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CLINICAL RESEARCH

Environmental Infection and Heavy Metal Analysis in More Than 400 Patients. Part I: Metal Analysis of Aluminium, Lead, Selenium, Zinc

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Abstract

Purpose: *Chronic diseases can develop through metabolic disturbances in trace elements and vitamins, and be maintained by environmental toxins. In order to gain more insight into these complex interactions and evaluate therapeutic regimens, we collected and analysed blood and urine from patients.*

Design: *Laboratory- and clinical-based survey.*

Materials and Methods: *Serum samples were obtained at the beginning of and during therapy from 489 patients (17–86 years; 308 males, 181 females; > 75% outpatient care, 1995–1997). Besides routine blood analyses, blood concentrations of trace elements, vitamins and environmental toxins were evaluated. The medical histories, analysis of metal ion serum concentrations (e.g. aluminium, mercury, lead, selenium, zinc) and urine analyses of metal excretions are reported and correlated.*

Results: *Serum aluminium concentrations were below 20 $\mu g\ L^{-1}$ in only 17% of initial analysis. Serum lead concentrations were below 20 $\mu g\ L^{-1}$in only 1.6% and between 20–50 $\mu g\ L^{-1}$ in only 52.1%. Serum selenium concentrations were above 100 $\mu g\ L^{-1}$ in only 14.5%. Serum zinc concentrations were below 70 $\mu g\ L^{-1}$ in 4.7%. Serial determinations during various diseases are reported, e.g. lymphoma, cirrhosis of the liver, pancreatitis, Crohn's disease, ulcerative colitis, tumours and neurological disorders. The medical history and biochemical findings, including heavy metal excretions of a patient with neurological complaints related to dental amalgam, are reported.*

Conclusions: *The results of the long-term observations suggest that serial determinations, e.g. of trace elements and environmental toxins, are essential because of the observed fluctuating serum concentrations. This is especially necessary in the pathophysiological evaluations and analyses of chronic disease development. Furthermore, serial determinations are necessary in order to adapt the appropriate therapeutic interventions and the doses of trace element therapy.*

Key words: serum metal ion concentration, aluminium, selenium, lead, copper, zinc, mercury, palladium, environmental toxins, chronic disease.

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INTRODUCTION

The increasing xenobiotic load on the human organism disturbs cellular-, and extracellular, biochemical and biophysical communications in the intra- and extracellular matrix. Therefore, it disturbs the cellular and mitochondrial defence mechanism. Alterations in energy metabolism and oxidative phosphorylation inducing chronic and degenerative diseases are the clinical consequences [1–6].

In daily medical experience this type of disease development cannot be exclusively determined within basic "routine" medical and blood analysis. Therefore, extended blood tests in more than 400 patients in my patient care unit (D. G. S. Thilo-Körner (T-K.)) were evaluated. These should improve the quality control of medical examinations, improve insight into the pathogenesis of disease development and extend therapeutic intervention therapy.

We present here the results of the metal serum analyses of 489 patients. In later reports, we will summarize the evaluation of the environmental, infection analyses and medical treatments for this group of patients.

METHODS

This evaluation involved 489 patients (17–86 years): 308 males (mean $48.6 \pm 12.2 \pm 0.75$ {mean ± standard deviation ± standard error of the mean} years), 181 females (mean $47.5 \pm 13.7 \pm 1.03$ years) who were seen between January 1995 and July 1997 in the internal medicine department of T-K. and later in an outpatient care unit (>75% as outpatients). Eighty five percent of the patients had a prolonged medical history (minimum of 6 months up to 20 years). The patients were examined medically. The blood tests were performed because of reported medical history, symptoms and pathophysiological considerations. Therefore, at the first consultation, not all tests were carried out for every patient. Treatment was based on medical history, reported symptoms and results of the laboratory tests.

