number of lymphocytes in spleen and lymph nodes of small intestines, normalizes their quantity in bone marrow and has no impact on thymus. The growing number of lymphocytes in the examined organs and tissues appears to be a mobilization of organism's adaptive reactions, when animals find themselves under the influence of pathological impacts (ionizing radiation).

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INTRAUTERINE INFECTIONS IN THE SYSTEM "MOTHER – AFTERBIRTH – FETUS"

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Infection process in fetus begins to develop when infection agents overcome complicated immunity system, starting from mother's common immunity and then up to histohematogenous barrier between mother' blood and morphofunctional formations of afterbirth. Then the agent penetrates through the barrier, overcomes afterbirth immunity system, penetrates through the second histohematogenous barrier of the afterbirth into fetus blood and after all overcomes fetus immunity system. Nowadays there is a necessity to work out preventive measures and treatment for a fetus during all the stages of intrauterine ontogenesis as well as the technique, which would allow to block the ways of infection spread into the system Mother – Afterbirth.

Background

Earlier we revealed two independent kinds of immunity forming in neurotropic virus infection: common barrier – extraneural and rehematoencephalic barrier – cerebrospinal [1]. During pregnancy afterbirth is being formed as an organ, connecting fetus with mother. It contains amniotic capsules and fluid, placenta, and umbilical cord. Infection disease agents, penetrating into fetus, are able to overcome barriers between morphofunctional formation of afterbirth and both mother's blood and fetus blood. [2, 3]

Research works of the last years show that intrauterine infection plays an important role in pathogenesis of those conditions, which recently were not regarded as infection pathology. The term "intrauterine infections" refers to the diseases, in which the infecting takes place during pregnancy or delivery and the mother is the source of infection. The term "intrauterine infections" is usually used to describe clinical signs of fetus and newborn infection diseases, revealed in prenatal period or straight after birth. They use in practical medicine the term "intrauterine infecting" to mark the fact of intrauterine infection, which happens more often, than clinical signs of the disease develop. The frequency of intrauterine infecting according to different authors fluctuate from 6% to 53%, achieving 70 % among prematurely born babies [4, 5, 6].

The aim of the research is to establish the frequency of infecting placenta and amniotic fluid in a newborn under different urogenital and virus infections in mother.

Materials and Methods

To resolve the task we examined 402 women in birth, 394 newborns of those mothers, 8 miscarried fetuses. We took during labor 402 amniotic fluid tests and 402 placenta tissue samples of those women.

All the women in birth were divided into the following groups:

A – women without any virus or urogenital infection according to laboratory tests. 172 subjects (control group).

B – women having virus or urogenital infection agents or the signs of infecting according to laboratory tests. 230 subjects (the main group), including:

- B1 – virus or urogenital infection agents or the signs of infecting were revealed only in women in birth – 76 subjects;
- B2 – virus or urogenital infection agents or the signs of infecting were revealed in a woman in birth, amniotic fluid, and/or in placenta tissue – 66 subjects;
- B3 – virus or urogenital infection agents or the signs of infecting were revealed both in women in birth and in their newborns. May be – in amniotic fluid and placenta tissue – 88 subjects.

There were 172 non-infected subjects in control group with normal indices of specific antibodies to herpes and cytomegalia agents and the absence of the elements of these virus and urogenital infections (chlamydiae, mycoplasmosis, ureaplasmosis) after

polymerase chain reaction (**PCR**) results. In the main group 230 subjects had different levels of specific immune globulins M and G to the given infection agents as well as positive PCR results.

All the intakes were done on the basis of Krasnoyarsk Clinical Maternity Hospital № 2 from 2002 till 2005.

We examined blood serum in newborns, afterbirths and back amniotic fluid in puerperas in groups A and B by PCR technique.

Peripheral blood and smears were taken from the subjects in the first stage of delivery. At the end of the second stage straight after the birth we took the samples of back amniotic fluid. Following the afterbirth stage we performed the cutting of placenta and amnion pieces by random. In cases of operative delivery the materials were taken on the operating table.

In 1 to 3 days after delivery we took peripheral blood samples for biochemical test from newborns in their ward. At the same moment the other blood samples were taken for testing DNA agents of the mentioned infections.

The Results of the Research

We traced the character and dynamics of infecting process in women, who were coming into delivery, by means of parallel determination of immune globulins in blood serum and the revelation of virus and urogenital infections DNA in vaginal smears.

So, in group B the IgG to cytomegalovirus (**CMV**) was revealed in 89.5%, to the virus of simple herpes (**SHV**) in 79.4%. There were no M immune globulins, which are responsible for acute process or for the exacerbation in chronic process to the mentioned viruses. Vaginal smears tests (performed by PCR technique) show cytomegalia virus DNA in 19.3% puerperas and herpes virus DNA in 13.8%. So, CMV as mono agent was revealed in 2% subjects, SHV in 9%. We marked high percentage of the associations of the given viruses with the agents of urogenital infections, which achieved 23%. The combination of DNA of these two viruses in one puerpera was not revealed by us (figure 1) [7, 8].

Percentage of urogenital infection agents was significantly higher in group B.

Totally in vaginal smears of all the infected subjects in the main group the Chlamidia trahomatis DNA was revealed in 63.2% cases. We analyzed the character of chlamydiae infection condition by immune enzyme technique (**IET**). We marked the presence of Ig M and the absence of Ig G in serum test in PCR positive subjects and regarded this as primary acute chlamydiae infection, which took place in 4.6% cases. In blood serum in 12.1% women both IgM and IgG were positive, which was regarded by us as reactivation or exacerbation of chronic chlamydiae infection. In blood serum in 73.8% patients Ig M to chlamydiae was absent. At the same time we marked diagnostically meaningful IgG titers, which can be estimated as chronic course of infecting process or as latent carriaging. In 9.5% women of this group both IgM and IgG to chlamydiae agent were not found, which can be connected with the peculiarities of immune response. We should mention that among mono infections chlamydiae corresponds to 23%, being on the first place in this niche.

We found ureaplasm DNA in smears in 38.6% and IgG to this agent in 28% patients. According to our data 36.8% women show mycoplasm DNA. Ureaplasmosis as mono infection was marked in 9% and mycoplasmosis in 7% cases.

The diagrams show the dominating position of different associations of urogenital infections - 27% (figure 1). The most prevalent are: the combinations of CMV, ureaplasmosis and Chlamidia trahomatis - 7% cases; ureaplasmosis and Chlamidia trahomatis – 4%; ureaplasmosis, mycoplasmosis and Chlamidia trahomatis – 4%. This is explained by rather high prevalence of these infections in the population [9].

The fact of determining immune globulins to the given infections does not testify obligatory on the development of infection process [10]. This is confirmed by IgG

presence in control group A, where infecting process in pregnant woman and in fetus didn't develop. So in this group 9% patients showed IgG to chlamydiae, Ig G to ureaplasm 3%, Ig G to CMV – 64%, and Ig G to SHV – 73%. Ig M in A group to the mentioned agents was not revealed.

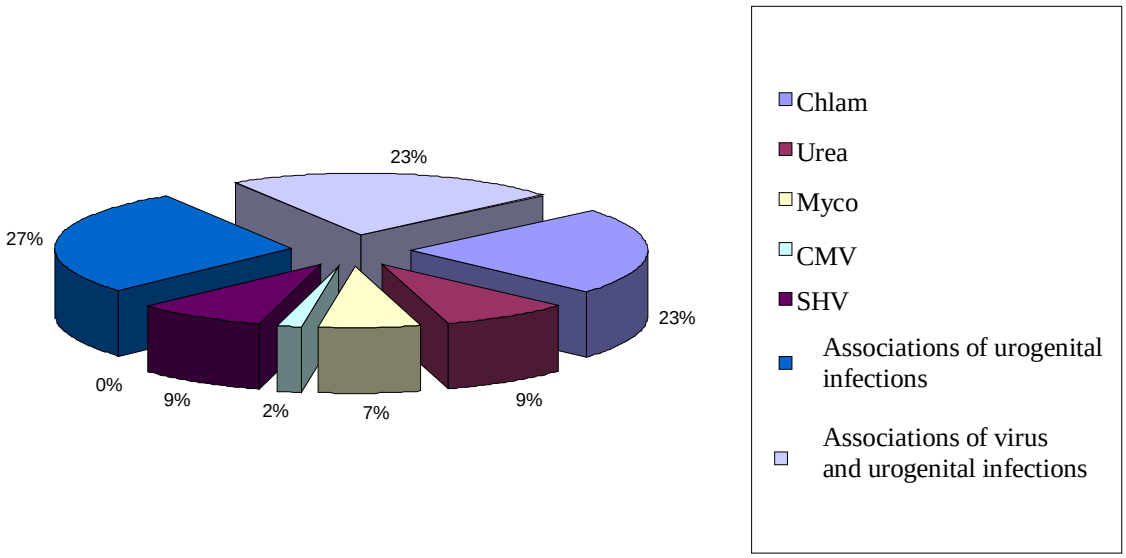

Figure 1. The prevalence of different agents of virus and urogenital infections in women of Group B (%).

We analyzed 402 afterbirths and 402 samples of amniotic fluid to reveal agent DNA of CMV, SHV and urogenital infections (chlamidiae, ureaplasm and mycoplasm). All the tests were performed by PCR technique.

We analyzed the data in details and obtained the following results. Out of 100% infected women only in 33% the infection was not distributed out of mother's organism. In two thirds of the pregnant women (67%), DNA of intrauterine infection agents were found in amniotic fluid or afterbirth or fetus (B2 and B3 groups). In 13% of the patients in the main groups, infection DNA passed fluid and placenta barriers and was recognized in newborns. In 10.4% cases infection DNA were marked in baby and in mother. In 2.6% cases infection DNA in a newborn differed from that one found in placenta and amniotic fluid (for example a newborn shows cytomegalovirus DNA but there was Chlamidiae and mycoplasm DNA in placenta and fluid).

So, in 87% mothers the infection agents passed natural barriers and went through placenta or amniotic fluid practically in 7 out of each 8 cases.

In groups B2 and B3 we revealed 43.5% cases with intrauterine infection DNA in amniotic fluid, 29% cases in placenta tissue and afterbirth cover, 27.5% cases in placenta and amniotic fluid.

Only in 10.5% cases we revealed chlamidiae DNA as mono agent. It was found in puerpera, in placenta and amniotic fluid. In 89.5% cases they were the combinations of chlamidiae, mycoplasm and ureaplasm DNA, CMV and SHV. In most cases they were different in placenta and amniotic fluid in one and the same woman.

We revealed 68% non-infected afterbirths out of 402 subjects in the main group. In 32% cases afterbirths contained DNA of the above-mentioned infections. The most prevalent were chlamidiae with the share of 19%, which made 59.4% of all the infected afterbirths. The second prevalent mono agents were SHV and mycoplasm, 3% or 9.4% of all the infections. In 2% cases we found DNA sectors to CMV in afterbirths.

We didn't reveal ureaplasm DNA in placenta (figure 2).

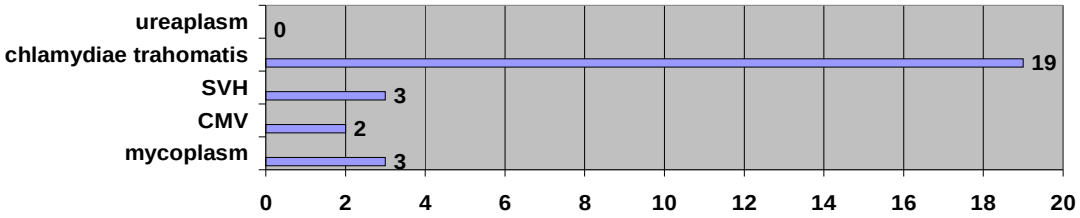

Figure 2. The results of placenta tissue tests for DNA sectors of intrauterine infections (IUI) agents in Group B patients (in %).

Only one combination of microbe associations was marked in placenta – chlamidiae and mycoplasm DNA, nearly 5%, which corresponded to 15.6% among the infected afterbirths.

57% of 402 samples of amniotic fluid in main group were not infected. Chlamidiae DNA was the most prevalent in amniotic fluid and in placenta (in 21% cases) which corresponded to 48.8% of all the infected samples. The share of mycoplasm DNA increased greatly and achieved 14% or 32.6% of all intrauterine infections. In 4% cases we revealed simple herpes virus in amniotic fluid and in 2% cases ureaplasm DNA. We didn't revealed cytomegalovirus DNA in amniotic fluid in the main group (figure 3).

So, in amniotic fluid in puerperas of the main group we marked the same associations of antigens as in placenta, i.e. chlamidiae and mycoplasm DNA but with smaller frequency of 2% cases or in 4.7% of all the infected samples [13].

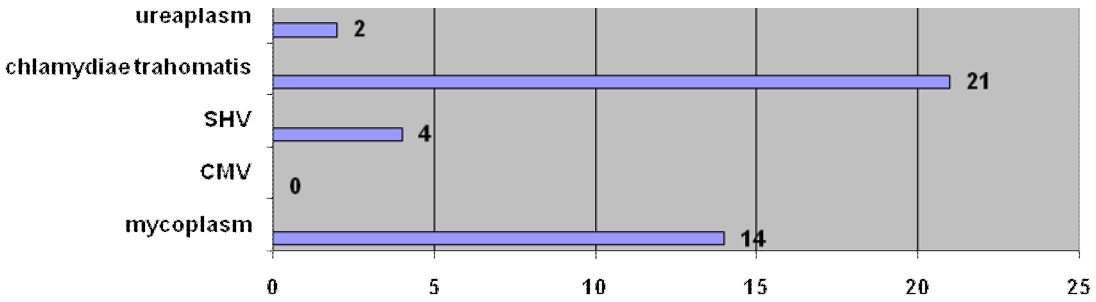

Figure 3. The results of the examination for IUI by PCR technique in amniotic fluid in Group B patients (in %).

All 394 newborns and 8 miscarriages of main group were examined by PCR technique for determining DNA specific sectors of the agents of perinatal infections - urogenital (chlamidiae, mycoplasm, ureaplasm) and virus (CMV and SHV).

According to the results of the tests there were no infected children in Group A (control group). There is no doubt, the results of Group B were the most interesting (the main group), in which all the mothers were infected and were potentially the "infection reservoir" for their babies [14, 15].

The majority of newborns of the main group (including miscarriages) were not infected according to serological test. Their share was 61.65%. The rest of the newborns had DNA fragments of one of the agents of intrauterine infection. Their share was 38.2%. It should be marked that we didn't reveal infection pathogens associations in any of the cases.

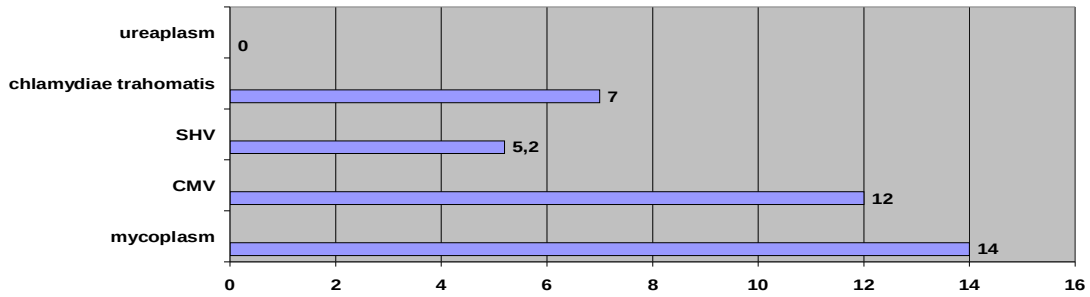

Figure 4. The results of blood serum tests in newborns for DNA sectors of intrauterine infictions agents in group B (in %).

The results of our tests for Group B newborns more often showed mycoplasm DNA. Their share was 14%. The second place in the prevalence belonged to CMV genome fragments in newborns. The share of these babies was 12%. The frequency of chlamidiae DNA in newborns was only 7 %, and SHV DNA was 5.2%. Ureaplasm DNA was not revealed at all (figure 4).

As it was mentioned above, all the IUI positive samples of blood serum in newborns contained DNA sections of representatives of some single agent. Having analyzed the share of each agent in common structure of intrauterine infection agents, taking into account DNA sectors in newborns, we received the following results: mycoplasm 36.4%, CMV 31.8%, chlamydia 18.2%, SHV 13.6%, ureaplasm 0%, associated infections 0% (figure 5).

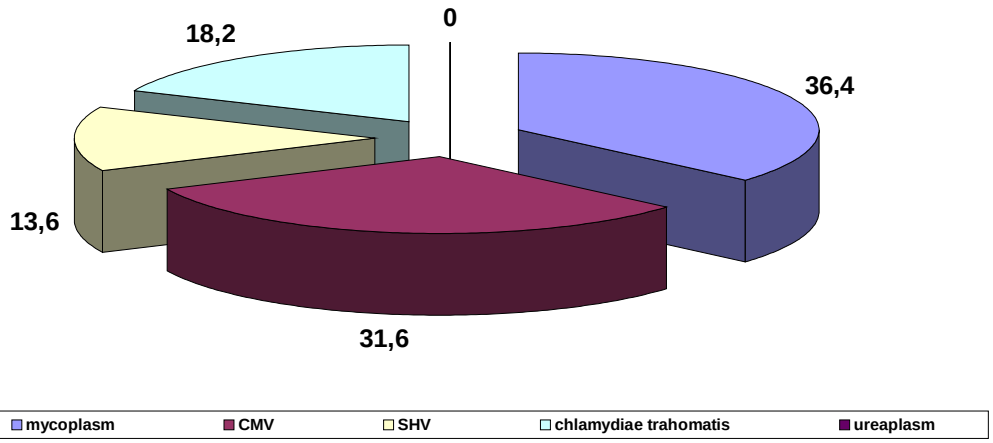

Figure 5. The shares of intrauterine infections agents in the stricture of the newborn infecting (in %).

So, having analyzed the received data, it became evident that dominating infections in puerperas are chlamydia and ureaplasm as well as different associations. In newborns mycoplasm and cytomegalia virus prevail.

So, the results of our research show that trans-placenta way of the infecting is the most typical for chlamidiae infection and less typical for cytomegalovirus or herpetic virus. For the last ones intro natal way of the infecting is more typical, which goes in conformity with researchers' generally accepted opinion [11, 12].

Conclusion

Three organisms function during pregnancy: mother, fetus and afterbirth. Each of them is developing its own immune system. But afterbirth immune system depends upon that one in a pregnant woman. Fetus protection against infection agents is provided by interactions between the developing immune system of afterbirth and immune system of mother and fetus.

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TECHNIQUE OF AN ESTIMATION OF RISK FOR HEALTH OF THE POPULATION OF THE PLANNED AND REALIZED INDUSTRIAL ACTIVITY, ADVANTAGE AND PROSPECT

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By the example of the large enterprise of Republic Kazakhstan comparison of use in practical ecological activity of a method of sanitary- hygienic standartization and a technique of an estimation of risk is carried out. The technique of an estimation of risk offers the complex difficult system of the calculations demanding for its carrying out highly specialized and well prepared personnel. The received data have an exact mathematical basis and more rigid hygienic estimation of interaction of the person with the chemical substances polluting atmospheric air. Absence of normative legal base at a republican level limits of use of the technique for practical application. At the international level creation of uniform legal base, global standards and the popular advisory coordination center with wide access to databases are actual.
Key words: techniques, an estimation of risk, health of the population, sulfur dioxide, nitrogen dioxide, hydrogen sulphide, atmospheric air.

Now in Kazakhstan there is no united conventional technique of an estimation of influence of industrial activity on health of the population.

We earlier carried out a comparative estimation of application in practical activities on preservation of the environment of domestic and foreign techniques according to the influence of harmful factors on health of the person (1, 2, 3, 4). The methodology of an estimation of risk to health of the population under influence of harmful factors of an environment is developed by EPA the USA (EPA US). Unification of requirements, principles, methods and criteria of an estimation of risk for the health connected to influence of chemical substances, polluting an environment, in view of documents of the domestic, foreign and international organizations carried out in Russia (5). Till now in Kazakhstan it has not received wide application though there are departmental documents and the separate literary data (6, 7, 8). The purpose of our work was the comparative characteristic of use of a method of sanitary- hygienic standartization and a technique of an estimation of the risk, executed in the large enterprise of Republic Kazakhstan.

Material and methods of research

The technique of an estimation of risk for health of the population (5) chemical substances polluting an atmosphere formed as a result of activity of a large developing industrial complex in comparison with control territory (the data of the Republic of Kazakhstan) is used. Calculations of size CPZ (sanitary protection zone) for the industrial complex including working, builded and planned factories, are executed by a department of protection of atmospheric air of Agency according to the legislation of republic and with use of the software allowed to application in territory of the country. The calculations are carried out for 3 substances, 2 groups of summation in 9 settlement points with an estimation of influence on health of the population of five settlements (A, B, C, D and E), located on the border of a sanitary - protective zone. The list of considered substances with the indication maximum concentration limit and a class of danger is resulted in table 1.

Results of research

Size CPZ for an industrial complex has made 7 kms that allows to provide a level of substances polluting an atmosphere on border of the nearest settlements below maximum permissible. The amount of emissions of considered polluting substances in an atmosphere is submitted in table 2.

The total amount of emissions of polluting substances in an atmosphere from the taken into account sources of working, builded and planned objects of an industrial complex makes 18435 tons one year. The structure of analyzed polluting substances is submitted by 60,23 % sulfur dioxide, 39,04 % nitrogen dioxide, 0,74 % by hydrogen sulphide.

Table 1. The characteristic of polluting substances

The name of substance	Maximum concentration limit	A class of danger of substances
Nitrogen (IV) oxide (Nitrogen dioxide)	0.085	2
Sulfur dioxide	0.5	3
Hydrogen sulphide	0.008	2

Table 2. Amount of emissions of polluting substances in an atmosphere

The name of the enterprise	Nitrogen dioxide		Sulfur dioxide		Hydrogen sulphide	
	gramme/ second	tonne/year	gramme/ second	tonne /year	gramme/ second	tonne /year
Factory 1	63.8	1887.1	177.8	5589.7	2.4	69.3
Factory 2	105.4	3321.9	156.0	4919.0	2.0	63.9
Factory 3	1039.5	1987.6	41.9	594.2	0.02	0.3
In total		7196.6		11102.9		133.5

Comparison with background concentration and referential dozes shows, that the amount of analyzed substances in an atmosphere at full designed capacity of the enterprise exceeds referential level that allows to use a technique for the quantitative characteristic of risks for health.

The first stage of risk assessment has allowed to define, that analyzed substances do not possess cancerogenic activity.

The index of danger is designed, as the relation of an influencing concentration chemical substance to it referential to a level.

$$HQ \equiv \frac{C}{RFC}, \text{ where}$$

HQ - index of danger,
C - concentration, mg / cube m,
RfC - referential concentration.

Indexes of comparative uncancerogenic danger are resulted in table 3.

Table 3. Indexes of comparative uncancerogenic danger

The name of substance	Indexes
Hydrogen sulphide	165.00
Nitrogen dioxide	15.75
Sulfur dioxide	2.80

As the designed factors of danger of substances exceed «one», the probability of development in the population of harmful effects at daily receipt of these substances during a life grows proportionally to increase in an index. The maximal uncancerogenic danger is represented with hydrogen sulphide - 165.00. According with degree of danger nitrogen dioxide is on the second place. Sulfur dioxide at ranging takes the third place.

The total index of danger (HI) is designed under the formula:

$$HI \equiv \sum HQi, \text{ where:}$$

HQi - indexes of danger to separate components of a mix of substances polluting an atmosphere.

The total index of danger (THI), characterizes allowable receipt and also exceeds «one».

The received settlement concentration of polluting substances testify that all considered substances are dangerous to health. The greatest contribution, both to total size, and to risk of influence on bodies of breath brings hydrogen sulphide. Then - dioxide nitrogen. Sulfur dioxide plays less significant role in formation of risk. The total risk is significant and makes 183,55. Biological action of substances potentiate influence on the same critical body, mainly respiratory system.

On the basis of the epidemiological data we carry out the calculation of risk of infringements development of a children health state. It is established, 38,05 of additional cases of diseases of pneumonia on 100 thousand person of the corresponding population, that is 9 % higher, than in control territory.

The maximal valid for one occation concentration of substances polluting an atmosphere from all three structures of an industrial complex are established for nitrogen dioxide - 0,63 maximum concentration limits on border of settlement A, for hydrogen sulphide - 0,41 maximum concentration limits on border of settlement D and for sulfur dioxide - 0,22 maximum concentration limits on border of settlement D (Table 4).

Table 4. The maximal ground concentration of polluting substances in settlement points

The name of settlement points	The maximal concentration in settlement points, in shares of maximum concentration limit				
	NO_2	SO_2	H_2S	Group of summation NO_2+SO_2	Group of summation H_2S+SO_2
Settlement A	0.63	0.14	0.33	0.65	0.44
Settlement B	0.29	0.14	0.30	0.35	0.36
Settlement C	0.20	0.07	0.16	0.20	0.20
Settlement D	0.48	0.22	0.41	0.65	0.61
Settlement E	0.43	0.09	0.25	0.50	0.31

The estimation of an exposition of analyzed polluting substances is carried out by calculation of daily dozes at their inhalation receipt with atmospheric air. For calculation all settlements located near the border of a sanitary - protective zone are taken. The established risks for health of the population (without taking into account the age) are submitted in table 5.

Table 5. The integrated estimation of an exposition

Polluting substances	The risk caused by inhalation influence of chemical substances in atmospheric air as a result of activity of an industrial complex				
	Settlement A	Settlement B	Settlement C	Settlement D	Settlement E
Sulfur dioxide	2,0E-02	2,0E-02	1,0E-02	3,1E-02	1,0 E -02
Nitrogen dioxide	1,5 E -02	7,0E-03	4,9E-03	1,2E-02	1,3 E -02
Hydrogen sulphide	7,5 E -04	6,9 E -04	3,7 E -04	9,4 E -04	5,7 E -04
Total receipt	3,6 E 02	2,8 E -02	1,5 E -02	4,4 E -02	2,4 E -02

Individual risk during all life, equal or smaller 1 x 10^{-6} corresponds to one additional case of serious disease or death per 1 million exposed persons and characterizes the small risk levels which are not distinguished from usual, daily risks. The risk from activity of the large industrial complex, designed for all analyzed substances influencing health of the population, living on border of a sanitary - protective zone exceeds this level.

For the hydrogen sulphide, the designed risk level is stacked in an interval more than 1 x 10^{-4}, but less than 1 x 10^{-3}, and is not allowable for the population. For sulfur dioxide and nitrogen dioxide the range of individual risk during all life more than 1 x 10^{-3} is not comprehensible for the population and demands carrying out of emergency actions on its decrease.

The established risk for health as a result of activity of a large developing industrial complex on border of a sanitary - protective zone is not allowable for the population.

Thus, the technique of an estimation of risk for health of the population offers the complex difficult system of the calculations demanding for its carrying out highly specialized and well prepared personnel. At the same time, the received data have an exact mathematical basis and, undoubtedly, more rigid hygienic estimation of parameters of interaction, than earlier known techniques that makes it attractive to use in system of complex difficult relations «the person - industrial activity». The absence of legislative normative legal base at a republican level limits opportunities of technique use for practical application.

At the international level creation of uniform normative-legal base and the global standards regulating interaction of the person and surrounding, including, the industrial environment is actual. Creation of the uniform, popular advisory coordination center with wide access to databases for carrying out of calculations of an estimation of risk to health of the population.

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AN EXTENSION OF THE COEVOLUTION THEORY OF THE ORIGIN OF THE GENETIC CODE

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Background: The coevolution theory of the origin of the genetic code suggests that the genetic code is an imprint of the biosynthetic relationships between amino acids. However, this theory does not seem to attribute a role to the biosynthetic relationships between the earliest amino acids that evolved along the pathways of energetic metabolism. As a result, the coevolution theory is unable to clearly define the very earliest phases of genetic code origin. In order to remove this difficulty, I here suggest an extension of the coevolution theory that attributes a crucial role to the first amino acids that evolved along these biosynthetic pathways and to their biosynthetic relationships, even when defined by the non-amino acid molecules that are their precursors.
Results: It is re-observed that the first amino acids to evolve along these biosynthetic pathways are predominantly those codified by codons of the type GNN, and this observation is found to be statistically significant. Furthermore, the close biosynthetic relationships between the sibling amino acids Ala-Ser, Ser-Gly, Asp-Glu, and Ala-Val are not random in the genetic code table and reinforce the hypothesis that the biosynthetic relationships between these six amino acids played a crucial role in defining the very earliest phases of genetic code origin.
Conclusion: All this leads to the hypothesis that there existed a code, GNS, reflecting the biosynthetic relationships between these six amino acids which, as it defines the very earliest phases of genetic code origin, removes the main difficulty of the coevolution theory. Furthermore, it is here discussed how this code might have naturally led to the code codifying only for the domains of the codons of precursor amino acids, as predicted by the coevolution theory. Finally, the hypothesis here suggested also removes other problems of the coevolution theory, such as the existence for certain pairs of amino acids with an unclear biosynthetic relationship between the precursor and product amino acids and the collocation of Ala between the amino acids Val and Leu belonging to the pyruvate biosynthetic family, which the coevolution theory considered as belonging to different biosyntheses.
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Background

Why the genetic code originated

There are two completely different interpretations on why the genetic code might have originated. The first is obtained by means of an extreme interpretation of the stereochemical hypothesis of genetic code origin which suggests that the genetic code originated because its organisation is somehow constrained by the stereochemical relationships between codons or anticodons and amino acids. This extreme interpretation seems totally absurd to me. The second interpretation that I am aware of has to do with the origin of peptidyl-tRNA: the key intermediate in the origin of protein synthesis.

Peptidyl-tRNA has no function per se, but in some models it has been assumed that the entire catalysis of the protocell was originally performed by this intermediate [1-4]. Its origin might therefore have been determined by interactions between covalent complexes of peptide and RNA (peptide-RNAs) and these interactions might have constituted one of the most elementary forms of protein synthesis [3,4]. This model shows that the interactions between peptide-RNAs must, at a certain evolutionary stage, have been directed by a template (pre-mRNA) which must have originally codified only the succession of interactions between peptide-RNAs [4]. This pre-mRNA is the most ancestral form of mRNA imaginable [4]. Finally, the evolution of these pre-mRNAs must have resulted in an mRNA codifying only for a limited number of amino acids [4]. This is the phase that defines the very origin of the genetic code. Clearly this is an historic interpretation of genetic code origin that is completely different from the deterministic one given by the stereochemical theory.

What is particularly important as far as this paper is concerned is that the evolution of these pre-mRNAs into mRNAs was char-

acterised by a progressive refinement of the interactions of the peptide-RNAs on the pre-mRNA templates and this refinement seems to have been made possible only when peptide-RNAs were transformed into amino acid-pre-tRNAs [4]. This is because there might have only been the modification, residue by residue, performed by the amino acid-pre-tRNAs on the evolving proteins that might lead to the complete specification of their sequences, and which made possible the birth of an mRNA proper but with codification limited to just a few amino acids [4]. As will become clear in the following, I maintain that these amino acid-pre-tRNAs came directly from the biosynthetic pathways of the first six amino acids evolving along the biosynthetic pathways of energetic metabolism and that they were the first amino acids to be codified on these still evolving mRNAs.

The biosynthetic relationships between amino acids are closely linked to the organisation of the genetic code

Ever since the genetic code was first deciphered, it has been observed that the biosynthetic relationships between amino acids are linked to the organisation of the genetic code. Indeed, Nirenberg et al. [5] acknowledged the existence of a relationship between amino acids of a similar biosynthetic origin and the codons specifying those amino acids. Although the examples of biosynthetic relationships reported by Nirenberg et al. [5] contain some inaccuracies, the authors were the first to suggest that the genetic code's evolutionary development might have been defined by the amino acids' biosyntheses. Jukes [6] also noted that some amino acids take part in the biosynthesis of other amino acids, such as serine which plays a part in the biosynthesis of tryptophan. However, these seemed to be isolated and not totally clear observations and Jukes [6] did not believe they could be generalised for the entire genetic code. Pelc [7] recognised that biosynthetic conversions between amino acids might have had an important role in defining the genetic code. However, it was Dillon [8] who, above all, suggested a metabolic model for the origin of the genetic code, although this author suggested amino acid biosyntheses that are only partly linked to those existing in living organisms. It was Wong [9] who fully recognised the importance, for the evolution of the genetic code, of the biosynthetic relationships between amino acids as they take place in actual organisms, suggesting what is now known as the coevolution theory of genetic code origin. This theory suggests that the genetic code is primarily an imprint of the biosynthetic pathways forming amino acids [9]. Consequently the evolution of the genetic code could be clarified on the basis of the precursor-product relationships between amino acids in their biosyntheses [9]. In other words, this theory suggests that only few amino acids (precursors) were codified in the genetic code; as other amino acids (products) developed from these, part of the codon domain of precursor amino acids was ceded to product amino acids [9]. Therefore, according to this theory, the genetic code might represent an evolutionary map of the biosynthetic relationships between amino acids [9].

While Wong [9] highlighted the precursor-product relationships between amino acids and their crucial role in defining the organisation of the genetic code, Miseta [10] clearly identified that the non-amino acid molecules that were precursors of amino acids might have been able to play an important role in organising the genetic code. Miseta [10] suggested the idea of an intimate relationship between molecules, the intermediates of glucose degradation, as precursors of precursor amino acids, and the organisation of the genetic code. This observation is also analysed by Taylor and Coates [11] who showed the relationship between the glycolytic pathway, the citric acid cycle, the biosyntheses of amino acids and the genetic code (Fig. 1) and, in particular, they point out that (i) all the amino acids that are members of a biosynthetic family tend to have codons with the same first base (Fig. 1) and (ii) that the five amino acids codified by GNN

codons are found in four biosynthetic pathways close to or at the beginning of the pathway head (Fig. 1)[11]. More recently, Davis [12,13] has provided evidence that tRNAs descending from a common ancestor were adaptors of amino acids synthesised by a common precursor and he also discusses the biosynthetic families of amino acids, suggesting their importance in genetic code origin.

However, there have also been authors who have suggested that some aspects of the biosynthetic relationships between amino acids were not important in genetic code origin [14,15]. In particular, Ronneberg et al. [14] criticise the coevolution theory above all because some pairs of amino acids used by this theory do not seem to be in a clear precursor-product amino acid relationship, although, more generally, they recognise that amino acids in a biosynthetic relationship tend to have codons with the same first base [14]. Di Giulio [16] responded to the criticisms made by Ronneberg et al [14] and, in particular, made numerous observations in favour of the coevolution theory. There has also been evidence indicating that the five families of amino acids, defined in accordance with a single amino acid precursor or a non-amino acid precursor, should have been randomly observed in the genetic code with a probability of 6 x 10^{-5} [17]. This indicates that the biosynthetic relationships between amino acids were fundamental in organising the genetic code.

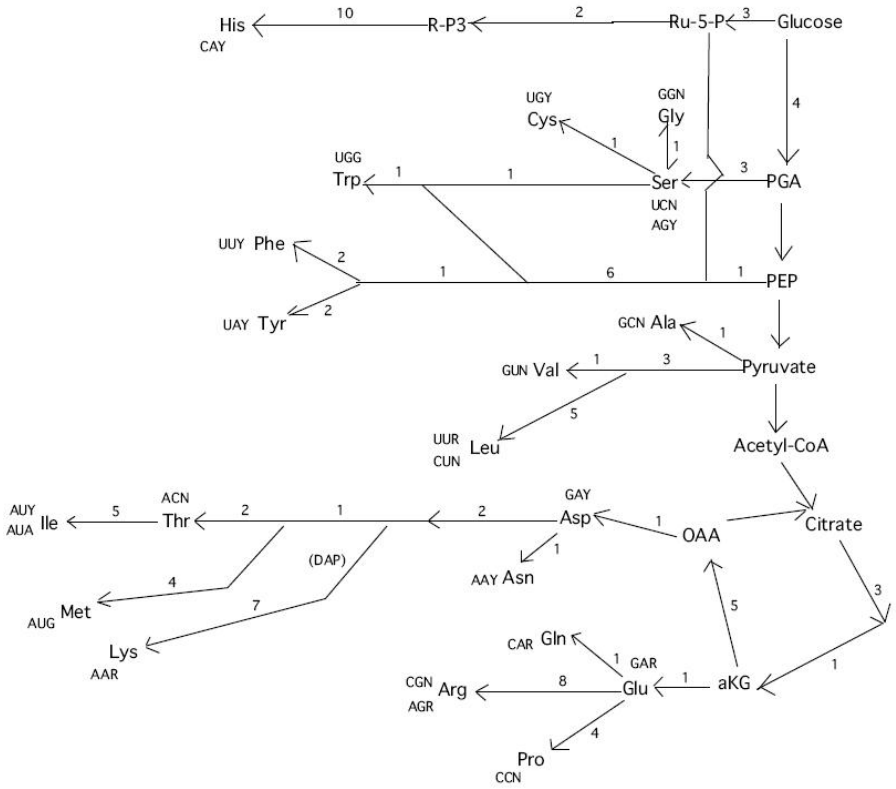

Figure 1. Biosynthetic relationships between amino acids, as defined by their biosyntheses and their relationships with the glycolytic pathway and the citric acid cycle. The figure was taken from Taylor and Coates [11] with a few modifications. The numbers indicate the biosynthetic steps. DAP = diaminopimelic pathway, aKG = alpha-ketoglutarate, OOA = oxalacetic acid, PEP = phosphoenolpyruvate, PGA = phosphoglycerate, R-P3 = 5-phosphoribosylpyrophosphate, Ru-5-P = ribulose-5-phosphate. The other abbreviations are standard.

