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The Role of Chromium Accumulation in the Relationship Between Airborne and Urinary Chromium in Welders

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Summary. Twenty-two welders working with high chromium alloyed electrodes have been examined. Biological monitoring of exposure was accompanied by measurement of the hydrosoluble fraction of chromium in the air. Several indices of early renal tubular damage were also determined.

The close relationship between airborne and urinary chromium suggests that the urinary excretion of the metal at the end of exposure, and particularly its increase above baseline values, are reliable indicators of absorption rate.

The measurement of the renal clearance of diffusible chromium—taken as an index of body burden—showed the influence of the lower exchange rate compartment on the relationship between environmental and urinary chromium. Although the degree of exposure was the same, the urinary excretion of chromium was higher in the workers with a greater chromium body burden.

The evaluation of some early nephrotoxicity indicators yielded no dose-effect relationship, even if a more frequent pathological "response" was observed in the subjects with a higher degree of exposure to chromium.

Key words: Chromium – Biological monitoring – Welders

Longitudinal studies on workers exposed to chromium in the chromium-plating industry showed that urinary excretion and renal clearance of diffusible chromium are two biological indices to evaluate the degree of current exposure and the body burden, respectively (Franchini et al., 1975; Borghetti et al., 1977). The results of epidemiologic studies on exposed workers are confirmed by an experimental investigation on rats (Franchini et al., 1978).

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Other authors have demonstrated a close relationship between hexavalent chromium in the air and urinary excretion (Gylseth et al., 1977) or urinary excretion of the metal corrected for creatinine (Tola et al., 1977). They suggest urinary chromium as a short-term exposure test. However, the biological monitoring is difficult because of the different physical-chemical states of chromium in the various plants and the differing individual absorption rate and excretory capacity.

The purpose of this study is to clarify the significance of the biological indicators of current exposure or chromium body burden, for a more exact definition of their correlation with the airborne chromium. The multiple relationship among airborne concentration, urinary excretion and accumulation of chromium was studied by determining the excretion of the metal at different levels of accumulation and exposure.

Furthermore, we examined the nephrotoxic action of chromium by evaluating several indices of early renal tubular damage and we searched for their possible correlation with the degree of exposure and body burden.

Materials and Methods

Production Scheme and Working Environment

The study was carried out on welders working in a tank manufacturing plant, where all parts of tanks are hand-fitted and high chromium alloyed electrodes are employed. Some subjects of this study worked inside the armoured cars, and therefore in a confine environment; more than one worker may weld simultaneously in the same hull; exhausters of fume are not always on or correctly directed. Other welders work "on benches", under much more favorable microclimatic conditions, at a constant temperature of 18° C, where the continuous wire welding in metal inert gas atmosphere is done.

Welding Fumes Sampling

The welding fumes samples were collected on cellulose nitrate membranes (Sartorius membranfilter SM 11306, ø 50 mm, mean pore size 0.45 µm) connected to an aspirator pump (Gelman EC 3,000). The filter holder was placed in the breathing-zone behind the welder's face mask. Flow rate averaged 12—15 l/min and the samples were collected for about 30 min each. About 15 fume samples (range of 12 to 16) were collected per worker. The one-month exposure monitoring in two subjects was modified as follows: flow rate averaged 4—5 l/min and the samples were collected for about 4 h each. Weekly exposure was resumed meaning two daily samples per worker, corresponding to a total number of ten determinations a week.

Welding Fumes Analysis

The total fumes concentrations were measured gravimetrically, by calculating the mass of the filter before and after the sampling, expressing the results in mg/M^3. The fumes were also analyzed to determine the metal content; for chromium the difference between total and hexavalent chromium was also calculated. According to recent studies (Vorphal et al., 1976) and to our own observations, a part of metallic chromium oxidizes to hexavalent state during the arc fusion. It is assumed that the hexavalent fraction coincides with the water soluble part (Tola et al., 1977).

The sample filters were boiled for 30 min in water. After filtration the solution was analyzed by atomic absorption spectrophotometry (Perkin-Elmer Mod. 403). The insoluble part of the original sample was treated with concentrated nitric acid and slowly and carefully evaporated to dryness. The sample was recovered with 5% nitric acid, transferred to 25 ml bottles and examined by atomic absorption spectrophotometry.

