Kuchma Igor L., Flyunt Igor-Severyn S., Ruzhylo Sofiya V., Zukow Walery, Bilas Volodymyra R., Popovych Igor L. Varieties of the state of exchange of nitrogenous metabolites (creatinine, urea, uric acid and bilirubin) and their immune accompaniment at rats. Journal of Education, Health and Sport. 2021;11(7):228-238. eISSN 2391-8306. DOI http://dx.doi.org/10.12775/JEHS.2021.11.07.021
https://apcz.umk.pl/czasopisma/index.php/JEHS/article/view/JEHS.2021.11.07.021
https://zenodo.org/record/5167845

The journal has had 5 points in Ministry of Science and Higher Education parametric evaluation. § 8. 2) and § 12. 1. 2) 22.02.2019.

Received: 12.07.2021. Revised: 20.07.2021. Accepted: 26.07.2021.

VARIETIES OF THE STATE OF EXCHANGE OF NITROGENOUS METABOLITES (CREATININE, UREA, URIC ACID AND BILIRUBIN) AND THEIR IMMUNE ACCOMPANIMENT AT RATS

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Abstract

Background. Earlier we found that even in intact rats, certain parameters of nitrogenous metabolism and immunity fluctuate in a fairly wide range, which further expands in cases of prolonged water loads. The links between the individual parameters of metabolism and immunity were revealed. Based on this, the **aim** of this study was to create groups that are homogeneous in the parameters of nitrogenous metabolism, followed by a search for the characteristic parameters of immunity. **Material and methods**. Experiment was performed on 60 healthy female Wistar rats, both intact and loaded with different mineral waters. The plasma levels and urinary excretion of the nitrogenous metabolites (creatinine, urea, uric acid and bilirubin) were determined. Immune status was assessed by thymocytogram, splenocytogram, blood leukocytogram and immunocytogram, as well as by phagocytosis parameters of blood neutrophils and monocytes. **Results**. The characteristic features of the members of the most numerous (29 animals) of the first cluster are moderately elevated plasma urea and upper borderline creatinineemia in combination with lower borderline uricemia. In members of the third cluster (22 animals), all seven parameters are in the range of normal. In contrast, rats of the second cluster (n=9) were found to have significantly increased levels of urea and creatinine excretion, as well as uricemia. Each cluster is accompanied by a specific constellation of immune parameters. The overall accuracy of the classification is 95%. **Conclusion**. The variety of states of exchange of nitrogenous metabolites is accompanied by specific constellations of immune parameters.

Key words: bilirubin, creatinine, urea, uric acid, immunity, rats.

INTRODUCTION

Earlier we found that even in intact rats, certain parameters of nitrogenous metabolism and immunity fluctuate in a fairly wide range, which further expands in cases of prolonged water loads [18]. The links between the individual parameters of metabolism and immunity were revealed [7,16]. Based on this, the aim of this study was to create groups that are homogeneous in the parameters of nitrogenous metabolism, followed by a search for the characteristic parameters of immunity.

MATERIAL AND METHODS

Experiment was performed on 60 healthy female Wistar rats 220-300 g. Of these, 10 remained intact, while others received drinking water of various compositions during the week. The day after the completion of the drinking course in all rats, at first, a sample of peripheral blood (by incision of the tip of the tail) was taken for leukocytogram analysis. Animals were then placed in individual chambers with perforated bottom for collecting daily urine. The experiment was completed by decapitation of rats in order to collect as much blood as possible.

The plasma level of the nitrogenous metabolites determined: creatinine (by Jaffe's color reaction by Popper's method), urea (urease method by reaction with phenol hypochlorite), uric acid (uricase method) and bilirubin (by diazoreaction using the Jedrashik-Kleghorn-Grof method). The same metabolites, with the exception of bilirubin, were also determined in the daily urine. The analyzes were carried out according to the instructions described in the manual [6]. The analyzers “Pointe-180” ("Scientific", USA) and “Reflotron” (Boehringer Mannheim, BRD) were used with appropriate sets.

