Hrinchenko B V, Snihur O V, Flyunt V R, Zukow W. Relationships between urina lithogenicity and neuro-humoral-immune factors in patients with chronic pyelonephrite and cholecystite. Journal of Education, Health and Sport. 2015;5(5):44-51. ISSN 2391-8306. DOI: 10.5281/zenodo.17369
http://ojs.ukw.edu.pl/index.php/johs/article/view/2015%3B5%285%29%3A44-51
https://pbn.nauka.gov.pl/works/557141
http://dx.doi.org/10.5281/zenodo.17369
Formerly Journal of Health Sciences. ISSN 1429-9623 / 2300-665X. Archives 2011 – 2014 http://journal.rsw.edu.pl/index.php/JHS/issue/archive

Deklaracja.
Specyfika i zawartość merytoryczna czasopisma nie ulega zmianie.
Zgodnie z informacją MNiSW z dnia 2 czerwca 2014 r., że w roku 2014 nie będzie przeprowadzana ocena czasopism naukowych; czasopismo o zmienionym tytule otrzymuje tyle samo punktów co na wykazie czasopism naukowych z dnia 31 grudnia 2014 r.
The journal has had 5 points in Ministry of Science and Higher Education of Poland parametric evaluation. Part B item 1089. (31.12.2014).

The authors declare that there is no conflict of interests regarding the publication of this paper.
Received: 15.02.2015. Revised 27.03.2015. Accepted: 15.04.2015.

RELATIONSHIPS BETWEEN URINA LITHOGENICITY AND NEURO-HUMORAL-IMMUNE FACTORS IN PATIENTS WITH CHRONIC PYELONEPHRITE AND CHOLECYSTITE

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SUMMARY

Objective. Despite a long history of research questions about the factors that determine lithogenicity urine remains open. **Aim:** to evaluate lithogenicity urine of patients with chronic pyelonephritis and cholecystitis and find her relationships with a concentration both in urine and plasma electrolytes and nitrogenous metabolites and the parameters gall-bladder motility, HRV, EEG and Immunity. **Results.** Lithogenicity urine Index (Lith) calculated by the formula: Lith=(Oxalates•Uric acid•Calcium/Magnesium•Creatinin)^{0,2}, is determined positive by Oxalates (r=0,55) and Uric acid (r=0,34) but negative by Creatinin (r=-0,54) and Magnesium (r=-0,32). Revealed significantly correlation Lith with Uric acid Plasma level (r=-0,30) and Gall-bladder postprandial Volume, most 30 min (r=-0,51). Discovered unexpectedly negative correlation Lith with both Baevskiy Stress Index (r=-0,33) and Sympatho-Vagal Balance Index HRV (r=-0,36). Among EEG parameters correlated with Lith δ-rhythm amplitude (r=-0,50), θ-rhythm asymmetry index (r=0,45) and α-rhythm frequency (r=0,32). Among parameters of Immunity correlated with Lith blood levels of $CD19^+$ B-Lymphocytes (r=0,34) and $CD16^+$ NK-Lymphocytes (r=0,30). Canonical correlation between urina Lithogenicity and Neuro-Humoral-Immune factors is veri strong: R=0,97. **Conclusion:** in patients with chronic pyelonephritis and cholecystitis there are relationships between urina Lithogenicity and neuro-humoral-immune factors.

Keywords: lithogenicity urine, neuro-humoral-immune factors, men.

INTRODUCTION

Even in 1978. HS Tiselius [22] proposed a formulas to calculate lithogenicity urine, which are based on the concept of lithogenic ability of calcium, oxalates and uric acid while litholytic ability magnesium and creatinine.

P Brundig et al. [3,4] found that in healthy people, and even more so in patients with oxalate urolithiasis, psycho-emotional stress (exams within 6 hours) on the day of his presentation, and the next day increased concentration of urinary oxalate, calcium and uric acid and decrease magnesium. Hence, the

authors concluded that the stress load significantly increases the risk of kidney stones by increasing urinary concentrations of lithogenic substances in combination with reduced of litolytic substances.

Among patients spa Truskavets' (Ukraine) is dominated by patients with chronic pyelonephritis, including calculary and aseptic urolithiasis and urinary diathesis, often in combination with cholecystitis [6,9,11,19]. These diseases, like many others, take place on the background of chronic stress [2,5,7,12,17,18]. On the other hand, neuroendocrine stress factors affect the parameters of the exchange of electrolytes and immunity [2,12,13,16-19].

