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Cross-Sectional Study of Platinum Salts Sensitization Among Precious Metals Refinery Workers

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A cross-sectional medical evaluation was conducted to determine respiratory and dermatological effects of platinum salts sensitization among workers in a secondary refinery of precious metals. Fifteen of 107 current employees and eight (28%) of 29 former employees, who had been terminated from employment on average for 5 years because of respiratory symptoms, had positive skin reactivity to platinum salts. Platinum salts skin reactivity was significantly associated with average air concentrations of platinum salts in employees' present work area. Workers with positive platinum salts skin tests had significantly higher prevalences of reported rhinitis, asthma, and dermatitis than negative skin test workers. They also had increased bronchial response to cold air challenge and elevated levels of total serum IgE. Platinum salts sensitization was not associated with atopic tendency as measured by sensitivity to common aeroallergens, but was strongly associated with cigarette smoking status. The findings indicate that cigarette smoking may be a risk factor for the development of platinum salts allergy. The persistence of platinum salts sensitization and high prevalence of adverse health outcomes among former workers demonstrate the importance of regular medical monitoring so that sensitized workers can be removed from exposure before they develop long-term health problems.

Key words: platinum refinery asthma, dermatitis, smoking, atopy, skin prick test, cold air challenge test, IgE, PFTs, ammonia, chlorine, formaldehyde, hydrazine, hydrogen chloride, nitric acid

INTRODUCTION

Platinum salts have been reported to induce allergic responses, including rhinitis, dermatitis, and asthma [Cromwell et al., 1979; Freedman and Kropey, 1968;

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Hunter et al., 1945; Murdoch et al., 1986; Pepys et al., 1972; Roberts, 1951]. While loss of platinum salts sensitization is said to occur after removal from exposure [Hughes, 1980], there have been few follow-up evaluations of sensitized individuals. Furthermore, risk factors for developing sensitization have not been clearly delineated, even though recommendations have been made for excluding prospective employees with a medical history of atopy [Hughes, 1980; Roberts, 1951].

The present investigation reports the findings of the largest epidemiological evaluation of platinum salts exposed workers conducted to date in the United States. The purpose of the investigation was to determine the prevalence and medical characteristics of platinum salts sensitization among exposed workers. Long-term sequelae of sensitization were evaluated by including workers who had been medically terminated in prior years. In addition, the possible roles of atopy and cigarette smoking as predisposing risk factors were evaluated.

The investigation was conducted on workers employed in a secondary refinery of precious metals. The 13-year-old facility reclaimed precious metals from scrap metal and expended catalyst used in the electrical and chemical industries. First, the industrial process involved burning the scrap to remove carbon and combustible substances followed by milling and sifting to yield a fine powder. The powder was dissolved in hydrochloric acid and chlorine followed by separation and concentration through sequential solubilization and precipitation to yield ammonium hexachloroplatinate or "yellow salt." The salt was calcined to produce a platinum sponge, which was redissolved and further refined. The platinum sponge was stored until orders were received for specific platinum compounds. The platinum compounds were produced in a separate area. The production process also utilized ammonia, chlorine, formaldehyde, hydrazine, hydrogen chloride, and nitric acid. The three major processes of burning and milling, refining to platinum, and producing platinum salts occurred in three areas that were referred to as "Recovery," "Refinery," and "Chemical Products."

Workers in the facility were routinely terminated for medical reasons after developing symptoms of "allergy." Personnel records of medically terminated employees indicated that between 1971 and 1979, 59 hourly employees were terminated for medical reasons, the majority due to apparent sensitization to platinum salts. The causes for medical termination were as follows: "allergic bronchitis" ($n = 45$, of whom 11 had bronchitis and dermatitis); "respiratory irritation" ($n = 4$); "allergic dermatitis" ($n = 3$); "allergic rhinitis" ($n = 1$); "conjunctivitis" ($n = 1$); and other or unknown causes ($n = 5$). For the years 1974 to 1979, the number of medical terminations due to allergic bronchitis or dermatitis represented 9.8% of the employees in the production areas of the facility per year. The work areas of the employees at time of termination were: Recovery—15%, Refinery—34%, Chemical Products—19%, Maintenance—11%, and all other areas—11%.