Finally, if we consider that other works have been carried out on the importance of biosynthetic relationships between amino acids and the genetic code [18-39], we come to the conclusion that there can no longer be any doubts on the hypothesis that the origin of the organisation of the genetic code was affected by the biosynthetic pathways of amino acids.

Results

The extended coevolution theory

In order to eliminate some criticisms on certain pairs of amino acids that are in an unclear precursor-product relationship [14,16] and, above all, to provide a more complete description of the very earliest phases of genetic code origin, I have been forced to suggest the following theory. This theory, which can be called the 'extended coevolution theory' as it is simply an extension or a generalisation of Wong's coevolution theory [9], states that:

"The genetic code is simply an imprint of the biosynthetic relationships between amino acids, even when defined by the nonamino acid molecules that are the precursors of some amino acids, i.e. that the organisation of the genetic code must only reflect the biosynthetic proximity between amino acids in the various stages of evolution of their biosynthetic pathways. This happened because the ancestral biosynthetic pathways took place on tRNA-like molecules and thus enabled a coevolution between these pathways and the organisation of the genetic code through the concession of tRNA-like molecules between biosynthetically close amino acids, which made possible the transfer of codons from one amino acid to another, while mRNA evolved, with the consequence that amino acids with correlated biosyntheses have contiguous codons in the genetic code".

This theory, which in a contracted and informal form has already been suggested [16], can be tested and all the evidence in favour of the coevolution theory is also in favour of the extended coevolution theory. The key point on which the two theories disagree regards the predictions on the earliest phases of genetic code origin, which are not well defined for the coevolution theory [9,40] while, for the extended coevolution theory their traces should be present in the biosynthetic relationships between amino acids that are precursors of other amino acids and the nonamino acid molecules that are precursors of precursor amino acids.

As shown in the following section, this main prediction of the extended coevolution theory seems to be corroborated by the observations.

The main prediction of the extended coevolution theory seems to be corroborated

According to the predictions of the coevolution theory, the codon concession mechanism between amino acids in a precursor-product relationship was based on tRNA-like molecules on which the theory hypothesises that biosynthetic transformations between amino acids take place [9]. Surprisingly, this prediction is confirmed by the existence of molecular fossils [33] representing the vestiges of these pathways (Tab. 1) hypothesised by the coevolution theory [9,19-21]. Although these biosynthetic transformations took place in accordance with the coevolution theory, only among the amino acids in a precursor-product relationship [9] is there no a priori reason why this should have taken place only between amino acids [28,31]. The coevolution theory seems to imply that all metabolism took place at that time on tRNA-like molecules [28,31] or, at least, that the entire metabolism of amino acids took place on these molecules. This view, i.e. that metabolism took place on tRNA-like molecules, has been hypothesised by other authors following arguments that might be totally different from those used here [41-43].

Therefore, if the metabolism of amino acids took place on tRNA-like molecules when the genetic code originated, the structure of the genetic code must contain traces linking the very earliest phases of genetic code origin to the biosynthetic relationships between the first amino acids to enter the

code and the non-amino acid molecules that were their precursors. This is because the very first amino acids that entered the genetic code and had non-amino acid molecules as their precursors, did so, as suggested by the extended coevolution theory, using the same mechanism employed by the pairs of amino acids in a precursorproduct relationship, i.e. exploiting the hypothetical existence of the biosynthetic pathways on the tRNA-like molecules that triggered the origin of the genetic code. This is the main prediction of the extended coevolution theory and how it differentiates the latter from the coevolution theory.

Fig. 2 reports the biosynthetic relationships between amino acids that presumably first originated from the glyPage colytic pathway and Krebs' cycle. All these amino acids are, with the exception of Gly, directly linked to nonamino acid molecules that are their precursors. (Although the biosynthetic pathways leading to Phe and Tyr and to His are directly linked to a non-amino acid precursor (Fig. 1), they seem too complex for an early evolution because they have at least ten biosynthetic steps in these pathways and so these three amino acids would evidently not fall within this classification (see Appendix)). As suggested by the extended coevolution theory, this might indicate that they were the first to originate during the evolution of the biosynthetic pathways of amino acids. (Gly is the only one of these amino acids that is not directly linked to one of these non-amino acid molecules of the glucose degradation pathway (Figs, 1, 2). Although the synthesis of Gly from Ser is well documented [9,44], the conversion of Gly to Ser also takes place normally [9,45]. For example, Gly is converted to Ser by reacting with formate in the presence of pyridoxal phosphate [9,45-47]. This favours the hypothesis that these two amino acids, Ser and Gly, were inter-convertible when these pathways originated).

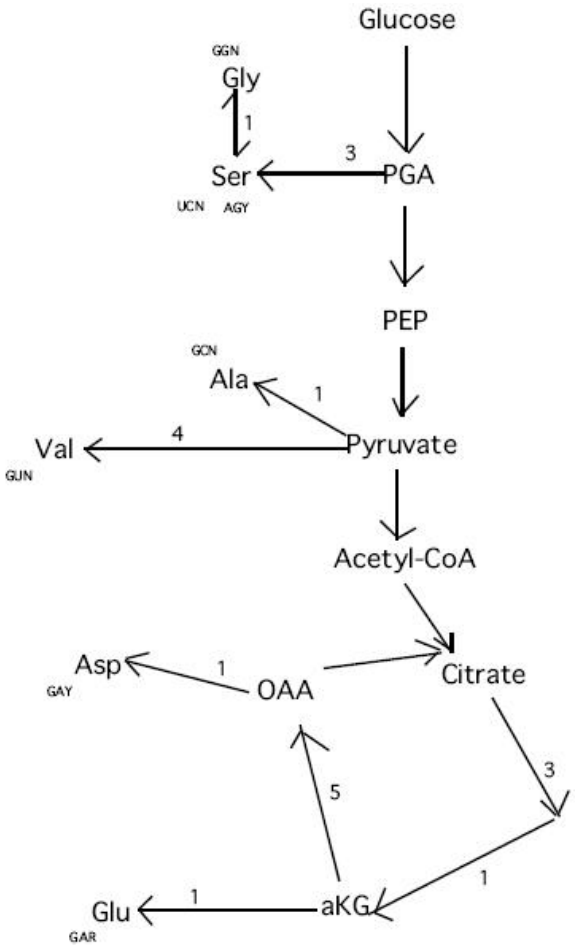

Figure 2. Biosynthetic relationships between amino acids and their precursor non-amino acid molecules, as defined in a particular stage of the evolution of the biosynthetic pathways of amino acids. With the sole exception of proline, these are also the amino acids that first appear in a study on the temporal origin of the appearance of amino acids [54]. See Fig. 1 for further information.

If these were effectively the earliest amino acids to originate from non-amino acid precursors of the energetic metabolism pathways (Fig. 2) and if the main prediction of the extended coevolution theory is true, then all these amino acids (Fig. 2) should occupy a particular place within the genetic code table because they should be witnesses of the earliest phases of the evolution of the genetic code. Indeed, as other authors have observed [11], with the exception of Ser, all these amino acids (Fig. 2) are codified by

codons of the GNN type. The distribution of these amino acids on these codons is not random and is obtained, by pure chance, with a probability equal to 3.9 Ч 10^{-4} (see Appendix).

Therefore, this observation that the first amino acids to evolve along the biosynthetic pathways are the same ones that are mostly codified by codons of the GNN type leads us to suppose, in compliance with the extended coevolution theory, that there existed a type of primitive genetic code (mRNA) that possessed only the codons of the type GNC (or GNG) and codified only for the amino acids Ala, Asp and Ser or Gly (or Ala, Glu and Ser or Gly) (Fig. 3) from which the GNS code codifying for Val, Ala, Asp, Glu, Ser and/or Gly (Fig. 3) might have evolved. This is suggested by exploiting the results of Ikehara et al [48] who, for quite different reasons, suggested a genetic code origin that is, in some respects, similar.

It should also be borne in mind that as these amino acids are the most abundant in the experiments of prebiotic synthesis and in meteorites [40] they had already attracted the attention of researchers. Indeed, Eigen et al. [49] had suggested a primitive code with codons of the GNY type, which is partly compatible with what is maintained here, partly because it might be derived from a GNC code (Fig. 3) [50].

Discussion

Some comments on the evolution of the genetic code, as suggested by the extended coevolution theory

The evolution of the genetic code as suggested here needs some discussion and clarification.

(i) Ser is not codified by any of the GNN codons whereas, on the basis of the considerations made here, it should be.

However, the fact that Ser is biosynthetically inter-convertible with Gly [9,44-47] might indicate that Ser was codified by some or all the codons that today codify for Gly in the GNS and SNS codes (Fig. 3), and only with the NNS code (Fig. 4), i.e. when the codon domains of precursor amino acids were defined as predicted by the coevolution theory, did Ser cede some codons (GGS) to Gly (Fig. 4). This seems to be corroborated by the observation that, as Ser is also codified by AGY codons contiguous to the GGN codons of Gly, this might imply that the latter codons codified for Ser in a previous evolutionary stage.

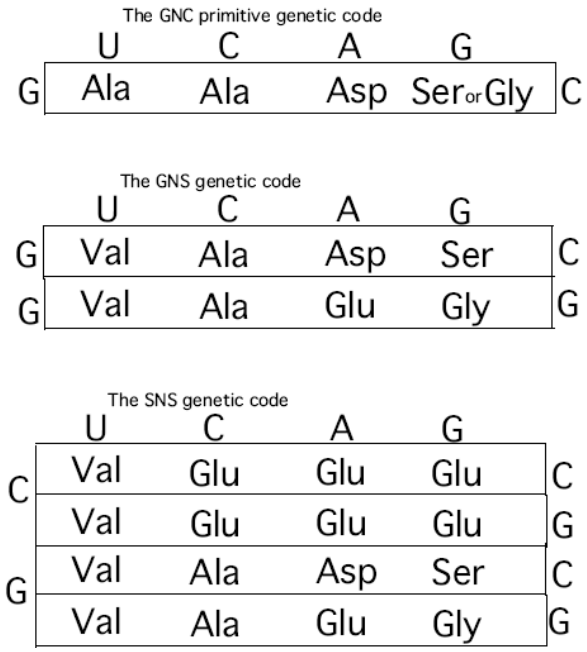

Figure 3. This shows three stages of genetic code evolution. All the abbreviations are standard. See text for discussion.

From the evolutionary stage (shown in Fig. 4) of the genetic code on, the evolution of the code is fully described by the coevolution theory [9] (see Di Giulio and Medugno [35] for details on the entry times of amino acids into the genetic code).

(ii) The closer biosynthetic proximity between the pairs Ser-Ala, Ala-Val, Asp-Glu and Ser-Gly, as shown in Fig. 2, seems to find confirmation in the genetic code structure in that: (1) Ser-Ala and Ser-Gly have contiguous codons in the genetic code, i.e. they differ only in a single base, although Ser does not occupy the last row of the genetic code; (2) the pair Asp-Glu occupies the same box in the genetic code, i.e. their codons differ only in the third base and these amino acids are the same ones that, at the evolutionary

stage of the biosynthetic pathways as indicated in Fig. 2, are more biosynthetically correlated; (3) the pair Ala-Val is part of the pyruvate biosynthetic family (Fig. 1) and their codons differ in only one base, a pyrimidine, even if these amino acids occupy the last row of the genetic code. All this seems to imply, in agreement with the extended coevolution theory, that amino acid pairs made in siblings by a non-amino acid molecule, i.e. the pairs Ser-Ala, Ala-Val, Asp-Glu and Ser-Gly (Fig. 2), the last of which might be in a precursor-product relationship [9], were particularly important in the earliest phases of genetic code origin because their organisation within the genetic code would also seem to reflect the closer biosynthetic proximity of these pairs (Fig. 2).

The NNS genetic code

	U	C	A	G	
U	Ser	Ser	Ser	Ser	C
		Ser	Ter	Ser	G
C	Val	Glu	Glu	Glu	C
	Val	Glu	Glu	Glu	G
A	Asp	Asp	Asp	Ser	C
	Asp	Asp	Asp		G
G	Val	Ala	Asp	Gly	C
	Val	Ala	Glu	Gly	G

Figure 4. This shows a stage of the evolution of the genetic code: the one in which the precursor amino acid codon domains are formed, as predicted by the coevolution theory [9]**.** See text for discussion

(iii) The here-maintained hypothesis that the amino acids that first evolved along the pathways of energetic metabolism (Fig. 2) formed the GNS code (Fig. 3) seems to rationalise why Asp and Glu are codified by GAN codons and not by ANN and CNN codons. Indeed, if the GAS codons had been attributed early on to Asp and Glu, they should have been both abundant on the first mRNAs and linked to them by a stronger historic constraint. Consequently, it would have been more difficult to concede them to product amino acids than the ANS and CNS codons making up the codon domain of Asp and Glu which instead must have been rare (see below) and also less historically constrained and, thus more easily transferable to the product amino acids, as seems to have happened. Therefore, this reasoning rationalises why Asp and Glu are codified by GAN codons and not ANN or CNN codons. Moreover, this strengthens the hypothesis of the existence of the GNS code for the very reason that Asp and Glu are codified by the GAN codons and not by some of those in ANN and CNN, as would have been more reasonable to expect considering the clearer biosynthetic relationship that Asp and Glu have with the product amino acids of their biosynthetic family compared to the less clear relationship they have with each other (Fig. 1). This should have resulted in a closer similarity between codons of Asp and Glu and codons of their product amino acids than with their own. The fact that this did not happen would seem to imply a very early involvement of GAN, or rather GNS, codons in genetic code origin because Asp and Glu are codified by these codons and not by those of the type ANN and CNN, as would instead be imposed by the clearer biosynthetic relationships with their product amino acids. In short, the codification of Asp and Glu by means of GAN codons might reflect the history of the very earliest phases of genetic code origin.

(iv) The evolution of mRNA as defined by the passage from the SNS (or GNS) code (Fig. 3) to the NNS code (Fig. 4) might have been highly facilitated if some codons were rarely used on mRNAs. In other words, let us admit that, for instance, there evolved in the SNS code: one or very few ANS codons codifying for Asp; one or very few CNS codons codifying for Glu: one or very few UNS codon codifying for Ser. It can be seen that in this way, all the precursor amino acid codon domains can be defined, i.e. the NNS code (Fig. 4), paradoxically without

there actually being all their codons present. Indeed, it is sufficient for the first base of any one codon to be recognised, although read in triplets [51], in order to define the NNS code relatively fully. If the rarity of codons had been preserved in the evolutionary stages following the NNS codes (Fig. 4), then an amino acid precursor might have easily ceded part of its codon domain to the product amino acid without generating considerable translation noise in this transfer of codons. Naturally, every passage between the codes GNC (or GNG), GNS, SNS and NNS (Figs. 3, 4) must have been characterised by the rarity of the types of codons because the system was evolving and, for instance, the majority of tRNA molecules had yet to evolve, i.e. there existed very few types of tRNA molecule. In other words, it would seem that it is the very evolution of the code that implies codon rarity, allowing a faster and more efficient evolution by means of the mechanism of the coevolution theory. This leads us to suppose that the SNS form of code might have only partly preceded the NNS form because it would take just one codon, for instance of the ANS type, to define an entire codon domain and, therefore, an entire evolutionary stage of the genetic code. In other words, the evolutionary stage of the SNS and NNS codes might be less sharp than apparently shown in Figs. 3 and 4. Moreover, this indicates that the mRNA of the NNS code might have been much simpler than appears from the same Fig. 4.

(v) Exceptions to the "rule" of precursor amino acid codon domains seem to be the codons UUG (Leu) and AGG (Arg) (in white in Fig. 4), but also the codon AGC (Ser) although the latter might be derived from codons attributed to Gly, as suggested by Wong [9], but in any case outside the domain of Ser (Fig. 4). In other words, the codons UUR and AGR are the only exceptions observed in the precursor amino acid codon domains because they do not biosynthetically belong to the codon domain of the precursor in which they reside. However, while the codons UUR (Leu) might have been captured with a secondary mechanism by the codons in Ser's domain, for the AGR codons (Arg) there might exist a fascinating explanation. It is possible that the AGR codons of Arg derive from the codon domain of Asp and not from that of Glu, which is the natural precursor of Arg (Fig. 1) in that Asp intervenes in one of the terminal steps of the biosynthetic pathway of Arg [14,16]. Therefore, for Arg, the CGN codons might derive from the codon domain of Glu via ornithine or citrulline [16], while the AGR codons might derive from the codon domain of Asp [14,16]. This might therefore be an extremely interesting case of a double entry of an amino acid in the genetic code through two different amino acid precursors, something which has also been hypothesised for Ser [9]. This would provide a strong corroboration for the mechanism by which amino acids enter the genetic code, as suggested by the coevolution theory.

Finally, the CUS codons of Val (Leu) also apparently belong to the codon domain of Glu (Fig. 4). This might corroborate the hypothesis that these codons were ceded from Glu to Val. Indeed, the early phases of the evolution of NNS codes are characterised by codification limited to only six amino acids (Fig. 4) and therefore, the relative biosynthetic relationships might have made the amino acids Val and Glu biosynthetic siblings (Fig. 2). Although not entirely free of criticism, this viewpoint cannot be categorically excluded.

Nevertheless, there seems to be a much simpler interpretation provided by the SNS code (Fig. 3). Indeed, if in this evolutionary stage all the SUS codons codified for Val (Fig. 3) there would not have been any need for a real transfer of codons from Glu, but this might have only depended on the passage from the GNS to the SNS code provided that the SUS codons continued to codify for Val (Fig. 3).

Conclusion

The coevolution theory [9] does not give a complete description of genetic code origin as it seems not to consider that the bio-

synthetic pathways of the amino acids that first entered the genetic code were important in the earliest phases of the origin of the code itself [9,40,52]. Whereas, with the extended coevolution theory it can be seen that there might have existed a GNC or a GNG code, but almost certainly a code of the GNS type, because the amino acids codified by these codons are in a clear biosynthetic relationship by means of their precursor nonamino acid molecules (Fig. 2) at the head of the amino acids' biosynthetic pathways and, therefore, must have characterised the earliest phases of genetic code origin.

The extended coevolution theory explains the existence, in the genetic code, of the pairs Phe-Tyr, Val-Leu and Thr-Met which are not in a clear biosynthetic relationship of precursor-product amino acids [14], by means of mere biosynthetic proximity. This is because, as the ancestral biosynthetic pathways take place on tRNA-like molecules, they enabled these biosynthetically close amino acids to have similar codons [16]. This cannot be achieved satisfactorily by the coevolution theory. For the sake of clarity and completeness, see also the comments already made on these amino acid pairs [16].

The coevolution theory [9] does not explain the presence of the codons of the amino acid pair Phe-Tyr inside Ser's codon domain (Fig. 4), whereas the extended coevolution theory explains its existence in this very domain through the mere biosynthetic proximity of the pathway leading to the synthesis of Phe and Tyr to that of Ser (Fig. 1).

Finally, the coevolution theory is unable to explain why Ala has codons contiguous to Val, even if it is clear that these two amino acids are biosynthetically correlated in that they are derived from pyruvate (Fig. 1). This theory even puts Ala and the Val-Leu pair in biosynthetically different domains [9,40], which seems to be mistaken. The extended coevolution theory, on the other hand, explains the relationships between these amino acids derived from the same nonamino acid precursor with the hypothesis that their ancestral biosyntheses took place on correlated tRNA-like molecules that allowed these amino acids to have likewise correlated codons in the genetic code [16].

Appendix

It is necessary to calculate the probability with which the amino acids Ser, Gly, Ala, Val, Asp and Glu can be observed in the GNN codons of the genetic code while also taking into account the distribution of the amino acids in the non-GNN codons. Fisher's exact test seems to be able to calculate this probability. If we consider that, of these 6 amino acids, only Ser is not codified by GNN type codons, we obtain for amino acids with non-amino acid precursors: (i) 5 of these are codified by GNN codons (= a), while (ii) only 1 (Ser) is codified by non-GNN codons (= b). For amino acids with amino acid precursors, we have: (i) 0 of these are codified by GNN codons (= c), and (ii) 14 of these are codified by non-GNN codons (= d). By applying Fisher's exact test we obtain a probability $P = 3.9 \times 10^{-4}$ (a = 5, b = 1, c = 0, d = 14) which is highly significant.

However, it could be objected that Val is 4 biosynthetic steps away from pyruvate, while Gly is not directly linked to PGA (Fig. 2) and therefore might not fall within the class of amino acids that evolved early on. To answer these strongly dubious questions, certain checks can be carried out.

Eliminating Val and Gly because they might not have entered the genetic code early on from the biosynthetic pathways' point of view (Fig. 2), we have P = 0.0035 (a = 3, b = 1, c = 0, d = 16). Therefore, under this hypothesis too, which actually seems extremely restrictive, we obtain a highly significant probability. Eliminating only Val (because Gly might have evolved very early on through interconversion with Ser [9,44-47]) or eliminating only Gly because Val is derived directly from pyruvate in a number of biosynthetic steps that, in qualitative terms, evolved rapidly and are not even numerous, we obtain a P = 0.0010 (a = 4, b = 1, c = 0, d = 15) that is still highly significant. In conclusion, these amino acids (Fig. 2) seem to

have correlated GNN codons because they evolved early on in the ancestral biosynthetic pathways.

Finally, if we consider that His and Phe-Tyr are also derived from non-amino acid precursors (Fig. 1), we obtain P = 0.0081 (a = 5, b = 4, c = 0, d = 11); If we remove Val or Gly we obtain P = 0.014 (a = 4, b = 4, c = 0, d = 12); whereas, if both Val and Gly are removed, we obtain P = 0.031 (a = 3, b = 4, c = 0, d = 13). These probabilities indicate that considering His and Phe-Tyr as amino acids deriving from non-amino acid precursor does not substantially alter the results of the statistical test.

Reviewers' Comments

Reviewer's report 1

Rob Knight, University of Colorado, Boulder CO, USA

This manuscript addresses an important question: whether there are traces in the pattern of codon assignments in the modern genetic code of its expansion from an earlier form, perhaps with simpler amino acids. The author addresses this problem from the perspective of his extensive previous work on the coevolution model, which argues that primordial genetic codes used simple amino acids that are produced in prebiotic syntheses and are encoded in the modern genetic code using codons beginning with G. For example, in previous work, he argued that the GNN-encoded amino acids Asp and Glu were early entries into the genetic code, and that the non-GNNencoded amino acids Asn and Gln arrived later, in part because of the distribution of the metabolic pathways producing them and in part because of the fact that in some organisms they are produced by tRNA-dependent transamidation rather than by direct aminoacyl-tRNA synthesis. In the present work, he elaborates on this theory by adding constraints on the simplest amino acids, and presents statistical evidence that supports the idea that this type of coevolution shaped the modern genetic code.

[Author's Response]

No reply.

Reviewer Comments

The main issue I have with the present version of the manuscript is that it dismisses or fails to discuss other patterns in the genetic code for which the statistical evidence is at least as good as that presented here. This is not to say that the manuscript fails to cite prior work adequately: for example, the discussion of the development of the coevolutionary theory in this manuscript is very complete, and provides a nice self-contained introduction to interested readers. However, I believe that the contention that "we come to the conclusion that there can no longer be any doubts on the hypothesis that the origin of the organisation of the genetic code was affected by the biosynthetic pathways of amino acids." is overstated given that all the cited literature in support of this hypothesis is the work of the present author. Similarly, the statement on page 3 "The first is obtained by means of an extreme interpretation of the stereochemical hypothesis of genetic code origin which suggests that the genetic code originated because its organisation is somehow constrained by the stereochemical relationships between codons or anticodons and amino acids. This extreme interpretation seems totally absurd to me." does not adequately address the mounting statistical evidence from several laboratories, especially the Yarus lab, that there is a relationship between coding triplets and modern codon assignments that should not be ignored (although it is possible that future research will provide some reason why this observation is an artifact of some currently unsuspected process). Similarly, a long list of investigators including David Haig, Laurence Hurst, Stephen Freeland, David Ardell, Guy Sella, etc. have found evidence that the genetic code is error-minimizing compared to other possible genetic codes. I believe that, to be useful, new work on the genetic code needs either to embrace these patterns and explain them, or to argue against them on some grounds other than personal incredulity. After all, if the structure of the natural world were intuitively obvious we wouldn't need

the scientific method, and it's important to take all the available data into account.

[Author's Response]

This paper presents a modification of the coevolution theory. I do not discuss other theories on the genetic code because, paradoxically, this is not 'the right place'. Even if other theories are well corroborated by evidence, I feel that my paper deals with such a specific issue – as the reviewer also acknowledges – that it 'rules out' comments on the other genetic code theories. On other occasions, I have not failed to tackle the problem raised by the referee [55,56] (see also below)).

The reviewer is making a serious claim: namely, that the biosynthetic relationships between amino acids are not in relation with the organisation of the genetic code. For instance, if we apply Fisher's exact test to the five biosynthetic families of amino acids [17], as the reviewer suggests, and then combine the five probability values in a single value, we obtain a highly significant probability ($\chi^2 = 34.8$, df = 10, $P < 10^{-3}$) (data not published). Ronenberg et al [14] also make a bitter criticism of the coevolution theory but, more generally, acknowledge that amino acids in a biosynthetic relationship have codons beginning with the same first base [14].

It is absolutely untrue that all the literature cited on this point is only my own. I have cited no less than 14 papers by other authors [5-13,16-22,34,37] which establish a relationship between the genetic code and the biosynthetic pathways of amino acids.

My suggestion refers to an extreme interpretation of the stereochemical theory, i.e. that if the origin of the genetic code were to start again from scratch, we would observe – according to this interpretation – the same assignments in the genetic code that we observe today. It is this extreme physicochemical determinism that seems so completely absurd to me.

A different argument regards the less extreme interpretations of the stereochemical theory. I have never neglected this theory (see, for instance reference [31]) and I have made it compatible with the coevolution theory [57], but I do not believe in the stereochemical theory because none of the presented evidence is, in my view, stronger, more important or more corroborative than the molecular fossils reported in Tab. 1 (see also replies to Reviewer 3).

All this evidence is compatible with the coevolution theory (see, for instance, reference [31] and replies to Reviewer 3).

My convictions are not based on grounds of personal incredulity but on molecular fossils (Tab. 1) which are 'eye witnesses' of the mechanism that gave origin to the genetic code (see also replies to Reviewer 3). If a different and credible interpretation of these molecular fossils were available, I would instantly renounce my convictions. There is nothing truly personal and unscientific in all this. I have taken all the data into account in Di Giulio [57].

Reviewer Comments

Similarly, it is not clear to me why the first amino acids to enter the code would be expected to be derived from other molecules that were not amino acids. If we assume that the genetic code arose in proto-cells that already had fairly sophisticated metabolism, e.g. the "RNA world" stage accepted by many researchers, it is less clear why pre-protein metabolism would not have generated a range of amino acids prior to genetic coding. Perhaps this point could be elaborated upon? For example, Eors Szathmary argues in the coding coenzyme hypothesis that we might expect complex amino acids to be introduced first, which is consistent with arginine's codon/binding site relationships demonstrated by myself and Michael Yarus.

[Author's Response]

I provide an extensive reply to this point with Reviewer 3. However, the Reviewer's question cannot find a simple answer because we do not understand the profound reason why the biosynthetic pathways of amino acids have to be in a relationship with the genetic code. Understanding this point might constitute the frontier research on genetic code origin [58].

It might have generated other amino acids, but their biosynthetic pathways seem to contain a quite different story than the one hypothesised by the Reviewer. Therefore, this point does not seem to require further elaboration (see also the replies to Reviewer 3).

It is possible: these are other heterotrophic interpretations on genetic code origin. In my view – and as I feel has been convincingly argued in this paper – the biosynthetic path-ways of amino acids tell other stories (see also some of the replies to Reviewer 3).

Reviewer Comments

The calculation in the appendix used to calculate the significance of seeing 5 of 6 amino acids that have nonamino-acid precursors in the GNN codon block (binomial using n = 5, k = 5, p = 6/20) is definitely incorrect because it fails to take into account the distribution of amino acids in other coding blocks. I think the correct calculation, if we use 20 coding blocks for the 20 amino acids, is to say that 5 coding blocks are GNN-encoded, 15 are not, and these distribute into 5 GNN-encoded, no-precursor blocks, 0 GNN-encoded, precursor blocks, 1 nonGNN-encoded, no-precursor block (for Ser), and 14 nonGNN-encoded, precursor blocks. Using Fisher's Exact Test on these data, we actually get a P-value of approx. 0.00038: almost an order of magnitude more significant than reported. However, some caution about the space of possible coding blocks is warranted, and showing that the test holds over a range of these assumptions would be useful. The other statistics should also be re-done using this approach. However, it should be noted that the statistical significance of these results does not come close to that reported either for the stereochemical or adaptive theories of the code's evolution, so a more ecumenical view at this point would appear to be prudent.

[Author's Response]

I have changed the statistical test. Fisher's exact test provides much more significant results (see Appendix). I have also introduced some new observations (see final part of the Appendix).

I have conducted several tests in addition to those shown in the Appendix. I feel that Fisher's exact test is the one that really must be used to calculate these probabilities because it can take into account the structure of the genetic code by means of amino acids codified by GNN codons and by non-GNN codons. I thank the Reviewer for this suggestion.

The probability of 3.9×10^{-4} (see Appendix) clearly indicates that the distribution of amino acids deriving from non-amino acid precursors is not in the least random in the genetic code. Even if this value is not close to the one associable to the stereochemical or physicochemical hypotheses, it nevertheless indicates that we have to explain it, which is what I have done in this paper.

I do not say that the stereochemical or physicochemical hypotheses are false, I simply explain what I observe using a prudent tone. Nevertheless, the stereochemical and physicochemical hypotheses cannot naturally explain what is observed in this paper.

Reviewer Comments

Finally, the conclusions seem to end rather abruptly with a discussion of specific product-precursor pairs. A more general concluding paragraph, including relationships between the present results and existing knowledge about the genetic code (including relationships to the adaptive and stereochemical patterns that have been shown using data from many laboratories) would be helpful for the general readership that Biology Direct attracts.

[Author's Response]

All the observations regarding the topic dealt with in the paper have been fully discussed. The paper is already overlong and its further extension with a discussion of the stereochemical and physicochemical hypotheses would be inappropriate in my view, partly because the observations reported therein are not easily reconciled with the stereochemical hypothesis, for instance, although there are models [57] that make the coevolution and the stereochemcial theories compatible. However, I feel that the Re-

viewer's suggestion is unsuitable as the paper does not aim to make a comparison with, for instance, the the stereochemical hypothesis. What the Reviewer suggests should be done elsewhere. Here I have introduced an extension of the coevolution theory and have not dealt with its relations with other theories.

Reviewer's report 2

Eugene Koonin, National Institutes of Health, Bethesda MD, USA

Reviewer Comments

This article strives to develop Wong's co-evolution theory to additionally specify the order of amino acid recruitment to the genetic code. The main salient observation is that, with the sole exception of serine, amino acids that are synthesized from non-amino acid precursors are encoded by GNN codons. These are supposed to be the first amino acids in the code. This is an interesting idea but I think it is based on certain assumptions that are not spelled out in the paper. First, I think way too much confidence is granted the original co-evolution theory. It is a viable explanation for some aspects of the evolution of the code but, to me, frozen accident + partial optimization for translational robustness work at least as well. Second, and somewhat more subtly, an important hidden assumption is that, at the stage of the code evolution, central metabolism was already in place, so that amino acid biosynthesis pathways evolved from central pathways. This is far from being obvious. From my viewpoint, a more sensible approach would be to assume that the first amino acids were those that are most readily produced abiogenically. Granted, this list significantly overlaps with Di Giulio's but there is also considerable difference, and I believe it matters.

[Author's Response]

I have dedicated entire sections to specifying the various assumptions and, in particular, the section entitled "the extended coevolution theory", so the Reviewers' comment appears strange.

There is nothing new in the fact that the coevolution theory is not generally appreciated, but we must say why. The frozen accident and partial optimisation for translational robustness are compatible with the co-evolution theory [31] (see replies to Reviewer 3). I repeat that I am convinced of the substantial correctness of the coevolution theory because: (i) the biosynthetic pathways are linked to the genetic code [5-13,16-22,34,37] and (ii) molecular fossils (Tab. 1) are 'eye witnesses' of the mechanism that structured the genetic code.

I reply extensively to this observation with Reviewer 3.

If the main suggestion of the coevolution theory is true, then there was a coevolution between the biosynthetic pathways of amino acids and genetic code organisation, implying that at least the metabolism of amino acids evolved when the genetic code evolved. Therefore, it is not utterly absurd to imagine that central metabolism was already in place because the biosynthetic pathways of amino acids start from there. Furthermore, the metabolic complexity of the RNA world has also been discussed (see, for instance, references [42,43]).

There is an overlap between the first amino acids to evolve along the pathways of central metabolism and those that are more abundant in the prebiotic syntheses or in meteorites. We will have to see which interpretation is right. This point is extensively discussed with Reviewer 3.

Reviewer Comments

The paper is written in a manner that makes it hard to figure out what is actually new.

I think it is worth to clearly formulate the difference from the traditional coevolution theory.

[Author's Response]

The Conclusions section answers this question.

The difference is reported in the Conclusions and on p. 9.

I think it is worth citing the following paper:

Trifonov EN. The triplet code from first principles.

J Biomol Struct Dyn. 2004 Aug;22(1):1–11

That presents a good overview of different approaches used to infer the order of aminoa cid appearance in the code.

[Author's Response]

I have introduced this reference [54].

Reviewer's report 3

Paul Higgs, McMaster University, Hamilton, Ontario

Nominated by Laura Landweber, Princeton University, Princeton NJ, USA

Reviewer Comments

The coevolution theory of the genetic code is a detailed and well-developed theory that describes the build-up from a simple structure encoding only a few amino acids to the current canonical code. Several important aspects of this theory make a great deal of sense to me, but other aspects seem less well justified. I will try to indicate the problems as I see them.

[Author's Response]

On the basis of what is written in this review against the coevolution theory, I do not understand what are the aspects of this theory that "make a great deal of sense" to this Reviewer.

Reviewer Comments

Firstly, I would like to relate this theory to the RNA World hypothesis, which supposes that there was a time early in the history of life at which both genetic and catalytic functions in organisms were carried out by RNA molecules. The genetic code and the translation process are the most important pieces of evidence that convince me that there was an RNA World. The whole point of translation is to take information from the mRNA and use it to make a protein. Furthermore, rRNAs and tRNAs are essential in the translation mechanism. Thus it seems clear that RNA came before the origin of the code. Although your papers and those of Wong do not mention the RNA World explicitly, it seems to me that the coevolution theory is perfectly consistent with the RNA World idea. Would you agree?

[Author's Response]

At a certain evolutionary stage. RNA must have become the 'master' of protocellular activity and from this point on I agree with the Reviewer's RNA world. Indeed I have published papers on this very topic [59]. In this paper, the coevolution theory is discussed in the terminal phases of the RNA world. There are also other papers of Wong's and my own on this issue [1-4].

Reviewer Comments

In my view, the late stage of the RNA World was already rather complex. I envisage cells enclosed by lipid membranes within which a well-developed, RNA-controlled metabolism was operating. These cells must already have solved the basic problem of accurate replication of relatively long RNAs (like rRNA), and they must have had a reliable energy input that could be coupled to the synthesis of large numbers of RNA polymers. The genetic code would have originated inside cells of this nature.

[Author's Response]

I totally agree: the genetic code originated very late on in the origin of life. In my papers I have stressed this point (see for instance reference [3]).

Reviewer Comments

One thing that is not clear in this paper is whether the metabolic reactions discussed are supposed to be catalyzed by RNAs or proteins. In particular, Figures 1 and 2 show that the synthesis of the earliest amino acids is related to the glycolytic pathway and the citric acid cycle. Since these are the earliest amino acids in the code, there could be no genetically encoded proteins prior to this. Are you therefore proposing that the glycolytic pathway and the citric acid cycle existed in the RNA World and that all the steps in these pathways were catalyzed by RNAs? This does not seem impossible to me, but it is a strong assumption, because it supposes that proteins have evolved to take over all the same catalytic steps formerly catalyzed by RNAs without changing any of the steps in the metabolism. Since the theory seems to depend on this assumption, it should be stated clearly.

