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## Section 1. Biology

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### The technology of rearing *Braconidae* in Vitro in biolaboratory

**Abstract:** In the article researches were given about creating artificial medium of diets in order to rear *Bracon* and choosing effective medium of diets. In our researches medium of diets which consists of some components was created and they were harmed with *Bracon* generations. According to it, generation of *Bracon*'s nutrition and developing three main types of medium were produced in order to rear *Bracon* parasite that was composed wax moths (*G. melonnella*) and (*H. armigera*) hemolymph, egg yolk, natural milk.

**Keywords:** *Bracon*, entomophagous, vermin, unripe cotton bell's caterpillar, wax moths, in vitro, artificial medium, hemolymph, egg yolk, genders proportion, inhabitation, result.

#### Introduction

Nowadays the safety of foodstuff is considered as one of the world global problems. More than 60 countries are suffering from this problem in the world. Increasing population of our country and exceeding demand for quality food, cultivating agricultural products and searching new sources of rearing is becoming problem [1; 2; 6].

That's why our motherland is paying attention widely to provide people with the safety of foodstuff in order to cultivate ecological healthy food and protect environment [1; 2; 3].

It is required much financial expenses to rear entomophages in laboratories in order to cultivate agricultural products and protect pests. In our Republic exist bio laboratories separate more than 140–150 thousand tons barley, maize, wheat to culture entomophages. It means that it causes great loss for food industry [1; 2; 3].

To carry artificial mediums in rear entomophages is considered as the best way and it notes the duties of directions such as produce them, save and select effective sorts [1; 2].

In rear parasite entomophages, using artificial mediums widely and automatizing them gives much opportunity to solve above mentioned problems [3; 4; 6].

It was investigated scientifically by learning inhabitation of *Bracon* parasite entomophages. In this article creating artificial diets medium for growing *Bracon* parasite entomophagous in bio laboratories, choosing productive diet medium and learning inhabitation of *Bracon* parasite entomophag, which reared in artificial way, was investigated scientifically [1; 4; 5; 6].

*Bracon* is reared widely in biolaboratories as an effective parasite which is against for rodent pests of agricultural plants. It was widely

spread in Uzbekistan and other countries of the world. By developing biological methods of learning insects for struggling against pests in the field of researching by these organisms is being paid attention much more. However, in spite of this few researches were done in the field of developing these organisms artificially. That's why we chose this branch [1; 3; 4; 5].

#### The materials and methods of research

Preparing of artificial mediums. The basic ingredient of medium is prepared insect hemolymph and in addition it is added chicken yolk, solution of cow milk (10 gr/100 ml water). In each 100 ml mixture, 40–60 thousand i.u of gentamisin is added. The mixture of diets are shown at the 6<sup>th</sup> table.

It is defined there is albumen, oil, water when it is checked ingredients of master caterpillar's type that belong to *Bracon* in nature. Ingredients of caterpillar resemble each other. That's why it is taken as a base hemolymph of wax moths' caterpillar to rear properly in laboratory. Besides, *Heliothis armigera* Hb, *Agrotis segetum* Sciss and cabbage white moths' pupal liquid is used for research.

Then it is dried with filter paper after taking water. When it dries, by cutting a small part of the tail or pressing to disjoin liquid, it is pulled with special syringe.

Natural milk mixture is added to hemolymph. In this case 1 gr of dry milk is dissolved at 10 ml distilled water and chicken yolk is added diet medium and put at ultraviolet lamp. It is rotated for 5 minutes at 2000 second speed in centrifuge. As a result, above separated additional oil and foam is distinguished. Diet medium should be kept in the clean, without microbe room and at 20 °C cool [1; 3; 5].

After medium has been ready, it is placed in special artificial caterpillars which are cleaned with 75% ethyl spirit made of poltilen.

The following laboratory tools and instruments are necessary to produce artificial caterpillar:

Particular thermostat, test-tube 50-PX, poltilen material 4mm, spirit 75%, ultraviolet lamp, petri plate, antiseptic pipette, centrifuge 2500, medical syringe 5 ml are necessity [1; 3; 4; 6].

Produce depicted artificial caterpillar:

A small part (1×1) of parafilm is extended 2 x 4 cm, absorbed in 75% alcohol for 15 minutes. Then it is dried with sterile printed paper, folded as a sack and fixed in order to stick both sides. 0,5 ml of mediums is placed by pipette into each parafilm box. When parafilm box is filled with mediums, it yields such depicted maggot. 15–20 small holes are opened with sterile entomologic needle for properly prepared artificial caterpillars. All the processes of the preparation are required to carry out in sterile room [1; 3; 4; 5].

Diet mediums which are ready are put in test-tube (50-PX), a day ago flown and nourished *Bracon*'s (*Bracon hebetor* Say) female genders are flown in 1 : 5 proportion.

In order to separate 100 mostly effective diet mediums, 3 kinds of diet mediums are prepared, they are investigated repeatedly 100 times. Their ingredients are following; [1; 3; 4; 6].

**First:** (A) Hemolymph wax moths (*G.melonnella*) (A<sub>1</sub>) 40,04%, chicken yolk (A<sub>3</sub>) 30,03%, milk (A<sub>4</sub>) 29,03%.

**Second:** (B) Hemolymph wax moths (*G.melonnella*) (B<sub>1</sub>) 45,01%, chicken yolk (B<sub>3</sub>) 28,02%, milk (B<sub>4</sub>) 26,07%.

**Third:** (C) Hemolymph unripe cotton caterpillar (*H.armigera* Hb) (C<sub>1</sub>) 50,04%, chicken yolk (C<sub>3</sub>) 25,03%, milk (C<sub>4</sub>) 24,03%.

In order to prevent diet mediums from microorganisms, gentamisin solution is added for each prepared medium 100 ml. i.u 40 thousand – 60 thousand i.u quantity.

#### Results of the research

In each experiment 200 artificial caterpillar are formed from diet mediums of above structure and each of them is experienced 100 times (1 – picture).

We chose a type of *Bracon* to be harmed with *Bracons*. *Bracon hebetor* Say, this type is tolerant, durable in extreme condition. It is practiced by means of choosing convenient state in developing each type to be harmed diet mediums with *Bracon* and in this condition it is put in thermostat.

Damaging the type of *Bracon* with diet mediums at + 28±1 °C temperature, at 68±3% moisture.



