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Clinical Findings of Irritation Among Chromium Chemical Production Workers

Herman J. Gibb, PhD,[1]* Peter S. J. Lees, PhD,[2] Paul F. Pinsky, PhD,[3] and Brian C. Rooney, MS[2]

Background *Several reports of workers in chromate production and chromeplating have indicated that exposure to hexavalent chromium is associated with skin and nasal irritation.*

Methods *A cohort of 2,357 workers first employed between 1950 and 1974 at a chromate production plant was identified. Clinical findings of irritation were identified by a physician as a result of routine examinations or visits to the medical clinic by members of the cohort. Percentages of the cohort with various clinical findings, the time from hire to occurrence of the first finding, and the mean and median annual hexavalent chromium (measured as CrO_3) concentration for the job title where the clinical finding first occurred were determined. A proportional hazards model was used to evaluate the relationship between hexavalent chromium exposure and first occurrence of each of the clinical findings.*

Results *Nasal irritation and nasal ulceration were the most common clinical findings reported, occurring in more than 60% of the cohort. The average time to first occurrence of these findings was less than 3 months, whereas the time to first occurrence of the other findings ranged from 10 to 22 months. Median exposure to hexavalent chromium at the time of occurrence for most of the findings was about 20 $\mu g/m^3$. The proportional hazards model indicated that ulcerated nasal septum, irritated skin, and perforated eardrum were significantly associated with ambient hexavalent chromium exposure; all clinical findings with the exception of conjunctivitis and irritated skin were associated with the calendar year of hire, with the risk being lower as the calendar year of hire became more recent. Annual average ambient hexavalent chromium concentrations generally dropped in the plant over the period of the study.*

Conclusion *Workers in the chromate production plant in this study experienced a variety of nasal and skin irritations. Irritated and ulcerated nasal septa, in particular, were quite common clinical findings, occurring in over 60% of the cohort, and they occurred in relatively short periods of time—less than 3 months from date of hire. Annual average concentrations of chromium may not be a good predictor of clinical findings of irritation.*
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[1]U.S. Environmental Protection Agency
[2]The Johns Hopkins University School of Hygiene and Public Health
[3]U.S. Environmental Protection Agency (Currently with the National Cancer Institute)
Institutions At Which The Work Was Performed: National Center for Environmental Assessment (8601D), U.S. Environmental Protection Agency, Ariel Rios Building, 1200 Pennsylvania Avenue, N.W., Washington, D.C. 20460; The Johns Hopkins University School of Hygiene and Public Health, 615 N. Wolfe Street, Baltimore, MD 21205

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*Correspondence to: Dr. Herman J. Gibb, National Center for Environmental Assessment (8601D), U.S. Environmental Protection Agency, Ariel Rios Building, 1200 Pennsylvania Ave., N.W., Washington, D.C. 20460. E-mail: gibb.herman@epamail.epa.gov

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INTRODUCTION

Nasal ulceration and perforation were reported among chromate production workers as early as 1827 [Public Health Service, 1951]. In a review of nine studies of chromate production workers conducted between 1901 and 1951, the prevalence of nasal septum ulceration was reported by the Public Health Service [1951] to range from 4.8 to 63.8% and the prevalence of nasal septum perforation from 8.6 to 71.6%. The Public Health Service [1951] found the prevalence of nasal septum perforation in six chromate production plants to be 56.7%. Of those who developed nasal perforations, 51% developed the perforations within 1 year from the start of exposure. Several studies of persons exposed to chromium in the workplace found increased risks of nasal irritation, ulceration, and perforation, skin ulcers, burns, and allergic contact dermatitis [IPCS, 1988; ATSDR, 1993; Cross et al., 1997]. Other than a study of 43 chrome plating workers in Sweden [Lindberg and Hedenstierna, 1983], little is known about the relationship of clinical findings of irritation and measured ambient chromium concentrations.

