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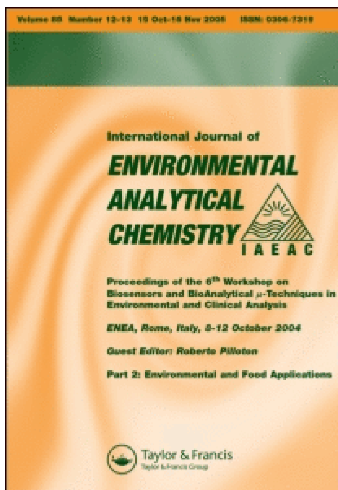

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OCCUPATIONAL EXPOSURE TO COBALT AND NICKEL: BIOLOGICAL MONITORING*

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Cobalt and nickel are industrially important metals which bear the risk of occupational cancer. In the health surveillance of workers biological monitoring provides a helpful means.

For urine, we apply a complexation and extraction of the metals in an organic solvent with subsequent ETAAS determination. Clean-up and enrichment steps result in sensitive procedures whose accuracy has been proven, e.g. by voltammetry. Metal excretions of occupationally unexposed persons have been measured (Ni, $n=123$; $m=0.6\,\mu g/L$; 95% < 1.8 μg/L; Co, $n=123$; $m=0.07\,\mu g/L$; 95% < 0.71 μg/L).

For blood and its compartments we minimized interferences by an eightfold dilution and by multistep decomposition before ETAAS determination. So we obtained simple and accurate direct procedures sensitive enough to monitor even low occupational exposures.

Forty workers of a cobalt foundry were investigated. Average air concentrations at different working places ranged between 49 and 1046 $\mu g/m^3$ which led to mean cobalt levels in whole blood between 4.9 and 47.9 μg/L and 18.9 and 438.4 μg/L urine, respectively. Between the individual blood (x) and urine levels (y) a significant linear correlation could be established ($r=0.862$; $y=7.52x-11.2$). In whole blood specimens, cobalt was bound not only to serum proteins but also to hemoglobin.

A second study was performed for 103 stainless steel welders. The external nickel exposure did not exceed two-thirds of the German Technical Guiding Concentration of 500 $\mu g/m^3$. The median nickel levels in body fluids were 3.9 μg/L (plasma) and 10.2 μg/L, respectively (urine). In none of the isolated individual erythrocyte fractions could nickel be quantified.

KEY WORDS: Occupational hygiene, nickel compounds, cobalt compounds, biological monitoring, blood, urine, preconcentration, chelation, extraction, ETAAS, DPASV.

INTRODUCTION

Nickel and cobalt are of great importance in occupational medicine. This importance is further stressed by the fact that certain compounds of nickel have shown to be carcinogenic for men. There are some hints that cobalt may have carcinogenic properties too. Biological monitoring of people occupationally exposed to these metals is therefore necessary. Because of their availability urine and blood are the materials most suitable for this purpose.

An ETAAS procedure for the determination of nickel in serum and urine has

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been accepted as a reference method by the International Union of Pure and Applied Chemistry.[1] This reference method has shown its great analytical reliability in international round robins. As in the case of an application of differential pulse adsorption voltammetry the ETAAS reference procedure necessitates however a complete mineralization of the biological matrix. Mineralization is an adequate procedure for a reference method, not for routine use. The latter, however, is by definition not the purpose of reference methods.

On the contrary to nickel there are only a few reports dealing with the determination of cobalt in urine and blood.

In this situation the working group, Analytical Chemistry of the German Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area (MAK-Commission), was occupied with the question of analytical methods for these parameters. It was our conception to have methods which are

- suitable for routine use in biological monitoring of great collectives;
- sensitive enough to determine the metal levels in biological material of persons not occupationally exposed.

As far as the detection limits were concerned the reference values published so far were used for orientation.

The values for cobalt and nickel levels in urine of people not occupationally exposed which were reported since 1970 decreased in the course of the last years to concentrations lower than 0.5 μg/L and 0.1 μg/L respectively for nickel and cobalt in urine. This decrease is more pronounced in the case of cobalt than in the case of nickel. We think that this decrease should be a consequence of the improvement of analytical methods in the last years.

