

## SERUM ZINC IN CHILDHOOD PNEUMONIAE

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One begins to discuss the biological significance of zinc when Raulin (1869) proves that zinc presents an obligatory element for the growth of *Aspergillus niger* and later on it is established that it is necessary for the normal development of plants (Maze, 1914) and animals (Todt et al., 1934)(4,5,7). The supervening versatile research enriched our knowledge about the biological role of zinc, i.e. it is a component of numerous metal enzymes, participates in the metabolism of nucleic acids and in protein synthesis, possesses a cell membrane stabilizing function and enhances erythrocyte affinity towards oxygen [5-7,11-13]. Dependence between zinc content in the organism and immunity as well as its relation to inflammatory diseases is of particular interest, indeed.

Zinc deficit induces various disturbances in the immune system - lymphoid tissue hypoplasia, disorders of lymphocytic count and transport, disturbed regulation of phagocytosis - mainly disturbances of cell-mediated immunity and subsequent reduced resistance towards infections [5,7,8,10,13].

Recently, numerous investigations demonstrate that zinc is reduced in almost all acute and chronic inflammatory diseases [7,8].

The purpose of the present investigations consists in the revealing of the influence of serum zinc on the nature of the course of childhood pneumoniae. The following tasks are to be solved in our trial:

- a) to examine serum zinc level in children with acute and protracted pneumoniae;
- b) to follow-up some immunologic parameters in these children;
- c) to establish a correlation between serum zinc level and these parameters of immunity.

### MATERIAL AND METHODS

Serum zinc level was examined in 50 children treated in the First Pediatric Clinic of the Department of Pediatrics, Higher Institute of Medicine, Varna, on the occasion of pneumoniae. The course of pneumonia was protracted (duration of the disease between 35 and 64 days) in 35 children. A part of these patients have come and admitted to this Clinic from other hospitals because of their severe state and/or because of resistance towards treatment administered there. In 8 cases the pneumonia appeared for the second or even for the third time during the previous two years. Blood picture was typical of an inflammatory disease in all children - accelerated ESR, leukocytosis, shift to the left of the differential count, most often there was a manifested anaemia, hypo- and dysproteinaemia. The course of pneumonia was acute in the rest 15 children (between 20 and 28 days long) and relatively more slightly expressed.

Zinc levels were estimated during the first days of the disease and on the days of hospitalization, respectively. Zinc was determined by means of Perkin-Elmer atom-absorption spectrophotometer (No 3030 B). Serum zinc was also determined in 10 healthy children aged between 2 and 12 years (6 boys and 4 girls) who formed the reference group (controls). Results were processed by the variation analysis and then compared with Student-Fisher's test. The following immunological parameters were studied in a total of 42 children: T-lymphocytes (active - Ta and total - Tt) after Willeram's method (rosette test); phagocytic activity - INT - after Lokai's method; CIC (circulating immune complexes) - after Hashkova's method.

## RESULTS AND DISCUSSION

Mean serum zinc level was 12.17  $\mu\text{mol/l}$  in the group of 50 patients aged between 2 and 12 years. Thirty-six children were in a compact group - between 4 and 10 years of age.

Serum zinc values between 10 and 18  $\mu\text{mol/l}$  [5,6,9] and between 12.20 and 24  $\mu\text{mol/l}$  [4,5,7,13] are considered normal in children and adults, respectively, in the literature available.

Serum zinc level was within the limits of 7.37 and 16.80  $\mu\text{mol/l}$  in children with protracted pneumoniae (fig. 1). Twelve children demonstrated values below 10  $\mu\text{mol/l}$  but six ones showed

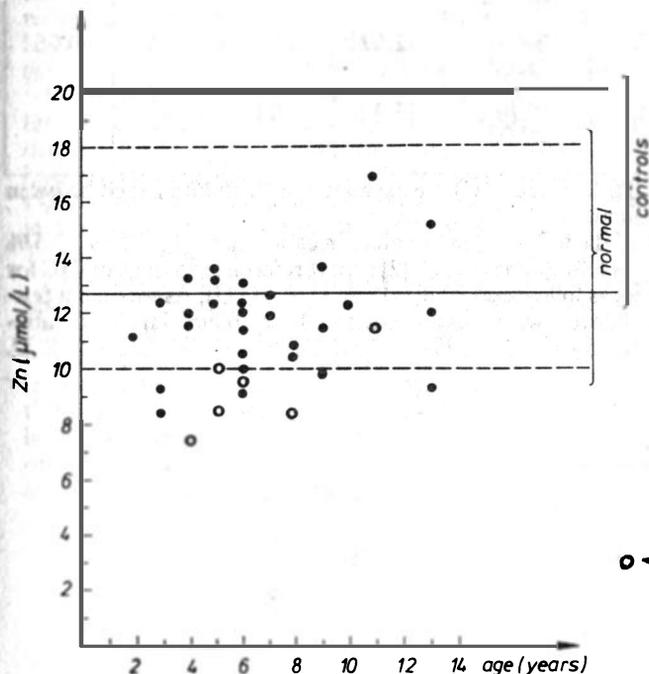


Fig. 1 Distribution of serum zinc levels in 35 children with protracted pneumoniae