[Author's Response]

We have discussed that the main catalyst in the early phases of genetic code origin was constituted by peptideRNA molecules, whose evolution resulted in peptidyltRNA like molecules and, therefore, in the origin of the genetic code [1-4]. Therefore, during genetic code origin, metabolic reactions were catalysed by covalent complexes of peptides and RNAs (see Background) also involved in the catalysis of the glycolitic pathway and the citric acid cycle (see also below). If peptides were already involved in the peptide-RNA complexes, as I maintain, then the problem that the Reviewer raises is non-existent because the protein component already present should eventually prevail – without violating the principle of evolutionary continuity – over the RNA component. These ideas have been presented in several papers ([1-4,59], and need not be repeated here. An entire section "Why the genetic code originated" introduces these ideas so I do not feel any more need be said. I remind the Reviewer that very early catalysts could have catalysed reaction classes and, therefore, there might have been a very small number of enzymes [60].

Reviewer Comments

At the end of the results section, you touch on the fact that the earliest amino acids in the code are the most abundant in meteorites and in prebiotic synthesis experiments. We have recently considered this question in detail [61]. By combining measurements from several meteorites, experiments on atmospheric discharge, hydrothermal vents, icy dust grains and others, we show that there is a consensus of which amino acids are easiest to form non-biologically. Our analysis shows that ten amino acids are found widely in these cases, and that these can be ranked in decreasing order of frequency as Gly, Ala, Asp, Glu, Val, Ser, Ile, Leu, Pro, Thr. The other ten biological amino acids are not found in these non-biological situations. We consider our analysis to be strong support for certain aspects of the coevolution theory. We refer to the ten listed amino acids as 'early', because we suppose these were the first incorporated into the code, whereas the other ten are 'late' because they could only have been incorporated after the evolution of biochemical synthesis pathways. The early amino acids that emerge from our analysis are almost exactly the same as those taken to be early in the coevolution theory. Furthermore, Trifonov [54] has also carried out a ranking procedure that predicts a very similar order.

[Author's Response]

These observations are partly consistent with the coevolution theory. However, Ile, Leu, Pro and Thr are product amino acids according to the coevolution theory and therefore appeared late on, while they are early according to the observations of Higgs and Pudritz [61]. Nevertheless, it is unclear whether these amino acids entered the genetic code through the biosynthetic pathways or through their availability in the environment (heterotrophic origin) (see also below). Whereas, in order to explain the codification of these amino acids by GNN codons by means of the scheme in Fig. 2, the extended coevolution theory need only add that the glycolytic pathway and Krebs' cycle were already operative. I have introduced a reference for Trifonov's works [54].

Although there seems to be general agreement about the distinction of early and late amino acids, our results make it clear that there are many different ways to make the early amino acids. These are easiest to form because they are thermodynamically least costly ([61]. In turn, this suggests that biochemical pathways might not be relevant at the earliest stages of genetic code evolution discussed in this paper. If these early amino acids were synthesized non-biologically, they might have been frequent in the environment and could have been used directly without requiring synthesis in the organism (heterotrophy). Alternatively, if they were synthesized by the organisms, the fact that they are easy to make suggests that many different reaction pathways would be possible, and that the pathways that were used in the RNA World may not be related to those

used today, thus casting doubt on the relevance of Figure 2.

[Author's Response]

I do not understand why the ease of thermodynamic synthesis of these amino acids should not have been exploited by the biosynthetic pathways of amino acids. It should rather be expected that the thermodynamic opportunities be exploited biologically. It is unclear why these amino acids should not be able to coincide. It is also unclear why the pathways used by the RNA world should be different from those used today. These pathways are fundamental and, once they were acquired it would have been difficult to change them. Does the Reviewer think that the metabolism of the RNA world was different from that of today? Why? And, in particular, why should the biosynthetic pathways of amino acids be different from those of the RNA world? Although minor changes are to be expected, the majority of the pathways present in the RNA world should have been preserved unchanged even in the later evolutionary stages. It must be borne in mind that most of the pathways in Fig. 1 evolved in a world in which the catalytic component might have already been represented, albeit partly, by proteins (peptides), at least those that were codified at that time, made up of only the amino acids in Fig. 2. Complexes of peptide-RNA catalysts, some of which were of heterotrophic origin, might also have been used for the syntheses in Fig. 2 with the additional condition that the first amino acids were codified only through the biosynthetic pathways in Fig. 2. However, the key point is that the amino acids in Fig. 2 are the same ones codified by GNN codons, and this association is statistically highly significant. If, more generally, we consider that the biosynthetic pathways of amino acids are linked to genetic code organisation [5-13,1622,34,37], then the relation between GNN codons and Fig. 2 becomes highly significant and might truly explain the very earliest phases of genetic code origin.

One interesting point of agreement is that the five most frequent amino acids in our list (Gly, Ala, Asp, Glu, Val) are exactly those coded by GNN codons, and this suggests something very similar to that shown in your Figure 3. In your results section, you mention GNN codons, but then say that there was a primitive code that possessed only codons of the type GNC or GNG from which the GNS code developed (where S = G or C). I do not understand the reason that the third position base was restricted to G or C. I would suppose that the wobble pairing at the third position in the anticodon-codon interaction is a fundamental aspect of RNA structure that would have been the same in the earliest tRNAs, *i.e.* I would assume that a tRNA with wobble base G could pair with codons ending C or U, and that a tRNA with wobble base U could pair at least with codons ending A and G (as occurs with most bacterial tRNAs today), and possibly with all four bases at the third position (as occurs with most mitochondrial tRNAs today). In other words, I think that the two-codon and four-codon boxes seen in the modern genetic code arise naturally from the properties of RNA structure and that these would also have occurred in the earliest code. In contrast, wobble pairing does not occur at first position, so there is no problem with having the first position restricted to G or C, as in Figure 3.

[Author's Response]

The GNC code was suggested by Ikehara et al. [48] and I make use of their results. The truly important point is that the biosynthetically early amino acids are codified by GNN codons. It is irrelevant which form of code, for instance GNS, GNR or other, was actually operative. However, the reason might be that, as all the codons start with G, it might have resulted in a general enhancement of G and C in mRNAs and it is also for this reason that the scheme in Fig. 3 was chosen. I also prefer the GNS codon because I believe that this took place at a very high temperature, thus favouring RNAs rich in G and C [3]. Therefore, I partly agree with

the Reviewer. More generally, I must say that this is not an important point and should not be overstressed.

However, Eigen et al. [49] also prefers codons starting with G (GNY). I prefer restricting the third codon position to just two bases because it is thus easier to achieve the evolution of mRNA [3,4].

Reviewer Comments

A key point of the coevolution theory is that, when a new amino acid is added, it takes over some of the codons previously assigned to its precursor. If all the amino acids in the current code are traced back to their earliest precursors, then we arrive at Figure 4 (or something similar, if we interpret 'C' and 'G' at third position as 'U or C' and 'A or G'). This code arises naturally from the logic of the coevolution theory, but there is no direct evidence for it, *i.e.* this is a prediction of the theory and not a basis for it. It does not follow on as an obvious step from the GNN code in a predictable way. There seems to be no reason why this rather bizarre pattern of placement of the earliest amino acids should have occurred. I find Figure 4 strange because it sets some difficult challenges for molecular recognition during the assembly of amino acyl-tRNAs. In particular, the shapes of the codon domains occupied by Asp, Glu and Ser are complicated. Presumably there were RNA catalysts that carried out the job of current amino acyl-tRNA synthetases. For correct charging of tRNAs, these synthetase RNAs would have had to distinguish large sets of tRNAs from one another, possibly by recognition of the bases in the anticodon. The anticodons for Asp tRNAs, according to Figure 4, would be GAU, UAU, GGU, UGU, GUU, UUU, and GUC (it should be remembered that pairing is antisense, so the first anticodon base pairs with the third codon base). To recognize this combination of anticodons would require some complex mixture of logical operations combining bases at all three anticodon positions, for example: IF (3rd base = U AND 2nd base C) OR (3rd base = C AND 2nd base = U AND 1st base = G) THEN charge with Asp. This would either require a very complex recognition process for a single synthetase, or it would require separate synthetases for each codon block that would carry out the same reaction of charging the tRNA with Asp. Neither of these options seems simple or parsimonious. The same would be true for other amino acids in this arrangement of the code.

[Author's Response]

The Reviewer is mistaken. There is direct evidence from the genetic code indicating, for instance, that the majority of ANN codons codified for Asp. Therefore, it is the biosynthetic relationships reflected in the genetic code that define Fig. 4. This is a prediction of the coevolution theory but it is also supported by the distribution of the biosynthetic pathways of amino acids in the rows of the genetic code (see, for instance, Taylor and Coates [11]).

Whereas, there is an obvious step which derives Fig. 4 from the GNN code. This consists of the fact that, once the codifications were assigned to the first six amino acids on GNN codons, it was necessary to immediately extend the meaning, as Crick also suggests [51], to many codons in the code, thus generating the code in Fig. 4. The Reviewer should read sections (iii) and (iv) of the Discussion more carefully. Fig. 4 is not strange and, in particular, the shape of the codon domain of Asp and Glu and Ser is linked to the rows of the genetic code which, as suggested by Taylor and Coates [11], are in relation with the biosynthetic families of these amino acids.

The coevolution theory does not necessarily envisage that the aminoacyl-tRNA synthetases were present at this stage of genetic code origin because the tRNAs might have been charged by means of the biosynthetic pathways of amino acids. There was no need for the aminoacyl-tRNA synthetases. The Reviewer's criticism is therefore weakened. Moreover, as stated in the paper, the mRNAs might have been simpler than Fig. 4 leads us to believe. See the subsections (iii) and (iv) of the Discussion, in which the complexity of

recognition maintained by the Reviewer is considerably reduced.

Reviewer Comments

An alternative that I favour at the moment is that the GNN code developed into a 'four-column' code in which all codons in the same column coded for the same amino acid: NUN = Val, NCN = Ala, NAN = Asp (and/or Glu) and NGN = Gly. This is an obvious simple step from the GNN code: all we do is relax the restriction that the first position must be G. It is very simple for molecular recognition by the synthetases because only the middle anticodon base needs to be recognized. For example, a single synthetase that adds Val to all tRNAs with 2nd anticodon base = A would be sufficient to assign all NUN codons to Val. Furthermore, the four column code explains why amino acids with similar physicochemical properties end up in the same columns of the code whereas amino acids in the same row (same first codon base) do not have similar properties. The difference between rows and columns shows up clearly when we look at the rates of evolution of 1st and 2nd position sites in proteins and the variability of these sites among species [62]. According to this argument, it is physicochemical properties that are important in determining where new amino acids are added to the code. Amino acids will be added into positions that were formerly occupied by amino acids with similar properties because this is minimally disruptive to the proteins encoded by the code at the previous step. As an example of the difference between this argument and the coevolution theory, consider Ile, which is assigned to codons in the AUN box. According to the coevolution theory, Ile ends up in this position because AUN was originally Asp and Ile is synthesized from Asp. According to the physical property argument, Ile ends up in this position because AUN was originally Val and Ile is similar to Val. It is well known that neighbouring codons in the canonical code tend to specify similar amino acids and hence that the code seems to be optimized with respect to randomly reshuffled codes [63]. The physical property argument summarized above explains how the optimality of the canonical code arises as a result of its evolution from the four-column code. The coevolution theory ignores this issue.

[Author's Response]

It is not obvious, and it indeed does not seem sensible, why a column code specifying amino acids Ala = NUN, Asp = NAN (and/or Glu) and Gly = NGN should have been created. Why should such a code have been created? Whereas the opposite is obvious for the coevolution theory. It would be sufficient to insert, from the GNN code, the other amino acids on the columns, according to their physicochemical properties, without passing through this fairly useless code, partly because there is no evolutionary link between these five amino acids (Val, Ala, Asp, Glu and Gly) and the other amino acids that will occupy the columns; and if this link had been based on the physicochemical properties of amino acids, it would have been inefficient because, for instance, in the column NGN = Gly, there are the smallest (Gly) and the largest (Trp and Arg) amino acids. Indeed, although the physicochemical properties are linked to genetic code organisation, they are not highly minimised and so these properties might have played only a subsidiary role in genetic code evolution [31,56].

If, on the other hand, the column code was obvious, then the code in Fig. 4 would be equally obvious because it is organised in rows, as Taylor and Coates suggest [11] the genetic code is organised. The GNN code, which the Reviewer also accepts, is a row code and, therefore, the next step in genetic code evolution must 'necessarily' be a code organised in rows because it evolves on row constraints existing in its precursor (GNN code) and not the one organised in columns suggested by the Reviewer which implies a radical change in the logic for the construction of mRNA.

The problem of the synthetases is nonexistent because, as already suggested, the coevolution theory can envisage the charging of tRNAs by means of the biosynthetic path-

ways of amino acids or, at least, can envisage a limited intervention of the synthetases.

The coevolution theory is compatible with the observation that the physicochemical properties of amino acids are better allocated on the columns of the genetic code. I have dealt with this issue extensively, see for instance Di Giulio [31].

Whereas, from the viewpoint of the coevolution theory, it is the rows (biosynthetic pathways) that are important for determining where an amino acid will be added, with the columns deciding only the reduction in the translation noise compatibly with the row allocation.

The coevolution theory considers this aspect. If we consider that, according to the extended coevolution theory, the GNN code preceded the current code then, as the amino acids evolved along the biosynthetic pathways organised in rows, the amino acids were allocated in columns in an attempt to reduce the physicochemical distances between amino acids [31]. If hydrophobic amino acids were allocated on a given column of the code (first column), then the majority of hydrophobic amino acids biosynthetically originating in the various rows would have the possibility to be allocated on the code's first column, and so on. In other words, the coevolution theory is perfectly compatible with the distribution of the amino acids' physicochemical properties in the genetic code [31].

Reviewer Comments

The amount of credence that one gives to the coevolution theory depends on the extent that one believes that amino acid synthesis occured on tRNAs. There are two cases where the evidence for this is very strong: Asp Asn and Glu Gln. These reactions occur on the tRNAs in both Archaea and Bacteria, as shown in Table 1, and Di Giulio [33] is cited as evidence that these are molecular fossils. The Ser Cys case would be another good example, but it is only found in Archaea, according to the table. The cases of Met fMet and Ser Sec are less relevant because they involve non-standard amino acids that do not have their own codons. It would be interesting to have more details on all the examples in Table 1. For any one of the examples, are all the enzymes that carry out this reaction homologous? This is particularly relevant if the function is shared by Archaea and Bacteria – it is necessary to argue that the sequence is homologous in the two domains in order to exclude the possibility that the function evolved independently. When one of these functions is present in a domain, is it present in the majority of species in this domain? This is important in order to rule out horizontal transfer of a gene from one domain to a small group of species in the other domain. As far as I know, Sec occurs patchily in unrelated groups of organisms, so even though the Ser Sec reaction occurs in all three domains, there is probably not a good case that it is ancestral. On the other hand, my understanding of the Asp Asn and Glu Gln cases is that these are really ancestral to the split of Archaea and Bacteria. Please could you summarize in more detail how strong the evidence is that all the cases in Table 1 evolved ancestrally to the split of the domains of life?

[Author's Response]

I have dedicated an entire paper [33] in an attempt to establish whether or not the pathways in Tab. 1 are ancestral traits. The conclusion of this analysis [33] is that there is no reason why these pathways (Tab. 1) should be derived traits. I cannot summarise the contents of that paper in this work. I cite that paper [33]. Three other references [19-21], and not only my own, are cited and indicate that these pathways might be molecular fossils (see below).

However, if the Reviewer accepts the ancestrality of the pathways Asp->Asn and Glu->Gln, why then should he not accept the ancestrality of, for instance, Ser->Cys? Does he perhaps think that these pathways were generated by different mechanisms? This seems absurd to me. There is absolutely no chance of these five pathways (Tab. 1) evolving independently without any clear selective pressure (see below). It is better to think that

these pathways are the expression of the same mechanism that produced them because they are 'homologues', i.e. they do the same thing.

Table 1. The biosynthetic pathways that transform one amino acid into another when the transformation takes place on tRNAs and their phylogenetic distribution. See Sheppard et al [53] for further information

Pathways	Phylogenetic distribution
$Glu\text{-}tRNA^{Gln}$->$Gln\text{-}tRNA^{Gln}$	Bacteria, Archaea and chloroplasts
$Asp\text{-}tRNA^{Asn}$->$Asn\text{-}tRNA^{Asn}$	Bacteria and Archaea
$Ser\text{-}tRNA^{Sec}$->$Sec\text{-}tRNA^{Sec}$	Bacteria, Archaea and Eucarya
$Met\text{-}tRNA^{fMet}$->$fMet\text{-}tRNA^{fMet}$	Bacteria and organelles
$Ser\text{-}tRNA^{Cys}$->$Cys\text{-}tRNA^{Cys}$	Archaea

The pathway Ser->Sec is certainly homologous, at least between Archaea and Eukarya [64,65], and so it should be extremely ancient. In Archaea and Eukarya, this pathway takes place in two steps, while it is in one step only in Bacteria [65]. However, all these enzymes are homologues, i.e. they share a common origin and so this pathways seems extremely ancient and is also very widespread, contrary to what the Reviewer says [66]. The pathway Ser>Cys has also been suggested as being present in the LUCA [67], However, the pathway Ser->Cys has only been found in a few archebacteria and so its phylogenetic distribution would seem to indicate, given its phylogenetic rarity, that it is a derived trait, as the Reviewer claims. Nevertheless, all these pathways (Tab. 1) are extremely difficult to evolve because they must necessarily create some intermediates, such as $Ser\text{-}tRNA^{Cys}$ which, if they ended up on ribosomes would have disastrous effects on cell life. Therefore, these pathways are difficult to evolve. This and other arguments are reported in Di Giulio [33], which concludes that all these pathways are molecular fossils of the mechanism that established the genetic code. The Reviewer is referred to my reference [33]. Finally, why should these pathways have evolved recently to do the same thing that an aminoacyl tRNA synthetase did so well? Why? Why replace an aminoacyl tRNA synthetase with another synthetase whose first step would charge an amino acid on a tRNA specific for another amino acid (for instance $Ser\text{-}tRNA^{Cys}$)? Why? I invite the Reviewer to write a paper on this issue, addressing these questions and those raised in Di Giulio [33]. The truth is that there are no answers to these questions and the only way that these pathways (Tab. 1) can be rationalised is to view them as ancestral traits. In conclusion, the evidence in favour of the ancestrality of these pathways is considerable (see [33]).

Reviewer Comments

If we accept for a moment that the Asp Asn and Glu Gln reactions evolved ancestrally to the split between the domains, the next question is whether these reactions were initially catalyzed by RNA or proteins. Asn and Gln are late additions to the code. A relatively diverse set of amino acids, such as the ten early amino acids listed above, could have been present in the code before Asn and Gln were added. Thus the first catalysts that carried out these reactions may have been proteins composed of the early amino acids. The fact that these reactions occur on tRNAs does not necessarily mean that they were relics of the RNA World. Similarly, the fact that these two amino acids are synthesized on

tRNAs does not necessarily mean that the metabolism of the earliest amino acids in Figure 2 occurred on tRNAs.

[Author's Response]

I do not understand the relevance of catalysts in these reactions. They could have been RNAs, peptide-RNAs or even proteins composed of early amino acids. I favour catalysis by peptidyl-tRNAlike molecules as the true catalysts at this stage of the genetic code [3,4]. This excludes nothing. These pathways have all the requisites to be molecular fossils of the RNA world ([31,33,68]).

If, as the Reviewer suggests, we accept that Asp->Asn and Glu->Gln are ancestral, then along with the other pathways (Tab. 1), this would strongly corroborate the coevolution theory. But this theory says that precursor-product transformations took place on tRNAs. However, why should only these transformations of amino acids take place on tRNAs? Evidently the implication is that the entire metabolism, or at least that involving all amino acids, took place on tRNAs and, therefore, the pathways in Fig. 2 could also take place on tRNAs. This conclusion is also suggested by other authors [28,31,41-43]. This is the extended coevolution theory. With this assumption, all the weaknesses of the coevolution theory are removed.

The fact that these two amino acids are synthesised on tRNAs does not necessarily mean that the metabolism of the amino acids in Fig. 2 took place on tRNAs, but all the pathways in Tab. 1, one of which takes place in two steps, might imply, more generally, that metabolism took place on tRNAs. Furthermore, Glu from Glu-tRNA^{Glu} intervenes in the biosynthesis of chlorophyll [31] and this, together with other observations on a more general role of aminoacyl-tRNAs in metabolism [69] might strengthen the hypothesis that the entire metabolism took place at this stage on tRNAs [31,41-43].

Reviewer Comments

If I understand correctly, all five examples in Table 1 are single step reactions catalyzed by a single enzyme. This is also a good reason to suppose that synthesis on the tRNAs is a relevant mechanism of synthesis for these amino acids in particular. However, most of the late amino acids with the exception of Asn and Gln have very long synthesis pathways involving many intermediates (as shown in Figure 1). There seems to be no evidence that any of these were synthesized on tRNAs. There are eight steps shown from Glu to Arg, for example. It seems to be stretching the theory too far to suppose that there were eight sequential reassignments of Glu codons to intermediate molecules, that all these intermediates have completely disappeared again from the modern code, and that all these reaction steps that formerly occurred on the tRNA have now been replaced by equivalent steps that occur without the molecules being attached to tRNAs. It is simpler to suppose that the pathways to synthesize these late amino acids were never associated with tRNAs, and that the intermediates do not appear in the modern code because they were never added to the code in the first place. Thus, the evolution of the synthesis pathways is important in allowing the diversity of the code to build up, but this does not influence which codons are assigned to which amino acids. If synthesis does not occur on the tRNA, there is no reason why the product amino acid should take over the codons of its precursor. Since most of the late amino acids have long synthesis pathways, it is likely that they arose in the protein world, and that the steps were catalyzed by proteins made from earlier amino acids. The situation may be different for Ile, Leu, Pro and Thr, which occur non-biologically and are thus included among the early group in our ranking, although they are less frequent than the simplest amino acids. These four also have relatively long synthesis pathways on Figure 1. These may have existed in the environment at the time the code originated if their rates of non-biological synthesis were high enough, or they may have been synthesized by RNA-catalyzed pathways. In either case, the protein enzymes catalyzing the pathways on Figure 1 would have evolved later and

there is no reason to suppose that these pathways are the same as those that existed when these amino acids were added to the code.

[Author's Response]

No. In the Ser->Sec pathway there are two biosynthetic steps. Absolutely not. As stated above, the first step regards the charging of an amino acid on a tRNA specific for another amino acid, which is a very dangerous hybrid because, if it ended up on the ribosomes it would be lethal. Therefore, there is no 'good reason' why these pathways should be used to synthesise these amino acids [33].

The fact that Ser->Sec takes place in two steps seems to indicate that this was possible, contrary to what the Reviewer maintains.

The intermediates that are not amino acids would not appear in the code. Only amino acids should appear in the evolving code according to the coevolution theory.

There is nothing strange in this. If biosyntheses took place on tRNAs then, when the code was completely developed, a strong selective pressure would have been triggered to remove tRNAs from metabolism because the tRNAs were extremely cumbersome and it is therefore not surprising that today we only observe the relics of these events (Tab. 1) [31].

Today it might seem true that syntheses on tRNAs were inefficient. Nevertheless, this is the very story that these fossils tell: synthesis on tRNAs.

However, there is evidence – again from molecular fossils – that biosynthetic pathways might have taken place on tRNAs. the pathway to His starts with a reaction producing N'-5'-phosphoribosyl-ATP, which is held to be a fossil of RNA [43,70].

The fact is that the biosynthetic pathways are linked to genetic code organisation [5-13,16-22,34,37] and therefore give credence to syntheses on tRNAs.

In several biosyntheses of amino acids, there are amino acids as intermediates. This implies, in agreement with the coevolution theory, that these could have been incorporated into the evolving code but were subsequently substituted [9,16]. However, I see no problem here with the coevolution theory, even if the biosyntheses were catalysed by proteins.

That the Reviewer's suggestion regarding the amino acids Ile, Leu, Pro and Thr is probably false and that, more generally, the Reviewer's entire argument regarding both the very early amino acids and the 'column code' is dubious, is demonstrated by the fact that the 'system' that led to the GNN code must have been extremely efficient because it was able to achieve a clear classification of amino acids only on the basis of their frequencies, separating them into two groups: Gly, Ala, Asp, Glu and Val in the GNN code, and Ile, Leu, Pro and Thr. Evidently an extremely efficient system! Is it possible that the system was able, only on the basis of frequencies, to incorporate into the GNN code only the first amino acids in the ranking of Higgs and Pudritz [61] without making an error and that the same system created the column code by extending the codification of these amino acids? This seems absurd because in the first phases there seem to be strong stereochemical constraints while, in the column code, these constraints are completely relaxed. Is this possible?

Why should the pathways be different? I have already answered this observation. It is better to maintain an old pathway if only to maintain evolutionary continuity. I fail to understand why the change of catalysts should entail a change of pathway even if, as already suggested, the majority of steps in Fig. 1 were catalysed by peptide-RNA complexes. (Finally, the coevolution theory does not clearly define the early phases of genetic code origin, i.e. the GNN code, because it considers that the precursor amino acids Gly, Ala, Val, Ser, Asp and Glu entered the code without following the biosynthetic pathways. The Reviewer adopts a similar standpoint in which the amino acids Gly, Ala, Val, Asp and Glu entered the GNN code without using the biosynthetic pathways. The extended coevolution theory has a different interpreta-

tion: the amino acids Ser, Gly, Ala, Val, Asp and Glu entered the code through the biosynthetic pathways. Therefore, the question is as follows: why should the amino acids Ile, Leu, Pro and Thr, which appear in prebiotic syntheses and are early in the ranking of Higgs and Pedrutz [61], not have been added to the code as the amino acids codified by the GNN codons, but entered the code through the biosynthetic pathways, as the coevolution theory suggests? This would constitute a difficulty for this theory because all these amino acids were present in the prebiotic environment and it would not be clear why some entered the code directly while others entered via the biosynthetic pathways. The extended coevolution theory removes this difficulty as it treats all amino acids in the same way: they all entered the code via the biosynthetic pathways. As already suggested, the Reviewer's hypothesis presents some inconsistencies. Why should only the amino acids Gly, Ala, Asp, Glu and Val have been codified by GNN codons while the other amino acids (Ile, Leu, Pro and Thr) were added to the code later on? Did this choice take place only on the basis of frequency? It seems to me that the frequencies are too weak a constraint to explain the clear distinction between these two groups of amino acids while the biosynthetic pathways seem to be a sufficiently strong constraint to explain these observations consistently with the allocations of all these amino acids in the code.)

Reviewer Comments

I have thus argued that while the case for the reactions Asp Asn and Glu Gln occurring on tRNAs is very strong, this cannot be generalized to other amino acids. Without this generalization, the central importance of precursor-product relationships in the coevolution theory breaks down. These two cases fit with the argument based on physicochemical properties and four-column code as well. If NAN codons were initially Asp and Glu, then it makes sense that Asn and Gln would also be added in this column because they are more similar to Asp and Glu than they are to the amino acids in the other columns. Thus the theories agree for these two cases.

[Author's Response]

All these pathways (Tab. 1) must be expressions of the same mechanism that generated them because believing that they might be derived from different selective pressures is absolutely absurd as no selective pressure can be clearly identified as having generated them [33]. Hence, if we accept the case of Asp->Asn and Glu->Gln then this must have been generalised among the other amino acids and, thus, the coevolution theory is strongly corroborated.

It is incredible how the Reviewer can say that the pathways on tRNAs involving the transformations Asp->Asn and Glu->Gln, which are a direct prediction of the coevolution theory, are also 'in agreement' with the columns theory for the simple reason that Asn and Gln are more physicochemically similar to Asp and Glu, respectively. Let's be serious: the two pieces of evidence are clearly different in quality and, therefore, the two theories are not at all equal on this point. This is because, if pathways on tRNAs, Asp>Asn and Glu->Gln would be historic evidence and hence of extraordinary importance in understanding the origin of the genetic code [33]. Whereas, the physicochemical similarity between these pairs of amino acids should have played only a secondary role in allocating Asn and Gln to the columns, as also predicted by the coevolution theory because it would be the necessary consequence of these pathways on tRNAs (see, for instance reference [31]). In short, although the two theories agree on this point, they receive different levels of corroboration: the coevolution theory is strongly corroborated by it, while the columns theory is not and it acquires only a subsidiary role.

Reviewer Comments

Finally, although any discussion of metabolic pathways in the RNA World is bound to be speculative, we can be much more concrete in discussing pathways in modern organisms. Figures 1 and 2 are presented as 'the' pathways for amino acid syn-

thesis, but I presume these are based on a particular organism like *E. coli*. I do not know to what extent these pathways are truly conserved between all species. Has anyone carried out this analysis using sequence data from complete bacterial and archaeal genomes? I would be interested to know what fraction of these complete genomes contains an enzyme for each of the steps in Figure 1. If enzymes do not exist for these steps, are there alternative synthesis pathways, or are the organisms reliant on taking in these amino acids as food? In general, are pathways of amino acid sequences in modern proteinbased organisms more conserved than some other pathways that might be considered to be less essential to cell function? If the pathways are not conserved in modern organisms, the chances that they would be conserved as far back as the RNA World are slim.

[Author's Response]

If logical-evolutionary analyses were conducted on these pathways and it was concluded that these were molecular fossils [33], it would not necessarily be true that the metabolic pathways of the RNA world are only speculations ([43,68]).

The majority of organisms use pathways essentially similar to those of *E. coli* [43,71]. I have been following this literature for many years and it does not seem to me that there are significant deviations from the pathways presented in Figs. 1 and 2.

There have not been analyses of this type or they have been very limited and nevertheless confirm the scheme of the biosyntheses of *E. coli* [71].

However, the intimate relationship between the biosynthetic pathways of amino acids and the organisation of the genetic code is such as to make the research suggested by the Reviewer superfluous because it is not possible that this intimate relationship holds only for the biosynthetic pathways of *E. coli* and its genetic code.

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CONCENTRATIONS OF CARDIAC TROPONIN I BEFORE AND AFTER OVARIOHYSTERECTOMY IN 46 FEMALE DOGS WITH PYOMETRA

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Background: Canine pyometra is a common disease in countries where routine spaying of young dogs is not common practice. This disease is known to lead to systemic inflammation potentially affecting multiple organs in the body, including the heart. Cardiac-specific Troponin I (cTnI) is a sensitive marker of myocardial cell damage, which can result from ischemia, trauma, toxins or inflammation. Dogs with pyometra are also exposed to anaesthesia which can potentially result in myocardial cell damage. The aims of the study were 1) to evaluate the occurrence of myocardial cell damage as indicated by increased serum concentrations of cTnI in dogs with pyometra and relate these to presence of systemic inflammation and 2) to evaluate the change in cTnI-concentrations after anaesthesia and surgery.
Methods: Serum cTnI concentration was measured preoperatively and one day after surgery in 46 female dogs with pyometra and 15 female dogs that underwent surgery for other reasons (ovariohysterectomy and mammary tumours).
Results: Forty-six female dogs of different breeds diagnosed with pyometra were included. The dogs had a median age of 8.5 years (IQR 7.5–10) and a median weight of 29 kg (IQR 9–32). Of the 46 dogs, 37 (80%) fulfilled the chosen criteria for systemic inflammatory response syndrome (SIRS) at inclusion. Thirteen (28%) of the dogs had increased cTnI concentrations (> 0.2 μg/l) before surgery and 18 (39%) had increased cTnI-concentrations the day after surgery. The cTnI concentrations in the 13 dogs with increased preoperative cTnI concentrations decreased in 8 dogs, increased in 4 dogs, and was unchanged in one dog. Seven dogs with nondetectable preoperative cTnI concentrations had increased postoperative concentrations. The only significant association between the studied laboratory or clinical variables (including SIRS) and cTnI concentration was preoperative percentage band neutrophils (PBN) and postoperative cTnI concentration (P = 0.016). In total, 20 dogs (43%) had increased preor postoperative cTnI concentrations. Seven dogs (15%) had pre-or postoperative concentrations of cTnI of 1.0 μg/l or higher.
Conclusion: Mild to moderate increases in cTnI appears to be common in dogs with pyometra before and after surgery, but the clinical importance of this finding is uncertain. None of the studied clinical variables were found to reliably predict increased preoperative cTnI concentrations. Because of the preand postoperative variation in cTnI concentrations, it was not possible to identify a negative effect of anaesthesia and surgery on myocardial cell integrity.

Background

Myocardial damage can be caused by multiple conditions including ischemia, trauma, toxins or inflammation. Cardiac-specific Troponin I (cTnI) is currently the most sensitive and specific marker of myocardial cell damage in the dog [1,2]. Cardiac-specific Troponin I is a protein that is expressed at high concentrations only in the myocardium. When cardiac myocytes are damaged, cTnI leaks into the bloodstream and can be detected in serum [1,3]. In normal dogs serum concentrations of cTnI are low or, most often, undetectable [4].

Canine pyometra is a common disease in countries where routine spaying of young dogs is not common practice. The condition may cause systemic inflammation, which may potentially damage multiple organs in the body, including the heart [5]. The presence of systemic inflammatory response syndrome (SIRS) may be predicted by certain clinical and laboratory parameters [6]. The systemic inflammation can, if not successfully treated, progress to multiple organ dysfunction syndrome (MODS) and death [7].

The safest and most effective treatment for canine pyometra is ovariohysterectomy [8]. However, anaesthesia and surgery may cause myocardial ischemia with subsequent myocardial cell damage, especially in individuals with systemic inflammation and impaired circulation [9]. In humans, the occurrence of perioperative ECG abnormalities

and "silent myocardial ischemia" is well recognised [10]. One study documented myocardial ischemia 12 hours postoperatively (as measured by increased concentrations of cTnI) in healthy women undergoing caesarean section [11]. It has been demonstrated that perioperative elevations of cTnI concentrations were associated with major cardiac complications up to 1 year after surgery [12].

Thus, myocardial injury is a potential cause of increased morbidity and mortality in dogs with pyometra before, during and after surgery. However, there are no reports concerning the occurrence and significance of perioperative myocardial damage in dogs undergoing anaesthesia irrespective of the underlying condition. The presence of myocardial damage may often be overlooked and difficult to detect when suspected if it does not lead to compromised cardiac function, arrhythmias or regional abnormal ventricular motion. Analysis of the serum concentration of cTnI can reveal both clinical and subclinical damage to the myocytes [9,13].

The aims of the present study were 1) to evaluate the occurrence of myocardial cell damage as indicated by increased serum concentrations of cTnI in dogs with pyometra and relate these to the severity of systemic inflammation and other clinical variables and 2) to evaluate the change in cTnI concentrations after anaesthesia and surgery.

Materials and methods

This study was approved by the Uppsala County local ethical committee.

Dogs

Forty-six female dogs diagnosed with pyometra were recruited to the study at the Department of Small Animal Clinical Sciences, Swedish University of Agricultural Sciences (SLU), Uppsala between January 2004 and December 2005. At the time of arrival, a physical examination was performed on dogs presenting with a history compatible with pyometra (polyuria, polydipsia, anorexia, vomiting, lethargy, fever, vulvar discharge, recent oestrus). Blood samples analysed for complete blood count (CBC) and cardiac-specific Troponin I (cTnI) were collected and radiography and/or ultrasonography of the abdomen was performed, and dogs diagnosed with pyometra were included in the study. Dogs whose owners did not agree to ovariohysterectomy, and dogs with clinical or laboratory findings indicative of other organ-related or systemic disease were excluded from the study. Recorded data obtained from the case history and physical examination included age, weight, rectal temperature, heart rate and respiratory rate. A second serum sample for analysis of cTnI was collected 12–24 hours after surgery.

Fifteen female dogs undergoing surgery for neutering (n = 12) or tumour mammae (n = 3) were recruited as control dogs. None of these dogs had a history or clinical signs indicative of other disease, and in the case of tumour mammae thoracic radiographs had shown that the dogs were free of visible pulmonary metastases. A physical examination was performed on all of these control dogs. Serum for analysis of cTnI was collected at presentation and 12–24 hours after surgery.

Diagnosis of pyometra

Abdominal radiography and/or ultrasonography were performed on all dogs. The radiological examination included left and ventrodorsal projections of the entire abdomen using the standard procedure at the Section for Diagnostic Imaging, Department of Clinical Sciences, SLU, Sweden. The diagnosis of pyometra was established when an enlarged (and, if ultrasonography was performed, fluid-filled) uterus was found, as previously described [14,15]. The diagnosis was confirmed by the presence of an enlarged uterus containing pus during the surgical procedure.

Diagnosis of inflammatory response syndrome (SIRS)

Dogs were grouped into two groups; SIRS-positive and SIRS-negative. Dogs that fulfilled two or more of the following criteria were considered SIRS-positive: 1) Resting heart rate > 120/min; 2) respiratory rate > 20/min; 3) rectal temperature above 39.2°C or below 38.1°C; and 4) total white blood

cell count (WBC) above 16 X 10^9 or below 6 X 10^9 cells per l blood or more than 3% band neutrophils [6].

Sample handling

Blood samples for hematological and biochemical analysis were taken from the distal cephalic vein into EDTA and serum Vacutainer® tubes (Becton & Dickinson, Meylon Cedex, France) and transported to the laboratory for analysis within one hour of collection.