Biochemical blood analyses consisted of routine analyses (differential blood counts, liver values, lipids, complement, cellular immunograms (T-,B-,NK-cells quantification), immunoglobulins, RAST food allergies, titers for yersinia (immunoblot), *Salmonella* ($n = 8$), *Shigella* ($n = 4$), *Candida* and *Aspergillus* as well as routinely between 15–30 different biochemical markers), xenobiotic toxins (e.g. p,p-DDE, p,p-1,1,1-trichloro-2,2-bis(*p*-chlorophenyl) ethane (DDT), hexachlorobenzene (HCB), polychlorinated biphenyls (PCB), pentachlorophenol (PCP), α-, β-, γ-hexachlorocyclohexane (-HCH); method: gas chromatography-mass spectometry [SIM]), serum ion and trace elements: aluminium, cadmium, copper, ion, lead (whole ethylenediaminetetraacetic acid-blood), selenium, zinc using the certified collecting tubes (Monovette system, Sarstedt Inc., Nürnberg, Germany) and appropriate standardized tests (atomic absorption, graphite channel technique; mercury: atomic absorption, hybrid technique). Metal determinations are routine analyses in our laboratory [7].

In 121 patients the total metal load was examined with 135 DMPS-test (dimercaptopropanesulfonic acid; 100 mg 10 kg^{-1} body weight); collection of urine before (I) and 120 min after (urine II) ingestion). In the two urine samples 18 different metals and creatinine were determined.

RESULTS

The primary analysis of aluminium concentration (Table 1) in 489 patients demonstrates that only 17% (n = 83) are in the double normal serum range of $< 20\ \mu g\ L^{-1}$. 1.8% (n = 9) are between 100 and 150 $\mu g\ L^{-1}$ and 0.4% (n = 2) showed more than 150 $\mu g\ L^{-1}$.

To verify that no contamination altered the aluminium concentration, the collecting tubes (Sarstedt Monovette with Li-Heparin/7.5 ml) were examined. Two days after incubation the

TABLE 1. Distribution of serum aluminium concentration ($\mu g\ L^{-1}$; normal range $< 10\ \mu g\ L^{-1}$) in 489 patients

Serum aluminium concentration $\mu g\ L^{-1}$	Percentage distribution
< 20	17
20–50	54.60
50–100	26.20
100–150	1.8
> 150	0.4

aluminum concentration was below 3 $\mu g\ L^{-1}$ (Dr Schiwara, Bremen, Germany; personal communication [8]).

The highest aluminium concentration (189 $\mu g\ L^{-1}$) was found in a female patient (aged 67 years) with Hashimoto thyroid autoimmune disease, *Candida albicans* infection, hyperlipidemia, headaches, chronic fatigue and tinnitus on both sides with increasing hearing loss. In a 48-year-old male patient the aluminium concentration was 182 $\mu g\ L^{-1}$. He reported Crohn's disease, hyperhidrosis and gold/steel/amalgam filled teeth, recurrent *Candida* infections of the gastrointestinal tract and toe nails, penicillin allergy, chronic fatigue, depression of varying intensity, cardiac arrhythmia and increased recurrent infections of the lungs and sinuses.

Observing the patients over a longer period, it becomes obvious that the aluminium serum concentration varies considerably. This is demonstrated by five patients with differing "main" diagnoses (Table 2): increasing recurrent infections of the upper respiratory system [Mu.(1), Lö.(2)], chronic lymphatic leukemia [Kö.A. (4)], immune thyreoditis [Ba.(5)]. One couple [Kö. (3, 4)] demonstrated different aluminium concentrations but live under the same conditions. Patient no. 6 had obesity (body mass index 35), uterus myomatosis and gallbladder stones as the main diagnoses.

A further example of varying aluminium serum concentrations was found in a 55-year-old male patient with xenobiotic toxin-induced chronic pancreatitis over 11 months of observation. Finally, he had to be operated on because he did not maintain the therapeutic, dietary regimen (Fig. 1). Four months before his operation, he cleaned his car with organic solvents and spilt them in the car which he drove during the following weeks. He suffered from a reactivation of his pancreatitis two days after cleaning the car.