In the blood, the parameters of immunity were determined as described in the manual [13]: the relative content of the population of T-lymphocytes in a test of spontaneous rosette formation with erythrocytes of sheep by Jondal M et al [9], their theophylline resistant (T-helper) and theophylline sensitive (T-cytolytic) subpopulations (by the test of sensitivity of rosette formation to theophylline by Limatibul S et al [12]; the population of B-lymphocytes by the test of complementary rosette formation with erythrocytes of sheep by Bianco C [3]. Natural killers were identified as large granules contain lymphocytes. In addition, the blasttransformation reaction of T-lymphocytes by PhHA was evaluated.

About the state of the phagocytosis function of neutrophils (microphages) and monocytes (macrophages) were judged by the phagocytic index, the microbial count and the killing index as well as the calculated on their basis bactericidal capacity for Staphylococcus aureus (ATCC N25423 F49) [5,11,15].

Immune organs weighed and made smears-imprints for counting splenocytogram and thymocytogram [2,4]. For them, as well as leukocytogram and immunocytogram, CE Shannon’s entropy was calculated [8,14,17].

Digital material is statistically processed on a computer using the software package "Statistica 64".

RESULTS AND DISCUSION

Preliminary screening confirmed the expected wide variability of parameters, so the sample was divided into three homogeneous groups-clusters (method of k-mean) [1]. If we take the range of norm: -1Z ÷ +1Z, it turns out that the characteristic features of the members of the most numerous (29 rats) of the first cluster are moderately elevated plasma urea (+1,22±0,31) and upper borderline plasma creatinine (+0,76±0,26) in combination with lower borderline plasma uric acid (-0,80±0,08). In members of the third cluster (22 animals), all

seven parameters are in the range of normal. In contrast, rats of the second cluster (n=9) were found to have significantly increased levels of urea and creatinine excretion, as well as uricemia.

Next discriminant analysis (method forward stepwise [10]) was conducted to identify exactly those immune parameters, in which the nitrogenous metabolism clusters differ significantly from each other. 19 variables were selected for inclusion in the model (5 from **thymus**, 4 from **spleen**, 6 from **blood** as well as by definition **uricemia, bilirubinemia, urea plasma and excretion**) (Tables 1 and 2), while others, including uricosuria, creatininuria and creatininemia, were outside the discriminatory model (Tables 2-6).

Table 1. Summary of Stepwise Analysis for Nitrogenous and Immune Variables ranked by criterion Λ

Variables currently in the model	F to enter	p-level	Λ	F-value	p-level
Uricemia, µM/L	41,8	10^{-6}	0,406	41,8	10^{-6}
Urea Excretion, µM/100g•d	20,9	10^{-6}	0,232	30,1	10^{-6}
Lymphoblastes Spleen,%	2,90	0,063	0,210	21,7	10^{-6}
Urea Plasma, mM/L	2,79	0,070	0,190	17,4	10^{-6}
T helper Lymphocytes, %	2,16	0,126	0,176	14,7	10^{-6}
Lymphoblastes Thymus, %	1,55	0,222	0,166	12,6	10^{-6}
Plasmocytes Thymus, %	1,43	0,248	0,157	11,1	10^{-6}
Endotheliocytes Thymus,%	1,40	0,257	0,149	9,95	10^{-6}
Lymphocytes Spleen,%	1,83	0,171	0,139	9,18	10^{-6}
0 Lymphocytes Blood, %	1,60	0,212	0,130	8,52	10^{-6}
B Lymphocytes, %	1,86	0,168	0,120	8,04	10^{-6}
Epitheliocytes Thymus, %	1,49	0,236	0,113	7,57	10^{-6}
Plasmocytes Spleen, %	1,72	0,191	0,105	7,22	10^{-6}
Spleen Mass Index, %	2,10	0,135	0,096	7,01	10^{-6}
Bilirubinemia, µM/L	1,75	0,185	0,089	6,76	10^{-6}
Microbial Count Monocytes	1,16	0,325	0,084	6,43	10^{-6}
Macrophages Thymus, %	1,24	0,300	0,079	6,16	10^{-6}
Entropy Leukocytogram	1,16	0,325	0,075	5,90	10^{-6}
Leukocytes Blood, 10^9/L	1,09	0,348	0,071	5,65	10^{-6}

Table 2. Discriminant Function Analysis Summary for Nitrogenous and Immune Variables ranked by Structural coefficient