Ovariohysterectomy

The dogs were premedicated with glycopyrrulate, methadone, acepromazine and carprofen. Anaesthesia was induced with propofol and maintained with isoflurane. In dogs that were considered an anaesthetic risk because of a severely compromised general condition (n = 5) anaesthesia was induced with diazepam and ketaminol and maintained with isoflurane. Ovariohysterectomy was performed using a standard ventral midline approach [16]. The procedure was performed within 24 hours in all dogs except one. The owners wished to delay surgery until after the weekend in this dog because of a good general condition. All dogs were treated with iv fluids before, during and after surgery. Approximately half of the dogs were treated with antibiotics perioperatively. All dogs received preoperative and postoperative opioids until discharge. No medications were given before the preoperative blood samples were collected.

Haematology, cTnI analysis and blood biochemistry

The CBC was performed using Abbott CELL-DYN 3500 (Abbott Diagnostics, Illinois, USA) in combination with manual microscopy in all cases except eight, where the haematology was performed using the QBC Vet Autoread (IDEXX Laboratories, Maine, USA). In these eight cases the CBC was performed in an emergency situation when the QBC Vet Autoread was the only option for analysis of haematology.

Troponin I was analyzed using a commercially available method (IMMULITE Troponin I, Diagnostic Products Corporation, Los Angeles, USA). This is an immunometric method where antibodies raised against human cTnI bind to existing cTnI in the sample. The lower limit of detection for the cTnI assay is 0,2 μg/l. The possibility of using this method for detection of cTnI in serum samples from dogs was investigated in an earlier study [17,18]. The upper reference limit for normal dogs in our laboratory was 0.2 μg/ l.

Adjunct serum biochemical analyses were not included in the study protocol but were performed in some cases, preoperatively (Table 1). ALT, ALP, creatinine and glucose were analyzed using a commercially available method (IDEXX VET TEST Chemistry Analyzer, IDEXX Laboratories, Maine, USA).

Statistics

All statistical analyses were performed using a statistical programme (JMP v 5.0, SAS, Cary, USA). Serum concentrations of cTnI from SIRS-positive and SIRS-negative dogs were compared using Wilcoxon Rank Sum Test.

The association between cTnI concentrations and haematological and blood-biochemical variables, and variables obtained from the physical examination were evaluated by a Spearman rank correlation. Values are reported as the median and interquartile range (IQR). The significance level was set at $p < 0.05$.

Results

Dogs with pyometra

The median age of the 46 dogs with pyometra at presentation was 8.5 years (IQR 7.5–10) and median body weight 29 kg (IQR 9–32). The group comprised 8 mongrel dogs and 38 dogs of 22 different breeds.

Control dogs

The median age of the dogs in the control group was 5 years (IQR 2–8). Median body weight was 27 kg (IQR 20–32). The group comprised 3 mongrel dogs and 12 dogs of 12 different breeds.

Table 1. Median and interquartile ranges (IQR) of preoperative plasma biochemical variables (ALT, ALP, creatinine and glucose concentrations) in the study population of dogs with pyometra

Biochemical variable	Median	IQR	Reference interval
ALT (u/l) (n = 27)	16 162 82 6.8	10–36 87–229	10–100 23–212 44–159 4.3–6.9
ALP (u/l) (n = 23)		67–100 5.9–	
Creatinine (μmol/l) (n = 33)		7.1	
Glucose (mmol/l) (n = 20)			

Preoperative cTnI-concentrations

All of the dogs in the control group had undetectable preoperative cTnI concentrations (Table 2). Of the 46 dogs with pyometra, 13 (28%) had increased preoperative cTnI concentrations (range 0.3–13.2 μg/l) (Table 3).

Postoperative cTnI concentrations

Two (13%) of the control dogs had increased cTnI concentrations the day after surgery (0.4 and 3 μg/l, respectively) (Table 2). Eighteen (39%) of the pyometra dogs had increased postoperative cTnI concentrations (range 0.3–6.4 μg/l) (Table 3). Of the 13 dogs with increased preoperative cTnI concentrations, 8 had lower, 4 had increased, and one had unchanged cTnI concentrations after surgery. In seven dogs with nondetectable cTnI concentrations at presentation, increased levels were demonstrated postsurgically.

Thus, in total, 20 dogs (43%) with pyometra had increased cTnI concentrations before or after surgery, and 7 dogs had preor postoperative cTnI concentrations of 1.0 μg/l or higher.

Preoperative blood biochemistry

None of the 27 dogs that had serum ALAT concentration analysed had a concentration exceeding the upper reference range. Similarly, only one out of the 33 dogs that had serum creatinine concentration analysed had a concentration exceeding the upper reference range for creatinine. Finally, 6 of the 23 dogs that had serum ALP concentration and 6 out of the 20 dogs that had serum glucose concentration analysed had a concentration exceeding the upper reference range.

SIRS groups and outcome

Eleven of the dogs with pyometra fulfilled all four SIRS criteria. Ten of the dogs fulfilled three criteria, 16 dogs fulfilled two criteria and 6 dogs one criterion for SIRS. Three dogs did not fulfil any of the SIRS criteria. Consequently the SIRS-positive group (two or more positive criteria) consisted of 37 dogs (80%) and the SIRS-negative group of 9 dogs (20%). All dogs except four were discharged within 48 hours of surgery. Reasons for delaying discharge in four dogs were resuturing of skin wound (n = 1), reduced general condition postoperatively (n = 1) and owner preference (n = 2). All dogs in the study recovered and survived the postoperative period (10 days).

Comparison of cTnI concentrations and clinical parameters

When the SIRS-positive and SIRS-negative groups were compared (both before and after surgery) there was no statistically significant difference in cTnI concentrations between the groups. The only significant association between the studied laboratory or clinical variables and cTnI concentration was preoperative percentage band neutrophils (PBN) and postoperative cTnI concentration ($p = 0.016$) (Figure 1). The preoperative PBN tended to be correlated with preoperative cTnI concentrations ($p = 0.059$).

Discussion

In total, 20 out of 46 dogs (43%) with pyometra had increased concentrations of cTnI at some time during the study, which indicates that increased cTnI concentrations are common during the perioperative period in dogs with pyometra. This finding is supported by the results of our previous study in which increased preoperative cTnI concen-

trations were documented in 12% of 58 dogs with pyometra [18]. The present study is different from our previous one because, to our knowledge, this is the first study that documents both pre-and postoperative measurements of cTnI concentrations in dogs with pyometra. It should be pointed out that only 7 of the 20 dogs with increased concentrations of cTnI (10 out of the total 31 samples with increased concentrations) had values ≥ 1.0 µg/l and none of the dogs measured higher than 13.2 µg/ ml, indicating that cTnI concentrations were mildly increased in the majority of cases. The lower limit of detection of cTnI in our assay is 0,2 µg/l. It is possible that the upper reference range for cTnI in dogs is lower than 0,2 µg/l and that a greater number of dogs would have had increased concentrations of cTnI if we had used a more sensitive assay, as recently described [19].

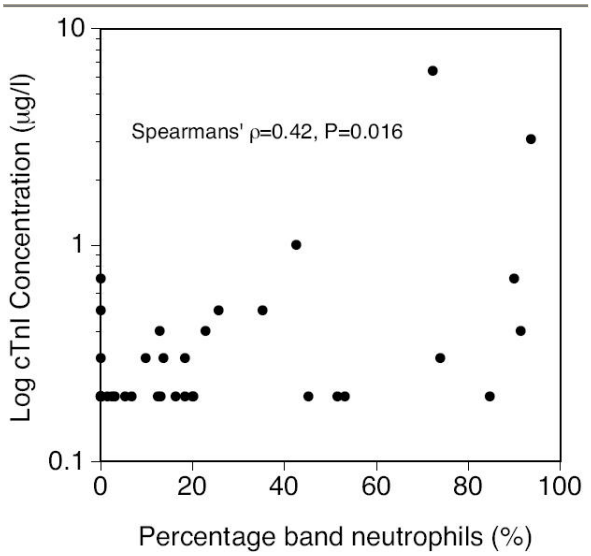

Figure 1. Scatterplot of postsurgical concentrations of cTnI by percentage band neutrophils in peripheral blood at presentation in 38 dogs (values missing in 8 dogs).

Table 2. Age, weight, reason for surgery (n = neutering, tm = tumor mammae) and pre-and post-operative serum cTnI-concentrations in 15 female dogs undergoing elective surgery (control group)

Case No	Age (years)	Weight (kg)	Reason for surgery	Pre-operative cTnI (µg/l)	Post-operative cTnI (µg/l)
1	9	28	n	< 0.2	< 0.2
2	4	38	n	< 0.2	< 0.2
3	6	22	n	< 0.2	< 0.2
4	4	8	n	< 0.2	0.4
5	5	20	n	< 0.2	< 0.2
6	9	31	tm	< 0.2	< 0.2
7	8	18	tm	< 0.2	< 0.2
8	7	22	n	< 0.2	< 0.2
9	9	10	tm	< 0.2	< 0.2
10	4	35	n	< 0.2	3.0
11	5	32	n	< 0.2	< 0.2
12	1	57	n	< 0.2	< 0.2
13	1	26	n	< 0.2	< 0.2
14	1	27	n	< 0.2	< 0.2
15	2	30	n	< 0.2	< 0.2

The clinical significance of mild increases in cTnI concentrations is currently unknown. Studies have shown an association between the degree of increase in cTnI concentrations and the size of myocardial infarctions in dogs [1,20]. However, it has been suggested that reduced renal function can cause an increase in cTnI in the absence of myocardial cell damage [21]. Most of the dogs in our study had preoperative creatinine concentrations determined. However, in 5 of the dogs with increased cTnIconcentrations the preoperative creatinine concentration was not known. Although alternative causes for mildly increased cTnI concentrations are possible [21], it is likely that the degree of increase of cTnI concentration in serum provides an estimate of the extent of myocardial damage in our dogs.

Table 3. Weight, age, white blood cell count (WBC), percentage band neutrophils (PBN), heart rate (HR), rectal temperature, respiratory rate (RR) above 20/min or not, pre-and post-operative cTnI-concentrations for 46 dogs with pyometra

Case No	Weight (kg)	Age (years)	WBC (×109/ml)	Neutrophils (×109/ml)	PBN (%)	HR (bpm)	Temp (°C)	RR >20	Pre-op cTnI (µg/l)	Post-op cTnI (µg/l)	SIRS-pos
1	32	6.5	32	1.8	72	120	39.1	Y	13.2	6.4	+
2	7	11.5	7	-	-	128	40.4	Y	< 0.2	< 0.2	+
3	11	7	11.4	5.9	0	80	38.6	Y	< 0.2	< 0.2	-
4	28	11	28	6.9	89	104	39.6	-	0.7	0.7	+
5	11	8	11.3	10.9	12	-	39.9	-	1.2	0.4	+
6	33	10	33.5	9.7	0	110	38.8	Y	< 0.2	0.3	-
7	29	3.5	29	-	-	140	39.3	Y	< 0.2	< 0.2	+
8	30	8.5	30	15.5	43	144	39.9	N	2.0	1.0	+
9	12	13	12	26.8	91	-	38.3	N	0.3	0.4	+
10	10	12.5	9.7	1.6	12	134	39.9	N	< 0.2	< 0.2	+
11	27	7.5	26.6	-	-	128	39.4	N	< 0.2	0.4	+
12	35	7.5	35	14.2	0	140	39.2	Y	1.0	0.7	+
13	20	8	20.2	18.4	16	210	39.9	-	< 0.2	< 0.2	+
14	22	9.5	22.8	37.5	13	138	39.8	Y	0.3	< 0.2	+
15	9	12	9	23.6	94	100	40.9	Y	0.5	3.1	+
16	26	8	26.2	22.5	10	130	38.6	Y	< 0.2	0.3	+
17	22	9	22	9.8	53	-	40.7	Y	< 0.2	< 0.2	+
18	5	10	5.4	6.6	52	124	40.6	-	< 0.2	< 0.2	+
19	32	9	32.6	15	5	88	38.6	N	< 0.2	< 0.2	+
20	32	11	31.6	15.5	14	-	39	N	< 0.2	0.3	+
21	31	10	31	17.9	20	90	38.3	N	< 0.2	< 0.2	+
22	23	10	23	-	-	90	39.4	N	< 0.2	< 0.2	+
23	23	9	23.2	6.8	35	90	40.1	N	< 0.2	0.5	+
24	15	6	15.5	23.7	45	128	38.1	N	< 0.2	< 0.2	+
25	24	7	24.5	12.6	18	-	40.3	Y	< 0.2	< 0.2	+
26	24	8.5	23.8	9.5	20	140	39.2	Y	< 0.2	< 0.2	+
27	29	11	29	17.7	7	128	39.3	-	< 0.2	< 0.2	+
28	45	6	45	-	-	-	38.7	N	< 0.2	< 0.2	-
29	7	10	7.5	-	-	150	39.7	N	13.2	1.0	+
30	22	11	22.5	9.1	85	100	39.3	N	< 0.2	< 0.2	+
31	8	9	8.2	21.9	1	116	38.7	Y	< 0.2	< 0.2	+
32	17	8.5	17	11.1	74	124	40.3	N	< 0.2	0.3	+
33	20	4.5	20	9.6	0	112	39.6	Y	< 0.2	< 0.2	+
34	26	7.5	26.3	12.7	2	112	38.9	N	< 0.2	< 0.2	-
35	35	5	35.1	27	0	120	39.2	N	< 0.2	< 0.2	-
36	20	10	20	-	-	110	38.8	N	0.3	< 0.2	-
37	12	6	12	-	-	124	39.6	N	< 0.2	< 0.2	+
38	37	7	37.3	8.8	23	108	39.8	N	< 0.2	0.4	+
39	25	7	25	15.6	26	128	38.7	Y	0.4	0.5	+
40	33	8	33	8.8	0	90	38.5	Y	0.3	0.5	-
41	41	7	41	21	0	90	39.3	N	< 0.2	< 0.2	+
42	25	0.9	24.6	8	0	92	40.5	N	< 0.2	< 0.2	-
43	29	10	29.2	33.4	18	80	38.9	N	1.2	0.3	+
44	7	8	7.3	26.7	0	136	39.7	Y	< 0.2	< 0.2	+
45	17	7	17	5.1	0	140	39.9	N	< 0.2	< 0.2	+
46	15	4	14.7	13.5	3	120	38.9	N	< 0.2	< 0.2	-

The last column indicates if the dog was classified as SIRS-positive (+) or not (-) using the chosen SIRS criteria. Where values for HR and RR are missing they were not noted in the records. Values for Neutrophils and PBN are missing in 8 dogs.

Detection of damaged myocardium may be useful for the clinician when managing a dog with pyometra because its presence could indicate that the dog might be at risk for adverse events such as ventricular arrythmias or unexpected death. Early identification of dogs at risk allows the clinician to take actions to avoid adverse cardiac events by monitoring the dog during the perioperative period and intervene early when indicated. Although none of the dogs had a history of known heart disease, one limitation of the study is that we did not rule out underly-

ing subclinical cardiac disease in any of the participating dogs.

A possible cause for the increased cTnI concentrations could be the presence of endotoxins into the circulation. Elevated plasma endotoxin concentrations have been documented in female dogs with pyometra [22-24] and is thought to be responsible for some of the clinical signs [23]. In most cases of canine pyometra, *Escherichia coli (E. coli)* can be cultured from the uterus [22,25]. Like other Gram negative bacteria, *E. coli* can release endotoxin during growth or when they die [26]. Endotoxins bind to receptors on cell-membranes and induce inflammation and cytokine production [26]. Depending on the extent of endotoxin release, the result is varying manifestations of inflammation, from local to systemic, and cellular damage, which could potentially affect myocardial cells and thereby result in elevated serum concentrations of cTnI. Indeed, SIRS has been documented to be part of the clinical picture in 57% of 53 dogs [27] and 53% of 59 dogs [18] with pyometra. In our study, 37 out of 46 dogs (80%) fulfilled the chosen criteria for SIRS. However, we could not find an association between a diagnosis of SIRS and increased cTnI concentrations. These results are in accordance with our previous findings [18]. The diagnosis of SIRS is difficult because some of the clinical parameters used to determine its presence (body temperature, respiratory rate, heart rate, neutrophil count) are influenced by the excitement and stress caused by the visit to the animal hospital and by the disease as such. This influence would lead to a falsely high number of SIRS-positive dogs in the study population. The criteria for a positive diagnosis of SIRS used in this study were chosen to minimize the risk of failure to identify SIRS, thereby minimizing the risk of the serious consequences to the patient that can arise when this diagnosis is missed [6]. With a high sensitivity of 97% there is a concurrent low specificity (64%), explaining the risk of false positive diagnoses of SIRS in our population of dogs. It is possible that a correlation between cTnI concentrations and SIRS could be found if we could more reliably diagnose the presence of SIRS in an individual animal. C-reactive protein has been found to be a valuable marker of SIRS in dogs with pyometra and may be of value in future studies of dogs suspected to suffer from SIRS [28].

As a group, there was no significant change in the cTnI concentrations before and after surgery in the 46 dogs with pyometra. However, this lack of significance does not mean that changes have not occurred in individual dogs. Indeed, in 8 dogs the cTnI concentrations decreased after surgery and in 11 dogs the concentrations increased. A possible explanation for the decreased concentrations on the day after surgery could be the normal metabolism and elimination of cTnI from the body. The half-life of cTnI is reported to be 120 minutes [9]. One explanation for increased concentration of cTnI postsurgically could be that anaesthesia and surgery may cause further damage to the myocytes, in particular in individuals with systemic inflammation and impaired circulation, because of potential perioperative myocardial hypoxia. This phenomenon is well recognised in humans [10,29,30] but has, to our knowledge, not been shown to occur in dogs. Another possible reason for myocardial injury during anaesthesia could be direct toxic effects of the anaesthetic agents. Ongoing myocyte damage because of SIRS or inflammation induced by systemically released endotoxin could also contribute to elevated concentrations of cTnI postsurgically. Two of the healthy control dogs in our study (which all had undetectable concentrations of cTnI preoperatively) had increased concentrations of cTnI after surgery. This could possibly be explained by the aforementioned perioperative hypoxia (or toxicity) and subsequent myocardial cell damage.

The only studied variable that was significantly associated with cTnI concentrations was preoperative percentage of band neutrophils and postoperative cTnI concentrations ($p = 0.016$). The preoperative PBN and preoperative cTnI concentrations tended

to be correlated (p = 0.059). A high PBN count in peripheral blood is considered a sign of a high demand of neutrophils in the tissues during inflammation [31]. The percentage of band neutrophils is, as mentioned earlier, one of the criteria used for the diagnosis of SIRS. Thus, the above-mentioned correlation might reflect myocyte damage caused by systemic inflammation.

Conclusion

Mild to moderate increases in cTnI appears to be common in dogs with pyometra before and after surgery, but the clinical importance of this finding is uncertain. None of the studied clinical variables (including SIRS) were found to reliably predict increased preoperative cTnI concentrations. Because of the preand postoperative variation in cTnI concentrations it was not possible to identify a negative effect of anaesthesia and surgery on myocardial cell integrity. Consequently, analysing serum cTnI concentrations from dogs with pyometra could possibly help detect subclinical myocardial damage. Further studies are needed to investigate whether increased concentrations of cTnI are associated with a higher risk of perioperative complications.

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Materials of Conferences

CLINIC CHARACTERISTICS OF PROFESSIONAL BRONCHIAL ASTHMA

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The object of the investigation is to identify the prevalence of professional bronchial asthma among the population of Kursk region and to optimise the therapy of the patients according to GINA 2006.

The methods of the investigation are the analysis of the medical histories of 1512 patients which are registered in Kursk Center of Professional Disease, prospective clinical trial of the patients with professional bronchial asthma.

Results: professional bronchial asthma was detected in 59 cases (4% of the patients with professional diseases), who earlier worked with professional hazard. Women prevail - 75% among the patients. The duration of the disease which is less than 5 years is registered among 14% of the patients, more than 10 years among 76% of the patient population. The majority is the patients of able-bodied population with the age from 30 to 60 – 66%, retirees – 34%. Concerning the level of control the professional bronchial asthma of 51 patients (86%) was partly controled and 8% - uncontroled. Such grades of severity and steps of treatment of professional bronchial asthma were determined: moderate bronchial asthma 2 step of treatment- 8%, bronchial asthma of average severity 3 step of treatment -41%, severe bronchial asthma 4 step of treatment -51% of the patients. Chronic cor pulmonale with Congestive heart failure 2A is diagnosed among 61% of the patients.The ground of the basic therapy is 2 combined medicines: Formoterol/Budesonide (Symbikort) and Salmeterol/ Flutikazone (Seretide). Fenoterol (Berotek N) and Fenoterol/ Ipratropiya bromid (Berodual N) were used according to the requirement. More than the half of the patients recieved Prednizolon enterally (from 10mg to 30mg per day) starting from the first days the disease was detected. All the patients used prolonged theophyllin.

Conclusion: the analysis of the recieved data allowed us to take reasonable steps in order to optimisethe treatment of the patients with professional bronchial asthma. 20 patients (34%) were transfered to the therapy with Symbikort in regimen -SMART (Symbicort Maintenance and Reliever Therapy). In this group of patients the increase of the level of the control of bronchial asthma was noted (the ACT-test was used to estimate the level of control) in comparison with the regimen of the therapy with fixed doses of combined (LABA and ICS) medicines.

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«BOL-CHITAL» - A NEW INNOVATIVE PRODUCT IN MAXILLOFACIAL SURGERY

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Maxillary bones are the most frequent locations of destructive changes, a considerable part of which is located at the level of teeth roots. These foci's development occurrence corresponds to a high level of complex cavities of teeth in the persons of both sexes in all age groups. The bony tissue reparative regeneration processes' optimization is one of the most important problems of reconstructive surgery, in the maxillofacial area, in particular.

The major task after the radicular gnathic cyst surgical removal is the defect correction due to new hard tissue formation stimulation. The operative therapy main method, according to many authors [5], still remains cystectomy with single-step resection of root apexes emerging into the cyst cavity. The resected teeth's function depression, the possibility of reinfection from the cut off microtubules and traumatism should be referred to disadvantages of the operation [6]. Besides, bone cavities lowering the strength of maxillary bones and able to cause functional and esthetic disorders remain after the excision of radicular cysts.

There appeared new trends in the gnathic cysts treatment, such as filling of bone cavities with biocomposite materials after cystectomy to prevent early complications. It is connected with the fact that at a standard operational intervention the blood clot reduction occurs and it often results in the bone cavity infection and subsequent complications. The filling of bone defects of jawbones with biocomposite materials after cystectomy is aimed at:

- the prevention of possible complications connected with the blood clot reduction and disintegration, and also the secondary infection of the wound;
- the optimization of bone tissue regeneration in the defect area and jawbones' form and function recovery.

For this reason, the materials used for the bone cavity filling after cystectomy should possess a range of necessary properties.

First, they should have good biocompatibility factors, be biodegradable and not cause inflammatory response in the patients.

Second, they should possess osteoinductivity, actively make osteoblasts and other mesenchymal cells form the bone.

And third, they should implement and steadily substitute the defect capacity, i.e. perform the osteoconductive function.

To solve these problems many stomatologists use native biocomposite materials as they practically do not trail foreign analogues and their cost is considerably lower than that of the imported ones. So, by the present time, the preparations "Hydroxyapol" and "Colapol" (by the "Polystom" firm), "Collapan-L" (by the "Intermedapatite" firm, "Ostim-100" (by the "Ostim" firm) and a range of other preparations are well studied and widely used in operative dentistry and maxillofacial surgery practice [1, 2, 3, 4]. The carried out bioexperimental studies testified that the material on the basis the chitosan-alginate complex "Bol-chital" also corresponds to all the demands placed on the implantation materials inducing the reparative osteogenesis [11].

The **purpose** of the present research has been the study of possibility of application and the definition of influence of the material on the basis the chitosan-alginate complex "Bol-chital" on bone tissue reparative regeneration processes at gnathic cyst excision.

Material and research methods

The problem set was settled by means of filling bone cavities with gel-auto-blood mass of the chitosan-alginate complex containing sulphated and non-sulphated glycoseaminoglycans, serum factor of cattle stock growth "adgelon". The method was carried out in the following manner according to the procedure developed by the authors [9]. The cyst focalization was defined with the help of OPG and intraoral roentgenograms. Under the local or general anaesthesia a section upon the dental process in the cyst location projection is performed, a mucoperiosteal flap is laminated, the cystectomy and, if needed, radiectomy are performed, the bone cavity is filled with the "Bol-chital" product gel mass after the cyst surgical removal with the following suturing of the wound tightly. The surgical sutures are removed in 6-7 days. 20 patients have been operated on the radicular cysts of maxillary and mandibular bones by the specified method.

Research results and their discussing

During the postoperative period a low-grade postoperative edema of soft facial tissues, insignificant pain sense modality and the alveolar bone's form steady recovery were registered in all the patients. In all the cases in the observed period from 3 months to 1 year a positive clinical effect with a complete (9 patients) or partial (2 patients) jawbone tissue recovery in the defect area was obtained within the average time-limits from 3 to 5 months after the operational intervention.

During the control examination in three months after the operative treatment the defects' contours in the roentgenograms are obscure. The reclaimed bone density approximated the density of the surrounding jawbone, the boundary of the bone and the defect being not seen in separate cases. The reclaimed bone shadow is homogeneous, nonstructural, with multiple small ossification foci and early formation of bone trabeculae.

Conclusion

The laboratory and instrumental control of the reparation proved the advantages of the offered method, which consists in the lack of allergenic properties in the "Bol-chital" product, its high compatibility with the bony tissue, its ability to agglutinate microbial cells and bind toxic products, its biodegradability, little traumatism at the implantation, pain-relieving effect, close sticking to the bone, the bony tissues' blood filling increase due to the formation of new vessels and influence of precursor bone cells on the differentiation.

Thus, the application of the offered method results in the reparative osteogenesis optimization, a quicker recovery of the bony tissue in jawbones' defects, allows performing denture in the patients in earlier terms.

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CHANGES OF ENZYMATIC ACTIVITY OF I AND II TYPE 11β HYDROXYSTEROID DEHYDROGENASE IN PLACENTAS OF GRAVIDAE WITH ACUTE HERPETIC INFECTION

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The hormonal profile change is registered at various infectious processes during gestation (Bazina M.I., 1999; Lutsenko M.T. and others, 2000). Practically always it is attended by cortisol concentration disturbance. The purpose of our work was the given hormone content analysis and its metabolism enzymatic activity estimation in the uterine cake in the course of gestation complicated with a herpetic infection attack.

52 mature placentas taken during the birth process from practically healthy mothers (24 cases) and women undergone laboratory detected herpetic infection attack (28 cases) served as the test material for the study. Depending on the gestation course the material was divided into two groups: control and basic ones. The cortisol study in placental homogenate was carried out by the method of enzyme multiplied immunoassay using the sets of the “Alcor Bio” CJSC (St.-Petersburg) in the spectrophotometer “STAT-Fax 2100” (USA). The detection of 11β hydroxysteroid dehydrogenase (11β-HSD I, 11β-HSD II) was carried out by the method of Lloyd (Lloyd Z. and others, 1982) in modification of the laboratory of etiopathogenesis and respiratory system recovery processes (Dovzhikova I.V., 2007).

When studying the influence of the herpetic infection attack, the cortisol content increase was registered not only in the peripheral blood of the pregnant (Lutsenko M.T., Dovzhikova I.V., Andriyevskaya I.A. and others, 2003), but in the placental homogenate as well. At the growth record of G antibody titer against herpes simplex virus (1: 12800) the material analysis illustrated the hormone amount growth 1,6 times (639,2± 2,70 nmol/l – at the herpetic infection attack; 395,3±1,51 nmol/l –in the control group).

To find out a possible cause of the hormone increased concentration the key insights of its metabolism were analyses. The activity study of the enzyme being responsible for the cortisol transformation into inactive cortisone and so protecting from glucocorticoid (11β-HSD II) abundance was carried out. In the control group the enzyme was detected histochemically in the placental plasmodium and villi, cytophotometrically its concentration in the control made 126,70±2,79 standard units. In the uterine cakes of the mothers with the pregnancy complicated with herpes attack the given 11β hydroxysteroid dehydrogenase isoform activity decrease (36,72±1,59 standard units) was registered. Undoubtedly, it affected the concentration of glucocorticoids, as the lack of II type 11β hydroxysteroid dehydrogenase will affect their hyperproduction.

We analyzed the activity of the enzyme being responsible for another direction of glucocorticoids’ transformation: 11-keto-form into 11-hydroxylic form - I type 11β hydroxysteroid dehydrogenase. Cytophotometrically in the control group the enzyme activity in the ***villi syncytiotrophoblast*** made 41,0± 0,85 standard units. At the herpetic infection attack the intensity of histochemical response to the detection of 11β hydroxysteroid dehydrogenase of the given form rose sharply (159,7± 2,95 standard units), that supposes the increase of cortisol production.

Thus, the herpetic infection episode was attended by changes in the work of various forms of 11β hydroxysteroid dehydrogenase. It was established that a low activity level of the enzymes inactivating corticosteroids in the uterine cake result in the action of high concentrations of glucocrticoids on the fetus (Dodic M. et al.,1999, 2002; Moritz K.M. et al., 2002; Yang K.,1997). A high cortisol concentration in the fetal blood can result in some pathologic processes in adult stage: hypertension, diabetes, adiposis (Alexander B.T., 2006; Myatt L., 2006; Yang K., 1997).

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THE IMMOBILIZATION OF ALKANE-TROPHIC MICROORGANISMS ON ORGANIC CARRIERS FOR REMEDIATION OF THE OILY GROUND

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Nowadays, during the remediation of the oily ground the selection of utilizable inexpensive natural carriers for alkane- trophic microorganisms on basis of the waste is very perspective. It provides the semi-functionality of the biological preparation-oily destructors, that has not only the ability to decompose petroleum pollution, but also to raise the biological ground activity, to provide positive balance humus, to active the microflora of the ground, to influence on rhizosphere of the plants favorably, to provide the adaptation of oily oxidizing microflora and to reduce the stress for microorganisms in a polluted environment.

The main purpose of the work was the substantiation of the ways of wastes' use of the fat-and-oil industry – sunflowers' seedcoats and its modification - as carriers for monocultures Rhodococcus erythropolis AC-1339 D and Fusarium sp. №56 and their associations during remediation of the oily ground.

There was carried out the modification of sunflower pod for increasing the adhesion properties, preliminary including the extraction of wax-like lipids from it by the light petroleum degreasing. After the solvent removal from the pod, exposured it by concentrated hydrochloric acid (within several hours), washed out by distilled water up to pH=7, then processed by 33% solution of alkali NaOH and again washed by distilled water before neutral reaction, finished the process by drying under 130ºC up to humidity 12-14 %. The generated modified carrier was used in the further researches. For just listed carriers was checked the absorption degree of microorganisms - oily destructors by the known procedure.

As a result of researches is revealed, that the application of modified sunflower pod with immobilized association of microorganisms Rhodococcus erythropolis AC-1339 D and Fusarium sp. №56 in the ratio 1:1 gives the significant increase of a biological degradation degree of petroleum (up to 10-20 %). The large specific surface of the carrier provides not complicated diffusion of substratum to cells of microorganisms- oily destructors and removal metabolite from particles. After the ground cleaning from petroleum the sunflower pod is like a siderate, improves the structural properties of ground, intensifies its moisture and air capacity and of course interchange of energy.

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BRONCHIAL ASTHMA - LOCAL IMMUNITY AND METHOD OF TREATMENT

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The purpose of our research was to study local immunity in patients with infection-allergic and atopic bronchial asthma (BA) and efficiency of a new treatment method. 30 BA patients were examined clinically and immunological. Also levels of antibodies to surface bacterial antigens and contents of IgA, IgG, IgM, IgD, IgE, slgA in bronchial secret and saliva were investigated. Along with low IgA content and absence of IgM and IgD compensatory function, hyperproduction of antibodies to gram-negative bacteria is registered. This form of BA is also characterized by significant decrease in slgA content and increase in IgE level. BA patients were treated by a complex of immunomodulators and local antihistaminic drugs. This method proved to be more efficient as compared to the basic therapy alone. Immunomodulators and antihistaminic drugs promote better and longer remission of BA patients.

BA patients suffering from respiratory airway inflammatory processes for a long time have serious morphofunctional disturbances in their bronchial mucous membrane. By immunohistochemical methods a marked rise of Type 3 collagen content in the mucous membrane basal layer was revealed; Type 4 and 5 collagen activity round the vessels as well as its content in basal membrane and in spaces between the epithelial cells increases. Against the background of the lipid peroxide oxidation rise the activity of ciliated epithelium reduce. Due to the complex anti-inflammatory therapy of BA patients (laser therapy, anti-inflammatory corticosteroids and cytokins) we succeeded to reduce bronchial airway obstruction by 30%; to abolish asphyxia attacks; to restore mucous membrane epithelium, ciliated epithelium activity.

Some revealed defects of humoral (decrease in IgA level) and cell immunity (decrease in the general amount of the T-lymphocytes and T-suppressors) in children with BA, together with hyperproduction of IgE and immune complexes made us search for new methods of directed therapeutic action on various sections of immunity. Immunal was used in 25 children suffering from BA at the age from 3 to 5 years. Immune status normalization was registered in 16 patients (64%). In the rest 36% the total number of lymphocytes increased significantly. In all patients IgE content and immune complexes level decreased. No increase in their contents was registered after 7 months observation.

Allergen-specific therapy is of pathogenic value in the treatment of BA in children. One year after the treatment, pronounced immunological effect was registered in 60 children (71.4%), while after two

years it increased up to 86% children. Specific immunotherapy resulted in normalization of T-lymphocyte functional activity, IgA, IgG and slgA serum levels in nasal secret. Prolonged therapeutic effect was registered in all clinical immunological data after the specific immunotherapy course.

We studied the functional state of central nervous and immune systems in patients with BA and effect of acupuncture on it. Positive result of acupuncture was obtained in 88.6% patients.

Along with objective clinical effect, i. e. ceasing of asphyxia attacks, patients' quality of life became much better: they gained optimism, eagerness to work, decrease of irritation and tearfulness, improvement of appetite and sleep. Immunological parameters also improved. Our results demonstrate high clinical and immunologic effect of acupuncture in BA patients with initial changes in central nervous system.

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IMMUNOTHERAPY AND MAST CELL ACTIVATION

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In the early phase of allergic reaction mast cells are the main cellular effectors of acute inflammation releasing preformed and newformed mediators. The release of mediators is therefore a marker of mast cell activation and could be used to evaluate early allergic reaction. From the preformed mediators histamine and tryptase can be currently assayed in biological fluids. Histamine can be originated in mast cells, basophils and probably from a pool of other cells or extra cellular spaces in respiratory mucosa. Tryptase is only released by mast cells, has a good stability in fluids and reliable assays are nowadays available. Tryptase is spontaneously released from mast cells in respiratory mucosal after allergen inhalation and its concentration in fluids for instance during pollen season corresponds to the intensity of allergic disease. Nasal challenge with allergen tries to reproduce natural exposure conditions and allows to evaluate on controlled conditions the kinetics and evolution of nasal allergy.

The study of tryptase release after nasal challenge with allergens is therefore a good and reliable method to evaluate mast cell response to allergens. In the last few years we have first tried to standardize the method for tryptase assay in nasal lavage fluid after nasal challenge and in a second phase applied this method to the evaluation of mast cells reactivity to allergen before and after specific immunotherapy in pollinosis.

Nasal provocation tests have been done before pollen season with increasing dosages of 10, 100, 1000 PNU._Tryptase assays in nasal washing have been done at 10, 20 and 30 min after provocation by CAP or RIA methods. Tryptases assays have been done before starting immunotherapy and after 2 years of immunotherapy. Nasal fluid has been always collected in absence of therapy with anti-histamine drugs in the last week, inhaled or systemic steroids DGCS or topical anti-histamines in the last 3 days.

The data obtained suggest that tryptase assays in nasal washing could be a useful addition in diagnostics of pollen allergy. A clear cut increase on tryptase concentration in nasal lavage fluid has been observed after nasal provocation. The results obtained suggest that a higher concentration of pollen extract (1000 PNU) is more reliable for the evaluation and that the more significant results are observed 10 and min after nasal challenge specific immunotherapy clear cut blocks the tryptase release provoked by nasal challenge decreasing the amount of tryptase released by mast cell after each one of the different concentrations employed but also slowing the release process as shown by the latter peak (20 min) observed after immunotherapy. These data point to an effect of systemic specific immunotherapy on nasal mast cell reactivity probably due either to a decrease of fixed IgE through high affinity receptors or to a blockade on mast cell releasability as suggested by the late peak (20 min.) of tryptase release.

Tryptase assays in nasal washing after provocation tests are a reliable, safe and useful additional method in diagnostics of pollen allergy and furthermore in the control of efficacy of specific immunotherapy. Mast cell reactivity in rhinitis can be studied by the assay of tryptase in nasal fluid after nasal challenge. An increase in tryptase in nasal washing is a marker of allergy to the extract employed. Specific systemic immunotherapy significantly decreases mast cell reactivity after nasal challenge with the same allergen as show by the decrease in tryptase release.