Because of the high rate of medical terminations, an investigation was conducted to determine the prevalence and medical characteristics of platinum salts sensitization among current refinery workers and workers who had been medically terminated due to allergic conditions in prior years.

MATERIALS AND METHODS

Environmental Measurements

The company's environmental monitoring data for 1977 to 1979 were available for analysis. Average air concentrations of platinum salts were determined for areas of the facility as geometric means of 8-hour time-weighted average air levels. In addition, environmental measurements for ammonia, chlorine, formaldehyde, hydrazine, and hydrogen chloride were made by Draeger Direct Reading Detector Tubes at a minimum of 10 locations in the Refinery and Chemical Products areas. Lower limits of detection for the sampling method were as follows: ammonia—3.5 mg/M^3, chlorine—0.6 mg/M^3, formaldehyde—0.75 mg/M^3, hydrazine—0.65 mg/M^3, and hydrogen chloride—1.4 mg/M^3.

Medical Examinations

A cross-sectional medical examination was conducted on current employees and a number of former workers who were medically terminated due to asthma, bronchitis, or dermatitis. Medically terminated workers were traced through the use of telephone books, driver license records, and word-of-mouth among current employees and neighbors at last known addresses.

The examination consisted of a work exposure and medical questionnaire; physical examination; spirometry before and after a work shift (current employees only); cold-air bronchial inhalation challenge test; skin prick testing to platinum salts and three common aeroallergens; and blood drawing to measure serum concentrations of total IgE and of specific IgE for platinum salts and common allergens.

Spirometry. FVC, FEV_1, and FEV_1/FVC were measured using an Ohio Medical dry rolling spirometer with a microprocessor according to the American Thoracic Society criteria [ATS, 1979]. Spirometry was performed by current employees before and after a midweek work shift. Former employees performed only a baseline spirometry. We considered a 10% or greater decrease in FEV_1 across the work shift to be a positive response.

Cold air test. Cold air challenge testing was performed using a system previously described [Brooks et al., 1990; Deal et al., 1980]. Baseline spirometry was established before each challenge. One subject with a $FEV_1 < 60\%$ of predicted was not tested further. Subjects breathed air cooled to $-40°C$ for 2 minutes at tidal breathing, followed by eucapnic hyperventilation at 60–65 L/min for the next 4 minutes. The minute ventilation was controlled by instructing the subject to constantly keep a reservoir bag full by matching its rate of emptying. Carbon dioxide was added to the inspired air to allow eucapnic hyperventilation. Spirometry was repeated at 2- and 4-minute intervals after hyperventilation. The response was considered to be the larger of the decreases in FEV_1 at the two posthyperventilation measurements.

For the analysis of the cold air test as a dichotomous variable, we considered a 9% or greater decrease in FEV_1 at either posthyperventilation measurement to be a positive response. We arrived at this value by analyzing the test results of 43 "normal" workers who reported no respiratory symptoms or past medical history of asthma or allergy, and had a normal physical examination, normal pulmonary function tests, and negative platinum salts and aeroallergen skin tests. The mean ($\pm$ SEM) % change in FEV_1 after cold air challenge in this subpopulation was -3.4 ± 2.8 %. Therefore, a 9% or greater decrease in FEV_1 represented an approximate value falling outside two standard errors from the mean of the change. This criterion is similar to values reported by other investigators [Deal et al., 1980]. A detailed evaluation of the utility and interpretation of the cold air challenge test is presented elsewhere [Brooks et al., 1990].

Skin prick tests. A standard procedure for skin prick testing was performed and interpreted according to previously described criteria [Bernstein, 1972; Biagini et al., 1985]. Disodium hexachloroplatinate (Na_2PtCl_6) and ammonium hexachloroplatinate ($(NH_4)_2PtCl_6$) were obtained from the company and tested for purity by the Experimental Toxicology Branch, NIOSH. The platinum salts were dissolved in Coca's solution and tested in 10-fold titrations ranging from 10^{-3} to 10^{-9} gm/ml. Positive control tests were performed with a 10^{-3} gm/ml histamine diphosphate solution and negative vehicle control tests with diluent solution. Preliminary skin test assays of all $(NH_4)_2PtCl_6$ solutions did not reveal evidence of nonspecific irritant responses in 39 nonexposed control volunteers. Subjects were also tested with extracts of three aeroallergens: ragweed, timothy, and dust at dilutions of 1:20, 1:20, and 1:10, respectively.