Step 19, N of vars in model: 19; Grouping: 3 grps

Wilks' Lambda: 0,071; approx. $F_{(39)}=5,7$; $p<10^{-6}$

	Clusters (n)			Parameters of Wilks' Statistics					
Variables currently in the model	**II (9)**	**III (22)**	**I (29)**	Wil-ks' Λ	Parti-al Λ	F-re-move	p-value	Tole-rancy	**Norm (10)**
Uricemia, µM/L	**1298** **218**	**871** **32**	**389** **28**	0,187	0,380	31,9	10^{-4}	0,579	662 108
Urea Excretion, µM/100g•d	**457** **91**	**166** **21**	**186** **22**	0,085	0,839	3,75	0,032	0,507	160 41
Macrophages Thymus, %	**3,44** **0,50**	**3,00** **0,26**	**2,90** **0,17**	0,079	0,897	2,24	0,120	0,463	2,70 0,42
Urea Plasma, mM/L	**7,07** **1,16**	**7,88** **0,62**	**9,51** **0,53**	0,087	0,816	4,40	0,019	0,479	7,42 0,54
Lymphoblastes Thymus, %	**6,78** **0,28**	**6,95** **0,21**	**7,41** **0,19**	0,085	0,839	3,74	0,033	0,451	7,40 0,27
Leukocytes Blood, 10^9/L	**10,0** **0,8**	**11,7** **1,2**	**12,0** **0,8**	0,075	0,947	1,09	0,348	0,580	12,7 1,9
Endotheliocytes Thymus,%	**2,44** **0,34**	**2,62** **0,20**	**2,72** **0,18**	0,104	0,686	8,92	0,001	0,284	2,60 0,31
Microbial Count Monocytes, Bac/Phag	**4,4** **0,5**	**4,6** **0,3**	**4,8** **0,4**	0,077	0,926	1,57	0,221	0,728	5,0 0,6
Lymphoblastes Spleen,%	5,11 0,54	**3,45** **0,27**	4,17 0,19	0,079	0,897	2,24	0,119	0,372	3,90 0,38
Plasmocytes Thymus, %	1,89 0,26	**1,71** **0,18**	2,17 0,15	0,077	0,927	1,54	0,227	0,597	1,80 0,25
Bilirubinemia, µM/L	5,13 0,79	**4,01** **0,39**	4,80 0,42	0,080	0,884	2,56	0,091	0,542	4,63 0,81
Plasmocytes Spleen, %	2,00 0,44	**1,73** **0,24**	2,14 0,26	0,088	0,807	4,65	0,015	0,299	2,50 0,50
B Lymphocytes Blood, %	15,9 0,6	**15,4** **0,6**	16,3 0,7	0,082	0,860	3,16	0,053	0,633	16,0 0,9
Epitheliocytes Thymus, %	7,6 0,7	**10,1** **0,5**	9,2 0,3	0,085	0,835	3,87	0,029	0,377	8,8 0,6
0 Lymphocytes Blood, %	20,5 2,4	**23,7** **1,2**	18,6 1,5	0,086	0,829	4,01	0,026	0,529	22,2 1,9
Entropy Leukocytogram	0,583 0,017	**0,594** **0,013**	0,557 0,012	0,076	0,934	1,38	0,264	0,702	0,596 0,018
T helper Lymphocytes, %	29,4 1,1	**31,9** **0,8**	30,6 0,7	0,087	0,814	4,45	0,018	0,561	31,5 1,0
Spleen Mass Index, %	0,284 0,018	**0,290** **0,015**	0,292 0,012	0,079	0,893	2,34	0,109	0,363	0,312 0,032
Lymphocytes Spleen, %	48,2 0,7	**48,3** **0,6**	48,1 0,4	0,082	0,869	2,93	0,065	0,617	48,7 0,9
Variables currently not in the model	**II (9)**	**III (22)**	**I (29)**	Wil-ks' Λ	Parti-al Λ	F to enter	p-value	Tole-rancy	**Norm (10)**
Creatininuria, µM/100g•d	**15,5** **1,2**	**11,5** **1,2**	**10,3** **0,8**	0,070	0,993	0,13	0,875	0,435	8,7 1,4
Uricosuria, µM/100g•d	**8,68** **1,61**	**5,82** **0,56**	**4,32** **0,41**	0,071	0,997	0,06	0,940	0,690	5,72 1,70
Creatinineemia, µM/L	**62** **11**	**75** **6**	**91** **6**	0,070	0,983	0,33	0,721	0,190	73 8