Reference levels of nickel and cobalt in blood and serum (Tables 1 and 2) show the same trend during the last 15 years. The nickel levels in serum and blood dropped from values up to 15.0 μg/L to at least one-tenth. The reference values for the concentration of cobalt in blood seem to be still lower than those for nickel (Table 2). Cobalt levels in blood as high as 15 and 7.7 μg/L have been reported 15 years ago. Since that time the reference values decreased by a factor of 100.

According to these normal concentrations of nickel and cobalt in biological material, the analytical methods should have detection limits of at least 0.1 μg/L.

The aim of great practicability and simultaneously great sensitivity of the analytical methods was fully achieved in the case of urine. For blood analysis practicability but not low detections limits could be realized.

MATERIALS AND METHODS

For the determination of nickel and cobalt in urine we used a chelatization-extraction procedure prior to ETAAS analysis.[2] 4 to 8 ml of urine are put into disposable polypropylene tubes. 0.5 to 4 ml of organic solvent containing the chelator is added to the urine volume. In this configuration enrichment factors up to 16 can be achieved. An ammonium salt of the hexamethylene dithiocarbamic

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Table 1 Nickel concentrations in serum and whole blood of occupationally unexposed persons as reported in literature (1970–1986)

Serum (*μg/L*)	*Whole blood* (*μg/L*)	*Authors*
2.6±0.8	4.8±1.3	Nomoto and Sunderman (1970)
2.6±1.0	–	McNeely *et al.* (1972)
4.6±1.4	–	McNeely *et al.* (1972)
15±5	–	Pekarek and Hauer (1972)
1.9±1.4	–	Janik and Kankowski (1973)
2.1±1.1	–	Nomoto (1975)
4.7±1.0	6.0±1.0	Zachariasen *et al.* (1975)
2.5±0.5	–	Gonzales *et al.* (1976)
4.2	–	Høgetveit and Barton (1976)
3.1±1.6	–	Mikac-Devic *et al.* (1977)
1.6	–	Spruit and Bongaarts (1977)
2.0	–	Spruit and Bongaarts (1977)
2.1	–	Høgetveit and Barton (1977)
1.9	–	Torjussen and Andersen (1978)
2.8±0.5	–	Salvadeo *et al.* (1979)
–	4.0	Pihlar *et al.* (1981)
5.6±1.2	–	Völlkopf *et al.* (1981)
–	1.41±0.37	Ostapczuk *et al.* (1983)
1.3±0.37	2.4±0.5	Pazzaglia *et al.* (1983)
0.46±0.26	1.26±0.33	Sunderman *et al.* (1984)
–	4.5 μg/kg (median)	Zober *et al.* (1984)
0.28±0.24	0.34±0.28	Linden *et al.* (1985)
1.7	–	Lewis *et al.* (1985)
0.62	–	Raithel *et al.* (1985)
1.0 (median)	–	Drazniowsky *et al.* (1985)
0.65±0.35	–	Andersen *et al.* (1986)
–	1.4 (median)	Christensen and Kirchhoff (1986)

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acid (0.05 M) is used for chelatization. Thirty percent xylene in diisopropyl ketone was the organic solvent. The tube is then shaken mechanically. The phases are then separated by centrifugation. Up to 50 μL of the organic layer is analyzed by ETAAS using normal or pyrolytically coated graphite tubes. After mineralization at 1000 °C atomization takes place at 2600 °C.

The described procedure for the determination of nickel and cobalt in urine has some outstanding advantages. The chelatization-extraction technique minimizes matrix interferences in the graphite tube. So aqueous metal standard solutions can be used for calibration. Time consuming standard addition technique can thus be omitted. Between-day imprecision of the methods was below 10%. The accuracy of the methods has been tested using flame atomic absorption spectroscopy in the case of nickel, and differential pulse adsorption voltammetry in the case of cobalt. Using only one disposable vessel for sample preparation, contamination problems are minimized and practicability optimized simultaneously. These characteristics together with minimal analytical background and high enrichment factors result in rather low detection limits. Using this method we are able to determine nickel and cobalt concentrations in urine as low as 10 ng/L.