Figures 1. Artificial caterpillar and developing the generation of *Bracon*

To compare *Bracon* generation of all diet mediums with (*H. armigera* Hb) caterpillars, cotton-plant caterpillars are also damaged with *Bracon* on. (1 – table).

The indexes of specifying *Bracon* generation's developing artificially made caterpillars in different expenditure limit.

Table 1. – (Experiments of the laboratory, 2014–2016 years) (+ 29 ± 2 °C, RH 78 ± 3%)

Types of diet mediums and their ingredients' expenditure limit%	The amount of damage% with parasite for artificial caterpillar.	Development degree of <i>Bracon</i> in diet mediums by days						All the numbers of generation days	Genders proportion ♂:♀	
		Egg	Larva	Pupa	Undone developing	Imago				
A			86,5	1,8±0,2	5,4±0,3	4,6±0,4	–	1,5±0,9	13,3±0,8	1:6
A1	A2	A3								
40,04	30,03	29,03								
B			61,3	1,3±0,5	3,3±0,9	4,8±0,9	1,8±0,2	–	12,2±0,5	1:1
B1	B2	B3								
45,01	28,02	26,07								
C			73,4	1,7±0,5	4,8±0,2	4,5±0,3	–	2,3±0,2	12±0,3	1:4
C1	C2	C3								
50,04	25,03	24,03								

According to it, the first diet medium (A) organizes damaging degree with *Bracon* 86,6% of all prepared diet medium, It takes about 13,3 days from eggs to imago (mature) period. Imagoes live 5,8 days. It takes 1,8 days to birth larvae from eggs, 5,4 days for larva period, 4,6 days for pupa period.

Genders of *Bracons* which went out from medium are male: female proportion will be 1:6.

In next diet medium (B) damaging degree of *Bracon* mediums will be 61,3%. It takes 1,3 days to go out larvae from eggs, in diet medium caterpillars inhabit 3,3 days and transform to pupa. Pupa period continues 4,8 days, imagoes develop a little and in pupa period they die in spite of observing their flying. In next mediums (C) *Bracon* damage diet mediums till 73,4%. It takes 1,7 days to appear larvae from layed eggs and they begin to consume nutrition.

Larvae develop for 4,8 days in this diet mediums and pupa period includes 4,6 days. Genders of *Bracons* flown from medium are male: females proportion is 1 : 4.

### Conclusion

It is defined during research that prepared all diet mediums are detrimented with *Bracon* generation, they layed their eggs there. But some of diet mediums die because of inconvenience for developing parasite generation.

According to mediums' structure the portion of only wax moths hemolymph (A) is 40,4 and in this diet medium *Bracon* parasites progress continuigly. The reason of it, there is average albumen and oil in the ingredient of hemolymph. They are convenient for developing parasite larva.

Thus, in order to develop and consume of *Bracon* generation well from above mentioned artificial diet mediums first medium (A) hemolymph wax moths (*G.melonella*) (A<sub>1</sub>) 40,04%, chicken yolk (A<sub>3</sub>) 30,03%, milk (A<sub>4</sub>) 29,03% is confirmed as the best diet medium to rear *Bracon* parasite.

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## To define the biological active matter-flavonoids in medicinal plants

**Abstract:** This paper summarizes the general flavonoids quantity, having antioxidant peculiarities where is situated in the southern-western Zarafshan ranges in Kashkadarya basin in medicinal plants such as *Origanum tyttanthum*, *Ziziphora*



clinopodioides Lam., Rheum maximowiczii, Trichodesma incanum, Alhagi pseudalhagi, Mentha asiatica Boriss, Peganum harmala L. The researches were held in spring, summer and autumn months in the leaves and stems of medicinal plants.

**Keywords:** flavonoides, antioxidant, free-radicals, Alhagi pseudalhagi, Mentha asiatica Boriss, Origanum tythanthum, Peganum harmala L., Rheum maximowiczii, Ziziphora clinopodioides Lam., Trichodesma incanum, extract, triton-100, 96% of spirits, lemon acid.

Flavonoids are not synthesized in organisms of animals; they are adopted in organism together with food. Flavonoids are biologically active combinations, they influence as antioxidant, protecting the organism from free — radicals, and intensify tolerance against to an influence of external factors. Flavonoids enter to natural antioxidants range; they may be used to correction of many diseases. If flavonoids are deficient in organisms, some diseases will be appeared. Flavonoids of some plants especially have to the vitamin P influence, they decrease the fragility of blood vessel, can be used as the gall and urine extracting means [2; 3; 6].

Flavonoids are wide spread in nature and they encounter almost in all high plants. Especially, Fabaceae, Asteraceae, Compositae, Apiaceae, Umbelliferae, Ranunculaceae, Rosaceae and other family members are rich to flavonoids. These group combinations will be as solution in cellular sap of all organs of plants. Flavonoids are more accumulated especially in flowering period of plants, then their quantity will be decreased. Plants usually more synthesize the flavonoids in the southern districts and in open, shiny lands than species of growing other territories [6].

In some medicinal plants so that in Centaurea cyanus L., Flores et Frustus Crataegi, Alabastra (Flores) et Fructus Sophorae Japonicae, Aronia melanocarpa (Michx) Elliot, Helichrysum arenarium D. C., Tanacetum vulgare L., Herba Hyperici (Hypericum perforatum), some biological active matters were defined, for example flavonoids were explored too. So, in flowers of Helichrysum arenarium, Tanacetum vulgare and Crataegus sanguinea Pall, the flavonoids were defined. They will be used as extract, fluid extract, nastoyka (a kind of liqueur) to cure some diseases [2].

It is known, flavonoids can be used for correction in rather more diseases. Utilization of pesticides in agriculture the environment are being polluted, in conclusion this chemical factors damage to animal and human organisms. When damaged with pesticides, peroxide oxidation process of lipids in mitochondria and micro soma of rat's liver was raised several times and activity of some ferments such as

ALaT, ACT and LDG were changed. To avoid from the poisoning and in correction we can use from plant antioxidant factors [1; 5].