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IMMUNOLOGICAL MONITORING OF PATIENTS WITH CHRONIC DISEASES IN THE COURSE OF IMMUNOREHABILITATION

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Comprehensive phenotypical characterists of immunocompetent peripheral blood cells (CD3, CD4, CD8, CD19, CD25, CD45RO, CD95 and HLA-DR) is presented. Proinflammatory cytokines (IL-lβ, IL-6 and

TNFα) and lymphokines of Thl-type (IFNγ and IL-2) were studied in serum of patients with chronic obstructive and nonobstructive bronchitis on the background of secondary immunodeficiency state (IDS), also patients with subacute and chronic rheumatoid arthritis (RA) in the course of immunorehabilitation (IR). Disorders in activation processes of immunocompetent cells in peripheral blood of patients with chronic bronchitis (CB) were revealed that manifested in a decreased quantity of activated T-lymphocytes expressing CD25 and CD45RO antigens, as well as significant increase in the number of CD95-cells. The levels of IFNγ and IL-2 were shown to decrease in blood serum of patients with CB, thus evidencing lower functional activity of Th1. Proinflammatory cytokines were demonstrated to prevail in blood of these patients. A step-by-step scheme for IR of CB patients with secondary IDS is suggested which can be also applied when treating patients with other immunopathological states. High efficiency of combined application of immunomodulators for system and local use in patients with CB of various severities was shown.

It was shown that RA patients are characterized by an elevated expression of activation markers on the surface of T-lymphocytes (CD25 and HLA-DR), significant increase in. the number of activated CD45RO-bearing T-memory cells and CD95-cells thus evidencing increased readiness to apoptosis. Direct correlation between the number of T-lymphocytes which express the marker of prolonged activation (HLA-DR) and duration of the disease in RA patients was established. It was shown that in serum of RA patients, proinflammatory cytokines prevail. Positive correlation between the levels of IL-lβ and IL-6 in serum and activity of the process was revealed.

Immunological monitoring at all IR stages of IDS patients was substantiated. The level of TNFα was shown to positively correlate with the number of CD95-cells in patients with chronic pathologic processes. Comprehensive clinical immunological analysis of a huge amount of clinical materials allowed elaborating technical approaches and tactics of IR of patients with disorders in immune system. It was shown that the choice of immunomodulators, scheme and methods of IR are determined by peculiarities of the clinical course of the disease, its severity, activity of inflammation process and immune state indices.

Results of ambulatory and sanatorium-resort IR programs were analyzed. They proved to be more efficient as compared to routine pharmaceutical and therapy measures. It was demonstrated that these complex IR programs should include adequate basic medicamentous therapy, set of immunomodulators of directed action, methods of nonmedicamentous treatment, as well as resort and preformed physical factors taking into account clinical immunological and pathogenic peculiarities of a person at every stage of IR. It was shown that step-by-step IR restores not only the number of regulatory immune cells, but also their functional activity and the level of proinflammatory cytokines which play an important role in the chronic inflammatory processes. It also provides stable clinical remission. It was demonstrated that prolonged, rational, complex, step-by-step IR allows to decrease the number of recurrences (by 95-98% in average), prolong remission by 4-to 5-fold, reduce drug uptake and improve ability for work and quality of life.

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IMMUNOLOGICAL ADAPTATION OF NEWBORN INFANTS WITH RESPIRATORY DISTRESS-SYNDROME OR PNEUMONIA

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The main peculiarities of neonatal immune system are:

1. The prevalence of immature CD5+ B-lymphocytes with high expression of sIgM and lack of sIgD which are able to produce polyreactive IgM, IgG1 and IgG_3; massive antigen binding with sIgM leads to immature B-cell apoptosis.

2. Low expression of CD40L on neonatal T-lymphocytes decreases their ability to differentiate to Th1 and to intensify macrophage reactions, to cooperate with B-cells and to be typically switch immunoglobulin classes synthesis.

3. Insufficiency of B7 expression on antigen-presenting cells (APC) which leads to non-professional antigen presentation to naive T-cells. Ratio of professional and non-professional APC has influence on priming or tolerance as a result of neonatal immune response. Small amounts of antigen can interact with a few mature B-cells and can be a base for specific humeral immunity development.

4. Heterogeneity of CD4+ lymphocyte subpopulation, the priority of CD45RA+ naive T-cells which act as suppression inductors and produce mainly interleukin-2.

The aim of our research work was to investigate dynamical changes of main immunological parameters (such as IL-I, TNF-α, IL-4, TGF-β serum concentrations (ELISA), lymphocyte phenotype (flow cytometry) and chemiluminescent response of peripheral blood phagocytes) during the early postnatal period in physiological conditions and in infants suffered from respiratory distress-syndrome (RDS) or pneumonia. We investigated 48 full-term newborn infants from moderate and high risk pregnancies during the first month of life.

It was found that serum levels of IL-lβ in cord blood of healthy neonates from moderate risk preg-

nancies were significantly higher than in peripheral blood of healthy adults (491,4±49,9 pg/ml versus 277,5±64,4 pg/ml respectively; p<0,05) but IL-4 serum concentrations in cord blood were significantly lower than those in blood of adults (27,4±10,2 pg/ml versus 126,3±27,2 pg/ml respectively, p<0,05).

During the first week of life in physiological conditions serum levels of proinflammatory cytokines and IL-4 significantly increased in comparison with cord blood levels. CD3+ and CD4+ cell numbers had the same dynamics while the number of CD8+ cytotoxic T-lymphocytes significantly decreased. The level of zymozan-induced chemiluminescence of peripheral blood leukocytes became significantly lower till the 7th day of life in comparison with cord blood. The values of immunological parameters under the physiological conditions were different from those situations when early postnatal period was complicated with respiratory distress-syndrome (RDS) or pneumonia (significantly lower serum levels of IL-I and TNF, reduced absolute numbers of CD3+, CD4+, CD8+ and B-cells. significantly higher level of spontaneous chemiluminescence in peripheral blood of neonates suffered from RDS or pneumonia versus healthy infants on the 5th-7th day of life. Recovery from pneumonia or RDS was accompanied with restoration of pro- and anti-inflammatory cytokine balance, elevation of absolute lymphocyte number and serum IgM level, reduction of natural killer number and level of expression of CD25+ receptor to IL-2 as well as normalization of spontaneous CL level.

So we describe the mode of normal early postnatal immunological adaptation in healthy full-term newborn infants and immunological distress-syndrome in neonates with RDS or pneumonia. The data are important for the further decisions concerning immunological intervention in neonatal period.

The work is submitted to Scientific Conference “Basic and applied research”, Brazil (Rio de Janeiro), February 19 - March 3, 2009. Came to the Editor’s Office on 22.12.2008.

TERRITORIAL HEALTH DIFFERENCIES IN RUSSIAN FAR EAST POPULATION

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The health of population is a biosocial phenomenon, as it depends both on the body features of separate people and external conditions. That is why the health level can be thought of as a factor of adaptation of a concrete population group to natural and socioeconomic environment of the territory reflecting how the given environment is comfortable for normal life activity of this group of people [1].

To study the Russian Far East population health we used the factors of life expectancy at birth (LE), men and women separately, in the rural and urban areas, and infant mortality.

The population health and territorial difference definition integral estimations were carried out on the basis of the health index calculated with the help of four LE factors and the infant mortality factor on the method of linear scaling. It is based on the definition of referential points (maximum and minimum values of indicators) and shows the position of a separate region between them. First, the calculation of special indexes on every factor is performed by the formula:

$$Y=(X-Xmin)/(Xmax-Xmin), \text{ to calculate the LE}$$
$$Y=(Xmax-X)/(Xmax-Xmin), \text{ to calculate the infant mortality,}$$

where Y – is a special index, X – the factor of this or that region, Xmin and Xmax – referential points [3]. The Y value varies anywhere from 0 to 1. Zero corresponds to the worst complex estimation, and 1 – to the best one.

The same minimum and maximum values (25 and 85 years accordingly) were chosen as the LE factor referential points. The smallest and largest values of the given factors were chosen as the minimal and maximal referential points for infant mortality in Russia in 2006 – 4,7 (St.-Petersburg) and 33,0 (Koryak AD) per 1000 of newborns accordingly. The spread in values of the chosen factors varied from 1,1 to 3,1 times.

The LE territorial differences manifest themselves considerably stronger in the rural area. A most vivid demographic feature of the FEFD subjects compared to average Russian factors is a tragically low rural area female LE level (Russia – 71,8 years). Even in the safest Republic of Sakha (Yakutia) in the Far East it is lower than the average Russian one (71,3 years). The rural area male LE in 2006 in the majority of FE regions, exclusive of the Republic of Sakha (Yakutia) - 60,2 years, is lower than the average Russian factor. The infant mortality factors in 2006 in the FE regions are higher than the average Russian one (10,2%) and vary from 10,6% in the Republic of Sakha (Yakutia) to 33,0% in the Koryak AD.

When calculating the LE index, first, we calculated and then summarized the indexes on separate components (men and women in town and village) weighted ¼. At the second stage the final health index was calculated as an arithmetic middling of the two special LE indexes and infant mortality.

We assumed that the health index maximum value fell on Sakha (Yakutia) – 0,73, the minimum value – 0,26 – on the Koryak AD. The difference between the minimum and maximum values of the health indexes among the Far East regions makes 2,8 times.

Proceeding from the obtained health indexes we marked out 4 groups of the FE regions by the health index value and the LE and infant mortality level combination. The first group with the population health level **above the average** was made up of Sakha (Yakutia) and the Primorski Krai, in the territory of which 45% of the FE population live. A relatively high LE and low infant mortality are typical of the given subjects' population. The **average** population health level is observed in the Khabarovsk Territory, Magadan, Amur, Kamchatka and Jewish Regions and makes 53,8% of the residents from the whole District population. The population of these regions has average LE and infant mortality values or one factor is lower and the other is higher. The population health level **under the average** is defined in the Chukchee AD (comprising 0,75% of the FE population), which a relatively low LE and high infant mortality are indicative of. The **low** population health level is defined in the Koryak AD with the part of 0,35% of the whole Far East District population. An extremely high infant mortality and low LE are common to the population of the given district.

An **index-map** with the FE regions' population health level territorial difference has become the result of our research.

The analysis of the FEFD population health state allowed coming to the following conclusions:

- The Far East as a whole has average and under-the-average health factors in Russia (the health index in the whole Russia in 2006 – 0,72).

- The LE factors irrespective of sex and the type of locality in the FE territory is much different from the average Russian ones and vary between 1 and 14,7 years.

- Regional differences in the population health state within the Far East are essential. The greatest territorial variability is typical of the rural area female LE, which makes 14,7 years. The rural area male LE makes 13 years. In the urban area the difference makes 11 years for both sexes.

- On the final health index value and the combination of LE and infant mortality index values there are 4 groups of regions marked out in the Far East with the differentiation on the health state. The majority of the FE subjects has an average population health level (53,7% of the FE population).

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Short Reports

INFLUENCE OF AN EXCHANGE OF SEXUAL HORMONES DURING THE OVARIAN-MENSTRUAL CYCLE ON THE VERBAL MEMORY AND LEARNING EFFICIENCY OF THE WOMEN-STUDENTS STUDYING PHYSIOLOGY

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In conditions of globalization in the CIS countries the reforming of the system of higher education takes place. Thus, in Republic of Kazakhstan the correspondence form of education has been reorganized into the distant one which, in turn, allows arranging an individual trajectory of studying considering various pedagogical, psychological and physiological factors [1].

One of the physiological factors that influences on mentality as a whole, on the personal behaviour, and on efficiency of his or her activity is a hormonal exchange, in particular an exchange of sexual hormones. It is especially important in the process of women studying. However, phases of the ovarian-menstrual cycle (OMC) in pedagogical activity generally are not considered, researches of this promlem mostly have strictly medical character. There are only a few publications on this issue. Some of them are related to the field of physical training and provide insistent recommendations to decrease physical activity during the period of catameniae [2], some works deal with decision-making processes in economy [3], and reveal the change of decision-making strategy of seller-women during their critical days (due to decreasing of the level of estrogens) who become less risky and more provident which is normally specific for seller-men.

Today influence of exchange of female sexual hormones not only on emotional processes, but also on cognitive sphere is proved [4-6] this resulted in recognizing of a new diagnostic category, namely premenstrual syndrome [7]. Thus, estrogens regulate plasticity of a nerve tissue and serves as the trophic factor. It can influence on formation of connections between neurons in cognitive areas – in the hippocampus and in the brain cortex [8]. Because of neurophysiological functions of hippocampus[9-10], estrogens improves verbal short-term memory, attention and training abilities[9; 12-13]. Estrogens, progesterones and their combinations also positively influence on the serotoninergic system which is carrying out neuro-mediation functions, that is transfering of nervous signals from one neuron to another, strengthen the brain blood-flow and the transport of glucose and its metabolism, and also activate formation of dendrites and synapses [9]. Therefore, in our opinion, in the professional training of female specialists the consideration of the particular qualities of sexual hormones exchange in OMC can be perspective, especially in professional spheres where the number of women prevails over, namely, pedagogical and psychological specialties. Besides, mentioned effects of influence of estrogens on cognitive functions have been received in the course of the researching of efficiency of the replaceable hormonotherapy for women in the post menopause [9; 12-13], but not investigating the analogous processes in the organisms of young healthy women. This aspect still demands additional special research. The maximum of estrogens is being produced during the ovulation period, that is, the 14^{th}-15^{th} day of the 28-day cycle, a minimum – during the catameniae period [6].

Considering that specifics, we have offered to 58 female students at the age of 18-25 years (excluding pregnant, given birth no more than 1 year ago, and having gynecologic problems students) to take the test by technique of 10 words which examines short-term verbal memory. The test was conducted 2 times: during the menstruation period (the 1-5 days of a cycle) and during the presumable ovulation period (the 12-18 days of a cycle adjusted to its duration). The maximum quantity of the reproduced words after the fifth presentation of stimulus was considered. Besides, we have compared the progress of the students – their grades for computer modular testing according to 5 points scale, with that of OMC period. Processing of the received data has been made by SPSS 14.0. We have applied Student t-criterion for connected selections.

According to the technique of 16 words $t_{emp.}$ =-6,64; according to the modular testing $t_{emp.}$ =-6,58; $t_{cr.}$ = 2,0 at $p \leq 0,05$ ($t_{cr.} \leq t_{empir.}$).

That is, distinctions of indicators are statistically authentic and in the menstrual period the indicators of short-term verbal memory are lower, than during the ovulation period.

According to the modular testing $t_{emp.}$ =-6,58; $t_{cr.}$ = 2,0 at $p \leq 0,05$ ($t_{cr.} \leq t_{empir.}$).

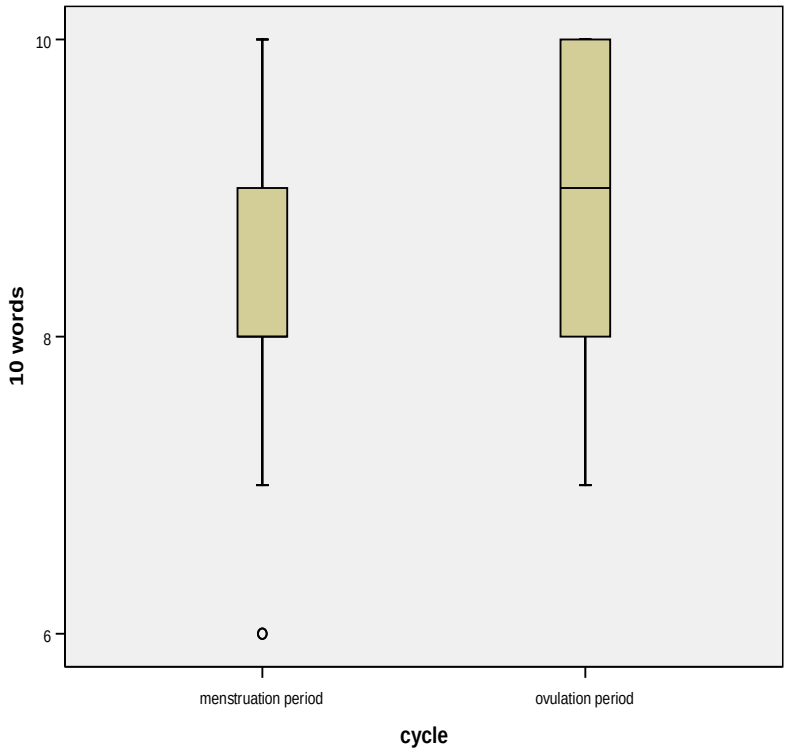

Diagram 1. Box plot of the indexes of the 'Ten Words Method' according to an ovarian-menstrual cycle

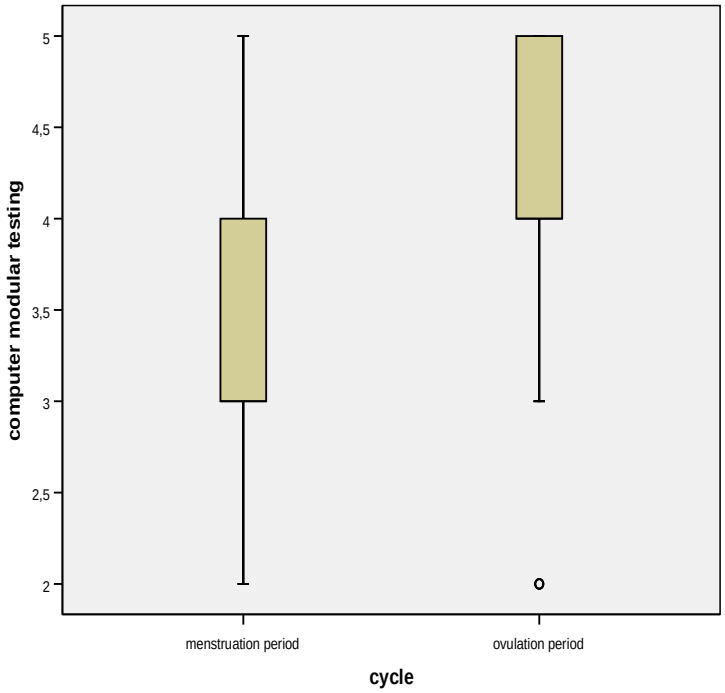

Diagram 2. Box plot of the indexes of the module testing of knowledge adaptation according to an ovarian-menstrual cycle

Moreover, the grades for modular testing reveal the same dependence: students' progress is rising during the ovulation period, i.e. during the peak period of estrogens concentration and, on the contrary, is decreasing with lowering concentration of these hormones.

Thus, it can be recommended for students to intensify their educational activity in respect of mastering of the new information and passing of control procedures in the middle of a menstrual cycle – during the period of the maximum estrogens concentration, and so more productive work of hippocampus, and to minimize the educational activity in the premesrtual period as well as during the period of menstruation.

It is clear, that such tactics of educational process is unlikely in conditions of the traditional form of education with the regulated schedule of learning process, but it can be realized in its innovative forms, for example distant education [2] while the subject of pedagogical process forms the individual trajectory of studying. It is also necessary to note that the received results are preliminary, considering multivariate character of researched phenomena and the necessity of their further complex studying.

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THE EFFECT OF *ESCHERICHIA COLI* TOXINS ON BLOOD MICROCIRCULATION IN VENTRAL MESENTERY OF WHITE RATS

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1. Introduction

Bacteria *Escherichia* is the basis of human and animal intestinal microflora. The group of entheropathogenic

E. coli causative colibacillosis has biomedical implication. The virulence of these bacteria associated, at first, by toxins production. The affect of *E. coli* toxins on physiological processes of microorganism particularly investigated.[1] At the same time response of intestine blood vessels on the action of toxins ex tempore in vivo is not describe practically. Changes in blood microcirculation system can be important diagnostic sign, reflecting the interaction of microorganism with surrounding internals' and tissues' cells. One of the perspective methods of evaluation of these changes in biomedical researches is speckle-microscopy[2-5]. Thereby, we carried on an investigation with this method to study the effect of *E. coli* toxins on blood microcirculation in the course of short intervals of time.

2. Methods and materials

2.1 Cultures

We studied exotoxin producing by strain *Escherichia coli* A5 and endotoxin producing by strain *Escherichia coli* B6. Each strain cultured in meat infusion bouillon at 37^{o} C separately. Daily strain cultures centrifuged at 600 g to get supernatants, which used for experiments.

2.2 Laboratory animals

An experimental animals (white rats) sedated by intramuscular injection of 5-Ethyl-5-(1-methylbutyl)-

2,4,6-pyrimidinetrione (*Nembutal*). Then we abducted the abdominal cavity and eviscerated the ventral mesentery. After the abduction we placed rat on the thermostabilizing stage of speckle-microscope. So, the loop of ventral mesentery was placed directly under the microobjective.

2.3 Speckle-microscope and its optical schemes

Optical scheme of speckle-microscope for investigations of random bioflow is shown in Fig. 1[2]. Beam of He-Ne laser (λ=633 nm) is focused into the spot of small radius (W_o =1.5 μm) on the investigated microvessel. Conventional optical microscope supplied by monochrome Mutech 1280-USB digital CMOS camera enables observation of blood flow in a vessel visually. Computer image analyzer processes consequence of the video images (frame-by-frame analysis).

As blood or lymph flows through the vessel or probing beam scans the investigated surface, the strongly focused laser beam is modulated in the waist plane. This leads to the formation of dynamic speckle pattern in the far zone of diffraction. Speckles of large size are formed in the case of small number of scatterers, so diameter of aperture of photodetector is essentially smaller then average speckle size. The temporal fluctuations of scattered intensity are detected by photoreceiver. Time-varying signal is amplified, recorded on the tape and processed further by computer[6].

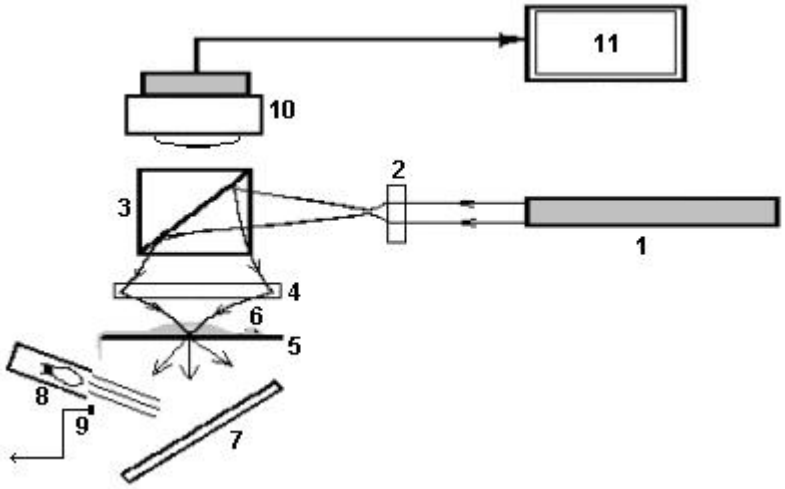

Figure 1. Optical scheme of speckle-microscope
1 - laser, 2 - microobjective with 10^xmagnification, 3 - beamsplitter, 4 - microobjective with 8^x magnification, 5 - stage, 6 - biological object (mesentery of white rat), 7 - mirror, 8 - lamp, 9 - photoreceiver with pinhole, 10 - TV camera, 11 - computer.

2.4 Original research

We brought a quantity one of the daily culture supernatant (~1ml) on the ventral mesentery loop and registered output signal of speckle-microscope for 10 second immediately. Repeated superimposing accomplished after 1, 2, 3, 4 and 5 minutes for dynamic process was studying. Blood flow characteristics before supernatant superimposing were used as control. The speckle-signal is amplified, recorded as avi-file and processed further by the computer with the original algorithm for MathCad 2001 program.

Obtained data are presented as changes of signal spectrum bandwidth (BDW) for each second during the time registration.

3. Results

We compared the effect of *E. coli* exotoxin and endotoxin on blood microcirculation in white rats ventral mesentery. Obtained results are presented in Fig. 2 and Fig. 3.

Fig. 2 shows the affect of *E. coli* A5 on blood microcirculation in capillaries. It is noted immediate increasing of blood flow velocity after superimposing supernatants.

Superimposing of *E. coli* B6 endotoxin shown lower fluctuations of blood flow velocity (Fig. 3).

4. Conclusion

Thereby superimposing of *E. coli* toxins caused immediate change of blood flow velocity in the course of short intervals of time. Thereat superimposing of *E. coli* A5 exotoxin offered the more intensive reaction, than *E. coli* B6 endotoxin. There was nearly twice increase of signal spectrum bandwidth in this case, while superimposing of *E. coli* B6 endotoxin resulted in increase of ~20 Hz maximum.

5. Acknowledgement

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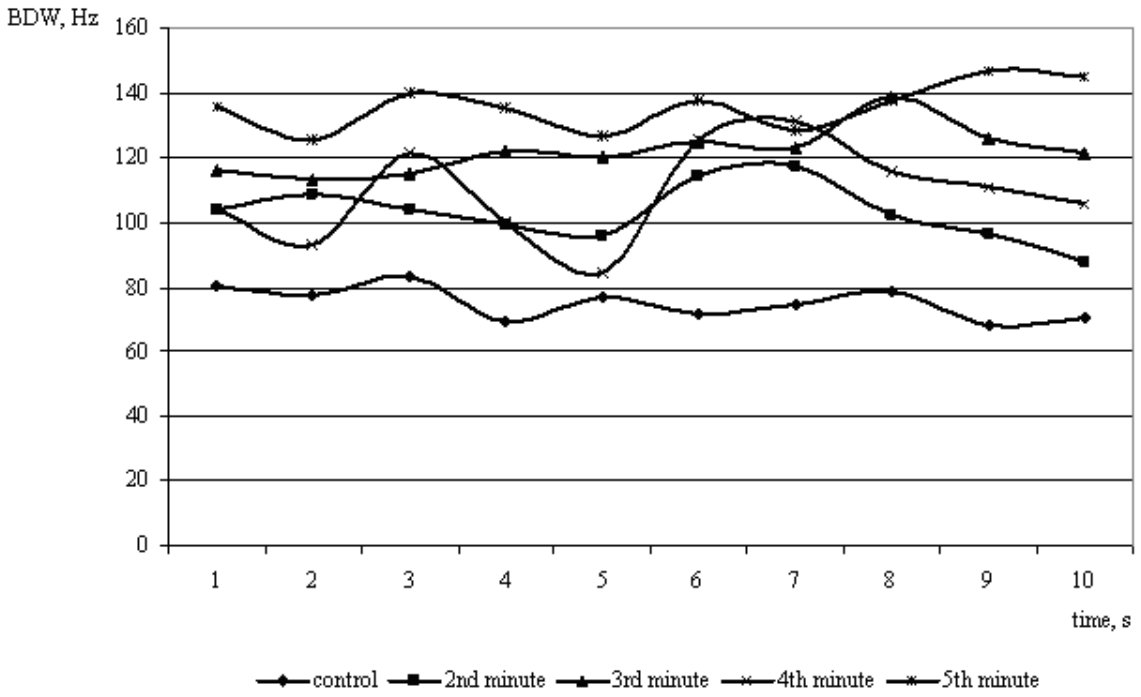

Figure 2. The effect of *Escherichia coli* A5 exotoxin on blood microcirculation in white rats ventral mesentery

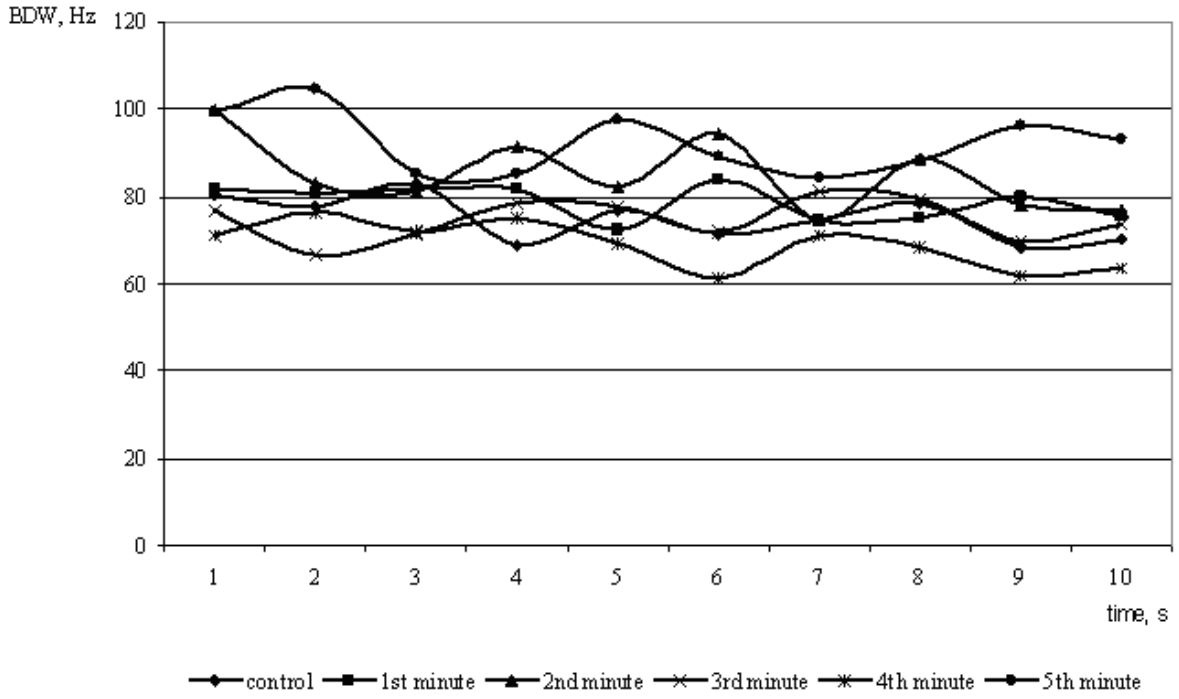

Figure 3. The effect of *Esherichia coli* B6 endotoxin on blood microcirculation in white rats ventral mesentery

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DEVELOPMENT OF THE NEW METHODS OF THE INSTRUCTION OF STUDENTS IN THE PEDAGOGICAL ACADEMY

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Within the framework of innovation educational programs psychology and directly psychology of thinking as object in the educational process of pedagogical VUZ (Institute of Higher Education) acquires special importance. Already by itself quality of formation implies the ability to think on the high level, to know how to solve complex problems, to find a way out in the difficult situation, to master objects and to use its knowledge with the high return both in the life and in the obtained specialty. Based on the example to Greece and Rome it is possible to distinctly trace bloom and drop in these empires - these processes invariably coincided with bloom and destruction of philosophical studies and schools. In the present stage considerable attention is paid the development of educational systems would not stopping, but only it was improved. Working as the assistant of the department of psychology, with the length of employment in the specialty of 8 years, for me it in practice is necessary to see the psychological unpreparedness of the students especially of the first courses for the educational process in VUZ (Institute of Higher Education), to what is devoted my work.
Keywords: psychology, education, innovation, program.

Problems with which, it is necessary to contend for the teachers of VUZ (Institute of Higher Education)

Interviews with the students from the first on the final fifth course instruction in VUZ (Institute of Higher Education) were carried out by me, furthermore, by them it was proposed to express its thoughts in the written form, with what problems they are encountered for the first time the years of instruction, also, in the process of further mastery of specialty. The assembled material, obtained in the course of a study, from the students of the first course attests to the fact that psychologically they experience difficulties in the educational process, all this is manifested in the insufficient perception of lecture material, but practical training does not contribute to the formation of skills and habits, necessary for the future profession, which affects the quality of the obtained formation. The principle of instruction in VUZ (Institute of Higher Education) strongly is differed from school instruction, and students pass the continuance of adaptation, which concludes only with the end of the second course. There is even expression “you will break two courses, from the third you will not depart”.

Somewhat better proceed the matter in the students, who passed the bases of psychology to school, but also, there are not all is smooth in this group of students. Our student freshman before the entering into VUZ (INSTITUTE OF HIGHER EDUCATION) became accustomed to associate with the teachers, and here he meets with the professorial-teaching staff, which principally is differed from the pedagogical association of school, and the system of instruction (this of lecture, practical training, work in the libraries, also, with the training literature of another size) in VUZ for them novelty.

It is completely obvious that school educational process has the essential omissions, connected with the teaching of such objects as philosophy and psychology. It is necessary to turn from traditional approaches to instruction in our young people in the school, and to the publishing houses, which work on the innovation technologies of the training process in short periods, to develop the training programs of schoolboys according to the requirements of present day. First of all, this concerns the objects of philosophy and psychology. Resolution of this question will make a real contribution to the adaptation upon transfer from one educational system into completely different plane of instruction. I.e. the entering of schoolboy into VUZ (INSTITUTE OF HIGHER EDUCATION) is accompanied by no adaptation this is the simply following stage of their development.

By the following problem, with which meets the pedagogical association of VUZ (Institute of Higher Education), this is the selection of profession, which for the majority of young people is serious problem. This the serious question as is correct to select specialty, since the quality of formation directly depends on the selection of profession. After conducting social psychological interrogation, after gathering in students (in the written form) their vision of the problem of the psychological selection of profession, the following picture appears: if student masters that profession, to which he does not have ability, then the cancelled career and/or the life of this student becomes sum. In this case the society acquires the unskilled worker and, simultaneously, loses the specialist of another profession, where the abilities of this student could appear. It is very important to note that the not always young person independently approaches the selection of profession, more frequent for it is decision of parents or other adult people. Resolution of this question also lies in the plane of the acquisition of qualitative formation in the school establishments and directly it depends on the teaching of philosophy and psychology.

Concerning other problems, which the students in the walls of VUZ (Institute of Higher Education) encounter - this is the inability to master objects in that river bed, as this present day and specialty requires. Knowledge are frequently interrupted, not ordered, is absent the competently built system of knowledge and in the majority of the cases this occurs not through the fault of student himself, not because of the poor teaching of this object by teacher, but because of the unpreparedness of student for the instruction in the psychological plan. Specifically, psychology of thinking can give to student the system of knowledge about how master object, in what direction move, on what to be oriented, to find correct approaches to the study of objects.

In our VUZ (Institute of Higher Education) insufficient attention is paid to this aspect of training students. I transfer the enumeration of psychological disciplines, which teach in our VUZ (Institute of Higher Education): general psychology and the history of psychology; psychology dependent on age; social psychology; special psychology; pedagogical psychology; the procedure of the teaching of psychology; psycho-geneticist; psychophysiology, all these objects give knowledge, but they do not teach, as it is correct to obtain knowledge. This omission is noted already from the school bench precisely here the absence of such objects as psychology of knowledge and thinking it affects what young people do not understand the skill of the perception of the integrity of instruction. This picture is observed also in VUZ (Institute of Higher Education).

On the basis obtained given from the students it is possible to make the following conclusion: is necessary introduction into the training process of schools and VUZ (Institute of Higher Education) not simply of psychology, but the inherent components, such as psychology of knowledge and thinking, when within the framework indicated disciplines will be given the principles of correct approach to the mastery of objects.

One additional problem, which indicate the students of the first courses (it it must be solved by the psychologists of VUZ (Institute of Higher Education) and by the system of training future teachers), has straight relation to the culture of school teachers. Being trained in the school, young people frequently encounter with the fact that instructors they do not know how to erect correct interrelations with the students, they do not know how adequately to react to their behavior, even if it causes irritation. Students note that in VUZ (Institute of Higher Education) them it does not be necessary to be encountered with this phenomenon, although the specific complexities in the interrelations of students with the instructors of higher educational institutions, certainly, exist, they bear another nature. It is understandable that the majority of students, that break discipline, subsequently do not enter higher educational institutions. However, formation

system VUZ (Institute of Higher Education) must prepare not only the qualified professionals in the specialty, but also study by training personnel for the school, by educational process, which, in turn, will be reflected in the adequacy of the behavior of school teachers in any most complex situations.

With existence of high-quality educational system in VUZ (Institute of Higher Education), the graduates of these institutions will know how to competently build interrelations with the children they to this will be trained. Are frequent the cases, when teachers exceed the scope of ethical standards, this behavior is unworthy of their formation and status, which indicate omission in the system of the formation of VUZ (Institute of Higher Education). It is necessary to develop psychological trainings corresponding to the world standards, with the aid of which the instructors of psychology will train students for the skill correctly to be oriented in one or other situation or another of pedagogical interaction and to seize the habits of the establishment of contact with the audience.

General with the students, after learning their opinion relative to the solution of this problem, it appeared, that not only the unpreparedness of the graduates of VUZ (Institute of Higher Education) is the sole reason, which lies at the basis of conflicts. The opinion of the students, with whom, was conducted the interview following: the teachers of schools themselves, without desiring this, provoke conflicts and they are obvious. First, when teaching is conducted monotonically the perception of material passes not at the proper level, moreover both for the students of those not desiring to learn and for the children, by which the formation is not unimportant, this situation leads to the stress of all participants in the process of instruction. Are in the second place, frequent the cases of the incorrect selection of the educational program (especially this it concerns “moved” programs, which require of the children, independent of their abilities, from the first years of instruction to independently master objects), which leads to the incomprehension of object and the development of conflict situation.

