

R. Hampel  
T. Kühlberg  
K.-P. Schneider  
Ä. Glass  
H. Zöllner

## Serum zinc levels and goitre epidemiology in Germany

### Serumzinkspiegel und Strumaepidemiologie in Deutschland

**Summary** Zinc is an essential element involved in many basic biochemical reactions. Animal experiments and clinical data support the hypothesis that in the presence of inadequate iodine

supply zinc deficiency may be a stimulus for the development of goitre. Within the framework of a study to record goitre prevalence and iodine supply of Germany we determined the serum zinc levels in 5 932 clinically healthy persons. The mean value was  $13.1 \pm 1.75 \mu\text{mol/l}$ . There were no differences neither in age, in sex nor in regional distribution. Furthermore there were no correlations between serum zinc level, thyroid volume and urinary iodide excretion. Only 1 % of all cases had low zinc levels ( $< 10 \mu\text{mol/l}$ ). Older people ( $> 40$  years) with lowered serum zinc levels showed significantly larger thyroids. We conclude that there is no relevant undersupply of zinc and therefore the trace element is not involved in the goitre endemy of Germany.

**Zusammenfassung** Zink ist für zahlreiche grundlegende biologische Vorgänge unentbehrlich. Aus Tierexperimenten und klinischen Beobachtungen gibt es bei Zinkmangelzuständen Hinweise auf gesteigertes Schilddrüsenwachstum und ein Absinken der zirkulierenden Schilddrüsenhormone. Im Rahmen

einer prospektiven Erhebung der Strumaprävalenz und der Jodversorgung in Deutschland bestimmten wir in 32 Regionen an 5 932 klinisch gesunden Personen auch den Serumzinkspiegel. Die mittleren Serumzinkwerte lagen bei  $13,1 \pm 1,75 \mu\text{mol/l}$ . Es gab keine Geschlechts-, Alters- sowie regionale Differenzen. Wir fanden keine signifikanten Korrelationen zwischen Serumzinkspiegel, Schilddrüsenvolumen, Knotenzahl in der Schilddrüse und der Urinjodidausscheidung. 1 % der untersuchten Personen hatten erniedrigte Zn-Spiegel, von denen die über 40jährigen ein im Median um 7 ml größeres Schilddrüsenvolumen aufwiesen.

Wir schlußfolgern, daß gegenwärtig in Deutschland kein Zinkunterversorgungszustand besteht und das Spurenelement für die Strumaendemie hierzulande keine Rolle spielt.

**Key words** Serum zinc levels – epidemiology of goitre – zinc supply in Germany – non toxic goitre

**Schlüsselwörter** Serum-Zink-Spiegel – Strumaepidemiologie – Zinkversorgung in Deutschland – Struma

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Prof. Dr. R. Hampel (✉) · T. Kühlberg  
Ä. Glass  
Abteilung für Endokrinologie  
und Stoffwechselkrankheiten  
Klinik für Innere Medizin  
Universität Rostock  
E.-Heydemann-Straße 6  
18055 Rostock

H. Zöllner  
Institut für Hygiene und Umweltmedizin  
Universität Greifswald  
Hainstraße 26  
17487 Greifswald

K.-P. Schneider  
Institut für klinische Chemie und  
Pathobiochemie  
Universität Rostock  
E.-Heydemann-Str. 6  
18055 Rostock

### Introduction

Zinc is an essential component of more than 70 enzymes. It affects important metabolic processes, cell division,

cell differentiation, growth, the immunological system, signal transmission, epithelial regeneration and endocrine functions (4, 9). Since the initial description in 1963 of a severe zinc deficiency in humans, increased clinical

attention has been paid to the trace element zinc as well (10).

Although it is nowadays considered certain that zinc deficiency is connected with greater susceptibility to infection, declining skin quality, reduced sensory perception, various defined dysfunctions, growth retardation and reproductive function disorder, the influence of zinc on the functional and morphological integrity of thyroid gland is still almost entirely unexplored. It is possible that zinc – like selenium – is a necessary co-factor for type 1 iodothyronine deiodinase, and reverse triiodothyronine and shares in the further metabolism of thyroid hormones (1, 8, 15). In cases of zinc deficiency, a lower serum thyroxine level has been observed both in animal experiments and in humans, together with higher TSH measurements, which proved reversible once the zinc deficiency had been overcome (1, 2, 8, 14, 15). In animal experiments zinc deficiency has given rise to goitre. Iodine and zinc have a synergistic effect on goitre formation (1).