To determine the quantity of flavonoids in the medicinal plants is the index of having essential biological importance. So the aim of our work is to define the general flavonoids quantity, having antioxidant peculiarities where is situated in the southern-western Zarafshan ranges in Kashkadarya basin in medicinal plants such as Origanum tythanthum, Ziziphora clinopodioides Lam., Rheum maximowiczii, Trichodesma incanum, Alhagi pseudalhagi, Mentha asiatica Boriss, Peganum harmala L. The researches were held in spring, summer and autumn months in the leaves and stems of medicinal plants.

It was used over the 1% of triton X-100 with the solution of 96% spirits for determination flavonoids in plant materials. A reaction was based to complex arising with the stable color as a result of boron solution of lemon acid in the flavonoids that separated from plant tissues. The arisen color complex was measured in spectrometer – 46 of 420 nm, the quantity of general flavonoids in medicinal plants was defined [4].

We conducted the researches in medicinal plants such like Origanum tythanthum, Ziziphora clinopodioides Lam., Rheum maximowiczii, Trichodesma incanum, Alhagi pseudalhagi, Mentha asiatica Boriss, Peganum harmala L. in various seasons growing in the southern-western Zarafshan ranges.

Results showed, that the quantity of flavonoids in medicinal plants in spring, summer and autumn seasons was different (table-1). The highest quantity of flavonoids in summer for Rheum maximowiczii was 3600 mkg/g, for Peganum harmala L. was 3525 mkg/g, in spring a quantity of it for Rheum maximowiczii was 2625 mkg/g, in Peganum harmala L. was 1800 mkg/g. As such, it was defined that in medicinal plants such as Peganum harmala L., Origanum tythanthum and Ziziphora clinopodioides Lam. in spring season a quantity of flavonoids was high. We observed the highest quantity of flavonoids in Mentha asiatica Boriss extract in summer season, which is used in medicine as spices.

Table 1. – A general flavonoids' quantity in some medicinal plants (mkg/g):

№	The name of medicinal plants	Spring	Summer	Autumn
1	Alhagi pseudalhagi	487.5±0.480	637.5±0.638	1950.2±1.99
2	Ziziphora clinopodioides Lam.	900±0.428	675±0.675	
3	Mentha asiatica Boriss	2250±2.25	3000±3	2550±2.55
4	Melissa	1838.5±1.838	1987.5±1.987	1275±0.758
5	Origanum tythanthum	2925±2.93	1400±1.4	1950±1.95
6	Trichodesma incanum	2100±2.1	1150±1.150	
7	Rumex	1875±1.875	2026±2.025	1764±1.763
8	Peganum harmala L.	1800±1.8	3525±3.53	1875±1.875
9	Rheum maximowiczii	2625±0.263	3600±3.6	

Its quantity was 2250 mkg/g in spring season, 3000 mkg/g in summer, 2550 mkg/g in autumn. The highest concentration of flavonoids in Origanum tythanthum was in spring season, it was 2925 mkg/g, in summer it was 1400 mkg/g, in autumn it involved 1950 mkg/g, for Alhagi pseudalhagi it was 1975,2 mkg/g and this quantity was much more than spring and summer seasons. The

high quantity of flavonoids was defined in sorrel plant in summer that it included about 2026 mkg/g. The flavonoids' quantity was high in spring and summer seasons in lemon herbs, but in autumn its quantity was low level.

The received results showed, that general flavonoids, having antioxidant influence, encounter in the composition of medicinal

plants such as *Alhagi pseudalhagi*, *Ziziphora clinopodioides* Lam., *Mentha asiatica* Boriss, *Origanum tythanthum*, *Peganum harmala* L., *Rheum maximowiczii*, *Trichodesma incanum* and its high quantity will be in summer for *Peganum harmala* L. and *Rheum maximowiczii*.

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## Section 2. Geography

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### Comparative study fodder plant in desert condition submontane in semidesert and utilization of amelioration

**Abstract:** The aim of our research was selection and in visitation of eco-biological and economically valuable peculiarities, more perspective prospects of food under their sorts, useful for creation of seed food agricultural lands and haymaking in piedmont semi desert of Uzbekistan. The task of the research contained comparative research of their rise and development, food and seed productivity, and food mass. Practical value of the work was concluded in that for the first time the condition of piedmont semi desert of Uzbekistan. Was given comparative complex mark according to eco-biological peculiarities and economically valuable signs of various prospects and sorts of food dwarf semi shrubs.

**Keywords:** natural condition, climate, pasture, types of food, sand layer, phenology, physiology, harvesting.

**Introduction.** Present situation of desert and semideserts pasture of Uzbekistan be characterized progressive degradation productivity and the quality of stern. Discount to present pass from heaven 260 types of stern plant from natural flora and distinguished more 30 available subshrub, differentiate from productivity and high suitability in extreme condition of desert [1]. Special activity in that acquire comparative from eco- biology research of important types of stern in semidesert, permit to cheat selection most avthailable types, quality of the arid stern plant for the amelioration submontane semidesert in Uzbekistan. In that actual mission and devote that work, itself representational total research of many years about comparative analysis and mark for the different types and quality submontane condition in semidesert in Uzbekistan.

**Aim and mission of research.** The aim of our research report is selection and observation eco-biology and more economical valuable specifics available types of stern in semidesert and its types, suitable for generation drizzle of stern land and haymaking in submontane semidesert in Uzbekistan. In task our research go in comparative study its growth and development, stern and seminal of productivity, mass of stern consist of condition in submontane was given comprehensive mark in Uzbekistan. Feature and economical valuable and differ from valuable of eco-biology of stern in semidesert, concern of ten types of economical family of chenopodiaceous and astrovs – chogon, qomforous, izen, keyruk, wormwood of tereskuni in Uzbekistan. Practical value of our work include basis of research of eco- biology and study different types and quality of semideserts dedicated valuable class and types for using in amelioration semideserts in pasture submontane of Uzbekistan.

Nature condition place where we conducting our exploration. Experimental work perform experienced field in Nurota. Experienced field located in zone submontane semideserts in southwest pediment centre of column Nurota its high 660–670 m. Climate characterized with snap rippling daily and annual number atmospheric fall-out with uneven prolapse [2]. Maximum number it prolapse in

winter- spring period. Average year fall-out period of average form 206 mm, average years temperature of air is – 13,4 degrees, absolute maximum temperature of air 43,1 degrees, absolute minimum is minus 29 degrees, average relative dump of air is 55,4 degrees. Wind principally in north side, after midday speed of wind increased.