Table 3. Variables of Thymocytogram currently not in the model

Variables currently not in the model	II (9)	III (22)	I (29)	Wil-ks' Λ	Parti-al Λ	F to enter	p-value	Tole-rancy	Norm (10)
Lymphocytes Thymus, %	71,2 0,8	**68,6 0,5**	69,1 0,5	0,070	0,990	0,20	0,823	0,133	70,3 0,8
Entropy Thymocytogram	0,533 0,011	0,559 0,007	0,558 0,007	0,071	0,996	0,08	0,926	0,138	0,538 0,011
Reticulocytes Thymus, %	4,89 0,51	5,05 0,31	4,52 0,13	0,070	0,993	0,14	0,871	0,562	4,70 0,54
Hassal corpuscles Thymus, %	1,78 0,15	1,93 0,09	1,98 0,09	0,071	0,995	0,09	0,911	0,430	1,70 0,17
Thymus Mass Index,%	0,025 0,003	0,028 0,001	0,030 0,002	0,069	0,967	0,66	0,524	0,597	0,028 0,004

Table 4. Variables of Splenocytogram currently not in the model

Variables currently not in the model	II (9)	III (22)	I (29)	Wil-ks' Λ	Parti-al Λ	F to enter	p-value	Tole-rancy	Norm (10)
Macrophages Spleen, %	7,89 0,51	**8,95 0,37**	8,03 0,34	0,070	0,984	0,31	0,732	0,461	7,90 0,50
Entropy Splenocytogram	0,754 0,008	0,751 0,005	0,754 0,004	0,071	0,994	0,12	0,888	0,136	0,753 0,009
Reticulocytes Spleen, %	14,8 0,6	14,8 0,4	15,1 0,3	0,071	0,997	0,06	0,944	0,415	14,3 0,6
Fibroblastes Spleen, %	8,3 0,5	8,3 0,4	7,6 0,3	0,069	0,971	0,57	0,571	0,642	8,2 0,7
Neutrophils Spleen, %	12,6 0,8	12,7 0,4	13,3 0,4	0,069	0,972	0,54	0,585	0,647	13,0 0,45
Eosinophils Spleen, %	1,11 0,26	1,68 0,17	1,45 0,16	0,070	0,986	0,27	0,761	0,695	1,50 0,34

Table 5. Variables of Leukocytogram currently not in the model

Variables currently not in the model	II (9)	III (22)	I (29)	Wil-ks' Λ	Parti-al Λ	F to enter	p-value	Tole-rancy	Norm (10)
Monocytes Blood, %	**3,67 0,70**	**4,32 0,59**	**5,45 0,38**	0,070	0,984	0,32	0,730	0,515	4,80 0,95
Lymphocytes Blood, %	59,6 3,7	60,9 1,7	60,5 1,2	0,070	0,984	0,31	0,737	0,757	60,7 3,0
Rod shape Neutrophils Blood, %	3,11 0,45	3,09 0,20	3,38 0,23	0,071	1,000	0,00	0,999	0,757	3,60 0,34
PMN Neutrophils Blood, %	29,2 3,1	27,6 1,5	26,8 0,9	0,069	0,973	0,52	0,600	0,793	26,0 2,2
Eosinophiles Blood, %	3,89 0,39	3,73 0,50	3,59 0,35	0,071	0,997	0,06	0,944	0,801	4,60 0,95
Basophiles Blood, %	0,56 0,24	0,23 0,09	0,31 0,09	0,068	0,961	0,76	0,473	0,791	0,30 0,15