In 380 patients, lead serum concentrations were determined before therapy was started. Because there seems to be no consensus on a "safe lead threshold serum concentration" the

TABLE 2. Variation of serum aluminium concentrations over 18 months in different patients

Patient	Serum aluminium $< 10\ \mu g\ L^{1}$					
1	70	21	25	52	30	26
2	79	26	84	39	45	66
3	56	125	28	79	57	43
4	71	25	39	17	30	
5	44	28	45	37	22	17
6	73	38	43	33	33	17

Patient information: (1) Mu.,A, 56 years old, male: IgA and IgG deficiencies, *Yersinia* infection; (2) Lö,H., 49 years old, female: hyperthyreodism, bronchiectasis, recurrent *Candida* and *Aspergillus* infections, DDT/DDE/PCB/PCP intoxication, food allergies; (3) Kö,H., 69 years old, female: rheumatic disease; cholecystolithiasis, *Yersinia* infections, food allergies; (4) Kö,A., 71 years old, male: chronic lymphatic leukemia; (5) Bä,K-P., 36 years old, male: immune thyreoditis; (6) Ni.,R., 38 years old, female: adipositas BMI 35, uterus myomatosis, toxic liver damage, T- and natural killer cell activation, cholecystolithiasis.

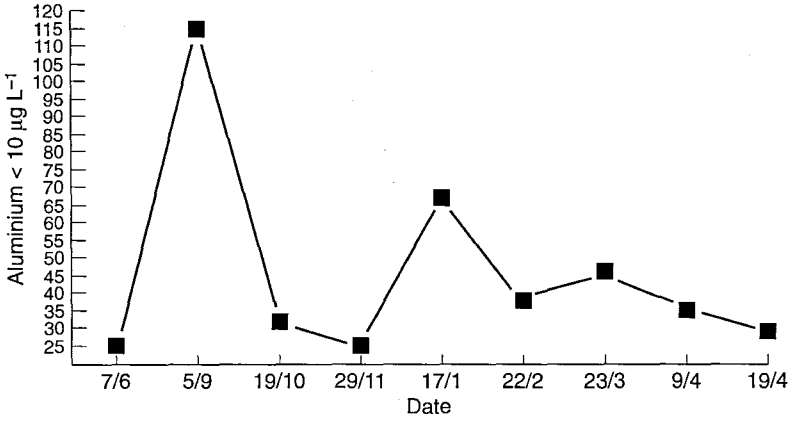

FIG. 1. Variations of serum aluminium concentration in a patient with recurrent chronic pancreatitis during an observation period of 11 months.

Patient information: Kr. HJ, 55 years old, male: CD4/CD8 between 3.55–6.06 (0.8–2.2); gallbladder fluid, obtained during cholecystectomy: HCB 9.8 $\mu g\ L^{-1}$; PCP 1.5 $\mu g\ L^{-1}$; lindane 0.04 $\mu g\ L^{-1}$; β-HCH 0.55; α-HCH 0.08 $\mu g\ L^{-1}$.

measured concentrations were divided. Only 1.6% were below 20 $\mu g\ L^{-1}$ (Table 3), 52.1% were between 20–50 μg/L (0.097–0.24 μmol L) and 34.5% between 50–90 $\mu g\ L^{-1}$ whilst 3.7% of the patients were between 90–120, 120–150 and 150–200 $\mu g\ L^{1}$ respectively. A lead serum concentration of more than 200 $\mu g\ L^{-1}$ (200–270 $\mu g\ L^{-1}$) was observed in 0.8% of the patients.

The individual variation of the lead concentrations is important in this respect [Table 4 (male); Table 5 (female)]. The diagnoses range from hypertension, heartbeat arrhythmia, depression, black tongue, uterus myomatosis, toxic liver damage or cirrhosis, disturbances of the lipid metabolism, environmental toxic load (e.g. DDE, DDT, PCB, HCB, lindane) and various combinations thereof.

Some of the female patients (1–4) had increased liver values (Table 5). Patient no. 5 had as the major diagnosis high pesticide (around 16 $\mu g\ L^{-1}$) and hexachlorobenzene levels (around 12 $\mu g\ L^{-1}$), combined with depression which had been treated with fluoxetin for about 12 years. After treatment, with for example 30 g vitamin C infusions, the blood concentrations of the environmental toxins were reduced. Furthermore, she was asked to clear her home of pesticides. Thereafter, she did not need any synthetic antidepressants and was finally able to live a normal life.