Biological Monitoring

The monitoring of one-month exposure to chromium was performed in two subjects, respectively 31 and 33 years old, who had not been previously exposed to chromium. During the study period they welded inside of tanks, using "basic" coated high-alloyed chromium electrodes (⌀4 mm).

The urine samples were collected at the beginning and at the end of four subsequent working weeks. The polyethylene bottles for sampling were pretreated with HCl and repeatedly rinsed with distilled water. Particular care was taken to avoid contamination.

The collected samples were immediatly frozen at −20° C and the analysis was performed at most a few days later. The renal clearance of chromium was measured on the Saturdays before and after the study: 10 ml venous blood was drawn into metal-free tubes; urine samples were collected for two periods of 2 h each. The clearance was calculated on the diffusible fraction of the metal, obtained by serum centrifugation at 1,750 r.p.m. for 30 min through filtering cones (Amicon CF 50) that allowed the collection of solutes with a molecular weight lower than 50,000.

Determination of chromium in urine and in ultrafiltered serum were performed by flameless atomic absorption spectrophotometry (Perkin-Elmer Mod. 300, HGA 72), according to Schaller et al. (1973). Urinary creatinine was determined by alkaline picrate autoanalysis (Autoanalyzer Technicon).

The following investigations were performed on a group of 20 welders of the same plant:

Urinary excretion of chromium at different times after ending exposure.

Relationship between airborne and urinary chromium at different levels of chromium body burden.

Urinary excretion of several early nephrotoxicity indicators (total proteins, beta-glucuronidase, lysozyme).

The mean age of our subjects was 40 years (range 25—57); their mean working time as welders was 18.9 years (range 2—40) and their exposure to high airborne chromium concentration averaged 9 months (maximum 2 years).

The renal clearance of diffusible chromium was measured on Saturday morning. The welders were divided into four groups of five people each, for an equal number of weekly analyses. After the determination of chromium renal clearance, each group was removed from exposure and every seven days for three weeks the workers came for the collection of urine only.

The environmental and biological monitoring of exposure was performed on different days during the week preceding the clearance measurement; each welder was examined once during a whole working day. Besides chromium and creatinine, urinary indicators of renal tubular damage were always determined.

A high beta-glucuronidase urinary concentration is related to epithelial lesion through the urinary tract. Excluding aspecific causes of cellular damage (intercurrent renal diseases) this appears to be an early indicator of renal tubular damage (Franchini et al., 1978). The determination was carried out by the method of Paul et al. (1967) as modified by Leonard (1974).

Lysozymuria indicates a more selective injury of the convoluted portion of the proximal tubule, and has the same significance of a low molecular weight proteinuria (e.g., beta$_2$-microglobulin). The measurement was performed according to Prockop and Davidson's method (1964) using Behringwerke kits.

Proteinuria was determined by Donaggio's method, as modified by Heremans (1958). Electrophoresis of unconcentrated urine was performed with high resolving power cellulose acetate strips (Cellogel RS, Labometrics).

Results

The composition of the material used by examined workers and the concentration of chromium in welding fumes are reported in Table 1. The environmental results

Table 1. Composition of employed materials. Total mass of welding fumes and chromium concentrations in the breathing zone are also reported. Welding was performed with high chromium alloyed "basic" electrodes or with continuous wire electrodes for metal inert gas atmosphere welding (MIGw)

Analyzed sample	Fe (%)	Mn (%)	Ni (%)	Cr (%)
∅ 4 mm coated electrode	64.5	7.5	7.4	20.3
∅ 2 mm electrode for MIGw	64.4	7.1	7.9	20.1
Armoured steel chips	92.1	0.8	0.1	1.4
Grinding powder	30.0	0.4	0.1	0.6

Type of Welding	Electrodes per h	Breathing zone levels (mg/M^3) as Cr		
		Total mass of fumes	Chromium concentration	
			Total	Hydrosoluble
Local exhaustion systems Off				
Coated electrodes (42 samples)	32 (26—40)[b]	17.4 (7.9)[a]	0.521 (0.212)	0.350 (0.127)
MIGw (26 samples)		15.5 (6.4)	1.000 (0.427)	0.090 (0.039)
Local exhaustion systems On				
Coated electrodes (84 samples)	16 (12—24)	2.0 (0.8)	0.048 (0.021)	0.020 (0.009)
MIGw (18 samples)		1.2 (0.4)	0.017 (0.007)	0.002 (0.001)

