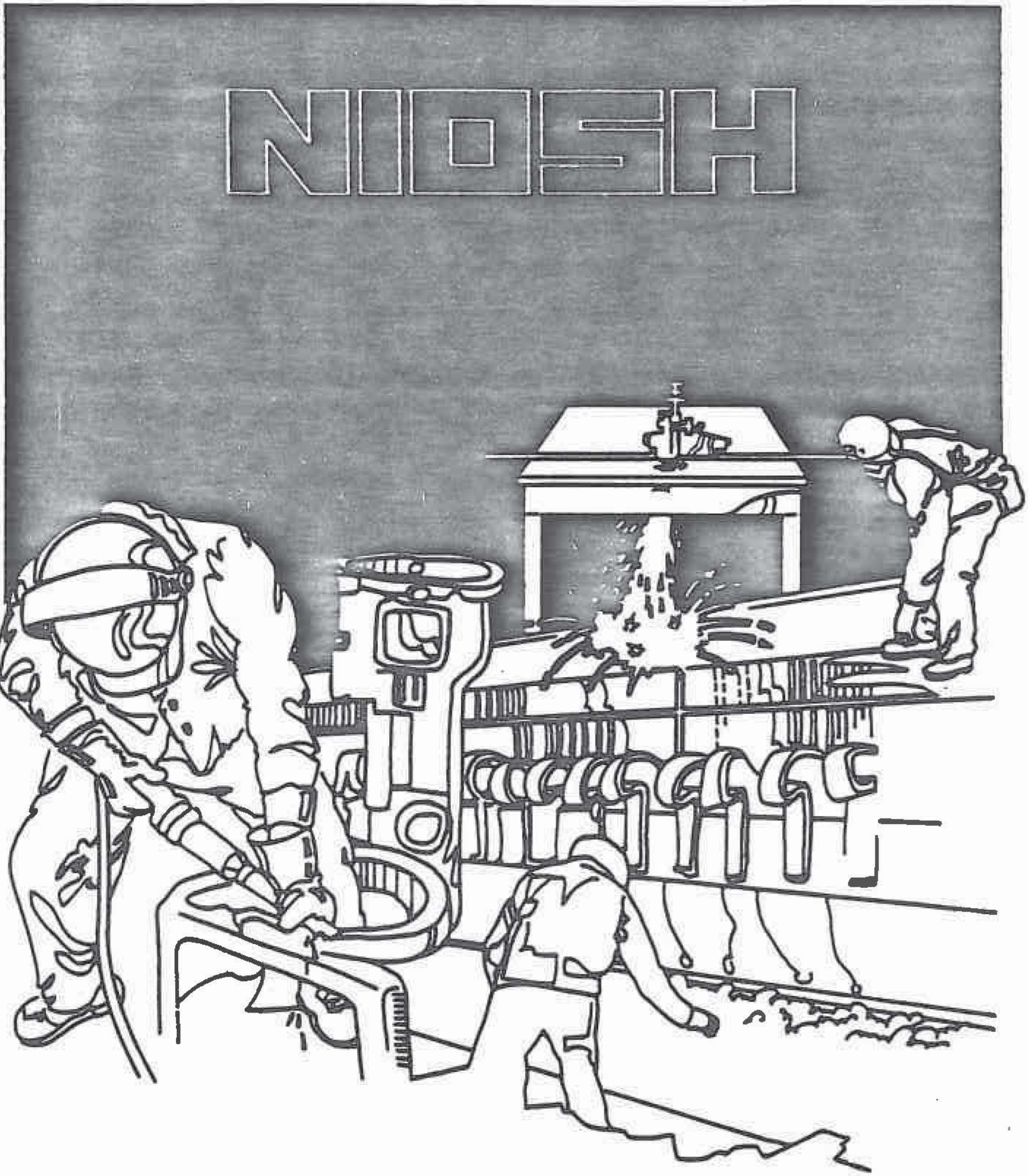

Health Hazard Evaluation Report

HETA 83-222-1631
METZ METALLURGICAL
SOUTH PLAINFIELD, NEW JERSEY

PREFACE

The Hazard Evaluations and Technical Assistance Branch of 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.

The Hazard Evaluations and Technical Assistance Branch also provides, upon request, medical, nursing, and industrial hygiene technical and consultative assistance (TA) to Federal, state, and local agencies; labor; industry and other groups or individuals to control occupational health hazards and to prevent related trauma and disease.

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METZ METALLURGICAL
South Plainfield, NJ

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SUMMARY

In April, 1983 workers at Metz Metallurgical in South Plainfield, NJ requested that NIOSH perform an investigation of health hazards at their plant. The request dealt with numerous exposures in this precious metals refinery, but focused on the health effects of the primary product, silver powders. Two hundred and twenty employees work in the refinery in extraction, foundry, chemical purification and precipitation, and drying, screening and packaging of metal powders. Silver powder exposures were high in several areas. Workers with the highest potential silver exposure were studied for the potential health effects.