Serum IgE. Total serum IgE was determined using a commercial radioimmunosorbent assay [Biagini et al., 1985]. Normal human serum values by this method are 60 ± 45 U/ml (mean ± SD). Platinum-specific antibodies were evaluated by the radioallergosorbent test. Detailed results of the immunological evaluation are reported elsewhere [Biagini et al., 1985].

Statistical Analysis

Analysis focused on the relationships between the skin test for platinum salts and the prevalence of health outcomes. We considered the result of the platinum salts skin test to be either positive (at any concentration) or negative. Definitions of the variables were as follows: rhinitis symptoms—itchy, watery eyes or itchy, watery nose while at work; asthma symptoms—wheezing, plus at least two other respiratory symptoms of cough, shortness of breath, or chest tightness; reported dermatitis—itching or burning of skin while at work; positive cold-air challenge test—decrease in FEV_1 greater than 9% after challenge with cold air; elevated IgE—total serum IgE greater than 225 U/ml; and positive aeroallergen test—positive skin prick test to at least one of ragweed, timothy, or dust.

We performed stratified categorical analyses using the Mantel-Haenzel prevalence odds ratio and chi-square analyses to test associations [Rothman, 1986]. Ninety-five confidence limits of the odds ratio were estimated using the method of Robins et al. [1986]. We also evaluated response to the cold air challenge test and total serum IgE as continuous variables, using linear regression. The distribution of total IgE levels was skewed upward, so it was normalized through logarithmic transformation prior to the regression. The relationship between platinum salts sensitization and work area air concentrations of platinum salts was evaluated using unconditional maximum likelihood logistic regression. The Statistical Analysis System was utilized for initial categorical analyses, for linear regression using the REG procedure, and for logistic regression using the CATMOD procedure [SAS, 1985].

RESULTS

Environmental Measurements

Analysis of company environmental monitoring data for 1977 to 1979, providing over 75 air measurements of platinum salts, is shown in Table I. Elevated platinum salt air measurements were noted in the Recovery, Refinery, and Warehouse areas, and often exceeded the OSHA governmental standard of 2.0 $\mu g/M^3$. Measur-

TABLE I. Measured Air Concentrations of Platinum Salts 1977–1979

Sampling location	Sampling days	Mean air concentration[a]	Percent of days above 2.0 $\mu g/M^3$ [b]
Residue	1	0.5	0
Recovery	9	5.3	56
Recovery, sampling	4	2.7	50
Refinery	3	10.7	67
Refinery, tray room	4	27.1	75
Analytical laboratories	3	0.4	0
Warehouse	8	8.6	75
Air conditioning unit	3	0.6	0

[a]Geometric mean of time-weighted average for an 8-hour shift, in $\mu g/M^3$.
[b]2.0 $\mu g/M^3$ was the OSHA Permissible Exposure Level at the time.

able concentrations of platinum salts were found throughout the facility, including in the air conditioning unit supplying air to the administrative offices of the facility.

Detector tube sampling for ammonia, chlorine, formaldehyde, hydrazine, and hydrogen chloride found that the maximum concentration for each substance was at "trace" or below the limit of detection in every sample obtained in the Refinery and Chemical Products area.

Medical Examination

Based on a review of the medical records, we determined that 49 workers had been terminated due to suspected platinum salts allergy (i.e., "allergic bronchitis," "allergic dermatitis," and "allergic rhinitis" stated as the reason for termination). We were able to locate 36 terminated workers; 29 agreed to participate in the study. At the time of the examination, the former workers had been terminated from employment on average for 5 years, ranging from 7 months to 107 months.

We conducted examinations of 29 medically terminated workers and 107 (87%) of 123 available current employees. Nine current employees were not available due to vacations, unrelated illnesses, or logistical difficulty in relieving them from their duties. The ages of the examined employees ranged from 20 to 61 with a mean of 34 years; 92% were male and 94% were white. There were no substantial differences in demographic characteristics between current employees and terminated workers.