Table 2 Cobalt concentrations in serum and whole blood of occupationally unexposed persons as reported in literature (1970–1986)

Serum (*μg/L*)	*Whole blood* (*μg/L*)	*Authors*
15	–	Welz and Weideking (1970)
0.23 ± 0.11	–	Behne and Diel (1972)
1.85 ± 1.32	–	Kasparek *et al.* (1972)
0.52 ± 0.43	–	Wester (1973)
7.7 ± 1.9	–	Muzzarelli and Rocchetti (1975)
0.02–0.06	–	Lins and Pehrsson (1976)
–	0.9–3.9	Curtis *et al.* (1976)
–	1.1	Ishizaki *et al.* (1977)
0.108 ± 0.06	–	Versieck *et al.* (1978)
–	0.2–1.3	Clementi *et al.* (1979)
–	10–80	Ward *et al.* (1979)
–	8–86	Ward *et al.* (1979)
–	0.5 ± 0.1	Alexandersson and Swensson (1979)
–	0.5	Lidums (1979)
1.6	2.4	Barfoot and Prichard (1980)
0.195 ± 0.015	–	Kasparek *et al.* (1981)
0.05–1.75 ♀	–	Masiak *et al.* (1982)
0.01–1.8 ♂	–	Masiak *et al.* (1982)
–	0.09–0.02	Ostapczuk *et al.* (1983)
0.15 ± 0.07	–	Andersen and Høgetveit (1984)
–	1.9 ± 1.1	Ichikawa *et al.* (1985)
–	0.24 ± 0.12	Christensen and Mikkelsen (1985)
0.28	–	Lewis *et al.* (1985)
0.1	–	Hartung (1986)

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This detection limit is sufficient to determine nickel levels in urine of occupationally unexposed persons. For instance, when looking at the cumulative distribution of nickel concentrations in urine samples of 123 women and men occupationally non-exposed to nickel, one half of all values are below 0.6 μg/L. The 95 percentile is 1.8 μg/L.

The same group of people was examined as to the excretion of cobalt in urine. The reference values are still lower there than in the case of nickel. Ninety-five percent of all persons showed cobalt concentrations in urine smaller than 0.7 μg/L. The median value is 70 ng/L. About one-quarter of all measured cobalt excretions could not be detected. They lay below 10 ng/L. This means that normal cobalt concentrations in urine are much lower than those reported till now. Still higher enrichment factors are necessary therefore to determine the whole range of normal cobalt excretion.

The analytical principle described for nickel and cobalt has shown its great efficiency also for the determination of cadmium and lead in urine.

For the determination of the metals in blood and serum we were not successful in applying chelatization-extraction procedures. For routine purposes we established an ETAAS direct method using standard addition technique for calibration.[3] To minimize matrix interferences we diluted the blood or serum samples with 0.01% Triton-X-100 to the eightfold volume. Further reduction of

Table 3 External and internal nickel exposure of different occupational groups

Working place	*Exposed persons*	*Average nickel concentration*		
		Air ($\mu g/m^3$)	*Blood/plasma* ($\mu g/L$)	*Urine* ($\mu g/L$)
Ni compounds	8	674	7.7 (b)	92.8
Co/Ni compounds	4	30	3.3 (b)	57.5
Co compounds	5	7	n.d. (b)	1.5
MMA, MIG welding	103	92	4.8 (p)	15.0

analytical background was achieved by a multistep thermal decomposition program at 100, 350, 500 and 1000 °C. Using this program there is only a minimal unspecific absorption left at the atomization step. The residual background is easily compensated with a deuterium source. The background absorption appearing just before the nickel signal is moreover clearly separated from the specific signal. The results are similar for determination of cobalt in blood.