[a] One standard deviation
[b] Range

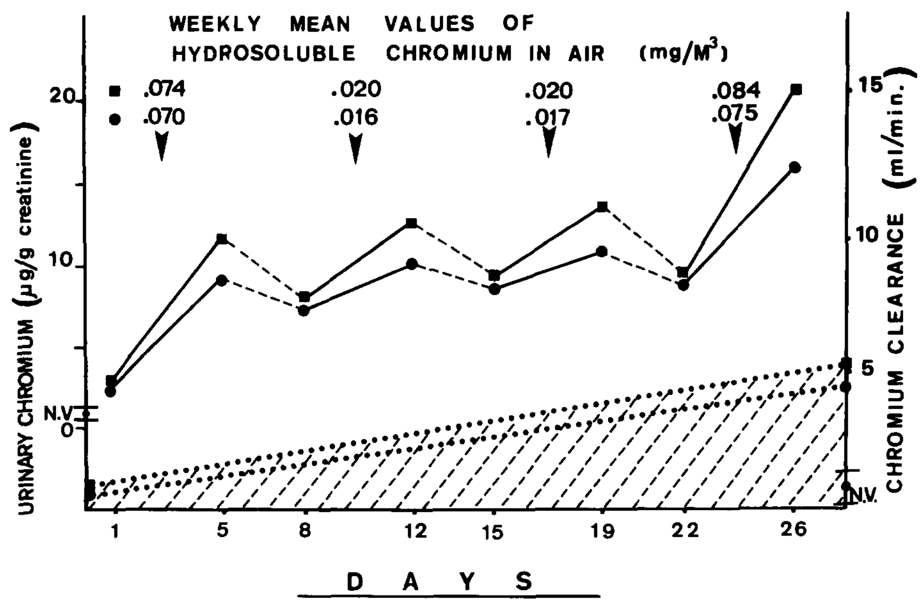

Fig. 1. Increase of baseline excretion during one month of exposure to chromium in two previously nonexposed subjects (■ F.V.; ● C.A.). Four subsequent weeks (uninterrupted lines) and the week-ends (dashed lines) are represented. For each working week the mean values of hydrosoluble airborne chromium are also reported: 4 h samples were collected at a flow rate of 4 l/min and weekly exposure was desumed meaning ten determinations a week per worker

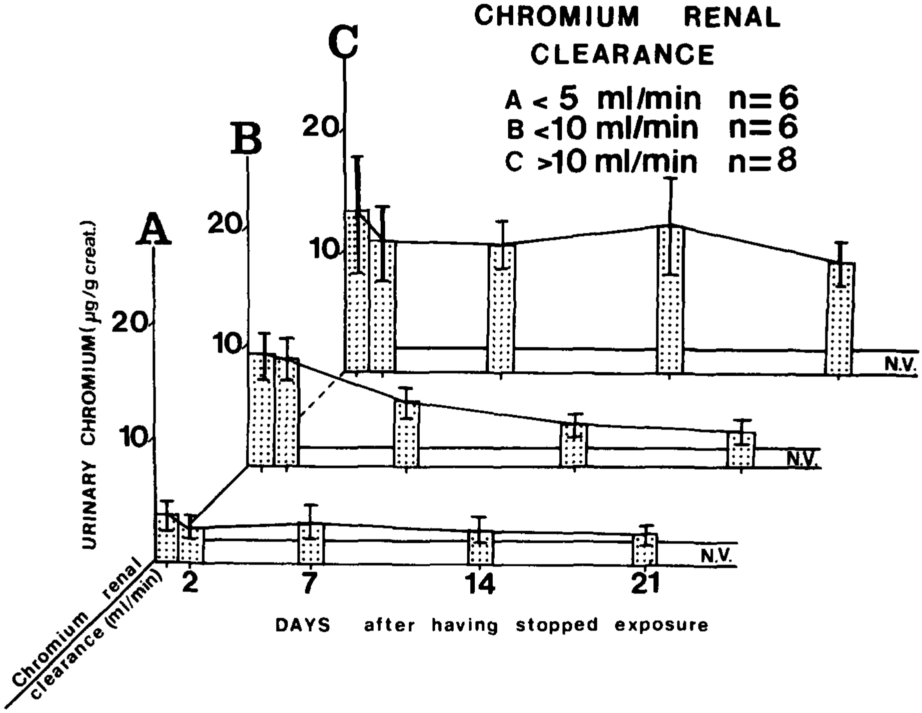

Fig. 2. Rate of reduction of urinary excretion of chromium during three non-exposure weeks in three groups of workers with different degree of body burden (as reflected by chromium renal clearance). Mean values (columns) and standard deviations (bars) are represented. The excretion remains high in group C, having a greater chromium body burden and a renal chromium clearance higher than 10 ml/min

are related both to the conditions (with or without exhausting systems) and to the rate of work (deduced from the number of electrodes consumed per unit of time).