The modern trend towards foodstuffs which are low in energy and rich in roughage could encourage zinc deficiency. It remains to be seen whether, in addition to the existing iodine deficiency in Germany, a possible undersupply of zinc may play a part in the epidemiology of goitre.

## Methods

In the context of a prospective investigation in 1994 of goitre prevalence, iodine intake and exposure to goitrogenic environmental substances (5, 6), we also collected serum samples in 32 regions of Germany to determine the serum zinc level in 5 932 clinically healthy persons of both sexes and all age groups. The fresh serum was immediately deep frozen and stored at -20 °C until analysis. The test subjects of approximately the same number for each age group and sex were recruited on a voluntary basis in each region from kindergardens, schools, professional training institutions, firms, old age homes and out of their own initiative. To minimize the diet induced undulations of serum Zn-levels as well as excretion of iodine in urine, all samples must be collected in the morning before breakfast. Unfortunately this is practically impossible in large epidemiological studies. However this limitation of the study would be statistically insignificant when applied to very large sample collection. To eliminate the influence of age on creatinine clearance in persons under 18 years after considering the body surface area we used the method after Remer et al. (11). This made it possible to avoid the misinterpretation of urine iodine excretion.

A detailed questionnaire on the history of the thyroid gland and on nutrition served to collect data on the iodine supply, possible iodine contamination, intake of me-



**Fig. 1** Goitre prevalence (% fat numbers) and urinary iodine excretion ( $\mu\text{g}$  iodide/g creatinine – number within the circle) in Germany ( $n = 5\,932$ ) (5, 6)

dicines and basic nutritional habits. By means of atomic absorption spectrophotometry (AAS) the determination of zinc in the serum was performed after deproteinisation with trichloroacetic acid.

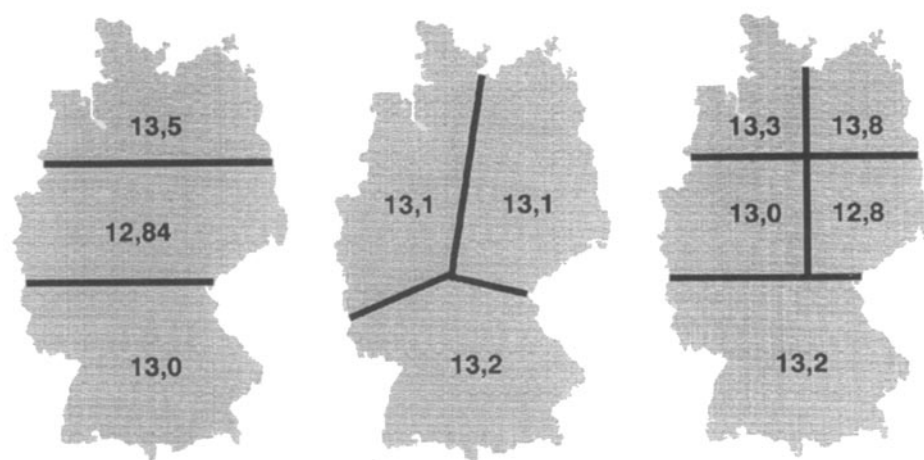
The statistical analysis was conducted with the help of the SPSS packet.

## Results

Of the 5 932 persons studied, 3 692 were female (average age  $41 \pm 17$  years) and 2 240 were male (average age  $39 \pm 18$  years). The goitre prevalence and the urinary iodine excretion as a measure of the alimentary iodine supply can be seen in Fig. 1.