Aim our investigation: to evaluate lithogenicity urine of patients with chronic pyelonephritis and cholecystitis and find her relationships with a concentration both in urine and plasma electrolytes and nitrogenous metabolites and the parameters gall-bladder motility, HRV, EEG and Immunity.

MATERIALS AND METHODS

The object of observation were 25 men aged 24-70 (mean 50±2) years, who were treated on Truskavets' (sanatorium "Vesna") from chronic pyelonephritis in combination with cholecystitis in remission. Most of these tests were carried out twice - at admission and after 10-12 days standard balneotherapy [12,19].

In the morning on an empty stomach background electroencephalogram was recorded in 16 monopolar leads (hardware-software complex "NeuroCom Standard" produced company "KhAI-MEDICA", Kharkiv) and electrocardiogram in II lead to estimate parameters of heart rate variability [1] (hardware-software complex "CardioLab +HRV" the same production). Details in our previous paper [21].

About the Gall-bladder tone and motility, that subordinates neurohumoral influences, we judged by its Volume on an empty stomach in the morning and after 5, 15 and 30 min after drinking cholekinetic (50 ml of 40% solution of xylitol). Used method echoscopy (echokamera "Radmir").

About phagocytic function of neutrophils [8,12] judged by activity (percentage of neutrophils, in which are found microbes - phagocytic index), intensity (number of microbes, absorbed by one phagocytes - Microbial Count) and completeness (percentage of dead germs - Index of Killing) phagocytosis museum cultures Staphylococcus aureus (ATCC N 25 423 F49) and Escherichia coli (O55 K59) from chemical-biological laboratory Hydrogeological Regime-operational Station.

Immune status evaluated on a set of I and II levels recommended by the WHO, using standardized methods described in manual [14]. For phenotyping subpopulations of lymphocytes the method of indirect immunofluorescent binding reaction monoclonal antibodies [15] from company "Sorbent" (RF) with visualization under fluorescent microscope. T-cellular immunity assessed by the following parameters: blood levels of a population of T lymphocytes phenotype of $CD3^+CD4^+$(helpers/inductors). State of killer link of immunity estimated by the content of $CD3^+CD8^+$-lymphocytes (T-killers) and $CD16^+$-lymphocytes (natural killers). The state of humoral immunity judged by the content of $CD19^+$ B-lymphocytes and concentration in serum of immunoglobulins classes G, A, M (radial immunodiffusion method) and circulating immune complexes (with polyethylene glycol precipitation method).

In urine selected during 24 h were determined concentrations oxalates and nitrogenous metabolites: uric acid, creatinine and urea, as well as electrolytes: calcium, magnesium, potassium, sodium, phosphates and chloride. Nitrogenous metabolites were determined in plasma. Used unified methods [10].

Results processed by methods of correlation and canonical analysis using the software package "Statistica 5.5".

RESULTS AND DISCUSSION

Lithogenicity urine Index (Lith) we calculated by modified formula:

$Lith=(Oxalates \bullet Uric\ acid \bullet Calcium/Magnesium \bullet Creatinin)^{0,2}$

According to the correlation analysis, the greatest contribution to Lithogenicity urine Index make concentrations Oxalates (r=0,55) and Creatinin (r=-0,54), less determining its Uric acid (r=0,34) and Magnesium (r=-0 32), while the contribution Calcium lean (r=0,08).

Analysis of the relationship between urina Lithogenicity Components evidence (Table 1), that concentrations Calcium and Magnesium are quite related, which we interpret as a manifestation of contrregulation to counteract sedimentation Calcium Oxalate. Instead concentration Uric acid is not associated with any urina Lithogenicity Component

Table 1. Correlations between urina Lithogenicity Components

Concentration	Oxalates	Creatinin	Uric acid	Calcium	Magnesium
Oxalates	1,00	-0,30	-0,09	-0,40	-0,31
Creatinin	-0,30	1,00	-0,09	0,10	0,23
Uric acid	-0,09	-0,09	1,00	-0,01	0,09
Calcium	-0,40	0,10	-0,01	1,00	0,60
Magnesium	-0,31	0,23	0,09	0,60	1,00

Relationships between Urina Lithogenicity and its Components documented in Tables 2 and 3 and visualized on Fig.1.