A high chromium concentration in both types of electrodes was observed. The percentage of chromium in the welding fumes varied from 3 to 6% (averaging about 5%): most of this was released in the hexavalent state during welding with coated electrodes (between 50 and 70%). The percentage of metal released in hexavalent state during metal inert gas atmosphere welding was quite low (between 7 and 10%). Without exhausters, despite the lower percentage, continuous wire welding caused a net exposure to the hexavalent chromium similar to that found for coated electrodes.

Fume removal systems greatly reduced the degree of exposure in both groups. However, it is important to point out that, owing to the interferences with the inert gas flow, exhausting has a negative influence on the quality of soldering done with continuous wire.

The biological monitoring of chromium exposure on two welders during four working weeks is shown in Figure 1. In particular, the changes of the basal values for urinary chromium corrected to creatinine during exposure time (solid lines) and during the week-end (dashed lines) are represented. The mean values of

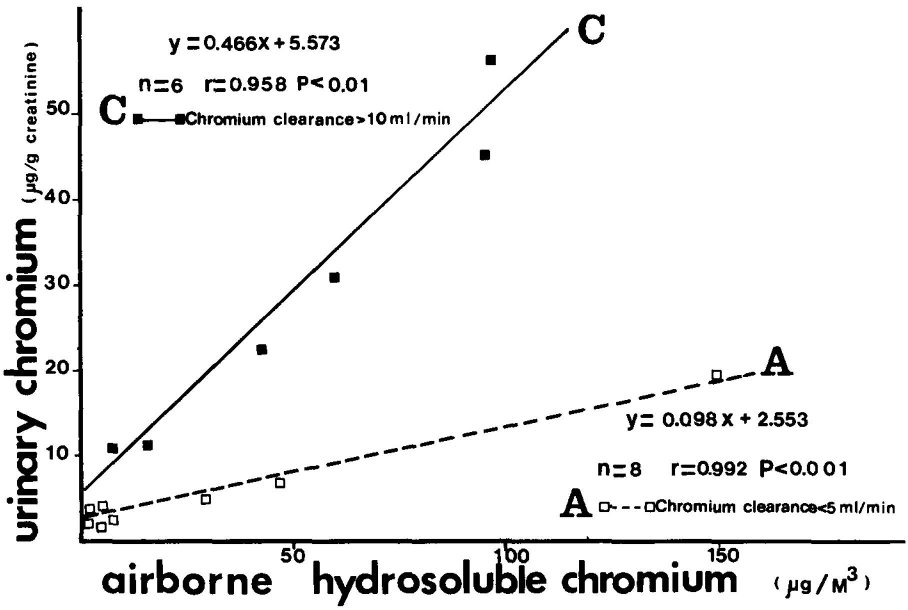

Fig. 3. Linear relationships between the airborne water-soluble chromium concentration and creatinine-corrected urine concentration at the end of exposure in two groups of welders