○ - Legend: Serum zinc levels in most severe pneumoniae

values over 13  $\mu\text{mol/l}$ . Mean value was 11.38  $\mu\text{mol/l}$  (table 1). Besides 6 children with the longest duration of pneumonia (between 42 and 64 days) and the most severe course of the illness demonstrated the lowest serum zinc values - between 7.37 and 11.20  $\mu\text{mol/l}$  (they are obelized on fig. 1). Mean serum zinc value in children of the control group was 15.82  $\mu\text{mol/l}$  or between 12.70 and 20.05  $\mu\text{mol/l}$  (table 1). Independently of the small control group (10 children only) these values correspond to literature data available [6,7,9,12] while the difference in zinc values in children with protracted pneumoniae is clearly manifested and statistically significant (i.e. there are lower borderline values and a lower mean value in these patients).

Serum zinc levels in children with acute pneumoniae vary between 8.40 and 18  $\mu\text{mol/l}$  (fig. 2). The upper limit corresponds to the mentioned in the literature. However, only two children have similar values (17 and 18  $\mu\text{mol/l}$ , respectively). Two children show values below 10  $\mu\text{mol/l}$  while serum zinc level varies between 10 and 15  $\mu\text{mol/l}$  in the rest 11 patients. Mean value for the whole group is 12.97  $\mu\text{mol/l}$  (fig. 2, table 1). In these cases, there are smaller differences as compared with values of children of the first group. However, in most cases serum zinc level is below or on the lower limit of the reference group as well as of referenced values accepted in the literature (the difference is statistically significant)(fig. 2).

Table 1

Serum zinc levels (in  $\mu\text{mol/l}$ ) in different groups of children

Groups	n	Limit of change	Mean value	S	t	p
Protracted pneumoniae	35	7.37 - 16.800	11.38	1.92	6.40	0.05
Acute pneumoniae	15	8.40 - 18.00	12.97	2.51	3.24	0.05
Healthy controls	10	12.70 - 20.05	15.82	1.93	-	-

Some immunity parameters (Ta, Tt, INT and CIC) are examined in 30 children aged between 4 and 12 years with protracted pneumonia.

Lebenson et al. (1) have established the following main values in children: for Ta - 22.0  $\pm$  2.5 % (19.5 - 24.5 %) and for Tt - 56.6  $\pm$  9.6 %. Maneva et al. [2] report referenced values of CIC for children aged between 8 and 16 years as follows: 20.30  $\pm$  12.90 U (8 - 33 U). As we do not possess any own referenced values for children, we use as comparison these obtained from our laboratory concerning adult patients: Ta - 15 - 35 %; Tt - 45 - 75 %; INT - 280 - 600 U; CIC - 8 - 30 U.