The students, when they shared their impressions about the school instruction, they noted that by it were encountered the teachers, object of which by them did not please itself, they considered themselves incapable of its mastery, but teacher knew how to interest them, lessons were passed during one respiration, it implicated them into very process of instruction. Experience of pedagogical activity as the teachers of chemistry and biology in the school and the assistant of the department of psychology in VUZ (Institute of Higher Education) of gave me to conducting of mini- conferences with the interested students. Taking into account the opinions of students, after discussing with them what style of teaching by them it is most acceptable for the best perception of material, I made the following conclusion that it is necessary to erect lecture and practical training on the specific principles:

- to implicate them into the process of instruction, after creating the atmosphere of discussions, debates, disputes, to grant to them the right to voice its judgments (this must practice from the school bench);

- within the framework educational programs to attain from the students of the fulfillment of course and abstract works taking into account of their own world view and attitude, allowing the conclusions, which can and not coincide with the conventional opinion. This will allow them to work creatively, to feel itself by capable of the uncommon solutions, it will free from the fetters of standards.

- to organize the mini seminars, where on the agenda must stand some problematic question and propose to students to express itself, as they independently can solve it;

- contact with the students must not be accompanied by sympathies and antipathies, no one must feel itself by that pinched or express the superiority, which often the teachers provoke by their relation;

- to reveal the most gifted young people not in the closed regime, when it cannot be to very participants in the competitions estimated, as their work it appeared in the comparison with those, who occupied the first places, and the work of conquerors were evaluated on what criteria. In this connection the principle of the attraction of students themselves to estimation of works and resolution of a question was used by me, who was worthy to participate in the competitions. This in the open form was conducted all students participated in the nomination for election. By this the principle of bias was removed.

The basic purpose of our profession - to prepare the qualified personals, capable at the proper level of managing our profession, only in this case we can say that the quality of formation in our country reached world standards. It is necessary to erect the system of the psychological thinking of students to the skill to obtain knowledge, to master profession, and systematic recommendations and benefits must be developed for this, standards for evaluating the professional fitness of student are created.

Since the educational system must serve for the good both the society and state and user himself - student, who on the base of the knowledge of those obtained in VUZ (Institute of Higher Education), must obtain worthy working place and become professional, as to the instructor of VUZ I made the attempt to systematize the basic problems of our formation by the eyes of students, was for which developed the enumeration of questions.

To students it was proposed in the written form to reflect the complexities, which they experience with the instruction in VUZ (Institute of Higher Education) and as far as possible to transfer these difficulties:

It is revealed:

1. The continuance of adaptation;
2. Selection of profession;
3. Skill to obtain knowledge on the objects;
4. Conflicts with the teaching staff.

To write in the free form about the ways, which (in their opinion), will solve these problems:

It is revealed:

1. To change educational system in the school. To introduce into the educational process as required object psychology, moreover those regions of this object, which give the skill to learn and to accept objects integrally, but not interrupted knowledge, they help to correctly select profession;
2. Two last year of instruction the teaching in the school must be the same as the higher educational.

What teacher they would want to see:

It is revealed:

1. Actively participating in the creative and educational process of students;
2. Correctly evaluating knowledge and the ability of students, impartial;
3. Confident in itself, respecting itself and its time, that knows how to preserve discipline and adapting to any unforeseen situation;
4. Respecting student and seeing in him creative beginning, capable of participating in the scientific activity.

What method of instruction they consider acceptable and, in what form they see the ideal teaching:

It is revealed:

1. In the form discussions, the assignment of visual and video of material, participation of students in the process of instruction;
2. It is possible to consider as the ideal teaching, when the mutual understanding of student with the instructor appears and teacher is capable to establish contact with the audience.

Why they selected this VUZ (INSTITUTE OF HIGHER EDUCATION):

It is revealed:

1. In order to obtain diploma about higher education;
2. In order to be arranged in the appropriate specialty;
3. They entered only into this VUZ (Institute of Higher Education);

4. To obtain knowledge and to make a career in the specialty;

What they want to obtain from the instruction in VUZ (Institute of Higher Education):

It is revealed:

1. Knowledge and habits for the adoption to the high-paid job;

2. Diploma;

3. Place is working.

What qualities of teacher prevent you from mastering material:

It is revealed:

1. Partiality

2. Inability to teach material, instruction in the form of monologue;

3. Indifference to the creative abilities of students, the unwillingness to spend its personal time;

4. When the knowledge of teacher is the crenulations' material, also, with the answer by students by their words of the essence of a question, but not by precise phrases from the textbooks, instructor begins to evaluate knowledge as not corresponding to understanding object.

Which contributes give the correct understanding of the object:

It is revealed:

1. Accessibility and simplicity of material;

2. Discussions;

3. Visual material;

4. Invitation to the occupation of person, who reached heights in this region and the consideration of material with it;

5. Professionalism of teacher and his erudition.

The results, obtained from the students, testify that it is necessary to orient its pedagogical activity toward the correspondence to their wishes, since the estimation of our activity is placed on the basis what professionals we will prepare to society and to state.

For the familiarizing of students with the creation the following methods were used by me:

1. It was proposed in the abstract form, without resorting to to the study of what or sources, to express its ideas to the system of the teaching in VUZ (Institute of Higher Education);

2. The consideration was conducted according to the results of the executed works, who more completely and more precisely reflected the existing problems, and it let to students themselves participate in the selection of conqueror;

3. To the students, who most fully illuminated problem, it was proposed already to work with the literature of analogous nature and to conduct comparative characteristic, as one and the same problem they attempt to decide in the different sources;

4. The system of the encouragement, when with the successful work of student and satisfaction of all conditions the following privileges, were allowed to it was used:

A) was placed test or examination with automaton;

B) was allowed free visit on the object, when the student gave the sufficiency of time out of the occupations to the object and he reported by the executed work;

C) the possibility to obtain additional marks to the examination c) was allowed.

The results obtained during the work with the students testify that it is necessary to change much in the system of the teaching in VUZ (Institute of Higher Education), should be reexamined the traditional style of the instruction of students. Today we precisely force students to acquire the knowledge, which must prove useful to them in the profession. The training literature and the systematic recommendations, developed for VUZ (Institute of Higher Education), do not provide for independent thinking and familiarizing of students with the training process, they do not teach the skill to reflect its thoughts in the written form. The system of the abstracts, course, control, the examinations, independent, etc, implies the commonplace skill to work with the strange material. The carried out experiment revealed, that the majority of students cannot express their thoughts and ideas on the paper, by it simpler compose summary of the existing literature,

than by itself present their idea. Answers to the questions presented by me, in essence, appeared by brief test account; however, approach itself to its own comprehension of educational process was pleased with all without the exception. It was expressed, that this is the first experiment and thus far they were not ready to this work, but already change itself in the approach to the instruction generated interest and students actively began to participate in this experiment.

Negative was the fact that young people, which entered into VUZ, were not ready to express their thoughts in the written form, to make a report, to participate in the debates, to have their point of view and to defend it. These are serious gaps in the system of the school preparation, when is not conducted work on training of the formed personality, which knows how to think independently. Another fairly complicated problem illuminated by students, was (I cite students themselves) "the session, when it is necessary to in time return tests, debts and, certainly, examinations". I.e., if the visit of occupations in the school was standard, then in the institute, in spite of entire seriousness of instruction, the visit of occupations, this is the prerogative of students themselves, and they because of the essential difference of instruction in the school and the institute were not fitted out and the passages of occupations affect the quality of the obtained formation. It is known that the visit by the students of objects directly depends on that as far as by them interestingly at the lectures and in the occupations.

Students illuminated another circle of the problems of those connected with the object psychology, they practically into one voice assert that psychology interesting object, gives some ideas about the personality, the interrelations, but it does not help with the knowledge of other objects, is not created the integral picture of peace, it does not help with the personal orientation in the society, etc, but as all other objects is the supplier of the specific knowledge and not more. In connection with this I will express my opinion that this problem appears not from the non professionalism of the teachers of psychologists, but from the imperfection of training and systematic literature, which is developed for other purposes. It is today simply necessary to reorient purposes and tasks, which in VUZ (Institute of Higher Education) must solve psychology and prepare the training system, capable of solving the basic problems of qualitative formation.

Conclusion

In the carried out scientific research experiment is made the attempt to reorient the traditional approach of educational process (commonplace obtaining of knowledge) to the work with the students, which makes it possible to actively assign them on the independent thinking, to the development of mental abilities, to the skill to analyze, conclusions, to learn to present its thoughts in the written form (is without which impossible science), to master the procedures of the instruction of objects, to find approaches and to develop the system of teaching, which makes it possible to better master material and to make psychology the object, which plays the key role in the development of innovation educational system. Was despite the fact that revealed a sufficiently large quantity of gaps in the educational programs (both school and higher educational of instructions), revealed, that involvement of students in the educational and scientific research processes, gives the perceptible results, which are expressed in the increased interest of students to the object, the percentage of truancies is reduced, independent work is stimulated, the level of the obtained knowledge rises, since for the possibility of participation in the debates, the expression of its own point of view, in students appears the personal motivation to the intensified study of object and appears the real possibility to manifest its knowledge before each other. The approach to the students, which deprives the possibility to preconceived relate to the knowledge, the personal qualities of students was in this work proposed, since the solution about that, whose work was executed most qualitatively, was

received by collectively, students themselves, when they did not know, they discussed whose work. Conquerors in such competitions had extra incentive for further improvement, since they felt, that they were selected on the objective criteria. In the completion one ought to note that was in this work made the first step and was created reserve for further improvement of the educational system of practical and applied nature, which in the future must become innovation and competitive.

Materials of Conferences

BRAIN WORK CULTURE FORMATION IN JUNIOR SCHOOL CHILDREN WITHIN DEVELOPING EDUCATION SYSTEM

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The developing education system created by a large collective under the leadership of D.B. Elkonin, V.V. Davydov, V.V. Repkin and others differs from other conceptions of developing education with its direct orientation to the problem of psychic, intellectual and personal development.

Proceeding from the problem of providing development, mental development of children in the process of academic activity, first of all, resting upon the views of L.S. Vygotsky about the leading value of the digested knowledge content for the intellectual development, a conclusion cardinally differing from the training practice applied in primary school, was made. In elementary school already the academic activity content should be directed at the digestion of theoretical knowledge as the system of scientific concepts, the acquirement of which develops the foundations of theoretical thinking and consciousness in learners. In the situation, when the content of education is made up of empiric notions and knowledge, there are necessary processes of memory and thinking fully formed before schooling in a child for their digestion. That is why the acquirement of such knowledge doesn't result in mental energy and abilities growth. In contrast to this, to be digested theoretical notions require new forms of thinking. The a priori knowledge digestion-mindedness of the academic activity in the practice of developing education opens real ways for the development of thinking and personal cognitive interests associated with the last.

The brain work culture level of school children defines all the sides and results of education: the quality of knowledge and skills being formed; the cognitive activity and development of learners' thinking and creative power; the learning work productivity and the level of academic load depending on the last; the efficiency of using educational opportunities of the academic activity; the readiness of school leavers to life.

As the formation of knowledge, working-out of educational-cognitive devices represents a long-term process: at the first, reproductive, stage school children use an explained device in standard academic conditions under the guidance of the teacher, and at the final, productive, stage they operate it in nonstandard conditions independently and creatively, performing the procedure of its application automatically, in the contracted form, i.e. without dividing this procedure into composite elements.

The work of the teacher on the organization of mastering this or that academic work device within the system of developing education is formed of such elements as: the device mastering original level diagnostics; the teacher's explanation of importance and necessity of mastering the given device; the instruction about its content and methods of mastering it; the delivery of practical exercises (merged with usual exercises delivered to digest a school subject); the current monitoring of the educational-cognitive skill formation course; its application in various situations; the fixation of the formed skill to work out a habit in school children to apply it independently.

It should be noted that in solving an important problem – to teach school children to learn – a close cooperation between teachers and parents should be exercised. From time to time the teacher should explain the parents which help is required form them while their children prepare their homework; teach them how to run the corresponding work, constantly guide them and correct their actions if it is necessary. But to do it the teacher himself should be equipped with special psychological knowledge about academic activity, its structure, formation, failure after-effect; he should digest the knowledge and skills to form educational-cognitive abilities of learners, methods and devices of this formation.

Thus, the brain work culture represents a complex multilevel model, in the process of education of which a complex approach is needed, i.e. the educational impact should be focused on the personality formation in its entirety.

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WAYS AND MEANS OF THINKING DEVELOPMENT IN PRIMARY SCHOOL AGE

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The problem of learners' thinking development and perfection is one of the most important problems in psycho-pedagogical practice. It is fairly considered that the main way to solve it is the rational organization of the whole academic activity. A specially organized game training of thinking can be considered as a supplementary, auxiliary way.

The weight of evidence suggests that a general base for any sound mental activity behaviour is the presence of three universal components of thinking as a minimum:

1. A high level of elementary mental operations formation: analysis, synthesis, comparison, segregation of the essential and other operations appearing as most divided elements of thinking;

2. A high level of activity, thinking unreservedness and plurality, manifested in production of a great amount of various hypotheses;

3. A high level of thinking organized and purposeful nature, manifested in a clear orientation to segregation of the essential in phenomena and use of generalized analysis outlines.

The main task of primary school is to guarantee the personality development of a child at a higher level compared to the pre-school period.

A source of the sound development of a primary school child is two kinds of activity. First, any child develops according to the past experience digestion of the mankind due to the inclusion into its contemporary culture. At the heart of this process there is educational activities aimed at the digestion of the knowledge necessary for the life in the society. Second, any child in the process of development realizes its possibilities independently due to its creative activity. As distinct from academic one, creative activity is not aimed at the digestion of general knowledge. It evokes self-activity and self-actualization in the child, the embodiment of its own ideas aimed at the creation of the new.

Performing the specified kinds of activity, children solve many problems and do it for different purposes. So, in academic activity training problems are solved to master any skill or digest one or another rule. In creative activity intellectually demanding creative tasks are solved to develop children's abilities. That is why, if a general ability to learn is formed in the process of educational activity, then within the framework of creative activity a general ability to search and find new solutions, unusual ways to achieve the required effect, fresh approaches to the offered situation consideration. If we speak about the present state of modern primary school in our country, then the central place is still taken by academic activity. At the lessons of the two main classroom disciplines – language and mathematics – children almost always solve training routine tasks. Their purpose is to reduce gradually children' searching activity with every following task of one and the same type and finally make it disappear at all.

The state of modern primary school one cannot call a normal one. On the one hand, the existed dominant influence of the knowledge and skills digestion activity thwarts children's intellect progress and creative thinking, first of all. In connection with such a system of teaching children accustom to solve the problems having always ready-made solutions, a single one, as a rule. That is why children become embarrassed, when a task has no solutions or, vice versa, has a set of them. Besides, children get used to solve problems on the basis of the already learned rule, so, they are not able to act independently to find any other new method.

On the other hand, constant solving routine problems impoverishes the child's personality, its attitude to itself, in particular. Little by little, children start evaluating themselves, their possibilities only through the prism of a successive or non-successive settlement of routine problems, which depends on the corresponding rule or definite knowledge digestion. Often it results in the fact that a positive self-esteem of a child depends not on the display of its invention or quick understanding, but on the diligence and carefulness in mastering rules and knowledge. However, that is not to say that in modern primary school there are no problems of searching character at all. But, first, the settlement of such problems is far from being intelligible to all children, but the most quick-witted ones; and, second, to solve these problems is not obligatory.

Thus, intellectual upbringing, thinking development is an important side in the primary school child personality development, in its cognitive sphere, in particular. An active search for relations between different events is typical of human reasoning. It is the orientation to the reflection of directly non-observed relations, segregation of principal and unequal, essential and non-essential details distinguishes thinking as a cognitive process from perceptions and sensations. The study of thinking is referred to the number of the most difficult and poorly developed problems of psychology.

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ON RATIO OF SPORTS AND PHYSICAL CULTURE

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There are a lot of different points of view on ratio of sports and physical culture. Most of Russian scientists consider sports to be a part of physical culture together with physical education, physical reaction and rehabilitation. But there are other scientists who argue that physical culture and sports only partially coincide or do not coincide at all. The fact that there are different points of view proves the complexity of the issue. Looking into the problem makes us pay attention to such crucial issues of the sport theory as the position of sports in the cultural environment and its cultural potential; problems and tendencies of sports' development as well. Comprehension of the problem of the ratio of sports and physical culture needs to differentiate the notion of "physical culture" and "physical training". Thus, it is necessary have new views on physical culture in the terms of new historical environment should be based on researches on the cultural phenomenon. Taking into consideration the fact that there are a number of the definitions of culture the main objective of the given article is not to give an original definition; We support the definitions given by other scientists. In this case the culture is experiences of a community or a people, fixed in people's behavior, verbal and institutional forms. These experiences comprise the system of human's activities. According to which an individual develops social relations, changes his or her inner nature. But what is the specific feature of the physical culture? The definition of the culture should reflect the fact that the culture the integrated mechanism of the social reproduction, all parts of which interact with each other and are not autonomous. Any phenomena the individual comes across are parts of the culture – political, moral, physical, etc. Therefore theoretically the physical culture can be considered as a specific area of culture. However it is hardly possible to consider it to be a separate part of the culture. Yet at the level of sociophilosophic, cultural analysis the notion "physical culture" must reflect in the consciousness specific features of different processes for perfection of physical and spiritual conditions. In the course of these processes natural and natural-somatic characteristics of a human being gain personal characteristics. In the beginning of these processes an individual is just a living thing, biologial body then an individual turns into a subject of activity. Human somatic is a certain type of natural and social unity, possessing sensitive characteristics (due to socio-cultural transformations).It should be emphasized that "human somatic" is a category showing the changes in the human flesh in the course of social modifications; so this category should be considered together with another very important and complex category as "spirituality". These notions are interconnected. Somatic has elements of spirituality and somatic is a form of spiritual existence in the physical world. Thus, physical culture is a part of cultural phenomena connected with the development of human flesh into human somatic (having overbiological substratum) and the inclusion of the natural individual in the world of culture. The area of cultural phenomena goes together with somatic existing of human beings, their physical condition. So the latter should be treated as a specific cultural value, it is necessary to achieve its perfection and improvement. Physical culture is not a homogeneous phenomenon; on the contrary it is heterogeneous, has a complex structure and is continuously ganging. It comprises various activities related to forming, developing and perfecting of human somatic. They form areas of physical recreation, rehabilitation, education (the ways to control an individual's movements), and upbringing. Let's assume that sports possessing its own features in relation to each of these areas; but being homogeneous in relation to physical culture are a part of its components cannot be considered as a phenomenon outside of its areas. Physical culture in a whole and each of its areas comprises activities realizing social transformations of a human body, development of movements, physical perfection and development of personal qualities. It is sports that make an individual be aware of limits of physical development, of the perfection of an individual's ability to move, physical force, and endurance. Meanwhile this very area an individual manifests his or her natural abilities which are necessary to maximize spiritual forces. Thus, in the area of sports to some extend enables realization and manifestation of a human being's existence boarders. And this applicability (essence) realizes sports within the framework of physical culture, instead of outside of them. Physical culture is the area defined, on the one hand, by nature (this area an individual begins to master after the birth, being still a natural non-social object); on the other hand the essence of all its intentions is the perfection of human somatic. Although perfection is an endless process (both in onto- and philogenesis) at every given moment of the social time it is finished. It is defined by means of a sport achievement; record, by the fact of overcoming the rivals and oneself. Consequently sports are not just a part of physical culture; it is the most important instrument of its self-development. Thus, the place of sports in ontological environment of culture in general and physical is defined first of all its ability to single out the boards of overall realization of abilities possessed by human somatic. Culture transforms an individual's natural forces, transferring them into a different- social – dimension, giving them a different way of existence implementing human creation and ensure in such a way reproduction of all the society in general. Physical culture develops and preserves human somatic. Sports participate in all

these processes, manifesting the highest human's achievements in the development of his or her somatic, mental and personal qualities. Therefore it is impossible to imagine sports without achievements, without certain objective to strive to records and to victory. The ambition to achieve certain results acknowledged by the participants of the competitions and fixed by the referees is the essential part of the sports. The result crowns all sportsman's achievements, shows the boarder of his or her personal abilities; and in serious competitions the boarder the mankind achieves due to this athlete. Therefore sports are is a struggle with winds, seconds, rivals and first of all with him- or herself. And yet this part of physical culture is something more than just the area where people try to find out who is faster and stronger. An athlete is a person acting on the bounds of his or her physical and mental abilities and always expresses people's ambition to try their forces.One more aspect of manifestation of qualitative homogeneity of physical culture as integrity and sports as a part of this integrity should be taken into consideration. Sports help to make somatic and mental abilities possessed by an individual visible and obvious. However we should not forget that a human being is natural and at the same time social. In the cultural-historic process natural organs are getting stronger transferring to a different dimension outside of a human existence. A human being appeared due to fact that natural abilities gained new cultural meaning. But on the other hand the problem of preserving and developing of an individual as natural creature. The solution of this problem is probably becoming the most important task of the whole physical culture and sports in particular.The root of many problems is the complexity and duality of human's nature, i.e. his or her abilities have different dimensions, different forms of existence including forms of existence "outside" the human's world. And the most crucial problem is the danger for an individual to "lose" the identity of a natural creature. Naturally enough that educated people both in the West and in Russia are worried that the power of artificial nature is developing much faster than an individual's strength given by nature. An individual needs physical culture in general and sports in particular not only because he or she is a hart of the culture but also because – a part of the nature. The mankind needs to restore natural forces and possibilities. That is why people use and perfect all the possibilities that help to avoid the danger of "loosing" an individual's natural features. The specific feature of sports is to demonstrate what an individual's natural features (even being socially modified) can and must be. An individual involved in all other areas of physical culture (and culture in general) can rely on these data.

Finally, reckoning on ration of sports and physical culture, a conclusion should be made the solution of this problem must be based on ration of a part and whole. Let us assume that these phenomena (physical culture and sports) are of the same quality. Otherwise they can be противопоставлять, their meaning in public mentality will result in reduction, and consequently either one phenomenon (those areas of physical culture which do not relate to the area pf sports) or other (sports itself) will be periodically вытеснять cultural functioning. It will lead to the wrong understanding of the given phenomena, physical culture сведется to P.T. classes; sports will become a part of ideology and commerce. Thus, physical culture is a part of cultural phenomena connected with the development of human flesh into human somatic (having overbiological substratum) and the inclusion of the natural individual in the world of culture. The areas of cultural phenomena are closely connected with human somatic, with their physical state. So physical state should be treated as specific cultural value which needs to be improved and perfected.

Sports to some extend manifest the boarders of an individual's abilities. And this applicability (essence) realizes sports within the framework of physical culture, instead of outside of them.

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TECHNOLOGY OF MODELLING OF AN INDEPENDENT RESEARCH WORK OF A FUTURE TEACHER

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Professional teaching requirements are constantly changing and enlarging. A person, who is going to become a teacher, should be able to act in modern culture, should possess the skills in projecting and to be competent in judging school's prospective technologies and to have one's own pedagogical position.

We consider the project activity to be an integral part of the professional competence of a teacher. Professional competence of a future teacher we regard as an integrative quality of a specialist, including theoretical and prognostic ability to follow his own developing path in an educational area in accordance with the personal qualities on the basis of real knowledge.

Teacher's project culture is a part of his pedagogical culture, the sum of project ways of the innovative reorganization of the pedagogical realty on the basis of prediction, planning, designing and modelling of the educational phenomena, processes and systems. The level of research skills determines the level of professionalism of a modern teacher.

During the experiment we proposed and tested the model of organizing the process of an independent research work in projecting and realization of peda-

gogical technologies among future teachers. The model was based upon the following principles: topicality of pedagogical knowledge as a real personal knowledge; continuity in modelling of an independent research work and in individual and differential help; movement from the imitating creation to the creative imitation and to the creative activity which is not stimulated contextually.

Here is the model of organizing the educational process in the institute of higher education for future teachers.

The first year of education is to be called a motivational-reflexive stage. During this time students realize the aims and peculiarities of teaching. The inner structure of lectures and seminars, which are too important for students, reflects a complicated emotional and moral atmosphere of relations and communication. It depends on the actualization of studying motives (first of all, pedagogical stimuli like a vivid narration of a lecturer, one's own school experience, emphasizing the practical importance of the studying material); a combination of emotionally-sensual and analytical processes in dialogical experience of the first-year students; students' reflexive experience which they gain, for example, during creative collective credits or analyzing the results of self-concept tests.

The second year of education aims to prepare students theoretically to the further work in school. The students make their own choice through the long-distanced communication and activity under conditions of the educational module, which pedagogical area represents a system of interconnected person-approving and educational situations with a lecturer and a student as the subjects. The second year is the stage of theoretical knowledge as the basis of practical experience; it proposes a free choice among the situations of partnership and personal self-expression. Reflexive value inclinations are supposed to start developing into the holistic foundation of "I-conception" of a teacher. Modelling of an independent research work of students allows to make the system an "open" one, where the elements of possible spontaneity are replaced by unpremeditation, potential readiness to percept the knowledge as the basis of practical skills, including the skills in projecting of pedagogical and educational systems. Constituent parts of the modeling process on this stage are: learning the content of a teacher's methodological and project culture; understanding the content image of the topic and the main idea of the research; creative work in projecting of the technology of the method of education.

The third year of education implies the choice of one's own "method", the possibility to express oneself, i.e. the project of pedagogical technology is developing on this stage. Personal self-expression is considered by scientists to be an extraordinary social-psychological phenomenon. It is a complex and multidimensional process of personal disclosure, in which a person displays his inner world. The condition under which this disclosure takes place may be the choice of one's own "method", projecting of one's own pedagogical technology. The peculiarity of a research work is that students may choose their own term-period and pace of work. In other words, students choose their own path toward the goal [1]. One of the situations, proposed by students, was a brainstorming search and a brainstorming answer as a synthesis of knowledge in different spheres.

Everyone had his own technology, but the backbone core remained unchanged. The first dimension of the work was "projecting of projecting": 1) The issue of "reaching the idea" is examined at the higher level; the notions "concept", "system", "structure", "project", "to project", "model" etc. are learned; 2) the structure of the work is introduced: introduction, importance of the topic, subject of research, leading ideas; the system of principles, fundamental for every established technology, is grounded; the scholarly apparatus of the topic, scientific novelty and practical importance of the work, its structure and prospects for approbation are examined theoretically and worked out; 3) the issues of creating chapters, paragraphs, conclusion and bibliography are considered. The second dimension was - learning the diagnostical, informative and procedural components of the project.

The fourth year of study broadens an educational sphere of a future teacher considerably: a school and children as real objects, school teachers as colleagues, coarse mates as teachers etc. determine the higher position of a personal representation. The new aspiration appears - for preserving one's own "I-conception" from the one hand, and enriching one's positions, asserting oneself, self-expression from the other hand. Future teachers learn to examine themselves, to evaluate their own work. The topicality and possibilities of an introduced individual project are analyzed in the movement of modern psychological-pedagogical and methodical problems of educational practical work. An individual author's point of view and peculiarities are revealed. Every project should have its "proper subjectness", "its own world-view", "its style and author's image". The peculiarity of this stage - is an integration of lecturers' efforts.

Modelling of an independent research work of future teachers – is the component of their general professional qualification, which determines the level of students' readiness for work in school. Readiness may be defined in two aspects, meanings, as a state and as a personal quality [2]. The aim of the fifth year of education is to disclose and approve the multistructure of an author's position as a creative source in pedagogical activity of a future teacher. There is a synthesis of philosophical and specialized knowledge, pedagogical technologies, psychological and methodical bases. The general system of renovation and modernization of education implies the further constructive development of other innovative projects, which

should be started in the system of higher educational institutions.

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QUALITY SYSTEMS OF RUSSIAN EDUCATIONAL INSTITUTIONS

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From the moment of Russia's accession to the Bologna Convention I higher education the necessity of creation and perfection of educational institutions' quality systems, which is conditioned by a range of factors, is traced more and more clearly.

The factors affecting HEIs on the part of the European Community and the state in the name of the Ministry of Education and Science of the Russian Federation can be referred to external ones. In the time of active participation of Russia in the Bologna Process a new structure of the education quality management system was formed. One of the orientations of the Russian education modernization system at the present time is the All-Russia education quality appraisal system (REQAS) organization, which motives HEIs to the dynamic development of their quality systems and the quality self-esteem within HEIs as the ENQA Quality Assurance Standards requires.

The demographic situation is also referred to the number of other external factors moving the HEIs in the given direction. At the International Forum "Education Quality Assurance" (Moscow, 2007) some depressive figures were read out aloud: if to take the quantity of potential enrollees of 2007 in the RF for 100%, then by 2010 their quantity will make about 70% from 2007 and by 2020 this factor will make about 50%. Consequently, the struggle for the enrollee will take more and more rough forms.

There are internal factors moving the creation of HEI quality systems besides external ones. These internal factors have a market orientation, and namely the will to polish the image of the HEI, to perfect its management and, consequently, raise the competitiveness at the market of educational services its graduates at the labour market.

The last century experience testifies that the competitive success is guaranteed by an effective management system. For the first time the theories of scientific management of education appeared in the 20's in the USA. They generally rested upon the theory of classical management and that of human relations. In the 70's M. Johnson became the first to offer the model of system management of education, the foundation of which the principle of cooperation and interdependence of all the components of the educational organization is put in.

At the end of the last century a classical model of the HEI quality management system was applied in educational institutions of Russia. Since 2000 a change to a HEIs' activity integrated assessment combining the procedures of licensing, performance review and state accreditation (the RF Ministry of Education Order from 12.11.99 N864 "On higher education institution activity integrated assessment"), the basis of which was the sanctioned check-list of the HEIs' activity factors, has been carried out. One of these factors was the "In-HEI quality control system", which in 2005 was changed to the factor 1.2.3 - the "In-HEI education quality assurance system efficiency". It compelled HEIs to work on the creation of the in-HEI quality systems, using various models for this purpose.

For the period of 2006-2007 a typical model of the educational institution quality system was created in Russia. The ENQA "Standards and Guidelines for higher education quality assurance in European Region and requirements and recommendations of international standards of the ISO series 9000:2000 (GOST P ISO 9001-2001, GOST P ISO 9004-2001). In the standard GOST P ISO 9000-2001 eight root principles (Focus on the consumer, Leadership of the manager, Involvement of workers, Process approach, System approach to management, Continuous improvement, Decision making based on facts, Mutually beneficial relations with suppliers), which provide a basis for the quality management system formation and development.

Together with the above represented principles we formulated the fundamental positions based both on the analysis of literary information and our own research and practical experience.

Position 1. The quality management system of an organization (or in the context of the typical model – the educational institution quality system) should be considered as maximally approximated to the organization management system.

It is registered in GOST P ISO 900-2001 that "the quality management system is a part of the organization management system, which is aimed at the achievement of results in accordance with the purposes in the quality area to meet the requirements and satisfy wants and expectations of the concerned parties. The purposes in the quality area supplement other organization's purposes connected with the development, financing, efficiency, environment, work safety and security. Various parts of the organization's management system can be integrated together with the management system into a single management system using common elements. It can simplify planning, resourcing, secondary targets definition and total efficiency evaluation of the organization". It is impossible to create an isolated, strictly defined quality management system without its being connected with other

kinds of activity at an enterprise. So, the quality management system can be considered as an organization's management system based on the quality criteria.

Position 2. The quality system of an educational organization is a socioeconomic system, which gets formed, develops and goes through all development stages (growth phases of the organization itself).

There is a quality system in any HEI already due to its management system self-organization (synergetics) and, consequently, quality system; it occurring irrespective of whether the front office is aware of the management and management quality theories or not. However, this quality system can reach various maturity levels in the process of formation. I.e., when a HEI proceeds to the quality system development, it already has a certain system "as it is" and compares it to the requirements "as it must be" stated in the quality system typical model.

The traditional quality systems inclusive of measuring, monitoring, planning, analyzing results, correcting and caution actions, elements of internal audit, working with the supplers (schools, colleges) and consumers (enterprises, organizations, students, graduates) are retained at state Russian HEIs in spite of the stormy shifts of the 90's. The non-state HEIs successfully found a lodgement in the market of educational services and oriented to their quality perfection, sunken to the competitive environment and being paid a careful attention on the part of the state and society worship the first quality management principle – "Orientation to consumer" from the very beginning of their existence, for it is consumers who are the source of their existence.

If to stick to the classification of maturity processes of R. Gartner [1], the majority of state HEIs is at the second level "definiteness", which is characterized by the customer response system availability, i.e. the consumers, their requirements have been defined; the consumers' requirements have been transformed into the efficiency criteria; the methods of work have been standardized on the basis of general procedures; the results are managed of the basis of the after-process control. To switch to the following – third level the quality management system formalization including a documental support of the found approaches to various activities performance and analysis is necessary by all means. Special requirements to the documentation emerge in the case, if a HEI develops quality management systems in accordance with the ISO requirements of the series 9000. The documentary system availability is one of the main requirements of these standards.

Position 3. At the educational institution quality system development according to the typical model (as well as the quality management system on ISO 9001) is recommended to build the created quality system into the traditional control (management) system of the organization and also to use all the existing quality system achievements of the maturity level it self-organized to.

The system should be created for every concrete organization, so, it is necessary to know its peculiarities, destination, working conditions and other factors. The efforts to adopt somebody else's experience, to take a pattern of other organization's documents seem to be unpromising.

Position 4. The educational institution quality system formation in accordance with the typical model recommendations should run according to its perception by the human factor, the higher and medium member leaders, first of all. The HEI quality system "is grown" and should get through definite growth phases.

Lately there appears much publishing about a formal approach to the quality system creation. Nowadays the quality management systems on the basis of the 9000 series ISO standards of the overwhelming majority of Russian enterprises, unfortunately, do not give the outputs, which they are potentially able to. For many Russian organizations' leaders the main thing at the 9000 series ISO standards introduction is not effective functioning, development and perfection of quality management systems, but their certification.

In the speech of V.I. Makolov (the Mordovian State University named after N.P. Ogarev) at the Vocational Education Quality Management Coordination Council in June, 2008, the main causes of low efficiency of the quality management systems created in HEIs are marked out: the quality management system "detachment" from the system of HEI management as a whole. The quality management system exists as though "in and of itself"; the formal introduction of the quality management system for the purpose of getting a conformity certificate only; the refusal of deep management transformations; the estrangement of top management from the quality management system; the orientation to substitute the quality management system by an aggregate of its documents; the formal introduction of the process approach and standardization of the practice; low volume of investments in the personnel development; the shortage of leaders; the non-involvement and low motivation of the personnel; the shortage of quality management system experts and low competence of the personnel in the area of modern methods and instruments of quality management; the priority of commercial interest in consulting firms' activities and not the formation of effective quality management systems.

It is impossible to pass the maturity stage "definiteness" without enlightenment and quality management training, planning of processes and quality system documentation. And this very stage makes the activity of a HEI "clear", sets everything in order, and allows noticing drawbacks and areas to improve. Then one can move to the following maturity level: to introduce cardinal changes in the organizational structure; make deep transformations in the activities; put

the process approach into action actively and thoroughly.

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REFLEXIVE APPROACH – SYSTEM MAKING FACTOR OF PROFESSIONAL COMPETENCE FORMATION

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Nowadays the competence-building approach has become one of the leading directions of education modernization. It is connected with the fact that a modern society needs a specialist possessing activity potential.

In this way, the professional development of the future pedagogue is closely interrelated to the development of a professional competence in him in the course of studying in a HEI, as under the present-day conditions the knowledge formation is not the main target of education (knowledge for the sake of knowledge). For a student, the future teacher, it is overwhelmingly important to acquire the ability to apply general knowledge and skills to settle concrete situations and problems arising from the reality.

Besides, the professional competence based on the fundamental-scientific education, emotionally valuable attitude to the pedagogical activity, educational work technology possession is a precondition for the formation of the future teacher's readiness for creative evolution of his personality.

In terms of the analysis of professional training efficiency criteria suggested by S.Ya. Batyshev [1, pp. 146-147] the following components of professional competence of the modern teacher have been marked out:

- independence in professional activity, which supposes an optimal choice of technologies and methods in educational work;
- the ability to diagnose pedagogical situations, make wise decisions; the ability to perform regular self-control;
- ability to adapt the training material and easily present it to students;
- ability to organize academic activity rationally, inducing students to master the subject actively;
- constant striving for self-education, searching for new forms and methods of the academic activity organization;
- knowledge of research work methodology, research skills possession and ability to organize research activity among students;
- constant reflection of one's activity, ability to critical self-analysis and self-control;
- creative attitude to work – ability to master innovative technologies and implement them in academic activity;
- liability for professional tasks' fulfillment.

It is worthy of note that nowadays the problem of the teacher's professional competence definition is the subject of psychologists', pedagogues' and experts' investigation. However, there is no common approach to the definition of this notion, competence classification in literature. A.A. Derkach defines professional competence as an ability of a human to solve a certain scope of professional problems [2].

But, unfortunately, in the given definition there is no attention paid to the problem of understanding of one's professional activity objectives by the human himself, to personal professional-pedagogical qualities' updating, i.e. the role of reflection in the professional competence structure and development is not mentioned. And this is one of the most important components of the future specialist's (and the teacher's in particular) professional competence.