Table 2. Canonical Weights for urina Lithogenicity and its Components

Variables	Root
Lithogenicity	-1
Oxalates	-0,670
Creatinin	0,303
Uric acid	-0,454
Calcium	-0,702
Magnesium	0,531

Table 3. Relationships between urina Lithogenicity and its Components. Regression Summary for Dependent Variable Lithogenicity

Regression Summary for Dependent Variable: LIT5

R=0,91; R^2=0,82; Adjusted R^2=0,80; $F_{(5,4)}$=37; $\chi^2_{(5)}$=73; $p<10^{-6}$; Std. Error of estimate: 0,07

Independent Variables	Beta	St. Err. of Beta	B	St. Err. of B	n=47 $t_{(41)}$	p-level
Intercpt			0,724	0,077	9,45	10^{-6}
Oxalates	0,606	0,076	0,375	0,047	7,94	10^{-6}
Uric acid	0,411	0,068	0,117	0,019	6,06	10^{-6}
Calcium	0,636	0,087	0,083	0,011	7,27	10^{-6}
Magnesium	-0,481	0,085	-0,130	0,023	-5,63	10^{-6}
Creatinin	-0,275	0,072	-0,036	0,009	-3,83	10^{-3}

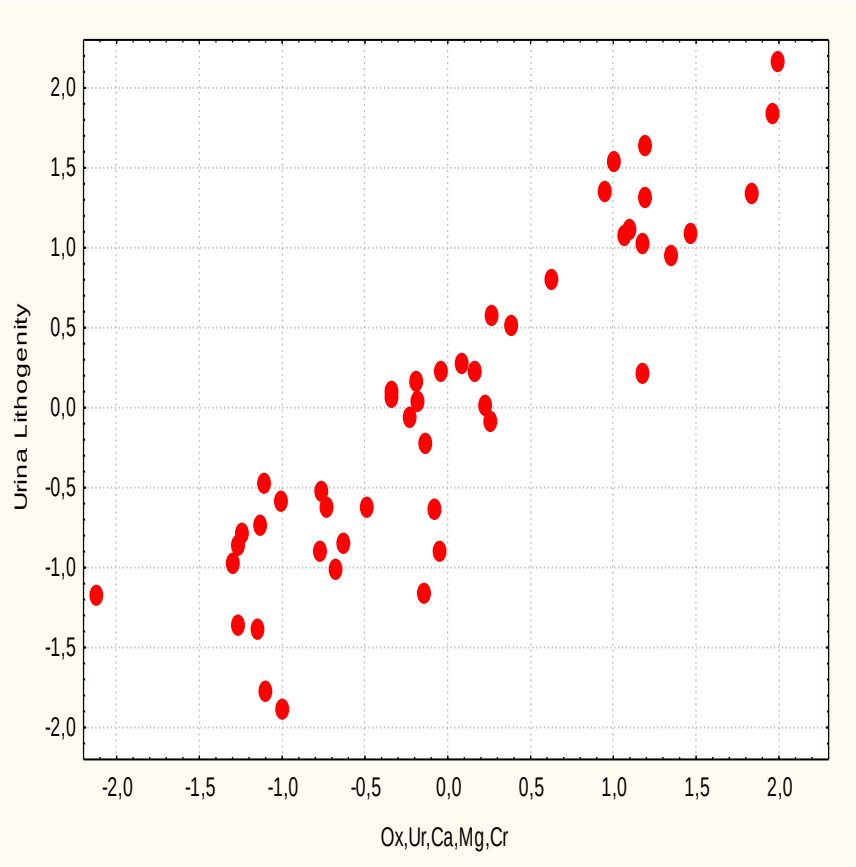

Fig. 1. Canonical correlation between urina concentrations of Oxalates, Uric acid, Calcium, Magnesiun and Creatinin (axis X) and Urina Lithogenicity (axis Y)

Urina Lithogenicity weakly correlated with Plasma levels Creatinine (r=0,20) and Uric acid (r=-0,30). There were no communications Lithogenicity with a concentration in Urina Phosphates (r=0,02), Chloride (r=0,06), Sodium (r=-0,04), Potassium (r=-0,06), Urea (r=-0,12), as well as Diurese (r=0,03).