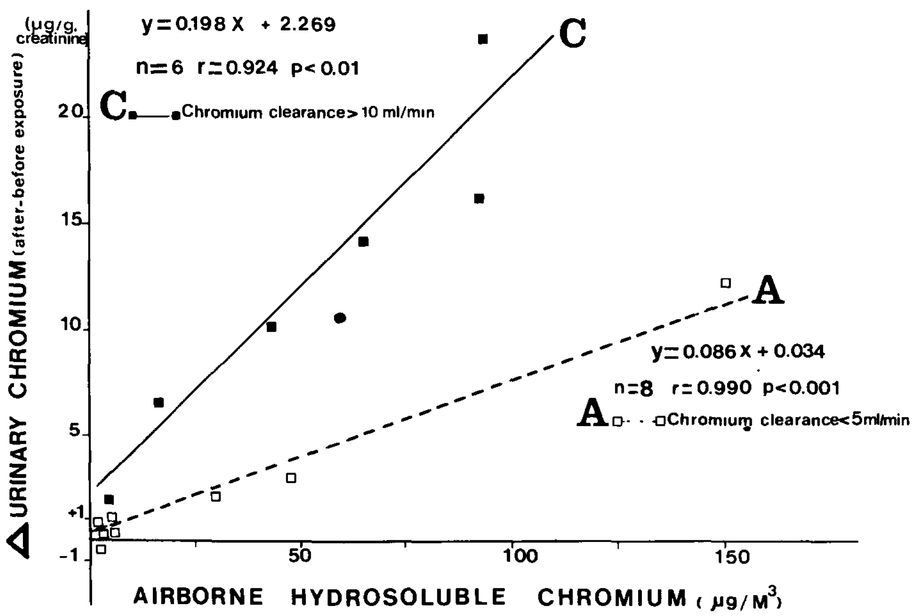

Fig. 4. Linear relationships between the airborne water-soluble chromium concentration and the rise of urinary excretion (corrected to creatinine) after exposure in two groups of welders

Table 2. Indices of renal tubular damage observed in three groups of workers, with different intensity and type of exposure to chromium. Alterations of these indices are more frequent in the more exposed groups, as shown by the urinary chromium and above all by the chromium clearance

Job and duration of exposure	Renal tubular damage indices						Exposure biological indices	
	[1] Beta-Glucuronidase (N.V. < 23 U/g creat.)		[2] Proteinuria (N.V. < 86 mg/g creat.)		[3] Lysozymuria (N.V. < 1.5 µg/mg creat.)		Urinary Chromium (µg/g creat.) mean ± SD	Chromium Clearance (ml/min) mean ± SD
	No. of workers	abnormal patterns	No. of workers	abnormal patterns	No. of workers	abnormal patterns		
A. Welding on stainless steel (4.5 ± 3.2 years)	39	—	39	—	39	—	5.3 ± 3.7	—
B. Special electrode welding on armoured steel (1.0 ± 0.4 years)	36	8 (22%) $\chi^2 = 7.51^b$	30	3 (10%) $\chi^2 = 2.03$	9	—	33.3 ± 6.9	8.8 ± 3.8
C. Chromium plating (8.9 ± 7.3 years)	24	9 (37%) $\chi^2 = 14.14^b$	24	4 (17%) $\chi^2 = 4.42^a$	24	1 (4%) $\chi^2 = 0.27$	24.5 ± 12.5	10.3 ± 5.1
Total	99	17 (17%)	93	7 (8%)	72	1 (1.5%)	—	—

[a] and [b]: Significant difference ($^a P < 0.05$; $^b P < 0.01$) versus group A

1 Beta-Glucuronidase: high molecular weight (>200,000) enzyme present in the kidney parenchyma at high concentrations. Increase in urinary beta-glucuronidase, in normal glomerular permeability conditions, is evidence of epithelial lesion through the urinary tract

2 Proteinuria: a urinary concentration higher than the mean normal value plus two standard deviations, with tubular electrophoretic aspect, was considered pathological

3 Lysozyme: low molecular weight (14,000—15,000) enzyme, physiologically filtered and almost completely reabsorbed at the tubular level. An increase in lysozymuria, without any serious haemopathy, is significant of specific proximal tubule impairment

N.V. = Normal value

airborne hydrosoluble chromium (as Cr) during the different working weeks are also indicated.

A progressive increase of the basal excretion values was observed on subsequent days: the rise was more significant in the period of greater exposure. The values at the beginning of following weeks also show the same increasing pattern, probably related to the incomplete excretion of the metal during non-exposure time. The accumulation was accompanied by a low, but significant, increase of the renal chromium clearance (dotted line).

The urinary excretion of chromium in three groups of welders after having stopped working is shown in Figure 2. The groups are distinguished according to metal body burden, as reflected by chromium renal clearance. Group A does not show any significant decrease in urinary levels, because of its low exposure. Group B shows a high rate of reduction of urinary excretion. Group C, with the greatest degree of accumulation, differs from the former two: the excretion remains high even after three weeks. It is worth to point out that the renal clearance for the subjects of group B has an average of 6.5 ml/min, which is much closer to group A than to group C.