Pedogenic breed serve fine-grained and deep deposition of skeleton, which characterized high afforest. In place prevail has light sierozem with wormwood and eferoids association. Content humus in there is 1–1,5%, nitrogen 0,05–0,09%. Horizont where is many gathering carbonate (scaling to lime, from 20%) standi in deep to 20–30 from 60–80 sm. Below plaster available horizont. In submontane semidesert Nurata sweep with eferoids types in semidesert. Base of plant intercession with *Carex pachystylis* J. Gay, *Poa bulbosa* L. *Artemisia, diffusa* Krasch ex Poljak, *Alhagi pseudalhagi* (Beib) Fisch, *Peganum harmala* and first year efemer.

**Object and method of research.** Object of research is 6 types of arid culture- chogon, qamforos, keyruk, izen, tereskina and wormwood. Experimental crop produce in autumn-winter period of year soil beforehand; work up. autumn ploughing in deep 22–25 sm, harrowing in two marking with lack of faith. Accounting field allotment 30m, replication experiment 4 time. In way of crop wide line between rows race 60sm. Norm of sowing for izen 3 kilo, keyruk and tereskina – 5 k, chogon and poliney – 0,5 k, 100% of economical family. Phenological survey according to take method of Beydeman survival of plant detect by basis of survives number, spring (may) plant and autumn (october) plant, as well asi according to year comparison with number appear sprout vegetation in first year. Plants growth of dynamics by force of monthly by population instrumentation (100 plants). Crop yield of sterns mass and family detect by method of directive department of sterns culture WIP (1979) and WNII (1978).

**Output and theirs discussion.** Near sunken sowing seed in deserts stern plants ascend early spring in period melting snow. First ascend (2–3 february) komforosma, teresken and polin. after 20 day (in first decade of march) izen, chogon, keyruk. In last



years first (2 decade of february) grow komforos, teresken, polin. secondly (in 1–2 decade of march) – izen, chogon, and keyruk. The phrase “beginning of flowering” pass in following sequence: izen – (1 decade of may), Chogon, qamforosma and glasswort (3 decade of may), teresken and polin (1 decade june). The seed of chenopodicious culture mature in 3 decade of october, in sequence – teresken – izen – keyruk – chogon – qomforosma, asid of (polin) only in 1 november and later. By duration vegetarians period of culture following allocate: keyruk (235 days) – teresken (240 days) – izen (243–255 days) – chogon (250 days) – qomforosma (255–265 days) – polin (255–265 days).

Survival cohort. In 6 years of life according to its survival allocate in following sequence: izen (80,1–85,3%), keyruk (75,3–78,2%), teresken (72–73%), polin (40–60%), chogon (45,3%), qomforos (36,4%). Rootage system. Study about rootage system separate in arid stern plants (in different zone) engage a lot of research people Amelin, Blagoveshenskiy, Petrov, Nechayeva, Shalit, Shamsutdinov and Rabbimov [3]. In condition of culture in submontane semidesert Nurota rootage system arid; stern plants in 5 year of life passage in different deep of chogon – 450 sm, keyruk – 325 sm, izen – 325 sm, polin – 250–300 sm, teresken – 250 sm. [4]. Horizontal distribution rootage according to its culture is found limit 150–200 sm in diameter.

**Altitude plants.** In average in 6 year of studying broadside of high (77–89) has izen, choga and polin. Keyruk already in his life achieve his more high average high 6 years level in this sign. Rest types of plant in his first year lower of average 6years level 24 sm (polini), 21sm (teresken), chogon, izen [5]. Productivity of stern and family. In average 6 years study of crop yield deserts stern of plant form 3,9–23,5 dry mass of stern. More crop field has izen (11,2–23,5), keyruk (18,9–20,3), and chogon (16,4) [6]. The copy

field family’s culture in average in 6 years study include 0,7–5,8. The highest crop field has keyruk (5,3–5,8), izen (3,7–3,9).

### Conclusion

1. In condition in submontane in semideserts Nurata region of Samarkand Uzbekistan dupe 6 years comparative complex study about 6 types of available deserts plant from chenopodiavious and acid subdumi and the life of subdumi.

2. In duration vegetarian period of culture sequence in following system: keyruk (235 days), teresken (240 days), izen (243–255days), chogon (250 days), qamforosaj (255–265), polin (255–265 days).

3. In condition of culture in the 5 year of life roofage system of studying types of pass in deep depth: chogon 450 sm, keyruk 325sm, izen 325sm, polin 250–300sm, teresken 250sm.

4. In high survival of plant in six years of theirs life has izen- 80–85,3%, keyruk – 75,3–78,2%, teresken– 72–73%, average of survive polin– 40–60%, chogon – 45,3%, qomforosa – 36,4%.

5. In average in 6 year corp field desert stern form of plant 3,9–23,5% dry stern mass. More corp field has izen – 11,2–23,5%, keyruk – 18,9–20,3% and chogon 16,4%. Copy field of family for culture in average in 6 years study has izen 0,7–5,8%, and chogon 2,7–2,9%.

6. According to complex economical ayailable mark more perspective for create higher productivity of pasture agrophytocenosis autumn-winter period in condition submontane semideserts Uzbekistana has subshrub – chogon and tersken and subshurbus types as izen, keyruk, polini.

In the condition of piedmont pasture in Uzbekistan was held comparative complex research in 6 types of more perspective deserted food plants out of pigweeds family belonging to vital. According to economically variable features more perspective for creation high productive pastoral of agro plant formation, autumn and winter usage in piedmont desert in Uzbekistan.

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## Section 3. History

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### «Politics is a dirty work, it is not for the refined female nature...»: how in 1917, Russian women were granted the suffrage

**Abstract:** One of the important achievements of the struggle of women and the Russian women's movement at the beginning of the crucial XXth century was the granting of universal suffrage to Russian women of all ages, nationalities and religions. This happened in 1917, after the February events, which can be called a significant historical event. This article will focus on the consideration of this important scientific and socially important problems.

**Keywords:** the February revolution of 1917, Russia, woman-suffrage, women.

The problem of women's political rights is one of those issues, the solution of which in Russia is more than a century old. Under present conditions, this problem is less relevant and linked to the taking place in the country of radical changes in the legal status of women in society.