Fifteen (14%) of the 107 current employees and 8 (28%) of the 29 terminated workers showed positive skin reactivity to platinum salts at concentrations of 10^{-3} to 10^{-9} gm/ml (Table II). Sensitization to platinum salts occurred among workers in all areas of the facility except the administrative offices. Platinum salts sensitivity generally varied directly with the environmental air concentrations of platinum salts in the employees' present work areas (Spearman correlation = 0.71, $p = 0.11$ based on six work areas). By logistic regression, the risk of demonstrating platinum salts skin test reactivity increased 1.13 times per 1 $\mu g/M^3$ increment in work area air concentration of platinum salts ($p = 0.01$).

Table III reports the prevalences of symptoms and medical test results between platinum salts skin test positive and negative workers. Skin test reactivity to platinum salts was associated with: increased symptoms of rhinitis, asthma, and dermatitis; $FEV_1/FVC < 70\%$; positive cold air challenge; and elevated total serum IgE. The

TABLE II. Work Area Distribution of Skin Prick Test Sensitivity to Platinum Salts Among Current Employees

Work area	Number of employees in area	Positive skin test	
		Number	%
Residue/recovery	15	1	7
Refinery	14	2	14
Refinery, tray room	3	2	67
Chemical products/salts	22	3	14
Analytical laboratories	19	2	11
Warehouse/stores	3	1	33
Maintenance	12	3	25
Manager/office	15	0	0
Other (electrician, boiler operator)	4	1	25
Total	107	15	14

medically terminated workers reported more symptoms and demonstrated more adverse test results than nonsensitized current employees.

Eleven (9%) of 133 subjects had baseline $FEV_1/FEV < 70\%$. A high prevalence of $FEV_1/FVC < 0.70$ (50% of 8 workers) was noted among terminated workers with positive skin reactivity to platinum salts. However, all of the terminees with positive platinum salts skin test smoked cigarettes. There was no significant association between platinum salts skin test result and $FEV_1/FEV < 70\%$ among current employees.

A significant change in FEV_1 across work shift was highly specific for overall atopic status, but not for platinum salts sensitization. Four persons had greater than 10% decrease in FEV_1 across the work shift. Each had a positive aeroallergen skin test and elevated total serum IgE. One had a positive cold air challenge test and another a positive platinum salts skin test.

Prevalence of aeroallergen skin test reactivity was similar among positive and negative platinum salts skin test groups (Table III) and was similar to that found in the general population. In contrast, cigarette smoking status was strongly associated with platinum salt sensitization. Approximately 80% of current employees with a positive platinum salts skin test were current smokers compared to 35% among negative skin test employees. Furthermore, cigarette smoking prevalence was elevated among medically terminated workers. All of the terminated workers with a positive platinum salts skin test were current cigarette smokers; 90% (19) of the platinum salts skin test negative terminees were current or ex-smokers.

Prevalence odds ratios for health outcomes among the platinum salts skin test positive versus negative current employees, adjusted for aeroallergens skin test reactivity and cigarette smoking status, are shown in Table IV. Platinum salt sensitization was significantly associated with increased prevalences of rhinitis symptoms, asthma symptoms, reported dermatitis, and a positive cold air challenge test, after controlling for aeroallergen sensitivity and cigarette smoking status. A positive platinum salts skin test also was associated with an increased prevalence of total serum IgE > 225 U/ml (POR = 3.5), although the association was not statistically significant ($p = 0.09$).

TABLE III. Symptoms and Test Results by Platinum Salts Skin Test and Work Status

Symptom or test result	Platinum salts skin test							
	Current workers				Former workers			
	Positive		Negative		Positive		Negative	
	Number	%	Number	%	Number	%	Number	%
Rhinitis symptoms	13	87	33	37	3	38	7	33
Asthma symptoms	10	77	18	22	4	50	8	40
Reported dermatitis	5	33	8	9	2	25	4	19
$FEV_1/FVC < 0.70$	2	13	4	5	4	50	1	5
Positive cold-air challenge	5	33	6	7	4	50	4	21
Elevated total IgE	4	27	7	8	5	63	4	19
Positive aeroallergen test	6	40	29	32	2	25	6	29
Smoking status—current	12	80	32	35	8	100	11	52
quit	2	13	22	24	0	0	8	38
never	1	7	37	40	0	0	2	10
Total	15	100	92	100	8	100	21	100