The relevant chromium excretion, even after three weeks, seems to confirm a considerable degree of accumulation for group C and, indirectly, the validity of renal clearance as an index of chromium body burden.

The linear relationship between airborne hydrosoluble chromium and the excretion of the metal at the end of one working day are represented in Figure 3. A and C indicate two groups of workers with different metal body burden, as shown by chromium renal clearance.

The correlation is good for both the examined groups, but the line calculated for group A has a greater slope and a higher regression constant, which confirms the relationship between chromium excretion capacity and the degree of body burden.

Figure 4 represents, for the same groups, the linear regressions between the airborne concentration and the increase in urinary excretion at the end of the work.

The correlations confirm that urinary chromium is a rapid exchange compartment indicator, but solely measuring the urinary excretion does not allow to evaluate the influence of chromium body burden, which is a factor modifying both the basal excretion values and the capacity of post-absorptive excretion.

The results of urinary indicators of nephrotoxicity study are reported in Table 2. The examined subjects are compared with other groups of workers with chromium exposure differing by intensity, type, and duration.

A high prevalence of pathological patterns was observed only in groups with greater exposure to chromium, proved by the values of biological indicators of exposure or body burden. None of the less exposed subjects showed patterns of renal tubular damage.

Discussion

The analysis of environmental data shows the great variability of the concentration of chromium in welding fumes. Continuous wire electrodes for metal inert gas atmospheres welding release a lower percentage of the most important biologically hexavalent chromium. Fumes exhausting further reduces airborne hexavalent chromium to very low levels. However, if one correctly uses an exhaustion system, the quality of welding is poor, because of its interference on inert gas flow. That is why the way in which it is currently used is inadequate for workers safety.

On the contrary, in coated electrodes welding, local exhaustion systems may be correctly used, obtaining a good soldering all the same. Therefore, not only the environmental concentration of chromium can be reduced, but also that of other metals.

The monitoring of two previously non-exposed workers confirms that urinary chromium represents a rapid exchange compartment indicator. Urinary excretion of the metal is quickly modified following exposure to coated electrodes welding fumes, where hexavalent chromium concentration is high.

The slower appearance of a urinary peak after trivalent or metallic chromium exposure is due to the slower absorption rate of these fractions of the metal. The slow excretion of that fraction of chromium with a longer half-time causes a high basal excretion line and may mask the further absorption of the metal.

Despite its early appearance in urine, hexavalent chromium is not completely excreted during non-exposure periods. The basal excretion progressively rises during the working week. A rising pattern is shown even by the values found at the beginning of subsequent weeks. The increased baseline excretion may be an indication of increased body burden.

Qualitative observations on exposed workers (Borghetti et al., 1977) and the close relationship between chromium concentration in renal cortex and chromium clearance in rats (Franchini et al., 1978) suggest that renal clearance of diffusible chromium in standard conditions permits ascertainment of the extent of renal accumulation and therefore approximate evaluation of body burden. Even after short-term exposure (one month) the two studied subjects have shown a rise of this index, confirming a slight, but significant chromium accumulation.

After a week following the last exposure, urinary chromium levels also provide useful indications on body burden (Fig. 2).

The greater chromium body burden is also associated with greater excretion levels at the same airborne concentration. On the other hand, that observation is implied in the concept that renal clearance increases as the accumulation rises. Moreover, it was experimentally verified on two groups of workers, divided according to the chromium clearance (high or low), taken as an indicator of chromium body burden.

In both the examined groups the different slope of the relationships of environmental hexavalent chromium concentration versus urinary excretion of the metal (expressed either as urinary concentration at the end of exposure in Figure 3 or as daily increase after exposure in Figure 4) furtherly illustrates the aforementioned concept and also mathematically makes the possibility of basing biological limit values on air TLVs groundless. If we base biological limits on airborne chromium concentration corresponding to TLV, we would be led to the absurd conclusion that the greater the chromium body burden, the higher the allowable urinary excretion level.

A hexavalent chromium concentration in the air of 0.05 mg/M^3 as CrO_3, which is the Italian TLV, corresponds to an urinary excretion of 8 μg/g creatinine in previously nonexposed subjects (group A) and of 17 μg/g creatinine in workers with a high chromium body burden (group C).