MATERIALS AND METHODS

A cohort of 2,357 workers first employed between August 1, 1950 and December 31, 1974 at a chromate production plant in Baltimore, MD was identified. The cohort is derived from that described by Hayes et al. [1979]; they identified 4,217 workers newly employed between January 1, 1945, and December 31, 1974. After excluding workers employed less than 90 days (N = 1,915), women (N = 160), and those with unknown length of employment (N = 24), work history (N = 16), and/or age (N = 1), the resulting size of the Hayes et al. study cohort was reduced to 2,101. The current study excluded those in the Hayes et al. cohort who began work before August 1, 1950 (N = 734) because on that date, the construction of a new mill and roast and bichromate plant was completed and extensive exposure information began to be collected. It was also decided to include workers in the current study who worked less than 90 days but began employment after August 1, 1950 (N = 990), to expand the size of the low exposure group. The resulting group of 2,357 males constituted the cohort for this study.

Physician findings as reported in clinic and first aid records were examined and abstracted noting the occurrence(s) of nasal irritation, ulceration, perforation, and bleeding, skin irritation and ulceration, dermatitis, burns, conjunctivitis, and perforated eardrum. If individuals were noted in the medical record as having more than one clinical finding (e.g., irritated nasal septum and ulcerated nasal septum), all findings were abstracted. For each individual, the date(s) of the first occurrence of each clinical finding were abstracted.

An extensive series of measurements of airborne hexavalent chromium concentrations over the period of 1950–1985, based on job title, provided the data for worker exposure estimates. An explicit objective of the exposure monitoring strategy as first laid out in 1950 was to determine usual or normal exposures by job title. During the period of 1950 until approximately 1964, airborne dust samples were collected using high volume air sampling pumps and Greenberg–Smith impingers with the sampling wand held in the worker's breathing zone. These were, of necessity, short term (tens of minutes) samples. Beginning in the mid-1960s, a system of exposure estimation based on 24-hour routine measurements from fixed-site monitors throughout the facility and regular observation of how much time workers with different job titles spent in the vicinity of each of these monitors was instituted. This system remained in use until 1985 when the plant closed. In 1977, this system was supplemented by routine full-shift personal sample collection, again based on job title, using NIOSH standard method P and CAM 169 [NIOSH, 1974]. Despite different dust collection methods throughout the period of this study, the sample analytical method remained constant, using minor variants of the s-diphenylcarbazide colorimetric method; all analyses were conducted at an in-house laboratory.

The exposure measurements (approximately 70,000 direct measurements) collected during this period were used to construct an exposure matrix displaying annual average airborne hexavalent chromium concentrations, expressed as mg CrO_3/m^3, by job title and year. The exposure matrix consisted of entries for 114 job titles over 36 years. All exposure data from fixed-site monitors were adjusted to better reflect personal exposures using the job-specific ratios of the fixed-site-based estimates and the personal estimates of exposure for the period in which the methods were used concurrently (1977–1985). Whenever data were available for a job title–year combination, exposure measures were directly entered into cells. If exposure data were missing for a particular matrix cell, exposure was modeled according to a standard protocol using exposure information from the same job title and similar years or from similar job titles and the same years.

The percentage of the study population exhibiting various clinical findings was determined. For each clinical finding, the annual average CrO_3 exposure for the job titles which individuals held at the time of diagnosis was abstracted for the exposure matrix and mean and median exposures calculated. The mean and median number of days from the date first hired to the date the finding was first reported was also determined. The date of a clinical finding was recorded by month and year while the date of hire was recorded by month, day, and year; therefore if the month of

hire and month of clinical finding were the same, the midpoint of the remainder of the month of hire was used as the date of clinical finding. For example, if the date of hire was March 20, 1956, and the clinical finding was March 1956, then March 25, 1956, was used as the date of clinical finding. If the clinical finding occurred in a month following the month of the date of hire, then the midpoint of the month in which the clinical finding occurred was used as the date of the clinical finding.

The proportional hazards model [Cox, 1972] was utilized to assess the possible relationship between hexavalent chromium exposure and first occurrence of each of the clinical findings. Hexavalent chromium exposure was entered into the model as a time-varying covariate; additional covariates were calendar year of hire and age at hire. The underlying time variable for the model was time since hire. Separate models were run for each of the 10 different clinical findings.