Field visits and medical examinations were conducted in March and August, 1984. Air sampling was conducted for silver powders, and participants received a work history, symptom questionnaire, and an ophthalmologic exam; urine was collected for the measurement of urinary creatinine and N-acetyl-B-D-glucosaminidase (NAG). Urine samples were collected and analyzed for silver and cadmium content and blood samples were collected and analyzed for silver content.

Airborne silver levels were found above the OSHA PEL of 0.01 mg/m3 in ten of 13 samples (range 0.0037-1.55 mg/m3, mean 0.303 mg/m3). Ninety-six percent of the 27 workers had elevated urine silver levels (range 0.5-52.0 ug/l, mean 11.3 ug/l). Ninety-two percent had elevated blood silvers (range 0.05-6.2 ug/100ml, mean 1.0 ug/100ml). Nineteen percent had elevated urine cadmium levels (range 1.9-76.0 ug/l, mean 11.8 ug/l). Respiratory irritation symptoms were reported in a majority of workers and nose bleeds were reported in 8 of 27 (30%). Deposition of silver in the cornea of the eye was detected in 5 of 8 (63%) of the long-term workers. Although not statistically significant, corneal deposition was associated with complaints of decreased night vision. NAG was significantly elevated in 4 individuals and was correlated with blood silver levels. In addition, the group's average NAG level was significantly higher than that found in a control population similarly tested. Estimated creatinine clearance was significantly lower in the silver exposed group than in an unexposed control group. Kidney function appears to have been adversely affected by exposures at work. Because of the exposure to cadmium, silver's role in causing the decrement in kidney function could not be definitely determined. Recommendations are given to reduce silver and cadmium exposures and to monitor the health status of workers at the plant.

Based on environmental, biological and medical results, it is concluded that a health hazard exists at Metz Metallurgical. Exposure to silver and cadmium dust and fumes are causing respiratory, eye and kidney problems among exposed workers. Exposures should be reduced and a follow-up medical suveillance program should be initiated.

Key Words: SIC Code 3341 (Secondary Precious Metals Smelting and Refining) Silver, Cadmium, Ocular Toxicity, Nepnrotoxicity, NAG

INTRODUCTION

In April, 1983 NIOSH received a request from employees of Metz Metallurgical Corporation, South Plainfield, New Jersey to conduct a Health Hazard Evaluation of their plant. The request mentioned exposures to formaldehyde, hydroquinone, acids, caustics, cyanide, metal fumes and silver compounds. In addition, the request cited employee problems with nosebleeds, headaches, tiredness and vision problems. In September, 1983, the investigation was assigned to the New Jersey Department of Health (NJDOH) under a cooperative agreement with NIOSH to conduct Health Hazard Evaluations.

In March 1984, a walkthrough of the plant was conducted and a short questionnaire administered to approximately 30 employees. On the basis of this inspection, exposure to silver was identified as the most significant exposure and therefore, a study protocol focusing on the effects of silver was developed. In August, 1984 in-depth field work including questionnaires, medical examinations, air sampling and laboratory tests was conducted.

BACKGROUND

Metz Metallurgical is a silver and other precious metal refinery. It uses pure metals (silver bars, cadmium, gold, platinum and paladium) as well as silver-containing wastes (spent chemical catalysts) for its raw materials. Numerous chemicals including nitric acid, hydrochloric acid, formaldehyde, caustics, hydroquinone and solvents are used in the refining process. Products from the plant include several grades of powdered metals and wire.

Approximately 220 workers were employed at the plant in 1984 in all phases of the operation. This included about 30 maintenance workers and 150 in production. There is no union representing employees at the plant.

Several processes are of interest to the present investigation. Silver powders are produced both for use in other plant processes, and for sale as pure silver. The powder is manufactured by adding silver nitrate, water and formaldehyde into a reactor vessel and heated. Sodium carbonate is then added and the product is decanted into a centrifuge on the lower level of the plant. Workers then manually scoop the silver cake from the centrifuge. During routine operations, workers stated that they experienced burning and reddened eyes. The powder is then dried, pulverized, screened and packaged in several grades in 55 gallon drums.

Metal bars, scrap and dust are melted in furnaces and poured into ingots in the melting area. Although some local exhaust ventilation is present, workers are potentially exposed to metal fume during melting and pouring procedures.

In the crystal area, silver nitrate is produced by dissolving silver bars in nitric acid and precipitating silver nitrate crystal. The crystal is dried on trays in ovens and then packaged.

Silver oxide is produced by adding sodium hydroxide to silver nitrate, heating and precipitating out the silver oxide powder. The precipitant is filtered and washed with water. The resultant mud cakes are then dried. The dried cake is hand scooped into a trough that leads to the packaging area.

Silver chloride and silver-cadmium oxide products are similarly produced. Materials are chemically combined, precipitated and then dried, screened and packaged. The major potential for metal dust exposure is during screening and packaging processes.

Silver flake is made by tumbling silver powder in steel drums with solvents and steel balls to flatten the particles. After tumbling, the silver sludge is dried, screened and packaged. Operators have potential exposures to silver powder, hydroquinone and solvents including methanol and petroleum hydrocarbons.

