

Nickel concentration of blood, urine and sweat after oral administration

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Healthy volunteers without nickel hypersensitivity were given 5.6 mg nickel orally. The nickel concentration was assayed in urine, serum and sauna-provoked sweat from hands and trunk before and after nickel ingestion. The nickel concentration in serum increased in all subjects, and in most cases in urine, but not decisively in sweat.

Key words: Nickel – oral provocation – serum – sweat – urine.

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Patients with a contact allergy to nickel often develop a chronic hand eczema of the pompholyx type (Christensen & Möller 1975a). We have earlier shown that this eczema may flare after oral ingestion of the antigen (Christensen & Möller 1975b), and this has lately been confirmed (Kaaber et al. 1978). Results of three recent studies (Menné & Thorboe 1976, Kaaber et al. 1978, de Jongh & Spruit 1978) speak in favor of a positive correlation between eczematous activity and urinary excretion of nickel. It therefore seemed warranted to establish the relationship if any between orally administered nickel on the one hand and nickel levels of body fluids on the other. Thus, in the present study, the nickel concentration in blood, urine and sweat was assayed in healthy subjects after oral ingestion of a nickel salt.

Material and Methods

There were 16 healthy volunteers, 10 females and six males, aged 20–35 years, with

no history of metal hypersensitivity. Morning urine was collected and a venous blood sample taken. Hands and wrists were washed for 3 min in a 5 ml PhisoHex®-tap water solution, and rinsed thoroughly with 300 ml distilled, deionized water (DDW). The hands were then air dried and dressed in polyethylene plastic gloves (Dispos-A-glove®) for collecting sweat. For the same purpose a 15-l plastic bag was applied against breast and abdomen. The experimental subject was seated in a 75°C dry sauna bath for 30 min. The sweat produced was collected by puncturing the plastic bag with Pasteur pipettes; cell-free supernatant was obtained by centrifugation.

Each subject was then given a capsule containing 25 mg nickel sulfate ($\text{NiSO}_4 \cdot 6\text{H}_2\text{O}$) in lactose with a nickel content of 5.6 mg. After 2 h the procedure with blood sampling, hand wash and plastic application was repeated and after a further .5 h the subject was seated in the sauna bath for another 30 min of sweat collection. All urine voided up to 7 h after nickel ingestion

Table 1. Temperature program

Spectrometer:				
Mode	Single beam			
Spectral lamp	Nickel hollow cathode			
Lamp current	7-8 mA			
Photomultiplier	R 372			
Slit width	0.3 nm			
Wave length	232.0 nm			
Recording	Peak height with recorder			
Scale exp.	× 5			
Flameless sampler:				
Type	Rectangular graphite tube with microboats			
Mode	Automatic			
Pressure	Atmospheric			
Purge gas	Argon			
Gas flow rate	20SC FH			
Indicated temperature (°C):				
20-600	600-1325	1325	1325-2700	2700
1	4	8	0	2

was sampled together. All blood, urine and sweat was collected in acid-washed containers.

In another experiment nickel provocation was carried out in six subjects as above but the second sweat collection was delayed until 6 h. Blood and urine were not sampled in this study.

For all the absorption measurements the Instrumentation Laboratory Inc (IL) 151 single-beam atomic absorption spectrophotometer was used along with an IL Model 555 Flameless Sampler. To record the absorbances a strip chart recorder (Philips) with a response time of 0.2 sec full scale was used.

The samples were pre-ashed in an ordinary laboratory oven. An aliquot of 30 μl serum, sweat or urine was directly placed in graphite microboats (IL) and 16 boats with samples were located on a probe plate made of titanium with appropriate dimensions for the laboratory oven.

The serum samples were preheated at 100°C for 5 min, 150°C for 2 min, 220°C

for 5 min and after that, up to 700°C for 1 minute. The urine and sweat samples were treated similarly except for a final temperature of 550°C . Prior to pre-ashing of the urine samples, 5 μl of conc. HNO_3 (supra pure) was added in order to eliminate salt effects.

After the pre-ashing treatment the graphite boats on the probe plate were taken out and left for a couple of minutes to cool. The graphite boats with the pre-ashed samples were placed in the graphite oven and the temperature program presented in Table 1 was run.

All samples were assayed in duplicate and mean values of the two results were accepted. The reproducibility of these assays was $\pm 5\%$.

Results

The *urinary excretion* of nickel before and after oral administration of nickel sulfate is shown in Table 2. One subject did not void any urine during the 7-h observation time. Among the other 12 subjects nine excreted more nickel after the ingestion than before.

In the 12 subjects in which *blood* samples were obtained before and after nickel administration, the nickel concentration in serum increased in all cases after ingestion (Table 2). The mean concentration before nickel ingestion was $4.9 \mu\text{g/l}$ (range 2-12) and after $23.6 \mu\text{g/l}$ (range 6-67).