In 421 patients the selenium serum concentrations were determined before any therapeutic intervention was started. Currently, in Germany the arbitrary normal serum concen-

TABLE 3. Serum lead concentrations ($\mu g\ L^{-1}$) in 380 patients

Serum lead concentration ($\mu g\ L^{-1}$)	Percentage distribution
<20	1.60
20–50	52.10
50–90	34.50
90–120	3.70
120–150	3.70
150–200	3.70
>200	0.80

TABLE 4. Serum lead concentrations in males ($\mu g\ L^{-1}$); determinations were carried out at different intervals in each patient

Patient	Serum lead concentrations ($\mu g\ L^{-1}$) with individual time differences							
1	170	70	30	40				
2	43	71	145	42	59	31	30	
3	200	100	120	110	80	110	90	130
4	140	150	220	200	140			
5	62	187	146	101	100			

Patient information: (1) He.,M., 39 years old: toxic liver damage (alcohol induced hypertriglycemia, recurrent *Candida* infections, gamma-GT between 25–180 $\mu g\ L^{-1}$, carbohydrate deficient transferrin $< 0.8\%$, further treatment and evaluation were denied by the insurance company because of "no medical necessity"; (2) Ze.,H., 40 years old: massive lipid disturbances, triglycerides 300–6500 mg dl^{-1}, DDE (14 $\mu g\ L^{-1}$), PCB-intoxication (36 $\mu g\ L^{-1}$), vitamin C deficiency; (3) Sö.,D., 55 years old: recurrent ulcera duodeni, insomnia, recurrent *Candida* infections of the lungs and gastrointestinal tract; (4) Ba.,K., 60 years old: hypertension, adipositas, massive pain at the amputated front foot right, selenium concentration 78, not done (n.d.), 99, 121, 92 $\mu g\ L^{-1}$ and aluminum concentration 25, 39, 58, 46 and 46 $\mu g\ L^{-1}$ respectively; (5) No.,G., 89 years old: toxic liver damage, cardiac arrhythmia, cerebral insufficiency, vitamin B6 deficiency.

tration range is still considered to be between 50–100 $\mu g\ L^{-1}$. According to these limits 8.3% of the patients had a selenium deficiency (Table 6). In 10.2% of patients, serum concentrations were between 50–59 $\mu g\ L^{-1}$, 15.9% between 60–69 $\mu g\ L^{-1}$ and 14.5% were above the, "normal" range of 100 $\mu g\ L^{-1}$. If the minimum selenium serum concentrations are above 100 $\mu g\ L^{-1}$ we find that 85.5% of patients are selenium deficient (Schrauzer, personal communication 1998).

Zinc was determined in the serum of 384 patients, of whom 4.7% demonstrated a deficiency, 81.9% were in the normal range and 13.5% above the serum concentration of 130 $\mu g\ L^{-1}$ (Table 7).

The importance of serial determination of serum concentrations of trace elements is demonstrated by a 60-year-old male patient with alcoholic disease. During the observation

TABLE 5. Serum lead concentrations in females ($\mu g\ L^{-1}$); determinations were carried out at different intervals in each patient

Patient	Serum lead concentrations ($\mu g\ L^{-1}$) with individual time differences							
1	170	70	40	60	60	23		
2	230	250	180	160				
3	142	130	105	115	80	86	62	107
4	150	150	190					
5	70	100	90	50	60	60	46	

Patient information: (1) Ni.R., 38 years old: adipositas, myoma of the uterus, the aluminium concentrations were 73, 38, 43, 33, 33, 17 $\mu g\ L^{-1}$ respectively; (2) Si,K., 43 years old: recurrent *Candida* infections, black tongue, PCP-HCB intoxication, IgE 190–273 E ml^{-1}; CD4/CD8 3.27–2.74 (0.8–2.2) changing CD4 cells 921–1950 (< 1452). Essential hypertension (190/120 mmHg), aluminium and selenium concentrations were 26, 37, 40, and 25 $\mu g\ L^{-1}$ and 54, 107, 116 and 156 $\mu g\ L^{-1}$ respectively; (3) Sche,J., 43 years old: *Cytomegalovirus* infection, toxic liver damage, loss of smell, pansinusitis, cardiac arrhythmia, acne after eating pork, describes herself as a "waste retainer", recurrent pulmonary emboli (5x), recurrent *Candida* and *Aspergillus* positive serology, IgE 454–972, T-cell activation, CD57 (NK-cell) depression at the beginning of the therapy 92(> 114), DDE/DDT between 2.78–1.41 $\mu g\ L^{-1}$, lindane 0.07–0.04 $\mu g\ L^{-1}$, various RAST-IgG positive at the beginning of the therapy as well as RAST-IgE: alder, hazel and birch; (4) Pi,R., 51 years old: liver cirrhosis (alcohol induced), gamma-GT around 60 U L^{-1}, CHILD B, hyperthyroidism, IgA 477 mg d^{-1}l (< 450), IgM 585 mg dl^{-1} (< 280), selenium concentrations 44, 61 and 59 and aluminium 48, 27 and 31 $\mu g\ L^{-1}$; (5) Ma.,A., 81 years old: depression (> 10 years) treated with fluoxetin, DDE (approximately 16 $\mu g\ L^{-1}$), PCB (4.13–7.45 $\mu g\ L^{-1}$), HCB-intoxication (around 12 $\mu g\ L^{-1}$), recurrent *Candida* and urinary infections.