In November, 1982 a walkthrough inspection was conducted by an industrial hygienist from the Somerset County Health Officers Association. His report cited potential exposures to cadmium and silver dusts, caustics, and nitrogen oxides and the need for review of health and safety policies, equipment and employee education. The report also recommended further medical evaluation of plant employees.

A Federal OSHA health inspection was conducted at the plant from 12/81 to 2/82 on the basis of a referral from an OSHA safety inpector. Citations were issued at that time for over exposure to silver in eight areas of the plant and for deficiencies in the safety equipment and procedures. The Federal OSHA standard for exposure to silver dust is a time weighted average (TWA) of 0.01 mg/m3 for eight hours. Airborne exposures to silver as measured by OSHA were:

Area	Silver TWA (mg/m3)
Melting	0.11, 0.15, 0.05
Nitrate Crystal	0.04, 0.05
Powder	0.38, 0.30
Flake	0.10, 0.63
Oxide	0.13, 0.35, 0.27, 0.12

On March 21, 1984 a preliminary evaluation was conducted by NJDOH utilizing a short questionnaire and brief examination of skin and eyes to detect changes associated with chronic silver exposure. All employees who worked at least two years in silver flake, silver nitrate, silver powder or the refinery area, maintenance workers with greater than 5 years of work experience at the plant, and workers from any area with more than 10 years work experience were asked to participate. All but two of the eligible workers agreed to participate. One of these individuals had gone home early because of illness and one individual was being patch tested that day for a possible contact dermatitis. In all, thirty-four employees agreed to participate.

Few chronic health problems were reported. The most frequently reported condition was high blood pressure, 6 of 34 workers. One individual had diabetes and two a history of ulcers. The most frequently reported symptom was nose bleeds, 5 of 34 workers. These symptoms were associated with silver oxide production. Three workers in the silver flake area had complaints of eye irritation, lightheadedness and fatigue. One individual complained of stomach pain relieved by antacids. Three individuals were noted by the examiner to have darkening of the whites of their eyes and one worker had multiple black pigmented spots on the side of his face from an oil explosion involving silver nitrate.

STUDY DESIGN AND METHODS

On the basis of our preliminary walk-through and evaluation of Metz employees, it was decided that additional testing would be conducted to identify and further define any health effects due to exposures at the plant. Although numerous exposures were present, silver was by far the highest exposure. Cadmium was also identified as a potentially hazardous exposure for several employees. Exposures to numerous irritants were also present at the plant but were more intermittent in nature, present primarily acute effects, and were therefore felt to be more difficult to address in the context of this HHE.

The study design was developed to identify exposure to silver and cadmium primarily using biological indicators of exposure (blood and urine metal levels) and health outcomes including reported symptomatology, physical examination findings and indicators of renal toxicity (creatinine clearance and enzyme excretion).

A. Environmental

On 8/16/84 personal air samples were collected by NJDOH to obtain further information about levels of exposure to silver present in the plant. Samples were collected and analyzed by NIOSH Method P&CAM 173 using a personal air sampling pump calibrated to about 1.5 liters per minute. Samples were analyzed by atomic absorption spectrometry.

B. Medical

On August 15, 1984 NJDOH returned to the plant to conduct a more extensive examination. Testing at that time consisted of a detailed questionnaire, slit lamp examination by an ophthalmologist, a weight measurement, urinary levels of silver and cadmium, a blood silver level, a blood chemistry including BUN and creatinine and a urinary n-acetyl-B-D-glucosaminidase (NAG) level. Estimated creatinine clearance was calculated from the serum creatinine, reported age and measured weight(1). Creatinine clearance was corrected to a standard body surface area of 1.73 m^3.

The 34 individuals included in the preliminary exam were invited to participate in the more extensive study. Twenty-seven workers agreed to participate. The seven individuals who did not participate in the second examination included 2 long term workers from non-silver areas, 3 workers from silver nitrate, 1 silver flake worker and 1 maintenance worker.

The questionnaire was administered by trained interviewers. The eye examinations were conducted with a portable slit lamp. The ophthalmologist was unaware of the work histories of the individuals he examined. He coded conjunctival and corneal findings on a 1-4 scale, based on a previously developed scoring system(2). Commercial laboratories performed the blood chemistry (METPATH) and urine silver(3) and cadmium(4) analyses (National Medical Laboratories). Blood silver analysis was performed by the NJDOH Laboratories(5) and NAG analysis was conducted by Cornell Medical Center(6).

Analyses for cadmium, silver and NAG were done on spot urine samples. Urinary silver and cadmium levels were reported as micrograms metal per liter urine. However, for all analyses relating urine metal levels with health effects (correlations and regressions), the urinary metal levels were corrected for urine concentration by expressing them as micrograms of metal per milligram creatinine.

Both systolic blood pressure greater than 160 mm Hg and urinary protein on dipstick of 2+ or greater have been associated with elevated NAG levels(6). Therefore, all statistical tests for NAG were done excluding individuals with either of these parameters.

An additional analysis of the effect of silver on NAG and creatinine clearance was conducted by comparing urinary NAG in the group as a whole with results of NAG in an unexposed control population. This group consisted of the first twenty-eight of fifty-one male workers from a tungsten carbide machine shop who were being studied for the pulmonary effects of tungsten carbide and cobalt exposure.