Half of humanity, which for centuries was not recognized as a subject of history, resolutely declare all of their rights to equal place with men in all spheres of socio-political and socio-economic life of the state, and more significant is their role in making important decisions.

In Russia, the attitude of society and government to the status of women began to change during the revolutions of 1917 and in subsequent periods. Just then, they have been the object of confrontation between different political forces, which was reflected in the consciousness and behavior of Russian women. In this regard, a special place was occupied by the revolutionary events of February 1917, which played a major role in the destiny of the peoples of the country, including women.

Prior to the twentieth century in Russia infringed the rights and freedoms of the individual. Men and women did not have electoral rights, take no part in the formation of state run public authorities. In accordance with Russian legislation, women were restricted in their rights to a greater extent than men. This is especially manifested in matters of inheritance and division of property. So, the daughter in the family, where there were sons, received 1/14 of the total immovable property, and 1/8 of the movable property. In the side lines women in the presence of men did not receive anything. After her husband's death the wife inherited, with children and without them 1/7 of 1/4 of the real and movable property [1, 66, 70]. Dowry and paraphernal property not included in this part.

Muslim women were also not in the best position. According to the Koran and Sharia, the woman was not equal to the man in the property and legal relations [2]. Their inheritance rights after the death of husband determined Shariah and Russian legislation. All wives of the deceased husband, received in aggregate of the entire property, "if children were – 1/8 part, if there are no children than all the wives get 1/4 part, and the remainder is given to other heirs". In the Russian legislation stipulated that — "each wife separately re-

ceived from the total an equal share" [3, 47]. Women's property rights were also infringed upon after the divorce. They are almost nowhere, not in the Koran, nor in the Russian legislation were clearly defined. In fact, in the division of family property, a divorced wife completely depended on her ex-husband [4, 208]. The woman's degraded position was legally fixed and sanctified by religious canons: the wife is obliged to obey her husband as head of the family, "to remain in love, reverence and unlimited obedience, to render him every kind of pleasure and affection as the mistress of the house" [1, 59].

But most of all women were infringing in political rights, and, above all, in the elective franchise. Russian legislation classified them as incompetent citizens who did not have a direct passive, the more active elective franchise. Although only a certain group of Russians women, who owned significant immovable and movable property, was granted the censorship right to participate in noble assemblies, communal and zemstvo elections [1, 135].

What was the basis of Russian legislation that determined the legal status of women? His moral support, as well as state policy in this matter, were religious dogmas about the relations between the gender, according to which the wife was created after her husband, was created for her husband, etc. In the domestic social and scientific thought, were widely disseminated traditional ideas about the natural preconditions for the inferiority of women, their secondary place in society and a family like "a woman, like a child, can not be anything but an object of influence". All these representations, of course, manifested themselves in laws relating to women, and fully corresponded to the state policy regarding them. After all, the legislation of the Russian Empire, which defined the status of women, was based on patriarchal and patriarchy views on their mission, according to which women's lack of rights is in the interests of women themselves, as well as the interests of the state and society as a whole.

Low legal status, weak mental consciousness, illiteracy, in this regard, the unclaimed of women, representing more than half of the population, acted as a kind of inhibitory factor in the development of the country, which caused the need to review legislation on the women's issue, the equation of women's rights with men.

Published in one of the domestic periodicals in the early XX century an article on this issue caused a great public response. Its author was a famous public figure A. Kiesewetter. Drawing attention to the status of a Russian woman, he wrote: "Old Russia, paying tribute to the fascination with ascetic femininity, recognized the woman as a social activist within the family house-building. The new Russia, having deprived the family meaning of the state organ, took away the position of a public activist from the woman. The Modern Russia will have to solve these centuries-old wavering. The family will remain a family, and the woman will keep her place of honor in her. However, it will perform and is performing on the arena of this public activity is not in the old, and in the modern sense of the meaning" [5, 1].

During this period, works began to appear on the topical issue of that time — the reform of the electoral system of Russia. In one of them it was said about the need to give Russian women a suffrage: "one of the first cases of reformed management should be to grant Russian women political rights equal with men" [6, 2].

The beginning of the XXth century was an important stage in the struggle for the political rights of women. During this period, according to the royal manifesto of October 17, 1905, democratic measures were promulgated, such as freedom of speech, of the press, of meetings, of religions and etc. However, after that came out the law on the procedure for elections to the State Duma of December 11, which gave voting rights only to men [7, 12]. The actual author of the manifesto is Count S.Yu. Witte, who on the appeal of the women's society to give an explanation replied, that during the preparation of this issue was not discussed. So, the legal capacity of women was not recognized and they were equated "to persons under-age, mentally deficient and under court". Opponents of political equality of women proceeded from the following arguments: when entering the path of social activity, a woman ceases to be a mother; few women aspire to political activity; the struggle for political rights has a great effect on the psyche, and therefore will negatively affect the family atmosphere; politics is a dirty job, not for refined female natures, and therefore the creative activity of the mother may be diminished and the quality of the race may deteriorate; he provision of electoral rights to women is premature, and others [8, 16].

During this period, the women's organizations operating in Russia noticeably stepped up their activities. From the very beginning of the creation of the parliament, they made repeated attempts to use it in solving the women's issue: they addressed the deputies, sent delegates to the commission, petitioned, etc. The editorship of one of the domestic women's editions appealed to Russian women to appeal to the State Duma with a protest against their lack of rights and demanding political and civil equality with men [9, 33–34]. Russian women's society, under a petition to the Duma for several months across the country, collected more than 5 thousand signatures, in which it expressed regret that among the people's representatives there is not women and no representative elected directly by the women themselves, so it puts before the Duma the issue On the political equality of women [8, 17]. All this affected the activity of the Duma and session were held on this issue more than once. However, it was not possible to achieve its solution. Despite the efforts of women's organizations, quite progressive positions of some factions and deputies, the State Duma did not take measures to equalize women's rights with men.