An external reason for the inclusion of reflection in the process of professional competence formation consists in the fact that competence is acquired by the student himself in the course of academic activity, which is organized as a thinking-activity or sensationally-outlived process of realization of their activity by students.

In connection with this the training of a competent specialist educationally is a reflexive process providing creation of conditions for self-education and development of professionally meaningful personal qualities. In the consequence of which, basing on the given problem and resting upon the idea of a reflexive approach to the process of education, we suggest the following definition of "professional competence".

Professional competence is readiness and ability of a person to understand its professional activity objectives, to update its professional-pedagogical qualities creating conditions for the perfection of self-actualization, self-reflection, self-development, self-esteem, self-concept as leading mechanisms of self-fulfillment.

The definition must follow that the formation of professional competence is only possible upon the condition of purposeful formation of pedagogical reflection in the teacher's consciousness. In this connection we consider the process of the future pedagogue's professional competence formation in the context of students' professional-pedagogical training.

The process of formation of professional competence represents a complex system including three main components: informative, procedural and personal ones, where the reflexive approach performs the

role of a system-forming factor and universal mechanism of the process of this formation.

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EXPERIENCE OF PARTICIPATION IN 7th GLOBAL CONFERENCE ON HUMAN DEVELOPMENT

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From November, 17 till November, 21st, 2008 in Japan there has taken place 7 Global Conference on Human Development on which have been presented not only themes for discussion, but also new approaches of training of youth revealed. The international institute of cultural affairs has proclaimed the following **approach:** Social change doesn't take place in a vacuum. The context of all change that impacts people is the set of cultural dynamics that determine how the collective defines itself, makes decisions, and acts out those decisions – as well as how individuals relate to others and to the whole, and the image those individuals hold of themselves and of the group. In order to achieve lasting, just outcomes, these cultural affairs must be centrally integrated into the development process. The basic approach through which we incorporate cultural affairs in human development consists of the following elements: **Participation.** In order for people to support and solidify change over time, they must be part of the change process from the beginning. And not just on the sidelines or as observers. Participation only produces results when the people who will be affected by change are engaged in defining the very substance of the matter, and then in shaping and implementing the change process itself. We enable this level of participation through unique, customizable, tried, and tested methods of participatory group dialogue, planning, decision-making, and implementation. **Comprehensiveness.** Every group of people is comprised of segments and divisions – from political parties to income levels to genders. Any change process that does not include the participation of all segments won't be implemented and sustained over time by everyone, thereby setting the process up for failure from the start. The simple process of inclusion itself is often a dramatic first step in the development process, bringing into dialogue for the first time marginalized and mainstream voices of a group on equal footing. The next step is to ensure sustained engagement of all parties over time. **Interconnectivity.** No problem is created or solved in isolation. The needs and challenges that produce the demand for change in the first place are inherently related to one another. Just as every person is defined in part by their social context, every social challenge is resolvable only within the context of other issues. When problems are analyzed from the perspective of their interconnectedness, a realistic path toward change becomes possible. Solutions that address multiple issues emerge, addressing underlying rather than surface problems, and expanding the number of people with a direct interest in a particular solution. The more people are invested, and the deeper the solution runs, the greater the probability that change will endure. **Duration.** Integrated human development can be a slow process, with fits and starts, spanning lifetimes and generations. Social structures and processes for managing change over time must be integrated into the cultural fabric, and must endure beyond the momentum of a particular issue or moment. This requires specialized, ongoing training for leadership from all segments and sectors. Social networks themselves must also be deepened, by building trust, improved communications, participatory leadership and governance structures, and healthy interdependency. **Neutrality.** The Institute of Cultural Affairs play a variety of roles, including facilitator, trainer, advisor, organizer, and mentor. In all of these roles, we operate as neutral outsiders, grounded in our core values but not in a particular outcome.

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EDUCATION MANAGEMENT TODAY

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Any frame of reference of a HEI (retraining center) can be represented in the form of an aggregate of processes. For every process the parameters of resources' quality, input/output data (results) are identified, the "input and output suppliers and consumers" are defined. The main processes (the value increase chain) – are the educational service life cycle ones, which create knowledge, abilities and skills directly and increase the value of the service. These processes are aimed at the users' and consumers' satisfaction. The supporting processes and procedures (monitoring) provide the value creation possibility and also functioning the processes and activities within the quality management system. Thereat, the sequence of these

processes, their efficiency criteria and methods should be defined; the availability of resources and information to support, monitor, measure and analyse the processes should be guaranteed and a system of measures necessary to achieve the planned results at the implementation of the processes and their constant improvement should be created. For all the elements of this typical circuit the quality measurers are established, the input data, processes, resources and data out quality specifications are recorded. The input data are the evaluations of knowledge of earlier studied disciplines' units most important to teach (some basic training is necessary), the input data suppliers are the teachers of the previous academics (from now on by academics we shall mean the experience of practical work with software and facilities together with the discipline as it is). The data out are the evaluations of results, the data out consumers are the teachers of the following academics. The resources are the personnel, programs, hardware components, methods, teaching materials and information. The quality is defined by the consumer's satisfaction level, training outcome, regularity of detection and elimination of training defects and other parameters. This is the quality management approach based on the cooperation of suppliers, executors and consumers, when each of them performs both the role of a "supplier" and "consumer" at the same time.

The education management requires a special scientific grounding of its participants. It is not carried out today for the lack of the developments necessary for this. That is why the education management participants follow their only personal experience and the declared pedagogical recommendations in their work. The abovementioned gives the ground to formulate the native education management main problem of our time: "How to provide the citizens of the country with good education in modern cultural-historical conditions at the resources being at the disposal of the native educational system?" Its settlement together with many other things requires the development of the conception and organizational and managerial logical-mathematical decisions optimization apparatus of academic activity by means of the calculated forecasting of their academic and economic efficiency, which would allow implementing the specialist training quality increase strategy at the limited resources and higher school motivations.

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THE HUMANISTIC ASPECT IN CHILDREN'S UPBRINGING IN RUSSIA

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There is one thing which units all of the humanistic thinkers all the time – the value attitude towards the child and his or her nature. Taking into account the many sided of the human nature all of them gave their preference to its different aspects: activity, sociality, cultural basis and ability to be changed in time. The European humanistic pedagogy tried to find instrumentals, which could help the child to become a member of society (a citizen) preserving his or her individuality.

The positive experience of European humanistic pedagogy was grasped, interpreted and enriched be Russian thinkers due to Russian culture and history. During the Middle Ages the pedagogy was interpreted into the human being vital practice and didn't possess the independence. Its type was determined by tendency of society development. Historian-cultured constants (statehood – orthodoxy) have advanced the educational practice of three types: family and domestic education, literary education and sacral education. Personality growth took place in the framework of high range values: Fatherland, faith, love, charity – in the way of obedience to secular and religious authority. Thus the tenor of man's life and habits, leading to God, emotional perfection and moral purity has been produced. The direct influence on the pupil was the mechanism of the upbringing, and the teaching, the word , the address to the heart, personal example, the engendering influence of Tutor's personality were the instrument of it.

The pedagogical contents of social conception of XVIII century, men's' mentality culture of that period of time have been enriched by teachings of I.Betskoy, E.Dashkova, N.Novikov, A.Radishchev, G.Teplov and others. Working out the pedagogical opinions of their own the Enlightenment epoch thinkers "pushed off " from the ideas about the person in his or her ontological and social essence and changed their mind about the ways of personality growth. The acknowledgement of the virtues to be a person's criterion has become a starting point for clarifying his or her social and civil essence. To the XVIII-th century philosophers opinion the human being can get his or her own way in the people society only, what is defined with his or her human nature: he or she being born helpless is not able to survive without guardianship and " to get profits" till others teach him or her. Brightly expressed anthropocentrism is also typical for abovementioned period of time: conviction that a human being with his or her requirements, interest and purposes is that what determines the development both of human society and to a considerable extent of

nature. The human being theme sounds more and stronger in works of I.Betskoy, N.Novikov, and A.Radishchev. Each of them interprets the sense and the purpose of human existence, the instruments for person upbringing of their own. N.Novikov the author of the term "pedagogue", who has written the pedagogical treatise "about child's upbringing and admonishment", in his reflections about upbringing formulates the fundamental purpose of upbringing like this: "The primary subject of upbringing is to educate children making tem happy and useful citizens". A person had to be well developed, intelligent and moral to become happy. Moreover N.Novikov binds man's morality and his or her intellectuality with the heart upbringing and mind education.

One of the peculiarities of Russian Enlightenment of the latest part of XVIII – early part of XIX century is the idea that the man is the reasonable being, the feeling being whose purpose of living is to achieve his or her fortune and to do good to the society.

The middle of XX century is the period of democratic ideal penetration into the native pedagogical thought. Thus, the main thesis W.Belinskiy put forward was: the upbringing is the condition of perfection achieved by man. Good upbringing can help the person to have perfection attained. It is determined by fatherland culture and by "private" conditions of the society. Love has to be an instrument and an intermediary of upbringing and "the humaneness" has to be a purpose. Some publicists (W.Belinskiy, A. Gertsen, N. Dobroliubov, and N. Tchernyshevskiy) attempted to try on social and personal meaningful purposes, considered the necessity of child's inborn forces development, what would be a foundation and condition of his or her socialization. Properly pedagogical part of upbringing was considered in that the adult has to help the child to form his or her "ego" (N.Pirogov, N.Dobroliubov). K. Ushinskiy possessing great pedagogical experience and vast knowledge in the sphere of contemporary philosophy, psychology and physiology came to the idea of necessity to join the comprehensive scientific knowledge about the child. This idea was realized successfully in the work "The man as subject of upbringing. The experience of pedagogical anthropology." unprecedented by volume and depth. The title of the work itself undicates the influence of Pirogov's ideas, who has directly named the man the subject and purpose of upbringing.

At the beginning of XX-th century the pedagogical values of humanistic tradition have gained the democratic phonation. The dominant replacement took place in ethic-pedagogical values: the unity "man and his/her life" was forced out by diad "man-society". The human being of the century boundary grasped himself both as the end and as the beginning: as the unity of physical reality, of spiritual experience and of intuitive faith. The best representatives of Russian culture of abovementioned period paid their attention to child's upbringing. Thus L.Tolstoy for example has wrote about what is really needed the child's upbringing. First and foremost this is the change of adults' way of living, whose actions, attitudes towards other people and convictions influence the child's behaviour right or wrong. The child assimilates instinctively and most hard the way of living of his or her parents, their attitude towards other people and life. Sermons and reprimands are not valid in upbringing in case their contents dissent from tutors actions. "In case you understand that there is only possible to bring up others through oneself, you do away with the question how you have to live. This idea of L.Tolstoy didn't lose its practical meaning till now. The modern psychology and pedagogy acknowledge that the child is more influenced by his or her family way of living and tutor's behaviour than by verbal instructions and orders: adult's action does bring up and not his or her word, though the last acts too. In this connection you have to remember: upbringing others you bring up yourself.

In the second part of XIX – early part of XX century the peculiar "pedagogical boom" had arisen in Russia: the society has realized the social meaningfulness of pedagogical activity, political transformations, acceleration of social and economic development have led to some reforms in the theory and in the practice of child's upbringing and education. The idea of necessity of comprehensive studying of the child and of his or her vital functions, of the researching of his or her physical, mental and moral development as of the base of pedagogical activity becomes dominant. W.Vahterev- the teacher – has affirmed that tutors are capable to build their activity only leaning against the knowledge of child's development regularity, forming by the number of natural sciences and scholarships. "The teacher's aim will be not to transform the child into the adult according to beforehand given norms, but to teach the child, to define his or her development tendency direction, to recognize his or her hereditary and acquired qualities and strengths, to help to develop them and to create favourable atmosphere for his or her hearty tendencies to become developed".

Russian pre-school pedagogy like to all social conception has constantly been socially oriented. The idea of social activity, of rendering service to progressive ideals of social development is present in labours of all Russian teachers of XIX-XX centuries one way or another. V.Zenkovskiy dedicated his first pedagogical work "Social upbringing, its tasks and ways "(1918) to the problems of social upbringing. Taking into account the axiom that the child's personality is able to be normally developed only in social conditions, he determines that "the problem of social upbringing consists in social activity development, in development of "the taste" to social activity, in education of solidarity spirit, of talent to get above one's personal egoistic intentions". The social upbringing in the above sense naturally has to be national, that is has to lean against national traditions, to accustom the

man to the historical work of his native land, to develop love to one's native land, feeling of duty. The common task of social upbringing as of child's activity development requires use of different instrumentals to be fulfilled. One of the instrumentals is the deliverance and the development of child's emotional life, resisting to common inertness, indifferentism. The social habits of hostels and contacts are outer discipline. The family, pre-school organization, school and at last out-of-school work with children – are of some more meaning for social upbringing. Each of them in its own way socializes child's life, educates his or her activity, independence, the feeling of collaboration and solidarity. The growth of spiritual wealth of child's personality is also essential for his or her social development. It is conditioned by that "the man is never given, is never completed, he or her is always "set", there is always endless perspective of spiritual development in the face of him or her. The child… lives with that what arises from the bottom of his heart, the process of personality rationalization, of conscious work on him-or-herself begins much later, and it changes the man a lot, at any rate it creates a deep turning point in the man's soul. The philosopher teacher affirmed with all his activity that in the early part of XX century the Russian pedagogy was in need of new approach to the children upbringing when common to all mankind values will be applicable in making choice of pedagogical technologies what we'll be able to observe in the work of child's pre-school institutions in subsequent years.

It is to report that in the soviet period of time (the early part of XX century – the eighties of XX century) the development of pre-school education was characterized as the State –Party system and the main task of government was to unite the kindergarten , the family and the atmosphere in solution of social and pedagogical problems.

The variations of pre-school education can be considered as the peculiarity of its third period (since the eighties of the XX-th century till nowadays). The self-determination of pre-school educational institution, well-grounded choice of educational programs and the forming of institution mission became the priority in management. During that time the teachers' activity in searching for new aims, contents, instrumentals and methods of work, organization forms of child's living in kindergarten have raised. Since nineties an active experimental work take place in great deal of kindergarten, rapprochement of science with practice is observed, and moreover practice often outstrips the scientific workings out.

We can observe that in the latest part of XX century the country's vital tenor has changed considerably. The national education has been reformed. The common idea in the development tendencies of all system of national education and pre-school branch is expressed particularly in passage to person competent education. To detach is the document which has determined the quality directions of modern pre-school education – "The conception of pre-school upbringing" (V.Davydov, V.Petrovskiy). According to it there are four main principles, which are fundamental for the expert evaluation of modern pre-school education in Russia: ***humanisation*** – the upbringing of humanistic direction of the child under pre-school age personality, of citizenship principles, of diligence, of respect to man's laws and liberties, of love to his or her family, native land and nature; ***the developmental type of education*** - orientation to child's personality, preservation and strengthening of his or her health, directions of taking possessions of thinking and activity ways, speech development; ***differentiation and individualization of upbringing and instruction*** – child's development in accordance with his or her dispositions, interest, talent and possibilities; ***deideologisation of pre-school education*** – priority of common to all mankind values, receding the ideological direction of kindergartens' educational programme contents. Those principles laid down the educational legislative acts and consequently the normative – instructive and program-methodic documents.

Thus, the key positions of modern pre-school education are:

1.The protection of metal and physical health of children under school age, the creation of at most comfort conditions of children sojourn at pre-school institutions and the maintenance of emotional well-being.

2. The humanization of ideas and principles of educational activity with children, expressed in principally new approach to organization of educational activity in kindergarten, based on leading activity of children under school age. The emancipation of child's life circumstances and activity and of tutors' work, the deideologisation of work's content with children.

3. The alteration of pre-school institutions' functioning and financing conditions. The inculcation of innovative technologies of children' teaching and upbringing, the creation of psychological services in the system of public pre-school education, the extension of variety and the improvement of the quality of given educational services.

4. The alteration of teaching staff training type for work at different pre-school institutions. The alterations, which take place at the pre-school educational institutions nowadays are due to their variations in a broad sense, trend to satisfaction of different educational requirements of various strata of society, state, to the survival at the competition conditions.

It is to state, that the pre-school education in Russia experiences the intensive reforming and development. At the modern stage of pre-school educational system development the main task of pre-school institutions work is to improve the quality of the educational services and to create the most optimum conditions for each child to be developed, for his or her

potential resources to be disclosed, for valuable person basis to be laid down.

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LIFE SELF-FULFILLMENT OF THE HUMAN: HISTORICAL-PSYCHOLOGICAL ANALYSIS

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The research results of development of ideas about life self-fulfillment in the process of movement of the psychological science from the classical ideal of rationality to the non-classical and post-non-classical ones are represented in the article. It was demonstrated that a system sophistication of the psychological science leads to the sophistication of the existing notions, the logic of "development" of which reflects the science developmental trends dominating in various historical periods.
Key words: life self-fulfillment, rationality ideals, classical type of rationality, non-classical type of rationality, post-non-classical type of rationality, science systemic levels, science developmental trend.

The psychological science objective developmental trends' analysis allows finding out that the problem of human nature, which is developed in the processes of creative transformation of the reality and demands constant arrangement and rearrangement of the life world and its fundamentals, is becoming the center of scientific interests of various scientific schools' and directions' representatives. The coming out of the science to the "New Frontiers" of rationality bears a relationship both to the integration of categories and principles (that is an evident feature of the science becoming more involved) and concretization of the notions "metaphorically framed up" at the previous level of rationality. The idea of "life self-fulfillment of the human" can also be referred to the number of such notions.

The logic of historical-psychological investigation allows correlating the case studies of psychological phenomena to the historical movement of the science oriented to more and more integral and multidimensional psychological reality study, behind which the movement to a whole person as the subject of psychological cognition "is revealed". In accordance with this the science itself is understood as an open self-organizing system, the development of which grows more and more sophisticated and it is provided by its development intrinsic logic leading the science to new problems, and the human community development, the result of which appears the deeper understanding of the proper (human) nature.

The historical-psychological analysis offers a clear view of the science movement trend in terms of various ideas' becoming so that "among all the possible development options only one will be accomplished – the poly-possibility of the movement will turn into a concrete way, the poly-variability of the future will turn into a concrete variation, which will be the content of the becoming history" [7; 36]. These very historical changes happening to the system the scientists "calculate" or predict the trends on. The rationality ideals – classical, non-classical and post-non-classical ones [8] – appeared to be such "points" in the course of the historical-psychological analysis of the life self-fulfillment ideas. These rationality types, "frozen moments of the system's self-development never-ceasing process", provide a means for the "revelation of becoming tendencies as potencies formed in movement and gaining strength to be implemented therein as well" [7; 42]. At every systemic level corresponding to the rationality ideals – classical rationality type, non-classical rationality type, post-non-classical rationality type – the "life self-fulfillment" phenomenon has different informative filling.

In the course of the classical rationality type analysis, where simple systems act as objects, it is found out that the given type is oriented to the opposition of Spirit and Matter, "internal" and "external", subject and object, and cognition consists in using such research method, which will provide the knowledge objectivity owing to obtaining the same result at any time and in any place for

any person. V.S. Stepin (2000) features the classical type of scientific rationality: the researcher's attention is focused on the object, which strives to eliminate everything referred to the subject, means and operations of activity at theoretical explanation and description; the purpose of the researchers is to get objective knowledge of the world; the ambitions and values of the science, which define the research strategies and methods of the world fragmentation, are determined as ideological mindsets and axiological orientations being dominant in the culture. All this provides a "unilinear causality and dismemberment of the research subject into elementary components" [3; 21]. In the view of the above said one can conclude that in the classical psychology the problem of human self-fulfillment was not specified: the psyche was understood in its adaptive function and the super-adaptive behavior phenomena were considered as nearly pathology [2].

In the non-classical type of rationality the subject for study is complex self-adaptive systems, where tough dichotonomy of the subject and object abates. V.Ye. Klochko (2007) marks the dialecticity of "non-classical mentality" overcome the statics of "what-has-become", escaped from the jaws of the past and come out to the primary dynamics, "catching" the development of "here-and-now", and grasping "what-is-becoming". The non-classical science merit is in the fact that it uses the ideation of a particular system level, discovering such phenomena as self-fulfillment, self-determination, self-actualization, etc. the science centering on the problem of human selfhood allows detecting the proper (human) nature manifestation through the environment transformation. So, in the works of C. Buhler the self-fulfillment appears an integral part of the human life journey. The life journey, as C. Buhler sees it, appears as a specific form of human life, the basic trends of which are want satisfaction, adaptive self-limitation, creative expansion and inner harmony establishment. Each of them can dominate in different periods of life of a personality, the self-fulfillment of which is possible within any of the trends: as well-doing (under one and a half years old), childhood end outliving (12-18 years old), self-actualization (the age of maturity), fullness (at the old age). C. Buhler noted that the completeness of self-fulfillment depends on the ability of a personality to make such aims, which are the most adequate to its inner nature. Being maximally close to the present, "what-has-become" is detected from this position; so, the given position can be referred to the non-classical ideal of rationality. That is why in the context of non-classical ideas there appears a possibility to define the problem of self-fulfillment and the term of "self-fulfillment" acquires the informative filling.

About a progressive sophistication of the scientific knowledge the ideas of self-fulfillment, which can become a reality in the presence of striving and desire of the human to become what he can become, so the emphasis is put on the taking place "here and now", on the present. It is the non-classics already, it is an evident movement, but it is not the integrity of times yet, not the unity of the human with the world – it is "caught" by the post-non-classics. Such forms of passage from the non-classics to post-non-classics "penetrate" practically all the works of Russian psychologists, who actualized the problematics of the role of the psychical in self-adjustment of the human (O. Konopkin, V. Mirosanova and others), the problematics of self-determination (D.A. Leontyev); and it promoted the self-fulfillment problem definition in the form of self-actualization and self-realization of the personality (A. Maslou, L.A. Korostylyova and others).

In the post-non-classical psychology the problem of life self-fulfillment is given a full twist. The post-non-classics' anthropocentrism, its axiological load, coming out to understanding the role of the psychic in human self-organization as an open system, the acknowledgement of the super-adaptive, transcendental, above-norm, above-situational in the human as his essential characteristics – all this allows opening a new as-

pect angle necessary for an adequate definition and solving the problem of revelation of the role and place of the psychic in the processes of vital self-fulfillment. In the conceptual apparatus of the psychology, which gave the post-non-classicism a variety of categories (self-development, self-actualization, self-determination, self-identification, self-becoming), the idea of "life self-fulfillment" is an extremely general category being developed through a collection of all the given notions and bearing a poly-disciplinary character. This affords ground for the investigators to detect those notion characteristics, which could not be opened, understood or felt from the positions of the previous ideas, but also to "place on record" the given notion sophistication in the science, using ontological foundations of the self-organization theory, behind which a consistent sophistication of the system organization "is revealed".

The conceptualization of the "self-fulfillment" idea not as the result of the life journey, not as the process actualizing this journey, but as a constant movement to sophistication, "opening new dimensions" [7; 138] allowing detecting in the world new opportunities, which, in accordance with the laws of "interrelationship" and "interaction restriction" [6], depend on the degree of conformity of the human to these opportunities (they will not be opened to some, some won't detect them and some, having found them out, will ignore them for a score of reasons, etc.), can serve as the starting point in their understanding. Acting in the context of various circumstances (internal and external, natural and cultural), the human realizes the ability to change himself and the world in accordance with his own movement logic, which expresses evolutionary-historical developmental trends of the society.

In the post-non-classical type of rationality the human life itself is considered as an every minute (every single moment) self-fulfillment withholding the life transspective. A "transspect", according to B.Ye. Klochko, - is an analogue of the idea of "becoming", but the analogue, which takes into account the direction for the development of an open self-organizing (self-developing) system as a regularly sophisticated spatial-temporal organization. A transspective is the post-non-classical science feature allowing detecting the possible directions of the human movement in the space of opportunities. The tendencies possess the virtue to be actualized, but only because objective laws of self-organizing systems' becoming are behind them [7; 95].

It should be noted that every new type of scientific rationality is described by a special, peculiar to it, science foundations; however, the new rationality type nascence doesn't result in the total disappearance of the ideas and methodological sets of the antecedent: "The non-classical science has not abolished the classical rationality at all, but only restricted the sphere of its action… the post-non-classical science becoming doesn't lead to the elimination of all the ideas and cognitive attitudes of the non-classical and classical investigation" [8;635]. In other words, different methods of thinking not only coexist, but react upon each other, conduct a constant dialogue and change in the process of this dialogue; that is why rationality supposes a dialogue of various cultural traditions, and the "internal unity of all the three rationality types found out in the dynamic chaos proves the becoming possibility in the generalized rationality modern culture" [1;241], in the context of which we manage to come out to the potential, which "is hidden" behind the achievements and possibilities of the psychological science. It is the tendencies that point out the most probable developmental directions in the space of the opportunities provided by the system and referred to the possibilities of the environment. What is meant here are the developmental trends of the psychological science moving to sophistication and leading the investigators to anthropologization as the science guiding developmental trend revealing the system-anthropological dependence of the human life self-fulfillment due to the natural integration of originally isolated scientific schools,

directions, psychological cognition principles (development, historism, consistency, conditionalism) existing separately, rationality ideals being a “private manifestation of the general developmental trend of psychology” [4; 226]. At the heart of adoption of the new perspective being reveled in the process of the psychological cognition development the anthropological choice, which can be put into effect only after coming out into the zone of proximate development of psychology – the “after-post-non-classical science” [5], lies.

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THE INFLUENCE OF COMPUTER GAMES ON THE COGNITIVE ABILITIES

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The purpose in front of researchers: to learn the psychological and psychophysiological consequences of the long-term unproductive activity forms in a cyberspace, the example of which is playing activity.
The research results of efficiency of mnemonic abilities have revealed significant distinctions between the experimental and the control groups on efficiency of all memory levels: mechanical, I.e. memorizing with support on functional mechanisms; to memory with appearance of semantic treatment, I.e. memorizing due to functional and operating mechanisms; to logical memory, I.e. with prevailing of regulative mechanisms (memorizing due to the functional system of mnemonic capabilities).
Key words: cyberplayers, cognitive abilities, cognitive ability, sensomotor parameters, functional systems realizing cognitive abilities.

The development of informational society, being based on creation and wideuse of information-communicational technologies in all spheres of social life, became the subject of the broadening circle of researches. Computerization, is not only the stage of scientific and technical progress, but it is also a new, higher level of civilization on the whole, which brings the substantial changes both in human activity and in his personal characteristics.

One of the discuss problems of cooperation between man and computer is a problem of psychical changes in the conditions of global informatization of the society. The development of information technologies goes very fast, concerning all spheres of human life, so that a new cultural and historical environment arises, the main criterion of which is computerization of human vital functions and transformation of computer in the forming element of culture. Computer activity, as a new type of the indirect activity, reconstructs its subject's consciousness, subject of cognition and subject of intercourse. Consequently, human perception and awareness of the world, processes of memory, thoughts, imaginations which are armed and simultaneously limited by the concrete-historical system of values, inherent to the certain social community, one or another culture (to the culture of computerization), changes.

Availability of computer technologies and usage expansion of it's possibilities both in professional and in a leisure sphere put a purpose in front of researchers: to learn the psychological and psychophysiological consequences of the long-term unproductive activity forms in a cyberspace, the example of which is playing activity.

According to the purpose, hypothesis and research tasks such psychological and psychophysiological methods were used in this work as:

1) Method of memory studying, by V.D.Shadrikov and L.V.Cheremoshkina, directed on definition of efficiency, a level of development and a qualitative originality of natural caused and lifetimely formed mechanisms of mnemical abilities (functional, operational and regulating) [16]. As a stimulant material were three figures of different degree the complexities consisting of direct crossed lines.

2) Method of time measuring the reactions of left- and right-parencephalons on visual, skin and auditory stimulants [8, 9]. On the indexes of time of motive reaction the functional state (level of cerebral structures activity) of sensory areas of right and left parencephalons, participation of the regulative and activating systems, was estimated in the process of intellection.

During the research two groups of examinee were selected.

An experimental group (cybergamers) consisted of college students, playing computer games during the last 6 years on the average for 6–7 hours a day. The number of examinees in the experimental group was 33 men (16 girls and 17 boys). A control group was made up by students with low cybergaming activity. The examinees's age was 16-19 years.

The results of questionnaire allow to say that the group of cybergamers differed from the control group by the expressed changes of the state of health. For the absolute majority of students protractedly and systematic playing the computer games rapid fatigueability, crabbiness, high degree of attention instability and considerable difficulties in their own conduct management, is marked.

The research results of efficiency of mnemonic abilities have revealed significant distinctions between the experimental and the control groups on efficiency of all memory levels (tab. 1):

• mechanical, I.e. memorizing with support on functional mechanisms (FM);

•to memory with appearance of semantic treatment, I.e. memorizing due to functional and operating mechanisms (FM and OM);

•to logical memory, I.e. with prevailing of regulative mechanisms (memorizing due to the functional system of mnemonic capabilities (FSMC)). The analysis of the results showed that the productivity of natural memory (functional mechanisms) and memory, provided by semantic treatment at an examinee, systematic playing computer games, is below as compared to the control group ($r<0,05$).

Especially it should be noted that distinctions between experimental and control groups were increased as far as complication of the material produced for memorizing. The efficiency of logical memory of active cyberplayers is meaningfully below, than for the representatives of the control group. These results allow to consider cyberplaying activity as a factor, affecting on efficiency of display of not operating, but regulative mechanisms of memory.

These results of lower efficiency of examinee's memorizing, systematic playing computer games, compel to study the features of functioning of their cerebral structures in the process of cognitive activity.

By the most adverse sign from the point of effective realization of cyberplayer's cognitive capabilities it is possible to consider lower functional state of all sensory areas of left- and right-parencephalons, which is registered on the decline of the sensomotor reacting speed on all produced signals. It enables to suppose that examinees, protractedly and systematic playing computer games, the time of information processing is meaningfully increased already on the stage of its perception.

The next important neuropsychological indicator of cognitive activity was a change of motive reaction time (increase - reduction) after the cognitive loading compared to quiet state. This index was used as an degree indicator of cerebral structures activating while memorizing the figures of different complication and served as convincing evidence of physiological cost of the expended efforts (table. 2).

So, for example, while memorizing figure 2 (the most simple material for memorizing) cyberplayers had a higher degree of cerebral centers activating. However, this group did not succeed to attain the level of cerebral structures activity, registered in the control group which had considerable superiority in the functional state of cerebral educations already in relative rest state.

While memorizing figure 3 (material of middle complication) strengthening of sensory areas activity of left- and right-parencephalons was fixed in both groups of examinees. Thus their right parencephalons activating was identical. However, the cyberplayers' left parencephalon was activated considerably weaker as compared to a control group in this situation . This fact rotined considerably less functional possibilities of examinee's left-parencephalons, protractedly

and systematic playing computer games, at complication of the memorized material.

Yet more expressed distinctions of functional possibilities of cerebral structures in the compared groups of examinees emerged on the stage of memorizing of the most difficult material (figure 9), requiring active involvement of regulative memory mechanisms. The produced loading of control the group examinees was accompanied not only with high-rate of the registered reactions but also with considerable increase of activity degree of sensory educations in the process of memorizing. While working with such a difficult material cyberplayers were caused the sharply expressed decline of the functional state left- and right-parencephalons. Otherwise, this cyberplayers' mental loading resulted not as activating, but as braking of cerebral structures.

The got results allow to do the following conclusions:

1. Examinees, playing the computer for 6-7 hours a day, characterized by a lower efficiency of memory and have a greater amount of complaints about their mental condition, showing up in restlessness, crabbiness, weakness of volitional processes and difficulties of conduct control as compared to the coevals.

2. Cyberplayers show the weakness of activating cognitive processes, that causes inability to maintain the protracted mental loading.

3. The conducted research let's to suppose that an excessive infatuation for computer games deforms cognitive capabilities and results in the decline of physiological possibilities of brain.

Table 1. The middle indexes of mnemonic capabilities efficiency (in sec)

Group of examinees	Time of the produced figures memorizing (in sec)		
	figure №2	figure №3	figure №9
Experimental (cyberplayers)	3,3±0,15	13,8±0,69	116± 5,8
Control	1,5±0,075	4,6±0,23	38±1,9

Table 2. Indexes of degree accelerations of sensomotor reactions, reflecting the value of left- and right-parencephalons activating on each of the experimental stages (in %)

Stages of experiment	diagnostics FM (figure №2)		diagnostics OM (figure №3)		diagnostics FSMC (figure №9)	
	right parence-phalon	left parence-phalon	right parence-phalon	left parence-phalon	right parence-phalon	left parence-phalon
Experimental (cyberplayers)	11,8	13,4	5,6	3,9	–2,2	–3,2
Control group	7,3	6,49	5,04	9,5	4,4	–3,1

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PRINCIPAL COMPONENTS OF BRAIN WORK CULTURE

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The brain work culture – is the synthesis of personal qualities, which together characterize a personal attitude to academic activity, the level of the personality's intellectual, organizational and technical, hygienic parts giving an opportunity to a pupil to perform any brain work qualitatively, efficiently and with the least possible troubles. Thus, the idea of "brain work culture" compiles four components: personal, intellectual, organizational and technical, hygienic.

The brain work culture represents a peculiar alloy of intellectual, organizational and technical, hygienic cultures of a personality, they being mediated by a personal attitude of the person to a given activity.

The brain work culture education represents a complex multilevel model including academic-organizational, academic-informative and academic-communicative skills.

The brain work culture of school children supposes upbringing of every learner individually. A personal attitude (the pupil's attitude to learning; orientation; interests; world view; inner life of the personality) appears the principal component affecting all the rest components compiling the brain work culture. When educating the brain work culture, a special place is given to the formation of a positive attitude of the pupil to learning. For the purpose of the formation of positive motivations to the process of education the formation of the following four interrelated impetuses begins from the 1st grade:

a) understanding of learning as the public and personal;

b) persuasion in the possibility and necessity of one's mental abilities development;

c) striving to simplify the academic labour and make it more productive;

d) displaying interest to the procedural side of learning-cognitive activity.

The learners' motivation reaches its highest level only when there appears a stable and efficient need for self-education, perfection of their intellectual abilities.

To develop motivations a special group of methods is used: an outward motion of positive attitude to learning; the disclosure of originality and topicality of the studied material; the organization of informative discussions; the habituation of pupils to implement corresponding requirements; the creation of success situation and the encouragement of pupils.

The central place in the idea of "brain work culture" is taken by the intellectual component. Intellectual skills while working with a book serve the operative side of the cognitive process providing qualitative acquirement of the informative side of the studied material.

The intellectual component is a decisive one at the work of a pupil with other sources of the educative information: spoken word, watching, cognitive problems, in the process of doing homework. The elements of personal and intellectual components appear as a peculiar "foundation", on the basis of which the whole process of education is build up. The organizational and technical and hygienic components promote the most economic and intensive digest of the learning material. A correct organization of the academic work includes a range of interdependent moments concerning external and internal conditions of activities. The following moments are referred to the external conditions:

- regular mode of working;
- workplace setup;
- definition of optimal order of preparation for every day.

Serious advances in the academic activity cannot be achieved without observing these conditions. Besides, the ability to get involved in work quickly, to work keeping mind from straggling and at a good bat, to settle down to homework in spite of the wish to walk or play, etc., can be referred to the internal conditions.

The education of a habit to systematic work begins from establishing a hard mode of working, without which serious advances in learning cannot be achieved. That is why to settle down to homework is necessary at one and the same time. One of important rules of preparation consists in beginning work immediately, as the longer a person delays the commencement of work, the greater effort will be needed to make him proceed to it, the longer the period of "getting involved" will be.

According to psychologists N.A. Menchinsky, D.N. Bogoyavlensky, Ye.N. Kabanova-Meller, when a person performs the work, which isn't of interest for him, two stages gradually change each other in his internal state. First, the person works hard, unwillingly, forcing himself. Everything is built on his conscious conation. The person works insufficiently effectively, though he spends much force on it. But, while he settles down to the task, the process of its implementation starts demanding less self-restraint, less conation. Often there appears an interest to the work being performed, or to its result, the work is exercised quicker and more efficiently. As psychologists say, the stage of arbitrariness is changed by the stage of post- arbitrariness.

Thus, a person delaying the work start lengthens considerably its first hard stage built on self-restraint. The longer this stage is, the more unpleasant the memories about the work are and the stronger the

temptation to delay the work beginning for the next time will be. That is why, teaching children how to learn, one mustn't disregard the working-out of a habit to hit the ground running.

Moreover, a school child must have a constant working place, a separate desk and a bookshelf would be best of all. Besides, nobody should disturb him at this time. Just as a habit to definite working time is developed in a person, so appears it to a working place, as well; that inclines the person to work, reduces the period of settling down to it.

Thus, the organizational and technical and hygienic aspects are important components of the brain work culture together with personal and intellectual ones. A specific content of the components' interaction structure is defined by the purposes and objectives of some or other academic work.

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PERSONALITY FORMATION PROBLEM IN TERMS OF METHODOLOGICAL POSITIONS OF AXIOLOGICAL APPROACH

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The carried out analysis of psychologists', sociologists' and philosophers' papers testified that the ideas of "personality development", "personality formation", "socialization" and also "individualization" often proved to be put into one and the same synonymic row. However, they are not interchangeable.