EVALUATION CRITERIA

A. General

As a guide to the evaluation of the hazards posed by workplace exposures, NIOSH field staff employ environmental evaluation criteria for 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 if their exposures are maintained below these levels.

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 evaluation 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 , and thus potentially increase the overall exposure. Finally, evaluation criteria may change over the years as new information on the toxic effects of an agent become available.

The primary sources of environmental evaluation criteria for the workplace are: 1) NIOSH Critera Documents and recommendations, 2) the American Conference of Governmental Industrial Hygienists (ACGIH), Threshold Limit Values (TLV's), and 3) the US Department of labor (OSHA) occupational health standards. Often, the NIOSH recommendations and ACGIH TLV's are lower than the corresponding OSHA standards. Both NIOSH recommendations and ACGIH TLV's usually are based on more recent information than are the OSHA standards. The OSHA standards also may be required to take into account the feasibility of controlling exposures in various industries where the agents are used; the NIOSH-recommended standards, by contrast, are based primarily on concerns relating to the prevention of occupation disease. In evaluation the exposure levels and the recommendations for reducing these levels found in this report, it should be noted that industry is legally required to meet the levels specified by an OSHA standard.

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 or ceiling values which are intended to supplement the TWA where there are recognized toxic effects from high short-term exposure.

In addition to using air levels of exposure, in this study we also consider the levels of silver and cadmium found in body tissues as an indicator of exposure. Since air levels cannot take into account the use of respirators, and silver and cadmium are retained in the body for some time after exposure, concentrations of metals in biologic tissue can be used as a relative index of exposure. Levels of urine cadmium thought to be safe have been identified by previous investigators and are adopted for use here. However, safe levels of silver in the body have not been identified, and we therefore use levels found in persons without any known exposure as an upper limit of normal body levels.

B. Toxic Effects

1. Silver: There are no known acute effects of exposure to silver metal. Certain silver compounds like silver oxide and silver nitrate are irritating and exposure to them has been associated with nose bleeds and abdominal pain(2).

With chronic exposure, silver binds to proteins in cells. Depending on the duration and amount of exposure, individuals may develop darkening of the whites of their eyes (conjunctiva) and darkening of the skin especially in sun-exposed areas. The darkening can be described as a slate-gray color. These skin and eye changes are not known to be related to disease, or altered function in these organs. Other than the cosmetic change described above, there are no other well documented effects from chronic exposure to silver(7).

Silver is deposited in the cornea of the eye. In a previous study of silver exposure, extensive eye examinations to follow up complaints of decreased night vision in workers with corneal opacities from silver did not uncover a cause for this complaint(8). Whether silver effects the kidney like other heavy metals such as mercury or cadmium has not been specifically investigated. One previous study in silver exposed workers found limited evidence of an effect of silver on creatinine clearance(2).

The current OSHA standard for silver is 0.01 mg/m3. ACGIH recommends levels below 0.1 for the metal and 0.01 for soluble silver compounds. Urine silver levels in an unexposed group are reported to average 1.61 ug/liter with a standard error of the mean of 0.15 (9). We have adopted an upper limit of normal for unexposed groups as the mean plus two standard errors, or 1.91 ug/l. Unexposed individuals have blood silver less than 0.27ug/100ml whole blood (5).

2. Cadmium: Acute exposure to cadmium fumes has been associated with chest pain, difficulty in breathing, dizziness and burning on urination. Exposure to cadmium oxide has caused flu-like symptoms which in some cases have progressed to fluid in the lungs (pulmonary edema) and death (10).

Chronic effects from repeated exposure to cadmium have included loss of weight, kidney disease, liver disease, bone disease with an increase in broken bones, chronic lung disease (emphysema) and anemia. Increased prostate cancer has also been reported among cadmium smelter workers (10).

The current OSHA standard for cadmium dust is 200 ug/m3 for an 8-hour TWA, and 600 ug/m3 as a 15 minute ceiling. On the basis of chronic kidney disease risk, NIOSH recommended an 8 hour TWA of 40 ug/m3 and 200 ug/m3 as a 15 minute ceiling. However, on the basis of recent evidence on the carcinogenicity of cadmium, NIOSH has recommended reducing exposure to the fullest extent feasible. The NIOSH recommendation for cadmium fume is the same as cadmium dust. Urine cadmium concentrations should be kept below 10 ug/l (11).

3. Medical: Elevation of urinary NAG is a sensitive indicator of kidney damage (10). In particular, elevated levels of NAG in urine suggest damage to the renal proximal tubule. Elevation of the enzyme level in hypertensive patients has been reported to be reversible in individuals whose hypertension was successfully controlled (11). A previous investigation of a worker population with no kidney toxin exposure showed an upper limit of normal as 79 units (nmoles substrate hydrolyzed per hour per mg creatinine). Upper limit of normal was defined as the mean plus three standard deviations(4). This upper limit was adopted for the present study.