In the process of the necessary change in the self-awareness of women in accordance with the requirements of the modern time, intervened objective factors in particular, the First World War. It affected the involvement of women in production, previously inaccessible to them works, as well as the activation of their role in public

life. The usual phenomenon were the women's gatherings and meetings. Acting and emerging women's organizations have expanded their activities. This was mainly due to the provision of assistance to soldiers who were at the front and rear in hospitals, as well as to «war victims» — refugees, orphans, invalids, families of mobilized people, etc. Therefore, in the conditions of war the urgency of the decision of a female question decreases. Despite this, it does not fall out of the center of public attention. This is indicated by the increase in articles in the periodical press and the publication of prominent public figures and politicians. They were united by one idea — the need to provide women with political rights "at a crucial time for Russia". In one of the works it was stated: "... if in peacetime the work of women in public organizations and in all other areas of Russian public life spoke for the need to give women full equality with men, but now, after the brilliant activity of women to help warriors and victims of war, new evidence of the need for equality" [10, 51]. However, there were other opinions: the authors were only partial advancement of women and the question did not see in the change of the existing system, but only in the gradual settlement of the current legislation. In one published in 1917 work, the author stated: "the State can be completely free and democratic only when it is not disenfranchised and deprived of the right to vote. All objections to the political rights of women are — ... a legacy of the time when the woman herself was so little developed that she did not raise the question of her participation in the political life of the country. Since the time when this question was raised, it could not have been given a different answer by the country, as positive" [11, 21].

After the fall of the autocracy in Russia, the pressing question of women's equality became more relevant and triggered a struggle of opinion in society. Different political forces had their own understanding of his decision. In their programs there were different demands for women's equality, as the revolutionary situation developed and deepened, various ways of achieving it were put forward. The observed increase in the share of women in production played a significant role in their involvement in the sphere of political struggle. Workers woman, representatives of a certain part of the intelligentsia, peasant women participated in strikes and peasants' actions against war, high prices, exorbitant exploitation. Along with general political demands, they put forward their demands, like the right to vote, equal pay, maternity protection, etc.

The intensification of women's participation in numerous political actions aroused genuine interest of the active political parties interested in attracting them to their side. This led to a noticeable increase in their environment of political agitation, especially among women workers. Women's organizations did not lag behind them, organizing meetings, rallies, lecturing on women's rights, their role in the current situation. Some of these political forces urged Russian women to support the war to a victorious end and the Provisional Government, others suggested together with the workers to demand the transfer of full authority to the Soviets and immediately stop the bloody war. However, the issue of enfranchisement of women remained acute. However, in their first declarations, the Provisional Government, while proclaiming universal suffrage without any censorship, religious or other restrictions, completely ignored the sign of gender. Another position in this issue was held by the Petrograd Soviet of Workers 'and Soldiers' Deputies, claiming that women were granted suffrage. Despite the measures taken and the very favorable conditions for the final resolution of this issue, it was postponed among other urgent issues until the convocation of the Constituent Assembly. The government promised to allow women to participate in elections to the Constituent Assembly, but

without the right to be elected to its composition. This caused discontent on the part of the female society. In Petrograd on March 19, the League for the Equal Rights of Women organized a mass demonstration with the participation of about 40,000 women, demanding that they be given voting right. After lengthy negotiations, the chairman of the Soviet of Workers 'and Soldiers' Deputies, N. S. Chkheidze, chairman of the State Duma, M. V. Rodzianko, Prime Minister G. E. Lvov gave explanations to the expecting demonstrators that the government under the «universal» suffrage understands its provision for people of both sexes. A. V. Tyrkova, one of the pioneers of the domestic women's movement, writes how one of the activists approached the demonstrators and declared to them: ... "Congratulations, citizens. We, Russian women get the rights" [12, 15]. This became a fact of their recognition as equal citizens. The next day the meeting of the League of Equality adopted a corresponding resolution [13, 1].

However, the question of the participation of Russian women in the elections to the Constituent Assembly on a par with men, was not yet fully clarified. In publications, the authors called on the public and, above all, the women themselves to clarify and finalize it. One of them said: "Women should not be satisfied with promises. They should ensure that the item on the distribution of suffrage to women is actually included in the draft law on elections to the Constituent Assembly currently being drafted. The participation of women in the Constituent Assembly, which must establish a new state system of free Russia, is especially necessary. All laws of the future Russian Republic concern not only men, but also women" [14, 14]. The next step was the meeting of the delegation of women

with the Prime Minister G. E. Lvov, where they handed their statement. The government returned to this issue in the course of discussion of the issue of drafting a law on elections to the Constituent Assembly. And after lengthy discussions on July 20, the government ratified the decision to grant all women who had reached the age of 21 the voting rights [14, 17]. This, of course, was an achievement of historical significance.

In such difficult conditions, Russian women sought electoral right and the right to participate in public and political life on a par with men. Russia was the fifth country in the world to secure the right to vote for women in the article "Provisions on Elections to the Constituent Assembly" dated September 11, receiving it later for 12 years after the men to whom it was provided by the "Regulations on Elections to the State Duma" of 1905 [15, 7]. Such a democratism in the policy of the Provisional Government, which so dramatically changed in such a short period, is explained by the fact that this question was resolved in the conditions of deepening the bourgeois-democratic revolution. It was to provide some thaw sing in the field of democracy in order to prevent the impending revolution. After all, the issue of the proclaimed equality of women did not affect the foundations of the existing system. And, agreeing to resolve the issue, many political forces counted on the support of women. However, in the summer of 1917 the first elections to municipality of domicile under the new rules showed all the formality of the rights granted to women, to which neither the parties nor the population themselves were ready. In the course of the events that took place in the autumn, there was a different situation in the socio-political life of the country, where Russian women had a completely different role.

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## Section 4. Machinery construction

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### Scientific substantiation of technical solutions for the improvement of the construction of the body of a hopper car for transportation of cement produced in the Republic of Uzbekistan

**Abstract:** The article describes the need to replenish the park of the Republic of Uzbekistan with modern freight cars. The questions of designing and putting into operation a new construction of a four-axial covered hopper car for cement transportation are considered. The main technical characteristics and results of strength studies of load-bearing elements of the body of a hopper car are given.

**Keywords:** hopper car, body, cement, transportation, method of final elements, coefficient of vertical dynamics, strength, load, model.

#### Introduction

Confident steps of Uzbekistan on the path of market reformations, constructing a modern democratic society, improving the living standards of the population necessitate the need to reform the basic sectors of the economy of the country. Under these conditions, residential building and its accompanying infrastructure — communal and social sector, transport and communication networks, production of modern building materials and structures — becomes the focus, which can and should serve as one of the most effective areas of capital expenditures and investment.