RESULTS

Medical (health clinic) records were available for 2,307 of the 2,357 individuals in the cohort (97.8%). Clinical findings and exposure measures are tabulated in Table I. Mean or median time on the job was considerably shorter for the appearance of irritated or ulcerated nasal septum (< 3 months) than for the other clinical findings (> 7 months). The percentage of workers with irritated or ulcerated nasal septa was relatively high ($> 60\%$).

The proportional hazards models indicated that ambient hexavalent chromium exposure was significantly associated with the occurrence of ulcerated nasal septum ($P = 0.0001$), ulcerated skin ($P = 0.004$), and perforated eardrum ($P = 0.03$). The relative risks associated with an increase of 0.1 mg CrO_3/m^3 were 1.20, 1.11, and 1.35, for ulcerated nasal septum, ulcerated skin, and perforated ear, respectively. The calendar year of hire was significantly associated with the occurrence of each clinical finding except conjunctivitis and irritated skin, with the risk being lower as the year of hire became more recent. Ambient exposure to hexavalent chromium in the production plant was known to generally drop over the period 1950–1985. Figure 1 demonstrates the decline in exposure for three selected jobs in the plant.

DISCUSSION

The percentage of workers experiencing some symptom of irritation in this cohort was relatively high. Over 60% of the cohort experienced nasal irritation, nasal ulceration, or both, at some time during their employment. In addition, the time to occurrence for nasal irritation and nasal ulceration was very short (both the mean and the median time to occurrence were < 3 months). With the exception of perforated eardrum, all of the clinical findings were observed in at least 10% of the population. The study of chrome platers by Lindberg and Hedenstierna [1983] found that workers exposed to chromic acid that exceeded a daily average of 0.002 mg/m^3 experienced septal ulceration and/or perforation. Two-thirds of workers exposed to a highest daily average of 0.020 mg/m^3 experienced septal ulceration and/or perforation. Unfortunately, the data of the current study do not allow direct comparison with that of the Lindberg and Hedenstierna study. Concentrations in this

TABLE I. Percentage of Cohort Reporting Various Clinical Findings, CrO_3 Exposure Concentrations at the Time of the Finding, and Time on the Job Prior to the Finding; Chromium Chemical Production Workers, USA

Clinical finding	% of Cohort ever having clinical finding	Mean (median) exposure at time of first diagnosis of clinical finding (mg CrO_3/m^3)	Mean (median) time on job in days from date first hired to date of first diagnosis of clinical finding
Irritated nasal septum	68.1	0.048 (0.020)	89 (20)
Ulcerated nasal septum	62.9	0.054 (0.020)	86 (22)
Perforated nasal septum	17.3	0.063 (0.021)	313 (172)
Bleeding nasal septum	12.1	0.049 (0.020)	418 (92)
Irritated skin	15.1	0.049 (0.020)	719 (189)
Ulcerated skin	31.6	0.058 (0.025)	373 (110)
Dermatitis	18.5	0.056 (0.028)	624 (216)
Burn	31.4	0.052 (0.022)	409 (133)
Conjunctivitis	20.0	0.049 (0.023)	604 (221)
Perforated eardrum	0.8	0.069 (0.023)	235 (10)