Table 6. Variables of Immunocytogram and Phagocytosis currently not in the model

Variables	II (9)	III (22)	I (29)	Wilks' Λ	Partial Λ	F to enter	p-value	Tolerancy	Norm (10)
Natural Killers Blood, %	**14,9 0,5**	**15,7 0,5**	**16,2 0,4**	0,070	0,992	0,15	0,862	0,545	15,6 0,9
Bactericidal Capacity Monocytes, 10^6 B/L	**51 13**	**74 17**	**103 22**	0,070	0,991	0,16	0,851	0,550	122 64
Microbial Count Neutrophils, Bac/Phag	**8,4 0,6**	**7,9 0,3**	**7,5 0,2**	0,069	0,975	0,49	0,617	0,516	8,6 0,6
Killing Index Neutrophils,%	53,0 2,8	**51,1 1,4**	54,5 1,1	0,071	0,996	0,08	0,919	0,728	50,7 2,0
Entropy Immunocytogram	0,886 0,007	0,884 0,004	0,875 0,005	0,070	0,987	0,25	0,776	0,624	0,874 0,006
RBTL of T-lymphocytes on PhHA, %	78,6 1,7	75,1 2,0	78,7 1,3	0,070	0,993	0,14	0,869	0,601	78,8 2,3
Plasmocytes Blood, %	0,89 0,22	0,75 0,12	0,78 0,12	0,071	0,997	0,06	0,938	0,419	0,47 0,15
T cytolytic Lymphocytes, %	16,0 0,9	16,1 0,7	15,9 0,6	0,069	0,977	0,44	0,648	0,477	16,0 0,8
Phagocytose Index Monocytes, %	2,9 0,2	2,9 0,2	2,8 0,2	0,070	0,991	0,16	0,850	0,553	2,9 0,2
Phagocytose Index Neutrophils, %	71,0 1,3	69,0 0,7	69,4 0,7	0,071	0,991	0,18	0,839	0,352	69,5 1,4

The distinctive information contained in the 19 discriminant variables is condensed into two roots. The first root contains 85% of the discriminatory potential (r^*=0,925; Wilks' Λ=0,071; $\chi^2_{(38)}$=127; $p<10^{-6}$) and second root 15% (r^*=0,715; Wilks' Λ=0,489; $\chi^2_{(18)}$=34; p=0,011).

Calculating the values of the discriminant root for each animal as the sum of the product of the raw coefficients on the individual values of the discriminant variables together with a constant (Table 7) makes it possible to visualize each rat in the information space of the roots (Fig. 1).

Table 7. Standardized and Raw Coefficients and Constants for Canonical Variables

Coefficients	Standardized		Raw	
Variables	Root 1	Root 2	Root 1	Root 2
Uricemia, µM/L	-1,111	-0,177	-0,0039	-0,0006
Urea Excretion, µM/100g•d	-0,609	-0,049	-0,0042	-0,0003
Lymphoblastes Spleen,%	-0,277	0,644	-0,2305	0,5352
Urea Plasma, mM/L	0,659	0,159	0,2219	0,0536
T helper Lymphocytes, %	0,063	-0,801	0,0172	-0,2185
Lymphoblastes Thymus, %	0,620	-0,233	0,6398	-0,2406
Plasmocytes Thymus, %	0,024	0,489	0,0296	0,6041
Endotheliocytes Thymus,%	0,998	-0,704	1,055	-0,7446
Lymphocytes Spleen,%	0,491	-0,103	0,1958	-0,0410
0 Lymphocytes Blood, %	0,374	-0,631	0,0524	-0,0884
B Lymphocytes, %	-0,100	0,644	-0,0317	0,2043
Epitheliocytes Thymus, %	0,538	-0,612	0,2776	-0,3154
Plasmocytes Spleen, %	0,747	-0,570	0,5826	-0,4441
Spleen Mass Index, %	-0,406	0,550	-6,013	8,155
Bilirubinemia, µM/L	-0,500	0,017	-0,2339	0,0079
Microbial Count Monocytes	0,342	0,064	0,1815	0,0339
Macrophages Thymus, %	-0,509	-0,043	-0,4503	-0,0383
Entropy Leukocytogram	-0,284	-0,222	-4,661	-3,648
Leukocytes Blood, G/L	-0,320	-0,079	-0,0698	-0,0172
		Constants	-12,15	11,32
		Eigenvalues	5,890	1,046
		Cumulative Properties	0,849	1