According to the most recent literature, urinary levels of 40—50 μg/l (Gylseth et al., 1977) or 30 μg/g creatinine (Tola et al., 1977) correspond to an air concentration of 0.1 mg/M^3 as CrO_3, that is TLV for hexavalent chromium in Scandinavian Countries. Considering the different TLV, our value of 17 μg/g creatinine seems to agree with that found by Tola (1977) and proposed as a short-term exposure limit.

The kidney may be considered a critical organ for chromium (Franchini et al., 1978), nevertheless any relationship was found between the degree of exposure or body burden and early nephrotoxicity indicators. Even if no dose-effect relationship was found, the examined welders more frequently showed pathological patterns with respect to welders with a lower exposure. This finding proved a renal dose-response relationship for hexavalent chromium.

Conclusion

Urinary excretion of chromium may be considered a rapid exchange compartment indicator and used as a reliable index of absorption rate, at least of the hexavalent fraction of the metal. Our results point out that the urinary concentration of chromium at the end of a working period reflects the recent exposure. For a more exact evaluation the daily increase above baseline values must be determined.

The renal clearance of diffusible chromium rises as the accumulation of the metal increases. Therefore, the chromium body burden influences the rate of port-absorptive excretion. The degree of body burden may be also evaluated by measurement of urinary excretion of chromium after a non-exposure week.

Without evaluating the degree of previous exposure, we consider the degree of recent exposure to be safe whenever the following conditions occur:

The urinary excretion does not significantly increase after a single working period, thus excluding a significant absorption of the metal.

The renal clearance of diffusible chromium is not significantly increased by occupational exposure, thus allowing us to rule out any rise of chromium body burden.

In our subjects, the abovementioned conditions were observed when the airborne chromium concentration was lower than 0.01 mg/M^3 as CrO_3, which corresponds to the TLV suggested by NIOSH (1975) for hexavalent chromium.

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References

Borghetti, A., Mutti, A., Cavatorta, A., Falzoi, M., Cigala, F., Franchini, I.: Indices rénaux d'exposition aiguë et d'imprégnation chronique par le chrome. Med. Lav. **68**, 355—363 (1977)

Franchini, I., Mutti, A., Gardini, F., Borghetti, A.: Excrétion et clearance rénale du chrome par rapport au degré et à la durée de l'exposition. Rein et Toxiques 271—281. Paris: Masson 1975

Franchini, I., Mutti, A., Cavatorta, A., Corradi, A., Cosi, A., Olivetti, G., Borghetti, A.: Nephrotoxicity of chromium. Remarks on an experimental and epidemiological investigation. Contr. Nephr. **10**, 98—110. Basel: Karger 1978

Gylseth, B., Gundersen, N., Langård, S.: Evaluation of chromium exposure based on a simplified method for urinary chromium determination. Scand. J. Work Environ. Health **3**, 28—31 (1977)

Heremans, J. F.: La réaction de Donaggio. Ses fondements biochimiques et ses applications en pathologie. III. La réaction de Donaggio dans les urines. Rev. Belg. Path. **26**, 264—311 (1958)

Leonard, C. D.: Urinary beta-glucuronidase in man: relation to urinary specific gravity and creatinine concentration. Clin. Nephrol. **2**, 41—43 (1974)

National Institute for Occupational Safety and Health: Criteria for a recommended standard... Occupational exposure to chromium (VI). Washington, DC: U.S. Government Printing Office 1975

Paul, W., Schapiro, A., Gonich, H.: Studies of uman kidney and urine beta-glucuronidase: biochemical characteristics. Enzyme **8**, 47—66 (1967)

Prockop, D. J., Davidson, W. D.: A study of urinary and serume lysozyme in patients with renal diseases. N. Engl. J. Med. **270**, 269—274 (1964)

Schaller, K. H., Essing, H. G., Valentin, H., Schäcke, G.: The quantitative determination of chromium in urine by flameless atomic absorption spectroscopy. At. Abs. Newsl. **12**, 147—150 (1973)

Tola, S., Kilpiö, J., Virtamo, M., Haapa, K.: Urinary chromium as an indicator of the exposure of welders to chromium. Scand. J. Work Environ. Health **3**, 192—202 (1977)

Vorphal, K. W., Jordan, P. T., Mathews, E. J.: Chrome alloy welding fume study. Am. Ind. Hyg. Assoc. J. **37**, 566—569 (1976)

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