The serum zinc results gave an average of  $13.1 \mu\text{mol/l}$  with a normal distribution. 95 % of the values were in the range  $9.7$  to  $16.6 \mu\text{mol/l}$  (Tab. 1). Presently the range considered normal is  $10$ – $18 \mu\text{mol/l}$  (13). The women evidenced a significantly lower average serum zinc level than the men ( $13.02 \mu\text{mol/l}$  versus  $13.34 \mu\text{mol/l}$ ). In the cluster analysis the women predominated with measurements slightly below the average for all the random samples. Nevertheless, these differences, which can be

**Fig. 2** Regional distribution of median serum zinc levels ( $\mu\text{mol/l}$ ) in Germany ( $n = 5\,932$ )



measured biometrically, are of no practical importance because they differ narrowly within the normal range. Irrespective of sex, the zinc levels were slightly lower over the age of 60. There was a positive correlation between zinc levels and body mass (Tab. 2). No statistical correlation were found between zinc and thyroid size, number of thyroid nodules or urinary iodine excretion, the main marker of iodine intake (Tab. 2). Also there was no regional variation in the zinc levels of the population of Germany (Fig. 2).

**Table 1** Serum zinc levels ( $\mu\text{mol/l}$ ) in 5 932 clinically healthy persons in 32 regions of Germany

	$\bar{X}$	s	median
all	13.1	1.75	13.0
female	13.02*	1.71	13.0
male	13.34*	1.79	13.0

\*  $p < 0.001$ ; 95 %-range: 9.7–16.6;  $\text{Zn} < 10$ :  $n = 59$  (1 %)

**Table 2** Correlations between serum zinc levels and other parameters

	r	p
age	-0.05	0.001
body mass	0.09	0.0001
thyroid volume	0.0065	ns
thyroid nodules	0.0071	ns
urinary iodide excretion	0.0092	ns

**Table 3** Serum zinc levels and thyroid volume (median) in relation to age

age (years)	Zn ( $\mu\text{mol/l}$ )	thyroid volume (ml)
< 40	normal	17.5
< 40	< 10	17.2
> 40	normal	23.1
> 40	< 10	29.9

We were able to confirm the known tendency of low zinc levels in pregnant women. 36 of the women in our sample were pregnant. Their average zinc level amounted to  $12.3 \pm 2.9 \mu\text{mol/l}$ . As thyroid size was mostly influenced by the age of the mother (22–38 years) and the duration of pregnancy (4th–36th week), low zinc levels showed no statistical correlation.

Only 1 % of the total sample produced zinc results less than  $10 \mu\text{mol/l}$ . Among persons over 40 years we observed a negative relation to the thyroid volume. The persons in this group had a thyroid on an average 6.8 ml larger than persons of the same age with zinc measurements in excess of  $10 \mu\text{mol/l}$  (Tab. 3).

## Discussion

Since zinc concentrations vary in the various tissues, the methods for obtaining the most reliable evidence of a true zinc deficiency are still a matter of debate. However, in epidemiological context, the serum zinc level is considered a sufficiently reliable parameter because hypozinaemia can be regularly demonstrated in cases of alimentary zinc deficiency (7, 12). Despite the reality of overeating in Germany in relation to energy expenditure, there is a trend towards consuming less meat and more fibre rich food. This might result in lower intake of zinc or in decreased zinc absorption (4, 7, 9). The average serum zinc levels quoted for Germany in 1992 amounted to  $16.8 \mu\text{mol/l}$  for men and  $16.2 \mu\text{mol/l}$  for women (3). The mean value which we ascertained for Germany in 1994 was considerably lower at  $13.1 \mu\text{mol/l}$ . Even so, this does not constitute a zinc deficiency. We were not able to prove a relationship between zinc levels and goitre prevalence, thyroid size, number of thyroid nodules or iodine supply. Only 59 persons (1 % of the sample) had zinc levels that were too low. Among these, persons over 40 years evi-

denced a considerably greater thyroid volume than those persons of the same age with normal zinc levels.

## Conclusions

There is no statistically relevant zinc deficiency in Germany. There is merely a trend to a greater thyroid volume from middle age onwards when the serum zinc

level falls below 10  $\mu\text{mol/l}$ . Estimation of zinc levels in elderly persons with goitre of unknown etiology is recommended. Presently the zinc status of the population of Germany is of no importance for the epidemiology of goitre.

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