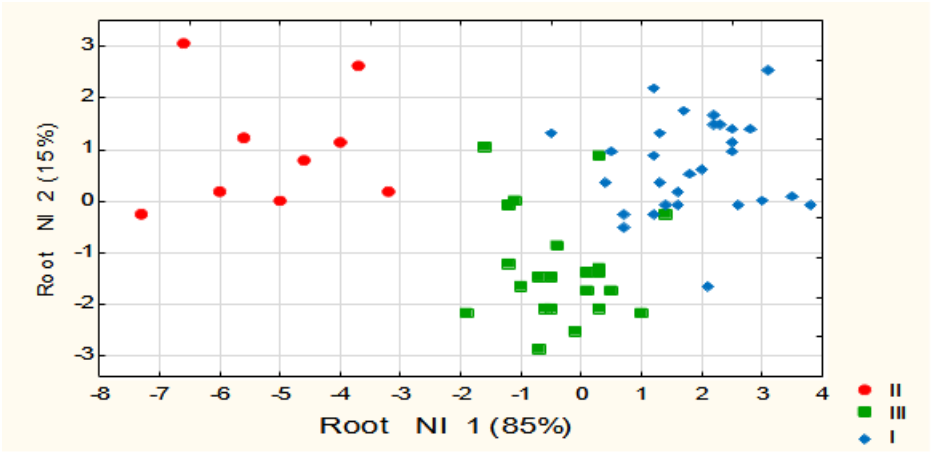

Fig. 1. Scatterplot of rats of differ clusters in space of Roots

As we can see, along the axis of the first root members of the cluster II occupy the extremal left position. This reflects their elevated or maximal for sampling levels of metabolites and macrophages of thymus and currently not in the model microbial count of neutrophils that correlate with the root **negatively**, and minimum for sampling levels in plasma of urea and creatinine as well as immune parameters that correlate with the root **positively** (Table 8).

At the opposite end of the axis of the first root are localized members of the cluster I, which are characterized by the **maximum**/**minimum** values of the same parameters. The intermediate position of the cluster III reflects, in turn, the intermediate values of the parameters, information about which is condensed in the first root.

Additional delimitation of the last cluster from the previous two occurs along the axis of the second root. The lowest localization of its members reflects the **minimum** for sampling values of bilirubinemia and immune parameters that correlate with the root directly, or the **maximum** for sampling values of inversely correlated parameters.

Table 8. Correlations Variables-Canonical Roots, Means of Roots and Z-scores of Variables

Variables	Correlations Variables-Roots		II (9)	III (22)	I (29)
Root 1 (85%)	**Root 1**	**Root 2**	**-5,12**	**-0,32**	**+1,83**
Uricemia, µM/L	**-0,478**	-0,339	**+1,86**	**+0,61**	**-0,80**
Urea Excretion, µM/100g•d	**-0,259**	0,339	**+2,28**	**+0,04**	**+0,19**
Creatininuria, µM/100g•d	Currently not in model		**+1,55**	**+0,64**	**+0,36**
Uricosuria, µM/100g•d	Currently not in model		**+0,55**	**+0,02**	**-0,26**
Macrophages Thymus, %	**-0,068**	0,028	**+0,56**	**+0,22**	**+0,15**
Microbial Count Neutrophils, B/Ph	Currently not in model		**-0,08**	**-0,39**	**-0,55**
Urea Plasma, mM/L	**0,124**	0,141	**-0,21**	**+0,27**	**+1,22**
Creatininemia, µM/L	Currently not in model		**-0,42**	**+0,12**	**+0,76**
Lymphoblastes Thymus, %	**0,100**	0,126	**-0,74**	**-0,53**	**+0,02**
Leukocytes Blood, 10^9/L	**0,059**	-0,038	**-0,45**	**-0,16**	**-0,12**
Endotheliocytes Thymus,%	**0,043**	0,009	**-0,16**	**+0,02**	**+0,13**
Microbial Count Monocytes, B/Ph	**0,029**	0,030	**-0,29**	**-0,22**	**-0,10**
Natural Killers Blood, %	Currently not in model		**-0,27**	**+0,03**	**+0,21**
Monocytes Blood, %	Currently not in model		**-0,38**	**-0,16**	**+0,22**
Bactericidal Capacity Mon, 10^6 B/L	Currently not in model		**-0,42**	**-0,28**	**-0,11**
Root 2 (15%)	**Root 1**	**Root 2**	+0,99	**-1,30**	+0,68
Bilirubinemia, µM/L	-0,014	**0,200**	+0,20	**-0,24**	+0,07
Lymphoblastes Spleen,%	-0,094	**0,403**	+1,01	**-0,37**	+0,23
Plasmocytes Thymus, %	0,060	**0,213**	+0,11	**-0,11**	+0,47
Plasmocytes Spleen, %	0,022	**0,138**	-0,32	**-0,49**	-0,23
B Lymphocytes, %	0,026	**0,128**	-0,04	**-0,22**	+0,12
Killing Index Neutrophils,%	Currently not in model		+0,36	**+0,07**	+0,60
Lymphocytes Thymus, %	Currently not in model		+0,39	**-0,71**	-0,51
Epitheliocytes Thymus, %	0,107	**-0,350**	-0,63	**+0,68**	+0,20
0 Lymphocytes Blood, %	-0,053	**-0,309**	-0,27	**+0,25**	-0,58
Entropy Leukocytogram	-0,071	**-0,223**	-0,21	**-0,02**	-0,66
T helper Lymphocytes, %	0,035	**-0,214**	-0,67	**+0,12**	-0,30
Spleen Mass Index, %	0,013	**-0,070**	-0,28	**-0,13**	-0,20
Lymphocytes Spleen,%	-0,008	**-0,034**	-0,18	**-0,14**	-0,22
Macrophages Spleen, %	Currently not in model		-0,01	**+0,66**	-0,08