It is an advantage of this method that the determination of the metals can be achieved without prior mineralization which is not only time-consuming but also prone to contamination. Deproteinization and matrix modification techniques led to inaccurate results. It is a disadvantage of this method that it is not possible to determine normal metal levels in blood. At detection limits of 1 $\mu g/L$ the occupationally elevated levels of nickel and cobalt in biological material can, however, be determined, making this method suitable for routine use in biological monitoring.

Using these analytical methods we examined occupational exposures to nickel and cobalt in a shipbuilding yard and in a foundry.[4,5] One hundred and three employees were engaged in welding of stainless steel using manual metal arc or metal inert gas techniques. In the foundry two minor collectives were exposed to nickel or cobalt compounds respectively, such as chlorides, sulfates, carbonates and oxides. One further group was exposed to nickel and cobalt compounds as well. The latter groups were engaged at three working places of the foundry, where, among others highly purified cobalt powder is gained for hard metal production. Thirty-one workers at four different working places were exposed to cobalt powder only.

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RESULTS AND DISCUSSION

Nickel Exposure

The average nickel concentrations in air, blood, plasma and urine are shown in Table 3. The first three lines show the external and internal exposures with nickel compounds of different solubilities. The nickel exposure of stainless steel workers is shown in the last line. At first glance these results seem to be rather confusing. But

there are some properties which they have in common. With the exception of the working place where cobalt and nickel salts are handled, the external exposure corresponds to the internal. The highest metal level in biological fluids was determined at the working place where nickel compounds are produced and packed, and the metal concentration in air was highest. The lowest external and internal exposures were measured in the cobalt salts department, where a minor nickel exposure has been detected. The welders occupy a median position in nickel exposure. It is interesting that the relations between the average nickel concentrations in urine and in air, of the different collectives, are in the same order of magnitude. Comparing our results with values reported in literature which have recently been reviewed by Sunderman *et al.*[6] it must be pointed out that external and internal nickel exposure of the welders investigated in this study is about one order of magnitude higher. This result could be verified by the values for chromium exposure.[7]

As in the case of urine the blood levels of the various collectives are in constant relation to concentration in air. It must be taken into account, however, that in the case of the welders the concentration of 4.8 μg/L corresponds to serum not to whole blood, as in the other cases. According to one of our results nickel could not be found in erythrocytes. This means that the nickel level in whole blood samples of the welders should be by a factor of about 2 lower than the value for serum. A value of about 2.4 μg/L fits better into the other results.

Correlating the nickel levels in blood and urine for all workers exposed to nickel compounds we got a statistically very strong relationship. According to this correlation the nickel level in urine is about eight times higher than in blood.

Nickel concentrations in serum and urine of welders, however, do not correlate statistically. It is interesting to note that other authors[8] reported the same observation. In spite of the missing correlations between nickel levels in blood and urine, in the case of welders on a collective basis, the relation between the nickel concentration in urine and in blood seems to be in the same order of magnitude as in the case of nickel salt production, irrespective of the different nickel species in the atmosphere. On summarizing: None of our observations is indicative for differences concerning the kinetics of uptake and excretion of nickel irrespective if nickel compounds or nickel welding fumes are incorporated. For the 103 welders, we found median values for nickel in plasma and urine were 3.9 and 10.2 μg/L, respectively. Ninety-five percentile values are 12.8 μg nickel per litre of plasma and 52.5 μg nickel per litre of urine.

Cobalt Exposure

Table 4 shows external and internal cobalt exposure of seven groups of workers exposed to cobalt metal and cobalt compounds. The average cobalt concentrations in the air of the different working places, reach from about 50 $\mu g/m^3$ (the American TLV-value) up to about 1000 $\mu g/m^3$, which is twice as high as the German Technical Guiding Concentration (TRK). The cobalt level in blood, as well as the metal concentration in urine, obviously parallels the cobalt concentration in air. There seems to be a correlation between the metal levels in biological materials and in air.