The idea of "personality formation" is used in two senses in native science. First, the formation of personality is considered as the development of the last, the process and result of the first. In this sense the idea of "personality formation" is the subject of a psychological study, the aim of which is to find out what is available (is revealed experimentally, becomes apparent) and what can be available in the developing personality in conditions of a purposeful educational impact. The second sense – is the formation of personality as its purposeful education. A.S. Makarenko called this process "personality engineering". This is a proper pedagogical treatment of the personality formation methods and aims division. The given approach supposes a necessity to find out what and how should be formed in the personality, so that it could meet socially conditioned demands, which the society places on it.

Thus, the idea of "personality formation" is wider in its content, and the idea of "personality development" is its component.

An axiological approach based on the acknowledgement of the personality development priority within one humanistic system of values, when their cultural and ethnic differences retain, traditions and creativity are equal, the necessity of the past and present schools study and use are acknowledged, appears as the initial methodological position.

The idea of "socialization" is used to specify the human and the society interaction. This idea has an interdisciplinary status and is widely used in psychology.

I.S. Kon determines socialization as "social experience digestion, in the course of which a concrete personality is created". A close to this one determination of socialization is given by B.L. Parygin, who thinks that the process of socialization represents entering a social setting, adaptation to it, certain roles and functions mastering, which, after their predecessors, is repeated by every separate individual for the whole history of his formation and development.

The personality social type-design practice tendencies (the digestion of social stereotypes and standards, role behavior models by an individual) allow considering socialization as the process of adaptation and integration of the human socially by means of the digestion of social experience, norms, orientations peculiar both for the society as a whole and separate groups.

By virtue of its natural activity a personality retains the tendency for autonomy, independence, freedom, the formation of its own position, inimitable individuality. The given tendency characterizes socialization as the process of personality self-development and self- actualization, in the course of which not only realization of the adopted system of social experience and relations, but also creation of new ones including personal, individual experience, occurs.

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Materials of Conferences

TUVA MOUNTAIN FORESTS' FIRE HAZARD

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Fires are becoming the primary factor of mountain boreal forest areas reduction of the Tuva Republic. The forests of the Region, meeting the bioclimatic zones: arid (Central Asian internal-drainage basins) and Western and Eastern Siberia boreal forest ones and the forest, perform an especially important climate regulating function in Central Asia. The subboreal forests, which grow within definite limits, determine a high sensitivity to excessive natural and anthropogenic impacts.

For the last three decades the anthropogenic origin fires dominate over wildfires. One of the first reasons for the forest fires to grow in number is connected with the introduction of "agricultural clean burns" in the 80-s. The prairies subjected to spring fires differ from clean burns by the minimal amount of precipitations (300-500 mm). In spring a sharp rise of the atmospheric temperature and little relative humidity result in the intensive snow cover vapor. The winds typical of this season lead to drying up the soil and vegetation. Quickly dried burning conductors of steppe and grove belts are very sensitive to fires. The wind direction and intensity define the fire situation and promote the steppe fire spread into the forest steppe. In dry weather days with strong winds the spring fires inflict a serious damage on the forest ecosystem of the Region.

The forest fires were mainly of natural character and were caused by dry thunderstorms in the Region before the 80-s. It was found out that for the period from 1996 to 2006 20% of the forest fires were caused by dry thunderstorms; in 2007 only 100 from 318 fires were caused by thunderstorms. A more global factor – the total warming – has probably an effect on the sharp increase of wildfires in number. The fire data testify that the fire number dynamics is clearly correlated with the amount of precipitations. During the driest years the number of fires reached 353 (1980), 380 (1989), and during the wettest year there were only 43 fires registered (1985). Besides, the fire data analysis of the Forest Management Agency of the Tuva Republic and Krasnoyarsk Base of Forest Air Conservancy testified that summer wilderness fires are localized along geological cracks. It requires an in-depth study of geologic-geophysical and geomorphological factors influencing the thunderous fire hazard formation in the mountain forests of the Region.

The anthropogenic origin forest fire increase is associated with the increase in demand for wild-growing edible plants of the taiga. During their harvest time neither traditional folk customs of solicitous attitude to plant resources nor fire caution measures are observed. The unique subboreal forests of the Region are greatly subjected to fires during berrying and nutting seasons because of badly put out bonfires, etc. For the period of 1996-2006 during the taiga berries (bilberry and blueberry) and cedar nuts gathering since July to the end of October there happened 298 fires and 94986,7 ha of the forest destroyed.

As a result, 33594,8 ha of forest area were destroyed with fires for 20 years (1959–1994). Then the fire taken forest area increased tragically: 546088,6 ha were destroyed with fires in 1995–2005, 60652,6 ha – in 2007. The total fire taken area made 60652,6 ha in 2007, the forest area of them making 43256,2 ha. An excessive increment of anthropogenic origin fires can result in negative changes in not only vulnerable forests of the Region, but also Southern Siberia mountain forests; and that can break the Siberian boreal forests' equilibrium having developed for a great while.

Since this year there are intensive local land methods in operation assisted by observation stations to detect forest fire foci less than 1 ha, and there works a satellite monitoring at the regional level. Such forest fire control method cannot inflict any appreciable damage at the timely detection of the fire focus. Such complex information got allows analyzing the current situation with forest fires, forecasting the fire hazard situation and carrying out the development analysis in the following and making the damaged forest areas inventory. Information technologies appear as an instrument of analysis, evaluation and monitoring of boreal forests of the Region, they being aimed at the optimal utilization of the last according to the sustained development concept.

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Materials of Conferences

EXPERIMENTAL RESULTS OF ELECTRIC ACTIVITY OF «ELECTRONIC - IONIC CONDUCTION» JUNCTION

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The "electronic-ionic conduction" junction is formed in chloride-silver electrodes, which have got application in various instrument making areas: medical – to take off human superficial biopotentials; geophysical – to measure constant electric fields of the earth; analytical tool engineering – as comparison electrodes. The main variables of the electrodes are as follows: electrolytic potential drifting on DC current; natural noise of the electrodes in various frequency diapasons; electrode impedance; polarization voltage. The electrical parameters of the junction depend on the technology of its production, and also the quality of the materials used.

With the measuring device resolution enhancement the threshold value declines and the minimal measured quantity decreases. Therefore, severe demands on the electrical parameters of electronic components, integrated circuits are placed and new technologies of their production are created or the current ones are perfected.

The transducers should also be perfected, as their noises are summarized additively together with measuring facilities' natural noise and lower the thresholds of measuring devices. Measuring of noise electric activity of the "electronic-ionic conduction" junction is a topical problem, as the existing devices can only measure the summarized junction noises and measuring facilities' ones, which exceed the junction noises significantly.

We have developed a plant to check up the chloride-silver electrodes – a computer-equipped PCE-2, wherein the junction natural noises can be estimated with the average nanovolt order value with the accuracy of not less than ±10% with the help of specially developed informational-measuring technology, the plant having passed the tests successfully in the RF Committee for Standardization, Metrology and Certification.

It allows comparing the junctions made with the help of various technologies for the purpose of their quality evaluation.

As a comparison there were made three electrode cells representing the system "electrode-electrolyte-electrode": "EC_1" – a pair of single-service chloride-silver electrodes of Italian production made according to the traditional technology of plating a sensing layer of Ag-AgCl on the basecoat; "EC_2" – a pair of chloride-silver electrodes made on the basis of porous ceramics of Tomsk Polytechnic University production, Russia; "EC_3" – a pair of nanoelectrodes made using modern nanotechnologies; Tomsk Polytechnic University production, Russia.

From the carried out experimental studies the following has been obtained:

- The minimal drifting on the DC current, which made 0,001 mcV/sec and is an order less than the EC_1 and EC_2 drifting, the EC_3 nanoelectrodes have, the electrodes of Italian production having the maximal drifting.
- The amplitude excursion of electrode cells' natural noises in various frequency diapasons is equal to:

- (0,01-1)Hz – EC_1- ±50nV; EC_2- ±6nV; EC_3 - ±5nV;
- (0,05-75)Hz – EC_1- ±300nV; EC_2- ±60nV; EC_3 - ±35nV;
- (1-500)Hz – EC_1- ±420nV; EC_2- ±120nV; EC_3- ±80nV;

- The electrode impedance average value at different currents and frequencies - I=0,1 mcA; 1 mcA; 10mcA; frequencies – 0,01 Hz; 0,05Hz; 0,15Hz; 1Hz; 2Hz; 75Hz; 10000 Hz – is equal to – the EC_1 resistance makes 1500 O; the EC_2 resistance makes 800 O; the EC_3 resistance makes 300 O.
- The polarization voltage depending on the flowing DC current value - 0,1mcA; 0,5 mcA; 1 mcA; 2 mcA; 3 mcA; 5 mcA; 10 mcA is equal to – the EC_1 polarization voltage changes from (– 1,5 mV) to (-31,18 mV); the EC_2 one - from (-2,5mV) to (-12,88 mV); the EC_3 polarization voltage changes from (-0,24 mV) to (-8mV). At the current change up to 0,5 mcA the electrode cell EC_3 made on the basis of nanotechnologies is not polarized.

As it is seen from the above material, the junction created on the basis of nanotechnologies has the highest characteristics from the obtained results. Nanoelectrodes have the least electrode potential drifting, natural noise level, impedance and practically are not polarized under the DC current influence.

Therefore, nanoelectrodes are the most promising for wide application in various instrument making areas: medical, geophysical and analytical.

The present work was carried out within the framework of the project РФФИ № 08-08-99069 "Development of scientific foundations of low-noise high-resistant nonpolarizable "electronic-ionic-conduction" junction formation on the basis of porous ceramics".

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Short Reports

INFORMATION OBJECTS AND INFORMATION UNITS

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Information object - generalized concept, which includes the structured information models and not structured descriptions. Information object (IOb)- descriptive set or information set, reflecting object of a reality and having an attribute of completeness of the description of this object or group of objects. It can include set of attributes, meanings and criteria.

As information unit (*IU*) in a broad sense name a certain subset of information set (*IS*), divided on criteria of completeness of the description (integrity) or qualitative attributes (*Qa*).

As information unit in narrow sense name information model having property of indivisibility by any criterion.

Thus, the information object and information unit is occupied by extreme positions. Information object - complete set, and information unit - minimal component of set. Allowable is the case, when set and is information unit.

As the information object has set of attributes, meanings(importance) and criteria of divisibility, the wide choice of various information units is possible, components and determining the given object.

The division into units is possible in width to formal attributes. In this case information units supplement each other for completeness of the description. Such division we shall name formal. The example can be served by(with) record in the table or in a database.

he division is possible in depth to semantic attributes. In this case units of the bottom level are enclosed in units of the top level. They can supplement semantic meaning of units of the top level, can be independent. Such division we shall name semantic. Besides the combinations of both approaches are possible. Thus, depending on a choice of a method of splitting and at set of criteria of splitting the different constructions of information units are possible. It as a whole creates ambiguity of application of the information approach.

The sets of connected information units (information models) can form various systems. Most known and frequently used are the systems of classifications

The choice for construction of information units of procedures of stratification and property of transitivity results in hierarchical system

The choice for construction of units of the descriptions of problem environment (events, phenomena, condition), results in concepts frame and slot.

If for construction of units to choose the generalized системно-structural descriptions, we come to concepts of system, subsystem and elements of system.

The choice for construction of units of communication aspect results in following information units: the message, phrase the offer, word a symbol [1].

The choice for construction of units of communication aspect results in following information units: the message, phrase the offer, word and symbol. The message is information unit of the top level, others are included into its structure.

It is possible and further to continue a similar line of constructions of information units. Thus application of information units enables to build the different descriptions, model and system and enables to connect these concepts at the analysis.

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LOGIC UNITS OF INFORMATION SYSTEMS

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Basic for information systems (IS) the processing not the information, and organized information or information models is. In IS are stored and processed the information models.

The information model has structure and parts.. It can be organized logically and is realized physically. The logic defines the theoretical description. Physical organization - realization on the computer or carriers as machine words or blocks. The logic description gives the basis to allocate logic units.

Logic unit IS - information object, which has property of indivisibility in aspect of structure and property synergetical in aspect of set of its parts. As against it information unit is connected to indivisibility of the description or different degree of completeness of the description [1].

In IS the basic procedures are: processing, storage, representation, transfer of the information. It determines appropriate logic units for such processes and systems.

For example, logic unit of a storage in relational Database is the record, and logic unit of processing - transaction. Logic unit of processing in IS is the information model, constructed under the decision of a concrete task

Logic units of representation in the computer diagram are the graphic elements. In GIS [2] logic units of representation are dot, linear and areal of

model. In systems of processing of the images logic units of processing are vectoral and rasterfl of model. In systems of transfer of the information logic units of transfer are: a symbol, word, offer, phras [3].

Use of logic units enables to carry out comparison and analysis between different areas of researches. They allow to create interfaces for information interchange between information systems and technologies.

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Materials of Conferences

WORK ACTIVITIES' MATHEMATICAL SIMULATION HEURISTIC ASPECTS BASED ON CONSTRUCTIVE GEOMETRY AS AUTHOR'S SPECIAL COURSE FOUNDATION

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In recent years the mathematical modeling on the basis of constructive descriptive geometry was aimed at work activities, the factors, parameters and components of which can be represented in the form of many-dimensional manifolds [1, 2, 3]. Such problems arising in practice in the processes of chemical changes, physical phenomena, socioeconomic events, etc., are impossible to be solved by classic methods of mathematical simulation, as the number of variables reflecting the corresponding multidimensional functional relationships exceeds the dimensionality of the real spatial area, wherein these processes take course. Together with that, the descriptive geometry is able to consider the many-dimensional manifolds as function spaces of many variables; that allows it to present such processes visually in the form of surface equations and their geometrical models, from which it is possible to forecast quickly optimum performances and parameters of the studied processes with the help of computer equipment.

The work activities, in terms of constructive geometry, are subdivided into the processes with the chemical substances non-reacting (first method) and reacting with each other (second method). Two methods of obtaining their models in the form of equations and graphic presentation have been developed for their simulation.

Mathematical modeling on the basis of constructive geometry is heuristic, as it is based on the ability to find out functional relationships by many-dimensional test values.

The laboratory research allowing obtaining multidimensional arrays of points by experimental methods and simulating real electrochemical and bioparametrical processes on their basis are included into the special course.

The special course includes:

1. Brief mathematical introduction.
2. Introductory mathematical practical course.
3. Introductory laboratory course.
4. Laboratory research.
5. Research assignments on process optimization.

Brief mathematical introduction.

The values, which are the factors, parameters and components, can appear as variables at the mathematical modeling.

In the chemical systems, wherein the substances do not react with each other, the number of components is equal to the number of constituents (first method). In the chemical systems, wherein the substances undergo reactions, the number of components changes in the process of reaction.

To apply the first modeling method the theorem is proved:

The sum of equations of right sections of a connective gives an equation of the surface bearing these sections [4].

The second method allows modeling the processes of the substances reacting with each other described by the carcasses of the surface spanned by a sheaf of imaginary axis sections bearing one-dimensional generators, parameter bearers of 2 – surfaces, 3 – surfaces, etc.

The purpose of the introductory mathematical practical course is to study theoretical foundations of obtaining work activities' mathematical models and overlearning surface equations and their geometrical models derivation according to tabulated values of real experimental measurement parameters of multifactorial and multiparameter processes in multicomponent systems.

The core attention in the process of mastering the brief mathematical introduction should be paid to the features of obtaining models incident with sections:

1) 9 experimental points are enough for a sheaf of planes, when to construct the whole studied surface with the required accuracy it is necessary to carry out experimental study in the total space and to obtain its model [5].

2) A sheaf of planes with an imaginary axis needs to have not less than 27 experimental points available to obtain the model and arrange its equation.

In accordance with the curriculum the special course contains as few practical hours based on the results of real research as possible.

To illustrate the abovementioned let us analyse one of the numerous samples of out research. The HAR IHPP-12 sewage waters were treated with induction current. Together with that we defined optical density by the agency of a PEC, hydrogen ions' pressure (pH) by means of an ion meter in the treated water and the HAR control sewage water in fixed time periods (Table 1).

As many parameters, factors and components changed in our research, our equations are sections of a certain multidimensional hypersurface, as a matter of fact.

Table 1. HAR waters' induction current treatment results, I = 1; 1,5; 2,5 A

N	T	PH	$\bar{p}H$	D_{start}	D_{end}	h	PH	$\bar{p}H$	D_{start}	$D_{end.}$	h	pH	$\bar{p}H$	D_{start}	D_{end}	H
I= 1 A							I=1,5 A					I=2,5 A				
1	0	8,6	8,6	0,085	0,085	1,5	8,6	8,6	0,085	0,085	1,5	8,6	8,6	0,085	0,085	1,5
2	3	8,6	8,2	0,085	0,068	2,5	8,6	8,2	0,085	0,065	2,5	8,6	8,0	0,085	0,056	2,5
3	6	8,2	7,9	0,068	0,049	2,5	8,2	7,8	0,065	0,036	3,0	8,0	7,7	0,056	0,035	3,5
4	9	7,9	7,7	0,049	0,039	3,0	7,8	7,6	0,036	0,032	3,5	7,7	7,5	0,035	0,032	4,0
5	12	7,7	7,5	0,039	0,036	3,5	7,6	7,5	0,032	0,032	3,5	7,5	7,3	0,032	0,028	4,0
6	15	7,5	7,2	0,036	0,035	3,5	7,5	7,1	0,032	0,032	3,5	7,3	7,1	0,028	0,024	4,0
7	18	7,2	7,1	0,035	0,035	3,5	7,1	7,0	0,032	0,032	3,5	7,1	7,0	0,024	0,024	4,0
8	21	7,1	7,0	0,035	0,035	3,5	7,0	7,0	0,032	0,032	4,0	7,0	7,0	0,024	0,024	4,0
9	24	7,0	7,0	0,035	0,035	3,5	7,0	7,0	0,032	0,032	4,0	7,0	7,0	0,024	0,024	4,0

According to the tabled values we obtain the studied process model

$$\Phi(D_{s.}, D_{e.}, pH_{s.}, pH', I, t, h) = 0$$

For a graphical presentation we cut it with two planes into 2 surfaces

$$D_{s.} = F(I,t) = 8{,}65\ 10^{-2} + (-4{,}43\ 10^{-3} I - 1{,}29\ 10^{-3} I^2) + (1{,}06\ 10^{-4} + 1{,}08\ 10^{-4} I - 6{,}17\ 10^{-3} I^2)t^2; \quad (1)$$

$$D_{e.} = \Delta(t,I) = (4{,}97 10^{-2} + 5{,}33 10^{-2} I - 2{,}22 10^{-2} I^2) + (1{,}99 10^{-3} - 1 10^{-2} I + 3{,}43 10^{-3} I^2) + 5{,}64 10^{-4} + 3{,}81 10^{-4} I - 1{,}24 10^{-4} I^2)t^2; \quad (2)$$

$$pH_h = \Sigma(t,I) = (8{,}52 + 5{,}49\ 10^{-1} I - 2{,}71\ 10^{-2} I^2) + (-2{,}38\ 10^{-2} - 1{,}29\ 10^{-1} I + 4{,}52\ 10^{-2} I^2)t + (-1{,}65\ 10^{-3} + 4{,}45\ 10^{-3} I^2)t^2; \quad (3)$$

$$pH' = \Psi(t,I) = (8{,}12\ 10^{-2} + 5{,}91\ 10^{-1} i - 2{,}13\ 10^{-1} I^2) + (-3{,}88\ 10^{-2} - 9{,}62\ 10^{-2} I + 2{,}96\ 10^{-3} I^2)t + (-4{,}62\ 10^{3} + 3{,}24\ 10^{-2} I - 9{,}11\ 10^{-3} I^2)t^2; \quad (4)$$

$$h = \Omega(t,I) = 1{,}51 + (-8{,}09\ 10^{-2} + 3{,}49\ 10^{-1} I - 8{,}88\ 10^{-2} I^2)t + (4{,}76\ 10^{-3} - 1{,}21\ 10^{-2} I + 3{,}17\ 10^{-1} I^2)t^2. \quad (5)$$

A combined graphical presentation of the equations (1)-(5) in the form of an extended multilevel Radishchev drawing allows depicting a hydraulic ash removal sewage treatment semi-parameter technological process under the action of induction currents in three-dimensional spatial area graphically and calculating optimal values of the parameters:

$$t_{opt}=20\text{min}, I_{opt.}>2{,}5\text{Amper}, h_{opt.}=4{,}0\ \text{mm}$$

and formulating a conclusion about the total absence of suspended matters in the waters treated with induced currents and the pH value of 7,0; that testifies to approaching to normal properties of the treated waters and the possibility of their being reused for the ash-slag pulp transportation. On the research base an application for an invention ("Hydraulic ash removal water purification device") was filed and a patent (№ 2199491) was obtained.

The purpose of the second laboratory course is to study the operating rules and mechanism of standard industrial gauges, which allow performing effective measurements of most important physical and chemical parameters of solutions and acquiring operating skills. In accordance with the curriculum the special course contains as few laboratory hours necessary to acquire practical skills of experimental measurements using pH meter, photoelectric colorimeter and spectrophotometer as possible.

A special attention in the introductory laboratory course should be paid to hard-and-fast carrying out safety instructions stated in the devices' service manual. The carefulness in performing all the operations of preparation and carrying out experiments and proper treatment of the devices are of great significance in the obtained measurement results' objectivity.

The laboratory research purpose is to study many-dimensional manifolds in the form of function spaces obtained in the process of experimental measuring of real technological processes' parameters in multicomponent systems and the formation of skills of practical application of methods of modeling multifac-

torial and multiparameter technological processes in multicomponent systems.

An important fact of the present special course mastering efficiency upgrading in conditions of creative atmosphere at solving topical technological problems lying in the area of students' vocational interests should be made a point on here.

From the experience of the present special course one may conclude that graduation and term papers on real production assignments of industrial enterprises can be one of concrete forms of such academic creative tasks; for example:

1. Mathematical modeling of multicomponent mixtures of non-reacting substances.

2. Multidimensional mathematical modeling for the purpose of work activities' optimization by the example of electric coagulation in sewage waters at their being treated with induction currents.

3. Mathematical modeling of an electrodeless electrochemical process in solutions at their being treated with induction currents and the like [6].

The purpose of research tasks is to reinforce the acquired earlier knowledge on modeling many-dimensional manifolds in the form of function spaces obtained in the process of experimental measurements of real technological processes' parameters in multicomponent systems and to form creative skills of practical application of mathematical modeling methods; for example:

a) Examination and optimization of the operating regime for a pipeline inner surface electrochemical metallization and passivation plant (patents № 2241075and № 2244766).

b) Mathematical modeling of a biochemical process at electrodeless disinfection of environmental waters (patent № 2264992).

c) Mathematical modeling of the chemical coal conversion process (patent № 2272825) and others.

4. Follow-up study perspectives. The introduction into HEI specialist training of the special course on mathematical modeling of technological processes on the basis of constructive geometry is intended for the formation of an up-to-date engineer able to independent exploration, finding and solving scientific and technological problems of sophisticated technology.

The special course is scheduled for 454 hours (90 lecture-hours, 108 hours of practice, 46 hours of laboratory research, and 210 hours for term papers among them) from the second to eighth semesters.

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Materials of Conferences

THE DEVELOPMENT OF THE METHOD OF THE DUST SUPPRESSION OF THE LEBEDINSK MINE-CONCENTRATING CONCERN'S HILLOCK

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At present an important ecological problem is the atmosphere pollution of the dust-ejection of a mining. One of the concerns exerting a negative influence not only on an environment but on a man is the Lebedinsk mine-concentrating concern, situated on Gubkin. The influence of it upon the environment is evinced by means of dusting the hillocks.

The problem concludes that the hillocks are fine-dispersive enough in its composition and after drying they are easy to be carried over with wind from the hillock's surface, exerting negative influence on an environment and a man not only on the concern's territory but close to the living houses. The hillocks of the Lebedinsk mine-concentrating concern contain in its composition of the order of 70% SiO2, about 10% FeO, 5% oxide Mg, also there are such biogenic elements in its composition as S, P, K, Ca. For an experimental study of the dust-carrying over of the hillocks of the LMCC the experimental plant was modeled and assembled. In the plant a constant speed of wind equal 12m/sec was founded and observed during all experiments.

The dust suppression was brought about two methods: mechanical and biological. Mechanical method concludes in a moistening the hillock's surface to average moisture about 11%.

When the hillocks are in a moist condition, coefficient of the dust-carrying over is insignificant and composes 0, 34%, but in case with the dry hillocks it reaches 7%, it's in 20 times more.

From literature it's known that the biological method of the dust suppression is used in the concern and it spreads only on the slopes of dam, at present it concludes in the usage of the perennial shrubbery plants (sea-buckthorn). In our experimental work it's studied the biological method of the dust suppression of all area of alluvium.

For the decrease of the quantity of the dust-carrying over the hillock's surface the perennial sorts of beans and cereals were used as experimental seedling. The seeds of the cultures were sowed on the hillocks in Petri cups with the different masses: 100, 1000, 5000 kg/he of the hillocks. After the experiments and generalization of the experimental facts it can do a conclusion that the most optimal mass for the dust suppression of the hillock for the area 1 hectare is 1 ton of seedling, the most optimal studied cultures are cereals and it's confirmed with the experimental facts.

As a result it was developed the technological scheme of the inculcation of the seedling in process of the magnetic separation.

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SOLUTION OF SOME ENVIRONMENTAL PROBLEMS OF KURSK MAGNETIC ANOMALY REGION

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Kursk magnetic anomaly (KMA) represents a unique iron ore basin. It is located in Central Black soil economic region of Russia and includes four areas engaged in iron ore mining: Belgorodski, Novooskolski, Starooskolski and Kursko-Orlovski. The total area of Kursk magnetic anomaly is approximately 150 thousand square kilometers. The iron content in the ore is within the limits of 14 to 57%, the greater part of which undergoes preliminary concentration and later is used in metal production. Ore concentration results in a concentrate with prevailing content of ore material and "tailings", consisting mainly of gangue. In Lebedinski mining concentrator (LMK), included into Starooskolski iron ore area of KMA, wet magnetic separation is used for concentration. The resulting "tailings" represent a pulp with the content of solid phase up to 30%, which is transported to the storage area (tailing storage) via pipeline. LMK land allotment, intended for tailing storage is as large as 1520 hectares, which exceeds the areas, allocated for the quarry – 1100 hectares. At present the accumulated volumes of wastes from wet magnetic separation (WMS) are about 80 mln tones. Taking into account the fact that production facilities are located on black soils, which are highly fertile agricultural areas, the problems of protection and rational user of land for Lebedinski mining concentrator are priority issues to be solved.

Judging from chemical and mineralogical composition WMS wastes of Lebedinski MC both currently produced and those from tailing storage are close to weak-ore quartzites. Rock forming mineral is quartz (over 60%), then magnetite (up to 8%), blende horny, iron oxides, pyrite, total iron content is from 10 to 17%. That is the reason that wastes from WMC, being finely dispersed, can be regarded as strongly ironed artificial sands and be used as basic ready made charge to produce pigment filling agents.

The pigments to be used in construction were produced at the department of industrial ecology of

the Belgorod state technological university named after V.G. Shukhov and were made by burning of basic WMC LMC wastes. Two regimes of treatment were regarded: soft heating and thermal stroke. Pigments as filling agents were obtained on the basis of currently produced WMS wastes as well as of those taken from the tailing storage. The most intensive coloring – red and brown – was obtained as a result of waste treatment at the temperature of 1000º C. The important characteristics of pigments, used for production of colored silicate materials are their coloring capacity and degree of inertness related to raw mix, especially lime. The results obtained showed that coloring capacity of pigments as filling agents (defined by means of adding lime [1]) on the basis of WMC wastes form tailing storage is higher that that of currently produced wastes, which is connected with different iron oxides content. However in both cases this characteristic is not lower than 1, thus, the pigments as filling agents obtained can be used for volumetric coloring of silicate materials.

The activity of filling agents was estimated by absorption CaO from solutions by basic WMC wastes and WMS wastes that underwent thermal treatment. As a result of thermal treatment of LMC WMC wastes their sorption capacity changes in relation to Ca^{+2} ions: from 65 to 80 mg/g in the course of soft heating and up to 125 mg/g with the use of thermal stroke for currently produced wastes; from 69 to 71 mg/g in the course of soft heating and up to 97 mg/g with the use of thermal stroke from wastes taken from the tailing storage. Activation processes which take place when thermal stroke is used , as well as action of iron oxides as a mineralizing agent at high temperatures, according to the research references [2], result in higher defects of the structure of quartz content in WMC wastes and growing inner stresses which they create. It is how the growing sorption activity of pigment filling agents during thermal stroke can be explained. The characteristics obtained in both cases constitute over 55 mg/g, which according to classification [1], characterizes pigment filling agent made on WMC basis both currently produced and taken from the tailing storage, made by means of soft heating and thermal stroke, as highly active. The pigment filling agents obtained were used for volumetric coloring of silicate brick and were introduced into the raw mix (lime 10%, sand 90%) in the amount of 5 to 70% instead of silica component. After thermal treatment the coloring of brick samples becomes weaker compared to raw samples, light tints were obtained – depending on percentage of pigment content – from light pink to light terra-cotta. The use of pigments instead of quartz results in considerable increase of compressive strength compared to the control composition. Maximum values – 29,5 and 28,6 MPa are achieved if the sample contains 50% of currently produced MWC wastes and those from the tailing storage, which is 76 and 51% higher than in the control respectively. Strength increase according to RFA results is connected with the synthesis of extra number of new formations – hydroferrites and low basic calcium hydrosilicates. Quartz contained in WMC wastes is characterized by high reactive ability due to thermal activation in the burning process, which provides higher synthesis speed, mainly of low base calcium hydrosilicates of tobermorite type and hydroferrites in the course of reaction with iron oxides, contained in pigment filling agents.

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Materials of Conferences

"MAGNITOGORSK IRON AND STEEL WORKS" JSC VALUE-BASED MANAGEMENT ON PRIOSKOLSKY FIELD DEVELOPMENT BY REAL OPTIONS METHOD

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When making a decision on realization of the project of own iron-ore base creation by an iron and steel plant a new approach including all the money flow discounting method advantages and leveling the given method disadvantages is necessary. The best suited implement for this purpose is the Real Options Method. Let us assume that the plant managers planned the following Real Options: the final product change option; the project intensive growth option; the project scale reduction option; the abandonment option; the activity arrest option.

The final product change option supposes producing end products of further processing with a more added value, which is in good favour in the market and can bring a supplementary economic effect to the "MISW" JSC when using given products in its production at the unchanged volume of the iron ore mined. It is offered to recover metal front ore to direct-reduced iron (DRI). The implementation of the option reduces the investments pay-off period and increases profits of the "MISW" JSC; and when using DRI as part of burden material of the "MISW" JSC electro-steel furnace, the plant gets additional economic and technical advantages.

The project intensive growth option supposes that, in case of iron ore raw material demand increase in the world market and "MISW" JSC, the plant can expand the Prioskolsky field production capacity owing to heavy ore reserves without large capital expenditures. The option realization allows the "MISW" JSC to be more flexible, when programming the production plan.

The project scale reduction option is conditioned by the market demand for iron ore raw materials and their prices, the activity of business rivals and other factors' influence. If the "MISW" JSC production volume is needed to be reduced due to the decrease in demand for steel, emergency or any other cause, the "MISW" JSC can be required to buy iron ore raw materials in the amount exceeding its demands according to the contract conditions. The "MISW" JSC possesses limited facilities to reduce iron ore raw materials acquisition from the SSGPO. Negative sequences can be reduced owing to the development of the Prioskolsky field. The project scale reduction is advisable to be carried out until the incremental cost reduction will positively influence the profit. The given fact allows intensifying the synergetic effect from the field development and increases the investment attractiveness of the "MISW" JSC. The implementation of the option allows the plant to be more flexible in the world's unsteadiness, than in the presence of a long-term fixed contract with the iron ore raw materials supplier.

The abandonment option gives an opportunity for the organization to stop the project at the market conjunction deterioration. Thereat, it can sell out all the assets at its disposal, compensating a part of negative profits, or use them in other projects; that allows the organization to get definite compensation payments. Capital investments in the Prioskolsky deposit development can be divided into several stages. In connection with this, as yet at the stage of planning there is an opportunity to foresee the variant of waiving the project after every of theses stages. At the project implementation some liquid funds, which can be sold by the "MISW" JSC at the price of 80% from their original cost value, are used.

The activity arrest option is effective at an intense price cut in the market. Let us consider the variant of the Prioskolsky deposit activity arrest for 2 years upon the preparation step completion. Thereat, the plant pays out wages to the employees for the purpose of competent personnel retention.

After a detailed analysis of every of the options the computation of net present value (NPV) of every kind of Real Options is carried out and expert evaluation of its probability (P) is defined, then the Prioskolsky deposit development real value is defined by the Real Options Method.

Table 1. The Prioskolsky deposit development value by the Real Options Method

№	Factor name	NPV	Probability	NPV with account of P
	Basic variant (25MIO.tons)	6 446		
1	final product change option	82 786	30%	24 836
2	project intensive growth option	59 811	30%	17 943
3	project scale reduction option	2 010	10%	201
4	abandonment option	-4 672	15%	-701
5	activity arrest option	3 421	15%	513
	Total:		100%	42 792

Thus, one can calculate an additional value of the Prioskolsky deposit development by the Real Options Method. The introduction of Real Options into the investment project structure and their evaluation allowed increasing its attractiveness significantly. The value of Real Options is equal to 36 347 MIO rubles. So, the expanded net present value makes 42 792 MIO rubles.

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DEVELOPMENT OF TOURISM INDUSTRY IN RUSSIA: PROBLEMS AND PROSPECTS

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Tourism is very favourable, progressive sphere of human life activity. Not so long ago our best experts in this area had to prove it in the highest cabinets to the highest authorities. But now, even the most skeptically officials can't help but recognize advantages of development of the given branch, capable to become one of the key spheres for any country of the world. By the way, some developed in this respect states receive incomes of the incoming tourism, comparable to what we have by selling raw materials. It is the real fact, without any exaggerations. But it is only one side of the coin. Tourism is very good because it is easy to travel, its cost is comparatively low to other profitable branches of industries. It is capable to solve and successfully solves many problems, including social ones. The first among them is a problem of employment.

It is necessary to remark, that World Travel and Tourism Council (WTTC) represents the industry of tourism after full economic analysis in such terms, as a total internal product (gross national product) and employment [1]. It allows us to compare a situation in the branch to a situation in other sectors of economy and the country as a whole. By the way, recently this organization has presented most detailed of ever offered the analysis of the Russian Federation's tourism industry. Practically all aspects of demand are presented.

According to the conclusions of the research, the tourism branch has great opportunities to influence on the future of economic and social development of Russia. The key data collected by WTTC, impress a lot. Employment just in the industry of tourism in 2008 will amount to 732 thousand workplaces (1% of all workplaces), and together with the interfaced branches of economy – 4,126 million (5,8% of all workplaces). The general share in gross national product of the industry of tourism and the interfaced branches of economy is considerable – 6,9%. By 2018 WTTC experts predict real annual growth of a share of branch in gross national product by 5,7%, and the general employment in this sphere and adjacent areas will have grown up to 4,563 million people [2].

WTTC president Jean-Claude Baumgarten declared: "Russia possesses sufficient potential to become one of the leading countries of the world in sphere of tourism within next ten years. I would like to approve of the major measures taken by Rostourism for stimulation of development of this branch, and to call the government, and also representatives of your industry and the society as a whole to listen to those recommendations resulted in this report to reach social and economic gains from development of tourism in full"[1].

These words are not idle talk, necessary only for the press covering this or that event. Not every country receives such honour, but only the country which the World Council considers perspective for the rise of tourism branch for the benefits of all world community. The report is also important because it changes foreign investors opinion about Russian tourism sector, for which WTTC is an indisputable authority.

So we can say that time for Russia has come. It testifies that our country represents the most perspective tourism market since WTTC cares about it. This advice offers concrete ways to decide our problems, prompting: where and how to invest more effectively, how to develop various branches of economy, directly or indirectly connected with the industry of tourism. Foreign experts advise us how short-sightedly and dangerously to build strategy of development of the Russian economy on raw materials export. Tourism can and should become one of the basic items of replenishment of the budget even for such an industrially focused state as ours.

Next decade Russia is predicted a place of one of the leading countries in the sphere of travelling. Come to think of it, chances to become a hospitable country for us are actually great. First, our incomparable natural sights say "yea". Secondly, our history full of peripetias and riches of cultural heritage. And, thirdly, the fact all this carefully had been hidden behind the Iron Curtain for years and years. But to receive the maximal feedback from tourism branch, it is required to solve a lot of problems. To hope for the market, which will correct everything by itself or for the efforts of domestic or foreign investors, is silly and naïve. Analysts consider that participation of the state is necessary. To decide problems in tourism and to develop new vision WTTC suggests meeting three demands:

1) the Russian management must give the priority status to the sphere of tourism;

2) businessmen should correlate interests of their business to people's needs, culture and environment;