TABLE IV. Relative Risk of Symptoms and Test Results by Platinum Salts Skin Test Among Current Employees, Adjusted for Aeroallergen Skin Test and Cigarette Smoking Status

Symptom or test result	POR[a]	95% CI	p-value
Rhinitis symptoms	8.3	1.8—37.8	0.001
Asthma symptoms	11.3	2.3—54.6	0.001
Reported dermatitis	12.6	2.2—72.8	0.001
$FEV_1/FVC < 0.70$	1.9	0.3—12.3	0.52
Positive cold-air challenge	7.7	1.5—38.3	0.003
Elevated total IgE	3.5	0.8—16.3	0.09
Positive aeroallergen test[b]	1.5	0.5—4.7	0.54
Cigarette smoking[c]	9.0	1.2—69.3	0.01

[a]Prevalence odds ratio of positive versus negative platinum salts skin test workers, adjusted for aeroallergen test status and cigarette smoking status (current, past, or never).
[b]Adjusted for cigarette smoking status.
[c]Current or past versus never, adjusted for aeroallergen skin test status.

In order to estimate the quantitative association between platinum salts sensitization and health outcomes, we performed a linear regression using percent decrease in FEV_1 following cold air challenge and total serum IgE as continuous variables; aeroallergen skin sensitization and cigarette smoking status were included as covariables. Platinum salts sensitization was associated with a 4.1% additional decrease in FEV_1 following cold air challenge beyond the average FEV_1 decrease of 3.8% among platinum salts skin test negative current employees ($\beta_{FEV_1\%} = -4.05$, $p = 0.001$). In other words, the average decrease in FEV_1 following cold air challenge was more than twice as much among the platinum salts skin test positive compared to skin test negative employees. Platinum salts sensitization was associated with an increase in total serum IgE of 46.9 U/ml above the average level of 53.9 U/ml among skin test negative current employees ($\beta_{\ln(IgE)} = 0.63$, $p = 0.09$). The increase in IgE was not statistically significant, but the power to detect an increase in total IgE of this magnitude in a population equal in size to the number of current workers would be only 40%.

DISCUSSION

Fifteen of 107 current employees and 8 of 29 (28%) medically terminated workers in a secondary refinery of precious metals showed positive skin reactivity to platinum salts. Workers with positive platinum salts skin tests had significantly higher prevalences of rhinitis, asthma, and dermatitis symptoms and positive cold air challenge compared to negative skin test workers. Nearly 10% of workers in the production areas per year were medically terminated due to apparent "allergy" symptoms. The results of this investigation clearly indicate that sensitization to platinum salts occurs at a substantial frequency among exposed workers in precious metals refining and are suggestive of an increased prevalence of occupational asthma and contact dermatitis in these workers.

Company environmental monitoring records provided evidence of elevated air concentrations of platinum salts in most operating areas of the facility. The average air concentrations of platinum frequently exceeded the OSHA standard of 2.0 μ/M^3 in the production areas. Furthermore, platinum salts were found in nonproduction areas, suggesting that once sensitized, a person could not remain employed at the facility without continuing to be exposed to the platinum salts. The correlation between air concentrations of platinum salts in the employees' present work area and the prevalence of platinum salts skin sensitization among current employees suggests an exposure-effect relationship between level of exposure and the prevalence of allergy.

The production process utilized ammonia, chlorine, formaldehyde, and other substances capable of causing irritation or allergy; however, the limited environmental monitoring results suggest that exposure to these other substances was low. It is unlikely that exposure to these substances was responsible for the adverse health effects, but it is possible that concurrent exposure to irritants even at relatively low levels could have potentiated the effects of the platinum salts exposure by increasing mucosal permeability. Biagini et al. [1986] reported such an effect in an animal model. They found that monkeys, experimentally exposed to platinum salts concurrently with ozone, demonstrated significantly increased incidence of platinum salts skin test reactivity and increased bronchial hyperreactivity compared to monkeys exposed to platinum salts alone [Biagini et al., 1986]. Unfortunately, the effects of concurrent exposure to irritants could not be evaluated further in this study.