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Table 4 External and internal cobalt exposure of different occupational groups

Working place	*Exposed person*	*Average cobalt concentration*		
		Air ($\mu g/m^3$)	*Blood* ($\mu g/L$)	*Urine* ($\mu g/L$)
Reduction	12	49	4.9	18.9
Electrolysis	11	239	18.6	112.8
Grinding	6	1046	47.9	438.4
Hard metal	2	–	7.7	30.8
Co-salts	5	149	20.5	144.6
Ni-salts	8	147	9.0	118.1
Co/Ni-salts	4	576	14.2	29.2

This is a very important observation because this may mean that there is no difference between metallic cobalt and cobalt salts with respect to uptake, kinetics and elimination of this metal. This hypothesis is further confirmed by the following observations:

There seems to be a constant relation between the cobalt concentration in blood and urine irrespective of the cobalt species taken up. Regarding all 40 workers there is a strong statistical correlation between cobalt levels in blood and in urine. According to this correlation the metal concentration in urine is about eight-fold higher than that in blood. In principle, this finding is supported by other field studies which have been recently reviewed.[9]

There is still another observation which deserves attention. Cobalt concentration in the blood samples of the 40 workers do not increase during the 8 hour shift. On a somewhat lower level of significance this is true also for the metal level in pre- and post-shift urine samples. This observation means that the workers are in a dynamic steady state according to uptake and elimination of the metal and that there is no hint that some cobalt species are eliminated from the human body more quickly than others.

On the basis of these observations and further reports in literature, the German MAK-Commission established a correlation between external and internal cobalt concentration for biological monitoring purposes. According to this correlation a cobalt concentration in air of $50\,\mu g/m^3$, the American TLV, corresponds to a metal level of $2.5\,\mu g/L$ in blood and $30\,\mu g/L$ in urine.

Biological exposure limits for nickel in serum and urine are in discussion now. Surely there will not be one limit value for all nickel species, but a common value for most nickel compounds. The difference between soluble and less soluble ones, as well as nickel in welding fumes, deserves to be discussed.

CONCLUSION

At the present time there are suitable analytical methods for biological monitoring of nickel and cobalt exposed workers. Further there are data correlating metal

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concentrations in air and metal concentrations in body fluids. It should be able today to estimate the total external exposure from cobalt and nickel concentrations in blood and urine. On this basis biological monitoring can be used routinely to minimize carcinogenic risk in special and health risk in common.

References

1. S. S. Brown, S. Nomoto, M. Stoeppler and F. W. Sunderman, *Clin. Biochem.* **14**, 295 (1981).
2. J. Angerer and K. H. Schaller, *Analyses of Hazardous Substances in Biological Materials* (German Science Foundation, VCH Verlagsgesellschaft, Weinheim, 1985), Volume 1.
3. J. Angerer and K. H. Schaller, *Analyses of Hazardous Substances in Biological Materials* (Deutsche Forschungsgemeinschaft, VCH Verlagsgesellschaft, Weinheim, 1988), Volume 2.
4. R. Heinrich-Ramm and J. Angerer. In: *Extended Abstracts from the Second Nordic Symposium on Trace Elements in Human Health and Disease* (WHO, CEC, EPA, eds.), 17–21 August 1987, Odense, pp. 70–73.
5. J. Angerer, R. Heinrich, D. Szadkowski and G. Lehnert. In: *International Conference Heavy Metals in the Environment* (T. D. Lekkas, ed.), September 1985, Athens, Vol. 2, pp. 11–13.
6. F. W. Sunderman, Jr., A. Aitio, L. G. Morgan and T. Norseth, *Toxicol. Ind. Health* **2**, 17 (1986).
7. J. Angerer, W. Amin, R. Heinrich-Ramm, D. Szadkowski and G. Lehnert, *Int. Arch. Occup. Environ. Health* **59**, 503 (1987).
8. A. Zober, K. H. Schaller and D. Weltle, *Research Report for Arbeitsgemeinschaft Eisen- und Metall-Berufsgenossenschaften* (DVS Verlag, 1985).
9. J. Angerer and R. Heinrich-Ramm. In: *Handbook on the Toxicity of Inorganic Compounds* (H. G. Seiler, H. Sigel and A. Sigel, eds.) (Marcel Dekker, 1988), pp. 251–264.

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