TABLE 6. Distribution of serum selenium concentrations in 421 patients

Serum selenium concentration ($\mu g\ L^{-1}$)	Percentage distribution
< 50	8.30
50–60	10.20
60–70	15.90
70–80	24.70
80–90	16.60
90–100	7.40
> 100	14.50

TABLE 7. Distribution of serum zinc concentrations in 384 patients

Serum zinc concentration ($\mu g\ L^{-1}$)	Percentage distribution
< 70	4.7
70–130	81.80
> 130	13.50

period and therapy over 15 months, his aluminium level varied considerably (Table 8). After a small decrease the aluminium concentration increased to 142 $\mu g\ L^{-1}$ on 25 August and then slowly went down to 23 $\mu g\ L^{-1}$ on 2 September. The lead and copper concentrations varied considerably. At the first consultation a severe selenium deficiency was found (25 $\mu g\ L^{-1}$), resulting in selenium therapy with 100 μg and later with 300 $\mu g\ day^{-1}$. The zinc concentration was stabilized by oral zinc substitution.

To determine the heavy metal load of an organism, the DMPS-test is simple, useful and routine. A representative example of the serial determinations of metals in the urine is demonstrated in the case of a female patient.

The 39-year-old adipose female patient had suffered from completely numb front thighs for 2.5 years, increasing headache, extensive pains in the feet and occasional intensive abdominal cramps. Previously she had been examined by an intermist and a neurologist. No morphological organ alterations were found. Therefore, she was considered healthy. She received vitamin B injections, which did not alter her symptoms. Besides other blood

TABLE 8. Fluctuations before and during therapy of: aluminium (AL), lead (Pb), selenium (Se), copper (Cu) and zinc (Zn) serum concentrations in a 60-year-old male patient with alcoholic liver damage

	AL	Pb	Se	Cu	Zn
7/13	42		25	115	
8/3	59	110	32	142	
8/7	38	90	63	136	
8/18	68	80	62	133	
8/25	142	70		145	
10/27	102	110	78	125	64
1/15	52	90	59	149	113
2/26	30	90	85	132	102
6/5	28	130	50	143	113
9/2	23	100	29	150	
10/7			92	137	
range	< 10 $\mu g\ L^{-1}$	$\mu g\ L^{-1}$	50–100 $\mu g\ L^{-1}$	79–131 $\mu g\ dl^{-1}$	70–130 $\mu g\ dl^{-1}$

TABLE 9. DMPS-test in a female patient (39 years old) with pain in the front side of both thighs with no explanation. After elimination of heavy metals and removal of teeth amalgam, pain reduced to zero during the following observation period. The CD4/CD8 ratio varied between 2.98–3.26 (normal 0.8–2.2).

	Urine I[1/96]	Urine II	Urine I[4/96]	Urine II	Urine I[2/97]	Urine II
Creatinine	2.52	2.34	2.06	1.99	1.78	0.87
Cadmium	n.d.	0.5/0.2	0.7/0.3	0.8/0.4	0.9/0.5	0.3/0.3
Cobalt	n.d.	1.2/0.5	1.6/0.7	1.8/0.9	5.1/2.8	4.2/4.8
Palladium	n.d.	<0.2	<0.2	<0.2	<0.2	0.4/0.4
Silver	n.d.	1.8/0.2	<0.2	2.6/1.3	<0.2	0.5/0.5
Mercury	3.9/1.5	330/141	4.1/1.9	208/104.5	<1	16.6/19

analysis we made use of the DMPS- and saliva-tests in order to evaluate a possible metal overload because of the 16 black amalgam fillings in her teeth.