RESULTS

A. Environmental

A limited number of air samples were obtained on 8/16/84 to confirm that the over-exposure identified by OSHA was still present. A total of thirteen personal air samples for silver exposure were conducted. Personal samples were obtained on individuals working in silver powder and oxide production and packing. Operators wear powered air-purifying respirators during most dusty jobs, thus airborne levels are only potential exposures. The average of the samples was 0.303 mg/m3, with a very broad range of 0.0037 mg/m3 to 1.550 mg/m3. Ten out of 13 samples taken were above the OSHA standard of 0.01 mg/m3. Previous monitoring by OSHA indicated silver exposures from 0.04 to 0.63 mg/m3 as presented in the Background Section above.

B. Medical

1. General

Twenty-seven male workers participated in the examination. Their average age was 41 years and they had worked at the plant an average of 9.1 years. Table I gives demographic characteristics of the study group. For all analyses of the urinary enzyme NAG, the four employees with systolic blood pressure greater than 160 or urinary protein excretion 2+ or greater on dipstick were excluded, leaving 23 individuals in the study group.

Based on inspection of the plant and job titles, individuals were categorized as working in one of six exposure groupings. The six areas were: silver crystal, silver flake, silver powder, melting, refinery and all over. The "all over" category included maintenance and supervisory job titles involving work in many areas of the plant. Table II presents the number of workers participating from each of these exposure groups.

2. Biological Monitoring

Results of biological monitoring for metals exposure (urine silver, blood silver, urine cadmium) are given in Table III. All but one worker (96%) had urine silver levels higher than expected in an unexposed population. All but two workers (92%) had elevated blood silvers and nineteen percent elevated urine cadmium levels.

Blood and urinary silver levels were similar between individuals from different work areas. The elevated cadmium levels were primarily in workers from the melting and powder departments where cadmium dust or fume exposure would be most likely.

Correlation coefficients between metals levels and age and years worked are given in Table IV. Urinary cadmium was significantly ($p<0.05$) related to years worked.

To check if the metal levels varied with cigarette smoking, mean urine silver, urine cadmium and blood silver concentrations were compared between current, never and ex smoking groups. No statistically significant differences were noted for blood or urine silver levels. Urine cadmium was higher in the never smoked group than in current or ex smokers indicating that the urine cadmium levels were not primarily caused by cigarette smoking. The mean cadmium levels by smoking group were, Never - 0.017, Current - 0.01, Ex - 0.004 ug/mg creatinine).

3. Respiratory System Complaints

Overall, 15 of 27 workers (56%) complained of mucosal irritation such as itchy, red or watery eyes, sneezing, runny or stuffy nose or sore throat. Thirty-three percent complained of lower respiratory symptoms such as cough, wheezing or tightness in the chest. Complaints of upper or lower respiratory symptoms were most prevalent in the crystal, powder, and melting departments. No significant association was found between smoking status and respiratory complaints.

Eight of 27 (30%) complained of nose bleeds. This included four of the five individuals in the crystal area. Respiratory system complaints had no statistical relationship with biologic monitoring results.

4. Vision

Six of 27 (22%) reported difficulty seeing at night. Results of the slit lamp examination showed 17 of 27 (37%) had conjunctival depositions with 10 of them rated greater than 1+. Six of 27 (22%) had corneal depostions, all of them scored 4+.

Individuals with corneal opacities were 3.5 times more likely to report problems with night vision than those with negative corneal slit lamp exam results. This association did not reach statistical significance.

Table V shows the distribution of slit lamp findings by years worked at the plant. Conjunctival discoloration increased with the length of time an individual had worked in the plant. All but one of the workers with corneal opacities had worked for more than 10 years. Over half of the workers with greater than 10 years at the plant had corneal opacities. Urinary silver, blood silver and urinary cadmium were not associated with presence of slit lamp findings, or with reported night vision symptoms.

5. Kidney Function

Mean results of urinary NAG and estimated creatinine clearance are given in Table VI. Kidney function parameters were compared between the study population and a control group of workers who were not exposed to silver or known nephrotoxins. Population characteristics, creatinine clearance and urinary NAG results of the two groups are given in Table VII. Five NAG results from the comparison group were excluded because of high blood pressure, leaving a comparison group of 23. There was no significant difference in age between the study and control group.

The silver exposed group's mean creatinine clearance was statistically lower than in the control group. Urinary NAG was significantly higher in the study group than in the controls ($p<0.01$), and the only abnormal NAGs (>79) were in the study group.

Further testing of the study group alone was conducted with the use of correlation and regression models to try to identify the most significant variable in the depression of creatinine clearance and elevation of urinary NAG. Correlation coefficients between metal levels and renal function parameters are given in Table VIII.

Estimated creatinine clearance was highly correlated with years worked at the plant, and age. To test the apparent relationship between urine cadmium with creatinine clearance, a multiple regression analysis was conducted with age and urine cadmium as the independant variables. Results of the regression are presented in Table IX. In this regression equation, age was significantly associated with creatinine clearance although the biological indicators of exposure, blood silver and urine cadmium, were not significant predictors (p>0.05).