In general, in the information space of the three discriminant roots, all clusters are clearly separated from each other, that is, they differ from each other in terms of four nitrogenous metabolites and constellation of the 15 parameters of immunity as well as 10 others that were not included in the model.

This distinction is documented by the calculation of the Mahalanobis distances between clusters (Table 9).

Table 9. Squared Mahalanobis Distances between clusters (above the diagonal), F-values (df=19,4) and p-levels (under the diagonal)

Clusters	II	III	I
II	0	**28**	**48**
III	**6,5** 10^{-6}	0	**9**
I	**12** 10^{-6}	**3,9** 10^{-3}	0

The use of classification functions (Table 10) makes it possible to retrospectively identify clusters II without error and the other two with one and two errors (Table 11), ie the overall recognition accuracy is 95%.

Table 10. Coefficients and Constants of Classification Functions

Clusters	II	III	I
Variables	p=,150	p=,367	p=,483
Uricemia, µM/L	-0,013	-0,031	-0,040
Urea Excretion, µM/100g•d	0,020	0,0007	-0,009
Lymphoblastes Spleen,%	10,47	8,136	8,701
Urea Plasma, mM/L	4,062	5,004	5,589
T helper Lymphocytes, %	4,221	4,804	4,408
Lymphoblastes Thymus, %	28,97	32,59	33,49
Plasmocytes Thymus, %	-0,360	-1,602	-0,340
Endotheliocytes Thymus,%	24,61	31,38	32,17
Lymphocytes Spleen,%	14,22	15,25	15,59
0 Lymphocytes Blood, %	2,229	2,683	2,621
B Lymphocytes, %	-2,290	-2,910	-2,573
Epitheliocytes Thymus, %	14,79	16,85	16,82
Plasmocytes Spleen, %	8,740	12,55	12,93
Spleen Mass Index, %	174,5	127,0	130,2
Bilirubinemia, µM/L	-1,035	-2,175	-2,664
Microbial Count Monocytes	7,785	8,578	9,037
Macrophages Thymus, %	2,200	0,128	-0,919
Entropy Leukocytogram	254,6	240,6	223,3
Leukocytes Blood, G/L	0,070	-0,225	-0,410
Constants	-758,9	-829,6	-834,0

Table 11. Classification Matrix for clusters
Rows: Observed classifications; Columns: Predicted classifications

Clusters	Percent Correct	II p=,150	III p=,367	I p=,483
II	100	**9**	0	0
III	90,9	0	**20**	**2**
I	96,6	0	**1**	**28**
Total	95,0	9	21	30

CONCLUSION

The variety of states of exchange of nitrogenous metabolites is accompanied by specific constellations of immune parameters.

CONFORMITY TO ETHICAL STANDARDS

Experiments on animals have been carried out in accordance with the provisions of the Helsinki Declaration of 1975, revised and supplemented in 2002 by the Directives of the National Committees for Ethics in Scientific Research.

The carrying out of experiments was approved by the Ethics Committee of the Ukrainian Scientic Research Institute of Medicine for Transport. The modern rules for the maintenance and use of laboratory animals complying with the principles of the European Convention for the Protection of Vertebrate Animals used for scientific experiments and needs are observed (Strasbourg, 1985).

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