In her saliva the baseline mercury concentration was 5.2 μg L. After 10 min. of chewing the mercury concentration increased 20.9-fold up to 108.8 $\mu g\ L^{-1}$. The results of the DMPS-test demonstrate a measurable concentration of silver (1.8$\mu g\ L^{-1}$ or 0.2 $\mu g\ g^{-1}$ creatinine) and a high concentration of mercury respectively (330$\mu g\ L^{-1}$ or 141 $\mu g\ g^{-1}$ creatinine) (Table 10). Urine excretion below 50 $\mu g\ g^{-1}$ creatinine has to be judged according to individual clinical history. After four months of treatment the test was repeated. A decrease in mercury and an increase in silver excretion in the urine were observed. After removing the amalgam fillings, the test was repeated after 13 months of treatment. There was a dramatic decrease in silver and mercury excretion. However, a measurable urine concentration of palladium was determined which was a result of the new gold inlay fillings which had a high palladium content. The last DMPS-test showed a decrease in creatinine to 0.87 mg L^{-1} (urine II). This suggested an alteration in kidney function independent of the normal serum creatinine concentration. Having reduced the mercury load, the patient reported that the neurological alterations and numbness decreased progressively. Unfortunately, she did not appear for further control in order to eliminate her palladium and/or evaluate possible palladium toxicity.

DISCUSSION

The increasing xenobiotic load of the biochemical, extra- and intracellular metabolism leads to an increased induction of chronic diseases [1, 2]. The symptoms thereby induced can vary considerably. Therefore, it is difficult to explain the pathogenesis and various alterations in the pathophysiological complexities of disease development in a linear way. The influence of nutritional factors on illness is well covered in an excellent source book of clinical research [8].

The problems with toxic metal exposure were anticipated by H. Schroeder in 1974 [9]. Over many years, Eric Underwood reviewed world-wide research on trace and toxic elements and his excellent book provides a detailed reference list applicable to this paper [10]. Therefore, increased metal load can induce various diseases such as immune disturbances, chronic fatigue syndrome, hypertension, various allergic and chronic diseases which have been evaluated with different methods [1, 2, 11–15]. Further basic and clinically oriented research should evaluate these aspects of synergistic interactions.

Aluminium, the third most frequent element on earth, is found in the brain, bones, lungs, muscles, liver, rectum and colon tissue and in erythrocytes [1, 16, 17]. However, the pathophysiology of aluminum accumulation and its induction of disease, especially in non-dialysed patients, has not been extensively examined.

Aluminium is considered to be a non-essential element in the human body. It is absorbed

in the gastrointestinal tract and mainly accumulates in the kidneys and parathyroid. It is excreted via the stools and, up to 90%, through the kidneys. Aluminium is taken up from the environment, nutrients and medications [18, 19]. Various interactions have been reported, e.g. with iron, zinc, fluoride, phosphorus, parathyroid hormones, transferrin, biosynthesis of neurotransmitters, hexokinase and transaminases, in erythropoesis and in diabetes mellitus [1, 20–22].

In patients with renal disease and especially in those on hemodialysis, blood aluminium concentrations of more than 50 $\mu g\ L^{-1}$ are considered toxic and increase the possibility of the development of, for example, encephalopathy and bone disease [16, 23, 24]. Aluminium is a possible factor in the induction of Alzheimer's disease as well as in alterations in the neurophysiology, because of its neurotoxicity and its accumulation in the grey matter [25]. It precipitates in the neuromelanin granules and enhances iron-induced lipid peroxidation [26, 27]. This may lead to alterations in mitochondrial metabolism. Ascorbic acid influences absorption in the gastrointestinal tract [28]. If this is in connection with vitamin-C deficiencies (below 3 mg L^{-1} or 17 $\mu mol\ L^{-1}$), which the author (TK) found in 43.2% of the male and 30.4% of the female patients (N = 176), it must be evaluated further [29].