The nickel concentration and sample volumes of *sweat* are also given in Table 2. In the 3-h study, sweat samples from the trunk were obtained in all cases before and after nickel administration. From the hands sweat could be collected before and after nickel administration in only eight of 13 subjects. The nickel concentration in sweat, from trunk as well as from hands, did not show any tendency to increase after nickel ingestion. In general, the nickel concentra-

Table 2. Nickel concentration in urine, serum and sweat before and after ingestion of 5.6 mg Ni. The volumes are given in parenthesis

Subject no.	Morning urine Total Ni µg	Urine up to 7 h after Ni ingestion Total Ni µg	Morning serum Ni µg/l	Serum 2 h after Ni ingestion Ni µg/l	Hand sweat before Ni ingestion Ni µg/l	Hand sweat 3 h after Ni ingestion Ni µg/l	Trunk sweat before Ni ingestion Ni µg/l	Trunk sweat 3 h after Ni ingestion Ni µg/l
1	2.1 (262)	1.6 (800)	2	27	8 (5)	5 (5)	9 (20)	6 (20)
2	16.5 (170)	5.5 (460)	12	67	158 (1)	No sweat	3 (20)	2 (20)
3	2.0 (152)	11.5 (220)	5	38	No sweat	11 (1.5)	2 (12)	8 (13)
4	1.7 (244)	4.3 (104)	3	9	No sweat	21 (1.5)	7 (10)	5 (10)
5 ♂	15.7 (190)	13.7 (390)	7	22	32 (9)	3 (18)	4 (40)	1 (30)
6	17.2 (350)	21.15 (235)	7	21	29 (5)	36 (3)	3 (18)	2 (18)
7	4.5 (140)	6.53 (284)	4	8	30 (2)	115 (2)	20 (10)	1 (10)
8	1.7 (90)	18.8 (250)	3	35	100 (1)	No sweat	7 (15)	7 (12)
9	1.2 (230)	3.0 (210)	3	No serum	51 (3)	43 (2.5)	4 (20)	3 (25)
10 ♂	0.5 (275)	3.5 (250)	5	7	No sweat	18 (3.5)	14 (22)	5 (16)
11 ♂	2.8 (220)	32.9 (310)	7	20	26 (6)	25 (3.5)	4 (25)	5 (20)
12	1.0 (95)	0	2	6	14 (5)	68 (3.5)	2 (15)	4 (12)
13	2.8 (105)	16.2 (170)	4	23	85 (5)	32 (5)	2 (8)	4 (12)

Subject no.	Hand sweat 6.5 h after Ni ingestion	Hand sweat 6.5 h after Ni ingestion
14 ♂	20 (8)	21 (20)
15 ♂	59 (10)	48 (10)
16 ♂	32 (5.0)	36 (4)
3	72 (3.5)	145 (12)
5 ♂	59 (10)	35 (30)
13	48 (3.0)	30 (6)

tion in hand sweat was higher than that in abdominal sweat.

In the 6.5-h study, the nickel concentration in trunk sweat was somewhat higher than after 3 h. Nickel excretion did not increase after provocation, either from the trunk or from the hands. On the whole, the individual variation in nickel concentration and sweat volume was great.

Two random samples of 5 ml Phisoex contained 0.32 and 0.75 μg nickel, respectively. Four random samples of 300 ml rinse water (including nickel in Phisoex) contained 114 and 111 μg nickel (subject no. 3), 35 and 34 μg nickel (subject no. 5).

Discussion

Normally, urinary excretion of nickel varies between 2.5 and 7.9 $\mu\text{g}/24\text{ h}$, the variation apparently being due to environmental exposure (McNeely et al. 1972, Spruit & Bongaarts 1977, Menné et al. 1978). Roughly the same amount was recorded in our study performed on morning urine samples. After oral administration of nickel sulfate, the excretion increased in nine of the 12 healthy subjects studied. These results agree with those of Menné et al. (1978), who found an increased nickel excretion in all of 13 patients with psoriasis or leg ulcer. Conversely, Kaaber et al. (1978) observed diminishing urinary excretion of nickel in patients on a low nickel diet.

Also blood levels of nickel vary with environmental exposure. Normal values of 1.6–4.6 $\mu\text{g}/\text{l}$ have been published (McNeely et al. 1972, Spruit & Bongaarts 1977) which is fairly close to the mean concentration found in our healthy subjects. In all subjects the serum nickel concentration increased after oral ingestion, the average increase being about five times.

It is known that nickel is excreted also in sweat (Hohnadel et al. 1973). Although our sampling technique and thereby

volumes differed somewhat from those of Hohnadel et al. (1973), we registered about the same nickel concentration in sweat from a similar anatomical region. In the two studies, variation between individual values has been great. The amount of nickel in hand sweat was generally higher than that from the trunk which should agree with the fact that hand sweat usually is more concentrated than that from the body (van Heyningen & Weiner 1952).

Certain amounts of nickel were found in the solutions used for hand wash. This can not, however, explain the regional difference since Bang Pedersen et al. (1974) found 3 min of hand wash sufficient to remove nickel from the skin surface.

There was no increase of sweat nickel from hands or trunk 3 or 6.5 h after oral ingestion. Although nickel is normally excreted in both urine and sweat, a sudden overload is obviously not reflected in sweat.

Comparing the nickel levels in the three body fluids studied, that of serum most regularly reflected the oral intake. It is thus recommended that serum nickel be followed in further provocation studies.

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