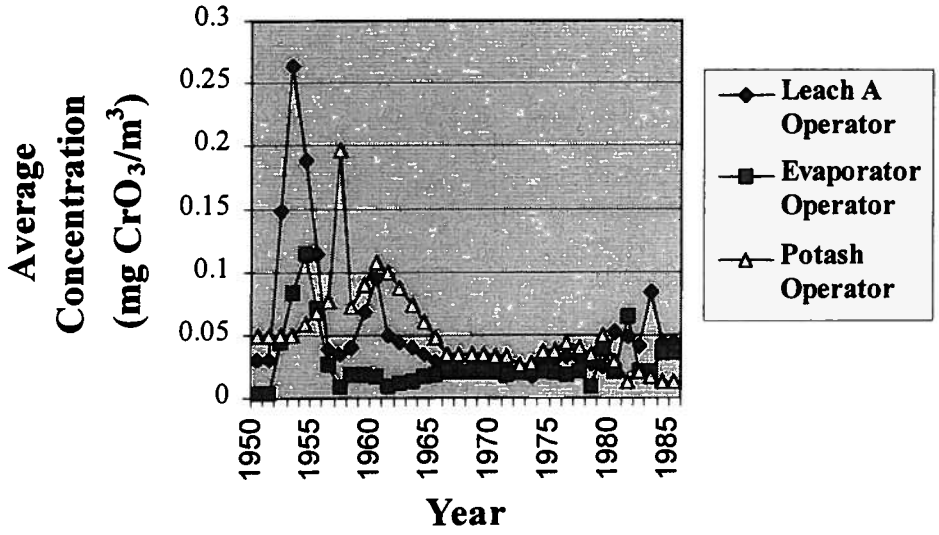

FIGURE 1. CrO_3 exposures over time for selected jobs; chromium chemical production workers, USA.

study such as those reported in Table I reflect mean *annual* concentrations; concentrations in Lindberg and Hedenstierna represent an average of 2–3 days measurements made following clinical findings. Furthermore, the irritative properties of chromic acid to which workers in the Lindberg and Hedenstierna study were exposed could be expected to be different from those of the chromate chemicals experienced in chromate production.

Variation in diagnosis in the current study could have changed over the time period of the study. Such variation could be the result of temporal changes in diagnosis by one physician or by differences among physicians. The extent of temporal variation is difficult to assess. With regard to variation among physicians, the variation would also be difficult to assess, but there were a relatively small number of physicians, probably fewer than five, over most of the time period of the study. There was only one physician in the plant at any one time.

For given diagnoses, Table I refers to mean and median CrO_3 concentrations at the time the clinical finding was recorded. These concentrations are the annual average concentrations for the job titles in which the workers were employed at the time of diagnosis. Workers may have worked in other jobs with other exposures prior to the time that the clinical finding was made.

Some of the clinical findings in this study could be considered nonspecific to chromium exposure. For example, burns could have included thermal burns. Conjunctivitis and irritated skin could also be considered nonspecific to chromium exposure. On the other hand, the nasal findings (irritated nasal septum, ulcerated nasal septum, perforated nasal septum, and bleeding nasal septum) would be considered more specific to chromium exposure.

It is unlikely that selection bias would have occurred in the current study. The fact that such a high percentage of workers experienced nasal irritation and ulceration suggests that the effect of chromium was not limited to a particular subset of individuals.

Survivor bias may have played a role in the percentage of the population with different clinical findings. Survivor bias described here is the bias in the results that may have occurred because not all of the cohort "survived" a normal working lifetime. There were many short-term workers in the population (over 40% worked less than 90 days).

The percentage of workers with nasal perforation was not as high in the current study as that reported by the Public Health Service [1951] in its cross-sectional study of six chromate production plants (17.3 vs. 56.7%, respectively). This difference is perhaps the result of improved industrial hygiene conditions over the years (the plant in the current study was rebuilt in 1950) but might also be explained by the inclusion of so many short-term workers in the current cohort. Despite the fact that there were so many short-term workers, there was a high percentage of workers who did develop nasal and/or other problems.

The proportional hazards model found that hexavalent chromium concentration was significantly associated only with the occurrence of ulcerated nasal septum, ulcerated skin, and perforated eardrum when the covariates were calendar year of hire and age at hire. The lack of a significant association of ambient hexavalent chromium concentration with some of the symptoms classically associated with hexavalent chromium (e.g., nasal irritation, nasal perforation, and bleeding nasal septum) may reflect the fact that the ambient hexavalent chromium concentrations used

in the proportional hazards model represent annual averages for the job in which the worker was engaged at the time of the clinical finding rather than a possibly more relevant shorter term average. Annual averages do not capture the extremes of episodic occurrences or even day-to-day fluctuation. The proportional hazards model did find that calendar year of hire was significantly associated with each of the clinical findings except conjunctivitis and irritated skin with the occurrence being lower as the year of hire became more recent. Annual average concentrations of ambient CrO_3 at the plant generally decreased over the period 1950–1985 (Fig. 1), which would be consistent with ambient hexavalent chromium being associated with the clinical findings, but other conditions in the plant may also be partly responsible for reduction in clinical findings in later years. These conditions could have included increased use of respirators and greater emphasis on personal hygiene measures.

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