An important observation was the finding of persistent positive platinum salts skin tests among medically terminated workers. This group of former workers, with no further apparent platinum salts exposure during an average of 5 years since termination, demonstrated a high prevalence of symptoms consistent with allergic conditions, $FEV_1/FVC < 70\%$, positive cold air challenge, and elevated total serum IgE. The findings suggest that allergic sensitization from work leading to termination may have prolonged sequelae. These findings differ from those reported by other investigators, where continued disease was not observed after termination of exposure [Hughes, 1980]. The most likely reasons for the difference are that exposures to platinum salts may have been higher and that there was no regular skin testing program in the facility for the early identification of sensitized workers. Periodic medical screening consisted only of a medical history and physical examination. Pulmonary function tests were obtained every 2 years, but there was no routine screening for platinum salts sensitization. It is important that workers with sensitivity to platinum salts be recognized early by medical surveillance and promptly removed from exposure.

Skin test reactivity to platinum salts and aeroallergens were not strongly associated in this study population. This finding is noteworthy in that one would expect that general atopic tendency would predispose to the development of new allergies [Bonner, 1984; Brooks, 1977; Chan-Yeung and Lam, 1986]. Furthermore, reports in the literature indicate that atopic status may be a risk factor for platinum salts allergy [Hughes, 1980; Parrot et al., 1969]. The prevalence of aeroallergen sensitivity among subjects in this study was comparable to that in the general population; however, among current employees, the proportion of aeroallergen skin test positive subjects was somewhat higher among positive platinum skin test workers compared to those with negative platinum salts skin tests (40% versus 32%). The difference was not statistically significant but the size of the study population was small. Due to the small size of the study population, we cannot make a definite conclusion as to whether atopy is a risk factor for platinum salts sensitization; it does not appear to be a strong risk factor.

In contrast, smoking appears to be a strong risk factor for developing platinum salts sensitization. Thirty-five percent of platinum salts skin test negative current employees were smokers compared to 80% of skin test positive current employees and 70% of medically terminated workers. The differences in cigarette smoking status among the platinum salts sensitization sub-groups are highly significant. It has been hypothesized that the mucosal lining of the airways of smokers are more permeable to inhaled agents, and thus there is a greater penetration of antigenic material and subsequent occurrence of sensitization. Our findings are consistent with studies of occupational exposures to green coffee bean, ispaghula powder, and tetrachlorophthalic anhydride, which noted increased specific IgE levels in smokers and associations between smoking and atopy [Chan-Yeung and Lam, 1986; Venables et al., 1985; Zetterstrom et al., 1981].

In order to evaluate whether the combination of atopy and smoking could have had a greater confounding effect than either factor alone, we performed each of the regression analyses both with and without a multiplicative interaction term for atopic status and cigarette smoking status. The associations of the health outcomes with platinum salts skin test results were not altered by including the interaction term and, in no analysis, was the interaction term statistically significant. Therefore, the presented analyses did not include the interaction term. This analytical strategy is sufficient to control for the confounding effects of atopic status and cigarette smoking in this study, but the statistical power is too low to evaluate the role of these variables per se on the health outcomes. More research is needed on the independent and interactive effects of atopy and cigarette smoking on occupational asthma.

The prevalence odds ratios were estimated only among current employees. Platinum salts skin test results among medically terminated workers would depend upon a complex function involving time since initial sensitization, degree of sensitization, and time since last exposure. Given the small number of medically terminated subjects, it is not possible to evaluate further the temporal course of platinum salts sensitization. Since it was clear from the medical records that all of the medically terminated workers had allergic symptoms leading to termination, we believe that virtually all of them would have had a positive test in the past.

The use of the prevalence odds ratio as an estimate of the rate ratio assumes that the duration of health effects, such as rhinitis or asthma, was the same among platinum salts sensitized and nonsensitized workers. Since development of symptoms following sensitization to platinum salts caused workers to leave work earlier, disease duration (i.e., length of employment after the onset of symptoms) likely was shorter for platinum salts sensitized workers than for those whose symptoms were not work-related. Therefore, the prevalence odds ratios among current employees are conservative estimates of the relative risk of symptoms due to platinum salts sensitization.