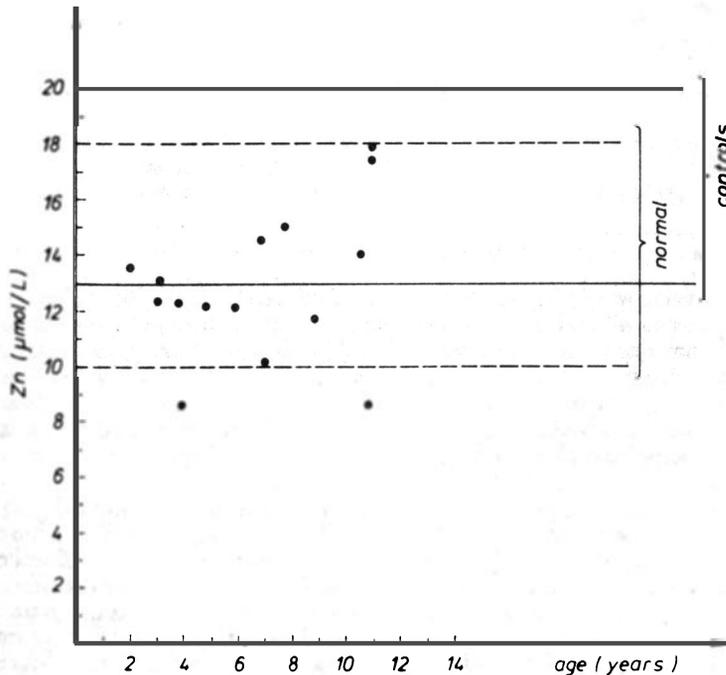


Fig. 2 Distribution of serum zinc levels in 15 children with acute pneumoniae

Active T-lymphocytes (Ta) are reduced below 15 % (between 10 and 15 %) in 19 children (in 63.33 per cent of the cases) with protracted pneumoniae which indicates a decreased cellular immunity in these children. It coincides with Matveeva' data [3] that there is a considerable lesion of cellular immunity in chronic and relapsing respiratory tract infections. Except for two patients with serum zinc level of 14 and 13.60  $\mu\text{mol/l}$ , respectively, these levels are below 12  $\mu\text{mol/l}$  in the rest 17 children and even below 10  $\mu\text{mol/l}$  in 6 of them. The course of pneumonia is more severe in these children. At the same time, Tt are within normal limits (between 45 and 69 %) in 22 patients (or in 73 per cent of the cases). Reduced phagocytic activity is established in 12 patients (or in 40 per cent) (INT below 280 U); an increased one - in 6 patients (INT over 600 U), and a normal one in the rest 12 patients (INT between 399 and 500 U). All of these 12 children with reduced INT demonstrate also reduced active T-lymphocytes (Ta below 15 %) and a serum zinc level below 12  $\mu\text{mol/l}$ . Examination of CIC does not demonstrate any abnormalities - CIC are between 8 and 22 U (mean value of 16 U) in 24 children (or in 80 per cent of the cases).

The same immunological investigations are carried out in 12 children with an acute course of the pneumonia. Ta values are reduced in 9 children (in 75 per cent of the cases). However, this decrease is less expressed than that in the first group, i.e. between 13 and 15 per cent. Serum zinc level varies between 10.41 and 13.28  $\mu\text{mol/l}$ , i.e. on the lower limit of the reference group and even slightly below it. At the same time, both Tt and CIC as well as INT do not show any abnormalities in these children. INT values vary between 300 and 420 U; CIC ones - between 9 and 24 U, and Tt ones - between 44 and 70 %.

Disorders of cellular immunity are established in more than the half of children with protracted pneumonia. They are manifested by Ta and INT reduction and low serum zinc levels. One should have in mind the role of zinc for maintenance of a normal phagocytic activity in the organism as well as the influence upon the count of active T-lymphocytes (the lower zinc level and the related inclination towards lymphoid tissue hypoplasia with subsequent Ta reduction, respectively). By this way, resistance capacities of the organism against respiratory tract infections are unfavourably influenced upon and thus restoration processes are delayed. There is a slightly expressed disturbance of cellular immunity in cases with acute pneumonia. It is manifested by Ta reduction accompanied by a less expressed serum zinc level decrease.

## CONCLUSIONS

1. There are significantly lower serum zinc levels in children with acute and protracted pneumoniae.
2. Hypozincemia is more common and more manifested in children with protracted pneumoniae - in 83 per cent of these cases against 50 per cent of children with acute pneumonia. Mean serum zinc level is considerably lower in patients with protracted pneumonia.
3. There is a reduction of the cellular immunity in about 2/3 of the children. These disturbances are most significant in children with the lowest serum zinc values.
4. Our investigations allow us to accept that serum zinc level reduction is directly related to the immunologic status (mainly to the cellular immunity) as well as to the severity and nature of the course of childhood pneumoniae.

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## СЫВОРОТОЧНЫЙ ЦИНК ПРИ ПНЕВМОНИЯХ У ДЕТЕЙ

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### РЕЗЮМЕ

При помощи атомно-абсорбционной спектрофотометрии авторы исследовали уровень цинка в сыворотке 50 детей, которые лечились по поводу пневмоний в Первой детской клинике кафедры педиатрии в Высшем медицинском институте в Варне. При сравнении с результатами исследования контрольной группы из 10 здоровых детей, у которых средняя стоимость сывороточного цинка была  $15.82 \pm 1.93$  микромол/л (нормальная стоимость составляет 10.0 - 18.0 микромол/л), у больных детей установлена ярко выраженная тенденция к гипоцинкемии. Более значительное понижение уровня сывороточного цинка наблюдалось у детей с протрагированным ходом пневмонии, у которых средняя стоимость составляла  $11.38 \pm 1.92$  микромол/л, в то время как у детей с острой пневмонией сывороточный цинк был на уровне  $12.97 \pm 2.51$  микромол/л. Приблизительно у 2/3 исследованных детей было установлено также понижение клеточного иммунитета, которое выразилось главным образом в уменьшении числа активных Т-лимфоцитов и в снижении фагоцитарной активности (INT). Эти отклонения наиболее значительны у детей с наиболее низкими стоимостями сывороточного цинка.

Результаты исследования дают основание полагать, что понижение уровня цинка в организме находится в непосредственной связи с состоянием клеточного иммунитета и с тяжестью и характером протекания пневмоний у детей.