During the recent period, a special role in the development was assigned to the industry of construction materials, an area determining the potential of the construction industry as a whole. Based on decisions of the President of the Republic of Uzbekistan there have been accepted and implemented state sectorial modernization programs on technical and technological upgrading of production in the industrial structure [1; 2].

The growth of requirements of the domestic market, rich natural resources and prospects for expanding the export potential create conditions for further development of the cement production. Currently, Uzbekistan disposes of a powerful cement industry, which produces about half of the cement in the Central Asian region.

Taking into account the significant advantages of the country, such as a favorable geographical location and advanced transport infrastructure expedient availability of transport units for the export of cement produced.

Among other means, railway transport is most adapted to mass transportation, operating around the clock, regardless of the time of year and weather. Railways are a universal means of transport for

the transportation of all kinds of goods at relatively low prime cost and high speed of delivery to the consumer.

Therefore, the availability of a fleet of modern freight cars, in particular the presence of hopper cars for transportation of cement will allow to carry out the timely delivery of the produced goods to the consumer.

#### The technical specifications and design of the new hopper car for the transportation of cement

Keeping in mind above mentioned, as well as to implement the resolutions of the President of the Republic [3; 4] designers of Subsidiary “Foundry-Mechanical Plant”, whose production base has been updated in accordance with [5], developed the design of the new hopper car for cement transportation.

The new four-axle covered hopper car model 19–9596 with the volume 61.6 m<sup>3</sup> and load capacity of 72.5 tons is designed for transportation of cement in bulk from the place of production to places of consumption or storage, having special receiving equipment in inter-rail space [6; 7].

The design of car body enables loading the cargo in mechanized way through four round loading hatch with a diameter of 620 mm. Charging hole covers securely protect the cargo from atmospheric precipitations, have simple and reliable locking mechanisms to operate.

The body has block and vertical sidewalls inclined at an angle of 50° with a thickness of sheathing 3 and 4 mm, respectively. Sheathing block walls – is made of flat sheet metal, the side – is from the curved profile with periodic corrugations.

In the lower part of the body in the inter-truck area there installed unloading hoppers. Each hopper has a discharge hatch of 500×400 mm, locking lid with labyrinth seal.



Technical specifications of the new hopper cars for transportation of cement model 19–9596 with volume of  $61.6 \text{ m}^3$  are shown in

Table 1.

Table 1. – Technical specifications of the hopper car for transportation of cement

Parameter	Indication	Quantity
The weight (tare), t	$m$	21,0
Cargo weight, t	$m_w$	72,5
Car weight (gross), t	$m_{car}$	93,5
The base carriage, mm	$2l$	7800
Car length over the end of the frame beams, mm	$2L$	10800
Car Length over coupler pulling faces, mm	$2L_c$	12020
Body volume (max) $\text{m}^3$	$V$	61.6
Constructional speed, km/h	$v$	120
Weight truck, t	$m_t$	5
Static deflection of the truck, mm	$f_{st}$	48
Dimension according to GOST 9238–83		1-VM

#### The research of a strength of supporting elements of a hopper car for the transportation of cement

Later, the young scientists of the department “Cars and car economy” of Tashkent Institute of Railways Engineering conducted theoretical studies to assess the strength of the proposed design of hopper car for transportation of cement model 19–9596 with volume of  $61.6 \text{ m}^3$  at axial load up to 23.5 tons [8; 9].

The strength of the body of a hopper car for transportation of cement in accordance with the requirements [10; 11] was estimated at two analysis modes:

a) the first rated conditions considered a relatively rare combination of extreme loads. The main requirement for the strength

based on this regime — is to prevent the appearance of residual deformation (damage) in the site or parts;

b) the third rated condition regime dealt with a relatively frequent possible combination of largest load characteristic of the normal operation of the car on a moving train. The main requirement for the calculation according to the regime — to prevent fatigue failure of parts or unit.

9596.00.00.000 steels elements of the body of a hopper car adopted in accordance with the design documentation project and allowed data voltage grades are presented in Table 2 [7].

Table 2. – Material and allowable stress elements of the body of a hopper car

Name of the element construction	Brand of steel	Allowable stress, MPa		
		I mode (stroke, jerk)	I mode (Compression, tension)	III mode
Centersill	375–10G2BD GOST 5267.0–90	375	337,5	230
The other elements of the frame	345–09G2S GOST 19281–89	345	310,5	210
The other elements of the car body	345–09G2S GOST 19281–89	345	327,75	220

In accordance with the requirements used for the steel modulus of elasticity was assumed to be  $2.1 \cdot 10^5 \text{ MPa}$ , the Poisson’s ratio was assumed to be 0.3.

The calculation was performed using finite element method using the technology of digital prototyping in the environment of modern engineering programs [12–13]. The volume finite-element model of the body of a hopper car was used to calculate. Body ele-

ments were simulated by linear finite volume elements with three degrees of freedom at each node: three displacement. Car trucks were simulated by elements such as concentrated mass. Elements such as the mass of the car were connected with the frame by means of an absolutely rigid links. Estimated assembly model includes elements of 61121 and 234959 units. General view and the view of the finite element model of the body of a hopper car are shown in Figures 1 and 2.

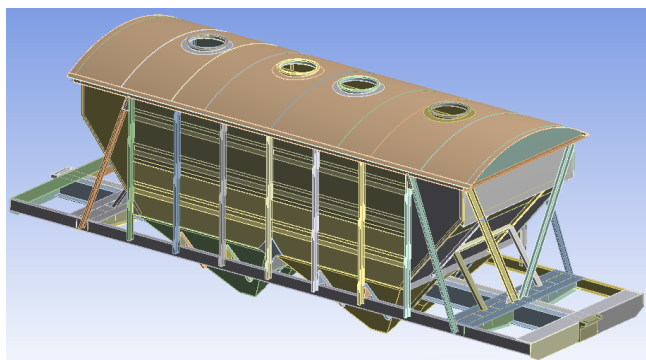


Figure 1. General view of the calculation model of the car body

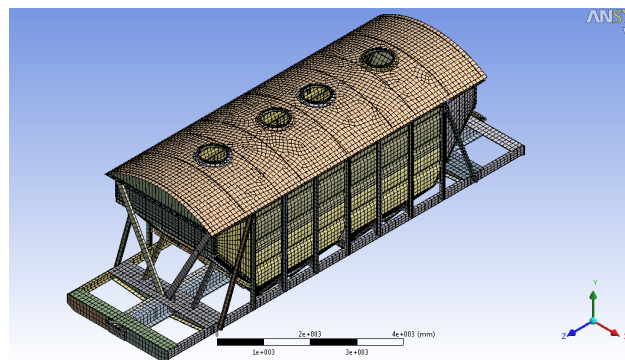


Figure 2. General view of the finite element model of the car body

The restriction of the vertical and transverse movements in the frame pivot assemblies; limited longitudinal movements in the plane of the rear and front coupler horn were adopted as the kinematic