Because of the lack of published information on aluminium serum concentrations in patients without chronic renal disease and failure, we report the serum concentrations of aluminium in 489 patients, combined with follow-up determinations. As far as we know, this is the first report of such a large group where aluminium was measured with the most accurate methods available. We have ruled out contamination during blood drawing or storage. Therefore, the reported concentrations have to be regarded as pathologic, suggesting a reduced excretion and/or an increased intake. Therapy with trace elements, vitamins and phytotherapy for the kidneys and the lymph fluid demonstrates a decrease in metal load. Further research is necessary in order to clarify the complex interactions of aluminium in patients with normal kidney function judged according to serum creatinine concentrations.

There is no safe level of lead in humans [1, 30–33]. Lead can lead to chemical sensitivity; it disturbs the glutathione system and other biochemical as well as mental processes [1, 31–36]. Lead can be ingested, for example, from sweets and the indiscriminate use of herbs [39, 40]. It can induce hypertension, allergies and pathological liver enzyme alterations. Provided that the observed fluctuations of lead serum concentrations are considered to be physiological, further research is necessary in order to explain these differences, the possible synergistic effect on other metals, and the modulation of the xenobiotic metabolism finally resulting in organ alterations and deterioration.

Selenium is regarded as an essential element as it is involved in more than 300 biochemical reactions [41–43]. Parts of our knowledge about the various functions of selenium have been recently summarized [41, 43]. Selenium influences, for example, the functions of cytotoxic lymphocytes and natural killer cells [44]. In a selected group of patients (with Crohn's disease) 40.9% showed selenium deficiency [45, 46].

The results suggest that selenium serum concentrations of more than 120 $\mu g\ L^{-1}$ reduce lead and aluminium serum concentrations. This observation has to be further evaluated in long-term studies. According to Schrauzer, all metals will influence the biochemical pathways of each other [41].

Germany is regarded as a selenium-deficient country. However, if one accepts the concentration range of between 50–100 $\mu g\ L^{-1}$, we were only able to detect 8.3% under 50 $\mu g\ L^{-1}$ and 11.2% under 60 $\mu g\ L^{-1}$ in a non-selected group of patients. However, many patients take vitamins and minerals, for example, in over-the-counter medication. This intake is seldom admitted to doctors. Therefore, it might not present the true selenium concentration.

If we accept that a selenium serum concentration of at least 100 $\mu g\ L^{-1}$ is sufficient, only 14.5% of the patients were in the "normal range". In times of increased demand a low concentration of around 60–100 $\mu g\ L^{-1}$ has to be considered as insufficient because

selenium is involved, for example, in the immunomodulation, selenium-dependent protein synthesis and for detoxification. Zinc shows a similar distribution to selenium. Zinc is an important element in our biochemical system. It influences more than 300 enzymatic reactions and modulates the toxicity of environmental toxins [1, 47].

Many publications have subjected mercury to special investigation [1, 48]. Mercury can be taken up, for example, from amalgam fillings, food and through exposure to interior latex paint [49]. It influences mental and neurological processes even at levels as low as 35 $\mu g\ g^{-1}$ creatinine [50].

Metal determinations over a longer period of time demonstrate that only serial determinations of serum concentrations will give an appropriate picture of metal intoxication and/or burden. The importance of metal analysis has been extensively demonstrated, for example, in infertile female patients [51, 52].

In spite of extensive medical and especially biochemical knowledge, it is still difficult to convince patients that metal intoxication may be an essential trigger in a vast variety of diseases and that continuous surveillance is necessary. It is even harder to convince medical insurance companies and parts of the medical community to incorporate these aspects into daily medical practice. Therefore, every effort should be made to eliminate pathological metal concentrations, to maintain them in acceptable minimal concentrations, and/or reduce great fluctuations, especially in patients with chronic diseases. This will assist the organism in its fight for a positive regulation of the xenobiotic and mitochondrial metabolism in order to cope with the burden gathered every day, especially in chronic disease.

Further basic and clinical oriented research is necessary to evaluate the various and synergistic influences of metals, the importance of trace elements [53], their induction or inhibition of our metabolism, resulting in biochemical and later on in morphological, alterations. If we learn more about the interactions, we may be able to improve our therapy in the care of chronically diseased patients.

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