The time of onset of symptoms also influenced the association between platinum salts skin test result and symptom prevalences. In an analysis not presented, subjects were stratified into those with symptom onset before or after start of employment at the facility. Employees with symptom onset before hire had prevalences of platinum skin test sensitivity comparable to those with no symptoms, while employees with symptom onset after hire had a higher proportion of persons with positive platinum salts skin test. Consequently, the strengths of association between platinum salts skin test and symptoms were stronger when cases were restricted to those with symptom onset after date of hire. For example, the POR for current employees with asthma increased from 11.3 to 17.9 (95% CI = 3.3-97.4, $p = 0.0001$) when the case definition was restricted to asthma symptoms with onset after date of hire. The PORs were similarly strengthened for the other symptoms. In the analysis presented, no adjustment was made for time of symptom onset in relationship to date of hire since the time of onset was based on subject recall and could not be verified. Therefore, the associations between platinum salts sensitivity and health outcomes reported in this paper are conservative estimates.

Since no comparison population was included in the examination, a number of strategies were used to interpret the findings. All employees, including nonproduction employees, were asked to participate so that internal comparisons could be made between high and low platinum salts exposure areas and between positive and negative platinum salts skin test subjects. We used the American Thoracic Society respiratory questionnaire modified with questions on asthma as developed for previous studies so that the prevalences of symptoms could be interpreted. The pulmonary function tests and immunology tests were performed according to standard methods so that reference normal ranges were available. For the cold air challenge test, which was not as well standardized at the time of the investigation, we established an internal standard by using the results of workers who had no respiratory symptoms and were negative on all other tests of allergy. The test values of this subgroup compared well with the few published reports on other populations. The specificity of the platinum salts skin test was evaluated by testing non-exposed volunteers at the investigators' medical center. Therefore, although no comparison group was available, the use of standardized tests, internal comparison groups, and external comparisons for some tests did allow interpretation of the findings.

In epidemiologic evaluations of occupational asthma, testing procedures must be safe and feasible to conduct at the industrial facility. Although the definitive test for allergic asthma is an inhalation challenge test, this test must be conducted in a clinical setting. Spirometry may be used to evaluate signs of reversible airways obstruction. Unfortunately, measuring changes in pulmonary function across a work shift is insensitive in identifying atopic status. Only four current employees had a substantial decrease in FEV_1 across their work shifts. All four were aeroallergen positive and had elevated total IgE levels, but only one was platinum salts skin test positive. Thus it also was not specific for identifying platinum salts sensitization. The sensitivity and specificity of the test in detecting changes in lung function due to work exposures were limited because the test was conducted over only one work shift. The test may be useful if performed repeatedly over several work shifts, or if frequent peak flow measurements utilizing a portable peak flow meter are obtained.

A positive cold air test was significantly associated with platinum salt sensitivity, independent of sensitivity to aeroallergens. Eighty-nine percent of persons with a positive response to the test had some immunologic condition—aeroallergen sensitivity, platinum salts sensitivity, or elevated total IgE. Thus it was highly specific for overall allergic status, but not for platinum salts sensitization. The cold air challenge test may be very useful in the evaluation of occupational asthma, but it should be interpreted only in conjunction with the results of other medical tests.

Treatment of occupational asthma is not satisfactory in the presence of continuing exposure. Generally, sensitized workers must be removed from exposure. Prevention usually involves a combination of agent substitution, environmental controls, use of personal protective equipment, and periodic medical examinations. Another strategy is to perform pre-employment screening to eliminate workers at increased risk. Atopic individuals may be at increased risk of sensitization due to some agents, but we could not demonstrate increased susceptibility in this study. Smoking appears to predispose individuals to the development of platinum salts sensitization after occupational exposure. Proper medical management in an occupational setting with potential exposure to an allergen such as platinum salts requires that workers be provided sufficient economic safeguards, including medical removal protection, retraining, and adequate compensation in the case of sensitization, so that they do not have an incentive to hide adverse health effects or prolong their exposure after sensitization.

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