The NAG values obtained in this study were not normally distributed and were therefore transformed for further analysis by taking their natural logarithms. A histogram of ln NAG (natural logarithm of NAG) approximated normal distribution appropriate for regression analysis. Correlation coefficients between biological indicators of exposure and urinary NAG are presented in Table VIII.

NAG was highly correlated with blood silver and age, and there was a borderline statistically significant correlation with urine silver. When the log of NAG was taken, these correlations were reduced. Nevertheless, ln NAG was still statistically associated with age (p<0.01), and statistically associated with blood silver levels (p=0.048). A similar correlation in the control group indicated no association between age and urinary NAG (r=-.0252, p>0.10).

Results of a multiple regression on Log NAG are presented in Table X. In this analysis, age was a highly significant variable (p<0.001). Blood silver contributed significantly to the variance in NAG (p<0.001), however, when controlling for age, blood silver lost statistical significance (p=0.137). Neither urine cadmium, nor years worked were significant variables in these equations.

DISCUSSION

This Health Hazard Evaluation was designed to identify health effects occurring at Metz Metallurgical caused by exposure to silver, silver compounds, and cadmium. Although the HHE request asked broadly about all health effects, the study was targeted toward the effects of the dominant exposure, silver. In addition to eye and respiratory complaints, special emphasis was placed on the evaluation of possible kidney damage from silver and cadmium exposure.

Twenty-seven of the workers considered to have the greatest potential for silver and cadmium exposure participated in the study. This small group limits the statistical power of the findings and precludes definite conclusion of rates of illness in the whole population. However, the findings do indicate acute irritation problems, and eye and kidney effects associated with plant exposures.

Limited information on actual environmental levels of silver exposure or other air contaminants was obtained. However, the samples collected during the study as well as previous air sampling by OSHA consistently showed high air silver levels, often above the OSHA standard of 0.01 mg/m3. Biological measures of silver exposure (blood and urine silver) were elevated in the majority of workers (96% urine silver and 92% blood silver). No correlation was found between elevated blood and urine levels and work area. This is not surprising since many workers used powered air purifying respirators in heavy exposure jobs. Urine cadmium was elevated in eleven workers above the recommended limit. This indicates that exposure levels for cadmium were also too high.

As has been reported in other studies of the effects of silver exposure, workers had symptoms of irritation of the respiratory system including eye, nose, throat irritation (56%) and lung symptoms such as cough, wheezing and chest tightness (33%)(2). Thirty percent of the study group complained of nose bleeds. There were very few complaints of abdominal discomfort. Silver compounds such as silver oxide and nitrate are irritating materials and probably account for these symptoms.

Difficulty seeing at night was reported by six workers in this group. Those individuals with corneal opacities were more likely to report night vision problems than those with no detectible opacities. This finding has been previously reported in silver workers(8). In this previous study an attempt was made to explain the association using electrophysiological measurements. Although unable to identify a physiological basis for the association, these investigators were unable to exclude reduced light penetration and scatter as a cause of the vision symptoms.

An attempt was made in this investigation to determine if there was an association between biological measures of silver exposure and kidney dysfunction. Since cadmium is a known kidney toxin and it is used at the plant, its effect was also investigated.

Kidney function was evaluated by the use of both a sensitive measure of tubular dysfunction, urinary NAG, and estimated creatinine clearance. Creatinine clearance was lower in the study group than the non-exposed control group. This finding is consistent with current knowledge of the effects of cadmium exposure (14). Estimated creatinine clearance was not associated however, with either blood or urine silver levels.

Urinary NAG was not statistically related to changes in urinary cadmium levels. Urinary NAG levels were significantly higher in the silver group than in an unexposed control group. NAG was positively correlated with blood silver, however, when controlling for age, blood silver was not a statistically significant predictor. In the control group, however, there was no association between age and urinary NAG. Although these findings suggest that silver is responsible for the elevated NAG levels, some question remains since the study group was also exposed to numerous kidney toxins including cadmium and solvents.

NAG is a measure of damage to the proximal tubule in the kidney. Creatinine clearance, on the other hand, is a measure of glomerular function. Excess exposure to cadmium has been associated with both tubular and glomerular dysfunction (14). However, in these studies, tubular dysfunction has been identified with the use of B-2-microglobulin instead of NAG. The relationship between NAG and B-2-microglobulin is not clear, since among mercury exposed workers elevated levels of NAG have been found in individuals with low or normal levels of B-2-microglobulin (15).

Elevation of urinary NAG above normal limits is thought to be a possible indicator of progressive renal damage. Elevation in NAG levels may decline to normal levels as individuals are treated for hypertension (13). Our finding of four silver-exposed individuals with NAG levels above the expected values and an association of NAG level with blood silver is suggestive of a toxic effect of silver on the kidney. However, on the basis of the present information it is not possible to determine if the observed NAG elevations are due to silver deposition, or other renal toxins such as cadmium. Whether or not these conditions will progress to permanent kidney damage cannot be answered in the present study. Measures to reduce exposure to irritants, silver and cadmium are indicated. Follow-up of the population for kidney disease is also recommended.