Mean Urina Lithogenicity is 1,00±0,05, ie 164% Mean norm (0,61±0,05). It is accompanied by increased average Baevskiy Stress Index: 200±38 at a norm 135±4 and Sympatho-Vagal Balance Index: 309±52 at a norm 234±8. This is consistent with the concept of relation Urina Lithogenicity and Stress. However, contrary to expectations, we note in our contingent **negative** correlation Lithogenicity with both Baevskiy Stress Index (r=-0,33) and Sympatho-Vagal Balance Index HRV (r=-0,36). Perhaps this is due to a chronic, but not acute stress?

Recently detected correlation between indices of the HRV and parameters of ongoing EEG [20,21]. In this investigation among EEG parameters correlated with Lithogenicity δ-rhythm amplitude (r=-0,50), θ-rhythm asymmetry index (r=0,45), α-rhythm frequency (r=0,32) and β-rhythm laterality index (r=0,24).

Revealed significantly correlation Lithogenicity with Gall-bladder postprandial Volume, most 30 min (r=-0,51). Gall-bladder motility reflect probably sympatho-vagal and humoral (cholecystokinin, glucagon ect) influences.

Fees Neuro-Humoral factors to combine determine urina Lithogenicity on 78% (Table 4, Fig. 2).

Table 4. Relationships between urina Lithogenicity and Neuro-Humoral factors. Regression Summary for Dependent Variable Lithogenicity

R=0,88; R^2=0,78; Adjusted R^2=0,74; $F_{(5,3)}$=18,0; $\chi^2_{(5)}$=40,5; $p<10^{-5}$; Std. Error of estimate: 0,09

Independent Variables	Beta	St. Err. of Beta	B	St. Err. of B	n=31 $t_{(25)}$	p-level
Intercpt			1,9556	0,1544	12,67	10^{-6}
Gall-bladder postprandial volume, %	-0,585	0,102	-0,0113	0,0020	-5,72	10^{-5}
δ-rhythm amplitude, μV	-0,461	0,100	-0,0047	0,0010	-4,60	10^{-4}
θ-rhythm asymmetry index, %	0,195	0,102	0,0020	0,0010	1,91	0,067
Uric acid plasma level, μM/l	-0,340	0,100	-0,6279	0,1856	-3,38	0,002
β-rhythm laterality index, %	0,327	0,100	0,0023	0,0007	3,27	0,003

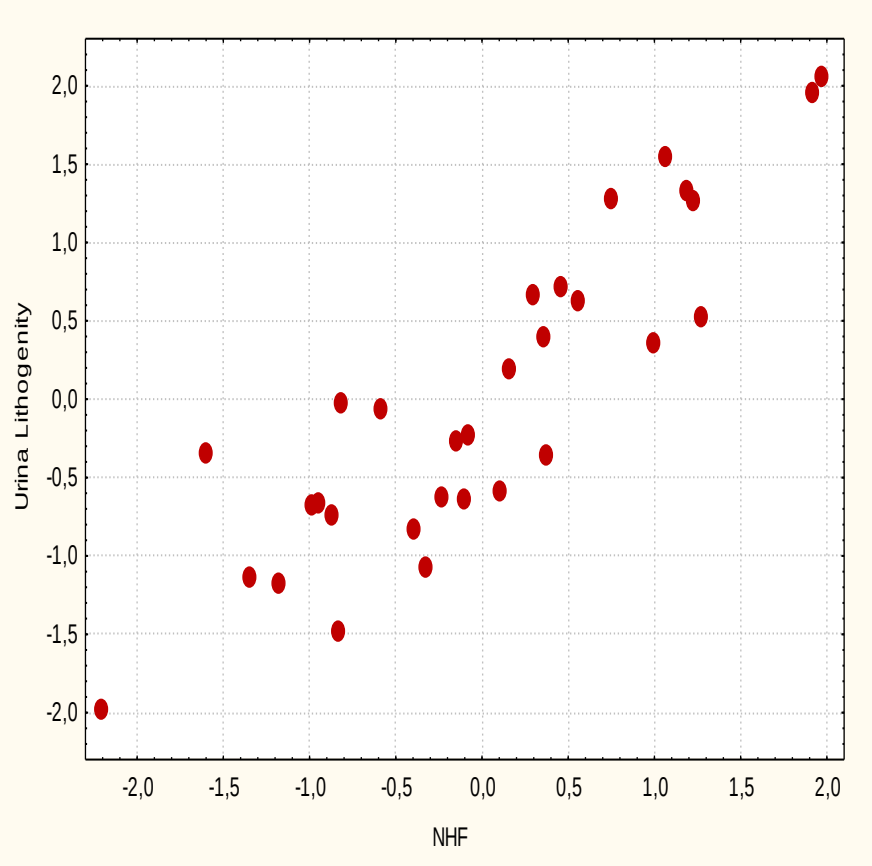

Fig. 2. Canonical correlation between Neuro-Humoral factors (axis X) and Urina Lithogenicity (axis Y)