SUMMARY

Exposure to silver and silver compounds above the PEL and exposure to cadmium is adversely affecting the health of workers at Metz. Two indicators of kidney function, creatinine clearance and urinary NAG, were adversely affected in the study population compared to an unexposed control group. Other health effects noted included changes in pigmentation of skin and eyes, reported difficulty seeing at night, nose bleeds and respiratory tract irritation. Exposures to silver, silver compounds and cadmium should be reduced. A follow-up medical monitoring program is needed to determine both the reversibility of the conditions found and to better determine their exact cause.

RECOMMENDATIONS

A. Environmental

1. Exposure to silver and silver compounds should be reduced to comply with the OSHA standard of 0.01 mg/m3 silver.

2. Exposures to cadmium should also be reduced to the lowest feasible level. Biologic monitoring for cadmium should be used to confirm that exposures have been sufficiently controlled.

3. Detailed studies of current ventilation systems should be pursued to identify primary sources of exposure to silver and cadmium compounds and a ventilation engineer should be hired to design improved exhaust systems.

4. Air sampling and biological monitoring results should be used to evaluate the effectiveness of the control systems. Problems which may result in elevated levels include both inadequate ventilation equipment or maintenance and inadequate respiratory protection. Where the use of powered air purifying respirators is found to be inadequate protection, the respirators should be carefully reviewed for design, maintenance and use.

B. Medical

1. A medical follow-up examination should be set up for the participants in this evaluation under the auspices of the New Jersey Department of Health. The purpose of the examination will be to clarify the cause of the kidney abnormalities found and to assess the reversibility of the findings. In addition, the follow-up will be designed to assist the company in assuring that controls put in place are adequate and developing the appropriate medical monitoring program for company follow-up. The following tests should be included in the follow-up examination:

Blood for silver,
Urine for silver and cadmium,
Urine for B_2 microglobulin and NAG,
Blood for BUN
Urine and Blood for Creatinine Clearance Calculation

REFERENCES

1. Cockroft DW, Gault MH. Prediction of Creatinine Clearance from Serum Creatinine. Nephron 1976; 16:31-41

2. Rosenman KD, Moss A, Kon S. Argyria: Clinical Implication of Exposure to Silver Nitrate and Silver Oxide. J. Occup. Med. 1979;21:430-435

3. Modification of method reported in Sachdev, West. Anal. Chim. Acta. 1969; 44:301

4. Modification of methods reported in AA Newsletter. 1966; 5:89, AA Newsletter. 1970; 9:119, Anal Chem. 1969; 41.1:24 and Anal Chem. 1962: 34.6:614

5. Howlett C, Taylor A. Measurement of Ag in Blood By AAS Using the Micro-cup Technique. Analyst. 1978:103:916-

6. Meyer, BR, Fischbein A, Rosenman KD, et al. Increased Urinary Enzyme Excretion in Workers Exposed to Nephrotoxic Chemicals. Amer. J. Med. 1984;76:989-998

7. Finkel, AJ, Hamilton A, Hardy HL. "Silver" in <u>Industrial Toxicology</u>. Boston, MA: John Wright, PSG, Inc. 1983

8. Moss AP, Sugar A, Hargett NA, et al. The Occular Manifestations and Functional Effects of Occupational Argyrosis. Arch. Ophthalmol. 1979; 97:906-908

9. Perry HM, Perry EJ. Normal Concentrations of Some Trace Metals in Human Urine: Changes Produced By Ethylenediaminetetraacetate. J Clin Invest. 1959; 38:1452-1463

10. Finkel, AJ, Hamilton A, Hardy HL. "Cadmium" in <u>Industrial Toxicology</u>. Boston, MA: John Wright, PSG, Inc. 1983

11. Lauwerys RB, Roels HA, Regniers M, etal. Significance of cadmium concentration in blood and urine in workers exposed to cadmium. Environ. Res. 1979; 20:273-279

12. Price RG. Urinary Enzymes, Nephrotoxicity and Renal Disease. Toxicol. 1982;23:99-134

13. Alderman MH, Melcher L, Drayer DE, Reidenberg MM. Increased excretion of runary N-acetyl-B-glucosaminidase in essential hypertension and its decline with hypertensive therapy. New Engl. J. Med. 1983;309:1213-1217

14. Falck FY, Fine LJ, Smith RG, et al. Occupational Cadmium Exposure and Renal Status. Amer. J. Indus. Med. 1983;4:541-549

15. Stonard MD, Chater BV, Duffield DP, etal. An Evaluation of Renal Function in Workers Occupationally Exposed to Mercury Vapor. Int. Arch. Occup. Environ. Health. 1983; 52:177-189

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1. Metz Metallurgical, South Plainfield, New Jersey
2. Requestors of this study.
3. NIOSH Region II
4. U.S. Department of Labor, OSHA, Region II

For the purpose of informing the affected employees, copies of this report shall be posted by the employer in a prominent place accessible to the employees for a period of 30 calender days.