Among parameters of Immunity correlated with Lithogenicity blood levels of $CD19^+$ B-Lymphocytes (r=0,34), $CD16^+$ NK-Lymphocytes (r=0,30) and active T-Lymphocytes (r=0,19) as well as serum level IgA (r=0,19). However, the correlation with microbial count is negative (r=-0,23). We interpret this as a defensive reaction of the immune system, aimed at preventing complications of urolithiasis pyelonephritis. Fees immune factors to combine determine urina Lithogenicity on 26% (Table 5, Fig. 3).

Table 5. Relationships between urina Lithogenicity and Immune factors. Regression Summary for Dependent Variable Lithogenicity

R=0,51; R^2=0,26; Adjusted R^2=0,17; $F_{(4,3)}$=2,7; $\chi^2_{(4)}$=9,5; p=0,050; Std.Error of estimate: 0,15

Independent Variables	Beta	St. Err. of Beta	B	St. Err. of B	n=35 $t_{(30)}$	p-level
Intercpt			0,514	0,355	1,45	0,158
$CD19^+$ B-Lymphocytes, %	0,276	0,160	0,019	0,011	1,72	0,096
$CD16^+$ NK-Lymphocytes, %	0,277	0,163	0,020	0,011	1,70	0,099
IgA serum level, g/l	0,211	0,161	0,088	0,067	1,32	0,198
Microbial count against St. aur.	-0,214	0,157	-0,005	0,003	-1,36	0,183

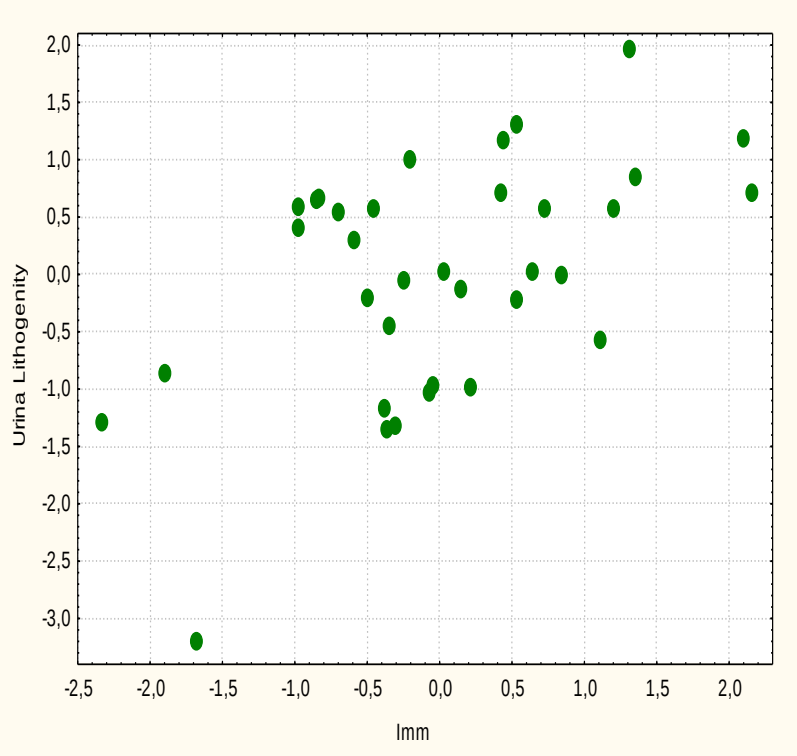

Fig. 3. Canonical correlation between Immune factors (axis X) and Urina Lithogenicity (axis Y)

Table 6. Relationships between urina Lithogenicity and Neuro-Humoral-Immune factors. Regression Summary for Dependent Variable Lithogenicity

R=0,97; R^2=0,94; Adjusted R^2=0,90; $F_{(9,1)}$=24,1; $\chi^2_{(9)}$=47,4; p<10^{-6}; Std. Error of estimate: 0,06