TABLE I

CHARACTERISTICS OF STUDY GROUP

Number		27
Mean Age (years)		41
Mean Seniority (years)		8.1
	years	
Number of Participants by Seniority	<2	2
	2-5	9
	5-10	8
	>10	8
Smoking Status		
	Never	4
	Ex	9
	Current	14

TABLE II

NUMBER OF WORKERS IN EACH EXPOSURE AREA

AREA	NUMBER OF PARTICIPANTS
All Over	4
Crystal	5
Flake	4
Melting	5
Powder	6
Refinery	3
Total	27

TABLE III

MEAN URINARY SILVER, BLOOD SILVER, AND URINARY CADMIUM LEVELS

	N	Mean	Range	Abnormal #	Abnormal %
Urine Silver (ug/l)	27	11.3	0.5-52.0	26	96
Blood Silver (ug/100ml)	26	1.0	0.05-6.2	24	92
Urine Cadmium (ug/l)	27	11.8	1.9-76.0	5	19

Upper Limit for Unexposed groups -			
	Urine Silver	<1.91 ug/l	(ref. 9)
	Blood Silver	<0.27 ug/100ml	(ref. 5)
	Urine Cadmium	<10 ug/l	(ref. 11)

TABLE IV

PEARSON CORRELATION COEFFICIENTS
BIOLOGIC MONITORING RESULTS, AGE AND SENIORITY

	Age	Seniority
Urine Silver	-.029	.218
Blood Silver	-.021	.017
Urine Cadmium	.194	.428*

* $p<.05$

TABLE V

PREVALENCE OF CONJUNCTIVAL AND CORNEAL CHANGES* BY DURATION OF EXPOSURE

Years Worked	N	Conjunctival 2+ or greater #	Conjunctival 2+ or greater %	Cornea 4+ #	Cornea 4+ %
<2	2	0	0	0	0
2 - 5	9	2	22	1	11
5 - 10	8	3	38	0	0
>10	8	5	63	5	63
Total	27	10	37	6	22

*Grading System for Evaluation of Pigmentation of Conjunctival and Corneal Silver Deposition (2):

Grade	Conjunctiva	Cornea
Trace	Equivocal pigment change in slit lamp view	Equivocal pigment change
1+	Detectable by slit lamp but not by unaided eye	Minimal pigment change at Descements membrane, centrally or perpherally just inside limbus
2+	Detectable without slit lamp on caruncle and/or inferior fornix	Present as in 1+, becoming patchy at one location
3+	Confluent involvement from caruncle to inferior fornix	Nearly generalized involvement of cornea at level of Descemet's membrane with relative spared areas remaining
4+	Marked involvement of conjunctiva elsewhere	Diffuse involvement throughout cornea at level of Descemets membrane

TABLE [illegible]

ESTIMATED CREATININE CLEARANCE
AND
URINARY NAG RESULTS

	N	Mean	Range
Creatinine Clearance ($ml/min/1.73m^2$)	26	84.6	59.6 - 119.7
Urine NAG (nmoles/hr/mgCr.)	23	52.4	12.0 - 224.0

TABLE VII

COMPARISON OF NAG AND ESTIMATED CREATININE CLEARANCE LEVELS
IN SILVER EXPOSED WORKERS
VERSUS
UNEXPOSED CONTROL POPULATION

	METZ	CONTROL
n for NAG Analysis	23	23
mean age	39.8	38.5
mean NAG (s.d.) (nmoles/hr/mgCr)	52.5 (46.3)	13.2 (11.8)**
# of workers with NAG > 79	4	0
N for Creat. Clear. Analysis	26	27
Mean Creatinine Clearance (s.d.) ($ml/min/1.73m^2$)	84.6 (14.6)	102.8 (23.0)*

(* $p < 0.05$)
(** $p < 0.01$)

TABLE VIII

PEARSON CORRELATION COEFFICIENTS:
BIOLOGIC MONITORING RESULTS, AGE, SENIORITY AND
RENAL FUNCTION MEASURES

	Creatinine Clearance	NAG	Log NAG
Urine Silver	-.005	.294	.215
Blood Silver	.178	.600*	.426*
Urine Cadmium	-.299	.118	.091
Seniority	-.419*	.153	.142
Age	-.805*	.649*	.634*
Creatinine Clearance	---	-.300	-.253

*p<.05

N=27 for creatinine clearance
N=23 for nag and log nag

TABLE X

REGRESSION EQUATIONS ON LOG Urinary NAG

INDEPENDANT VARIABLE	DF	B	p	r-square
Constant	21	2.4	<.001	.283
Age		0.03	.009	
Constant	20	3.2	<.001	.182
Blood Silver		59.1	.048	
Constant	19	2.02	<.001	.470
Age		0.03	.005	
Blood Silver		37.4	.137	

TABLE IX

REGRESSION EQUATIONS ON ESTIMATED CREATININE CLEARANCE

INDEPENDANT VARIABLE	DF	B	p	r-square
Constant	24	126.5	<.001	.684
Age		-1.0	.009	
Constant	24	87.4	<.001	.089
Urine Cadmium		-319.8	.138	
Constant	24	82.4	<.001	.032
Blood Silver		219.4	.383	
Constant	23	126.5	<.001	.669
Age		-1.0	<.001	
Urine Cadmium		-158.6	.238	

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