Independent Variables	Beta	St. Err. of Beta	B	St. Err. of B	n=23 $t_{(13)}$	p-level
Intercpt			1,95	0,31	6,19	10^{-4}
α-rhythm asymmetry, %	-0,180	0,106	-0,0018	0,0010	-1,70	0,113
α-rhythm amplitude, μV	-0,468	0,115	-0,0112	0,0027	-4,07	10^{-3}
δ-rhythm amplitude, μV	-0,574	0,111	-0,0052	0,0010	-5,16	10^{-4}
CD19 B-Lymphocytes, %	-0,354	0,103	-0,0281	0,0082	-3,44	0,004
Gall-bladder postprand. vol., %	-0,544	0,093	-0,0105	0,0018	-5,85	10^{-4}
Microbial count against St. aur	-0,173	0,085	-0,0046	0,0023	-2,03	0,063
IgA serum level, g/l	0,454	0,114	0,1815	0,0457	3,97	0,002
θ-rhythm frequency, Hz	0,370	0,105	0,0515	0,0147	3,51	0,004
Active T-Lymphocytes, %	0,402	0,085	0,0146	0,0031	4,74	10^{-3}

Overall, selected Neuro-Humoral-Immune factors associated with Lithogenicity veri strong (Table 6, Fig. 4).

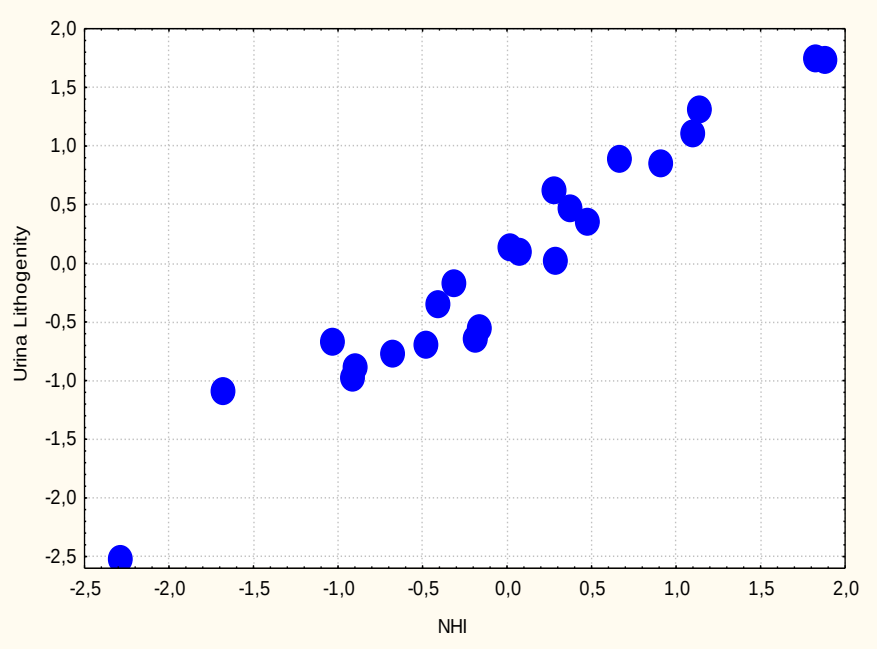

Fig. 4. Canonical correlation between Neuro-Humoral-Immune factors (axis X) and Urina Lithogenicity (axis Y)

We result opportunely matrix of relationships between Neuro-Humoral-Immune factors (Table 7).

Table 7. Relationships between Neuro-Humoral-Immune factors

Variables and its Codes	DV	AV	THz	AT	V30	MC	TA	IgA	CD19
δ-rhythm amplitude DV	1,00								
α-rhythm amplitude AV	,46	1,00							
θ-rhythm frequency THz	-,38	,28	1,00						
α-rhythm asymmetry AT	-,24	-,46	-,06	1,00					
Gall-blad postpr vol V30%	-,17	,11	-,05	-,30	1,00				
Micr. count vs St. aur. MC	,16	,23	-,06	-,26	-,30	1,00			
Active T-Lymphocytes TA	-,01	-,12	-,27	,23	,23	-,29	1,00		
IgA	,30	-,12	-,37	,57	-,44	-,08	,11	1,00	
CD19 B-Lymphocytes	-,45	-,57	-,11	,46	-,16	-,02	,35	,25	1,00

It confirms the existing concept of neuroendocrine-immune complex [16,17].

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