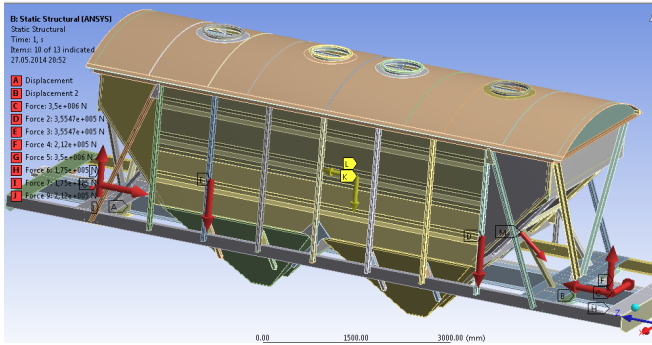


Figure 3. Kinematic and force boundary conditions for dynamic compression forces on the car according to I and III design mode (stroke)

In accordance with the requirements [11] of the body of a hopper car for the transportation of cement was estimated on the strength of the first (stroke, jerk, compression and tension) and third (stroke, jerk, compression and tension) calculated regimes.

The combination of loads acting of the body of a hopper car for transportation of cement in the first and third modes of settlement was determined in accordance with the requirements.

Longitudinal force of inertia of the body and trucks of hopper car was determined by multiplying the weight of the body and trucks by the normalized value of the longitudinal acceleration. Acceleration was applied during the calculation of the model of the body of a hopper car.

Longitudinal force of load inertia  $N_u$  was determined by the formula

$$N_i = N \frac{m_w}{m_{car}}, \quad (1)$$

where  $m_w$ ,  $m_{car}$  – respectively the mass of the cargo and the car weight (gross),  $t$ ;

$N$  – outer longitudinal impact force, MN.

Inserting data into the formula (1) we obtained that the force of inertia of the cargo was for the first mode under the stroke  $N_i = 2.71$  MN, under the jerk  $N_i = 1.94$  MN ( $N_i = 0.77$  MN for the third mode).

Vertical force at the non-central interaction of automatic couplers  $P$  was determined by the formula

$$P = N \frac{e}{b}, \quad (2)$$

where  $e$  – the difference between the levels of the axes of automatic couplers;

$b$  – the length of the rigid rod, formed of dual-clutch automatic couplers.

Inserting data into the formula (2), we have found that the power at the non-central interaction of automatic couplers was for the first mode with the stroke of  $P = 175$  kN, with a jerk of  $P = 138$  kN (compressive  $P = 125$  kN, tensile  $P = 110$  kN), for third mode was of  $P = 25$  kN with the impact and compression,  $P = 27.6$  kN with the jerk and stretching).

Active (static) maximum pressure of the load thrust for per unit of the body wall area made up  $3438$  N/m<sup>2</sup> on the first rated regime, while it was  $15435$  N/m<sup>2</sup> on the third rated regime.

The pressure load on the block wall was  $124059$  Pa.

Transverse forces of interaction between the cars in the curves  $P_t$  were determined by the formula:

– under compression

boundary conditions. Kinematic and force boundary conditions for different calculation modes are shown in Figures 3–4.

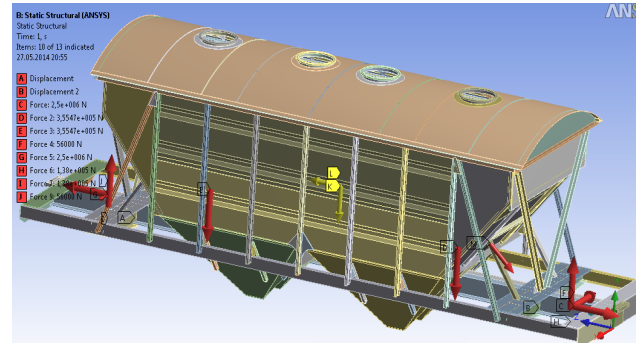


Figure 4. Kinematic and force boundary conditions of tensile dynamic forces on the car according to I and III calculated regimes (jerk)

$$P_t = N \left[ \frac{\delta \cdot L}{l^2} \left( 1 + \frac{L}{a} \right) + \frac{L_c}{R} \right] \frac{l}{L}, \quad (3)$$

– under tension

$$P_t = N \frac{L_c}{R}, \quad (4)$$

where  $2l$ ,  $2L$ ,  $2L_c$  – respectively the car database, the distance between the thrust plates of couplings and car length on the axes of automatic couplers clutch;

$a$  – the estimated length of the coupler body;

$R$  – curve radius, according to the requirements [11]  $R = 250$  m;

$\delta$  – the possible lateral movement of the pivot section of the car body due to gaps in rail wheelset track, in the axle guides, rods and elastic deformations of springs.

Substituting these into the formula (3) and (4), we have found out that the transverse forces between the cars in curves for the first mode when compression is equal to  $P_t = 200$  kN, and tensions  $P_t = 160$  kN.

The coefficient of vertical dynamics of the  $C_{vd}$  in accordance with the requirements [11] is determined by the formula

$$C_{vd} = \frac{C_{vd}^{ave}}{\beta} \cdot \sqrt{\frac{4}{\pi} \ln \frac{1}{1 - P(C_{vd})}}, \quad (5)$$

where  $C_{vd}$  – the average probable value of the vertical dynamics of the coefficient is determined by the formula (6);

$\beta$  – allocation option, according to the requirements [11]

$\beta = 1, 13$ ;

$P(C_{vd})$  – confidence level, which determines the ratio of the vertical dynamics, according to the requirements [11]  $P(C_{vd}) = 0.97$ .

The average probability of a value determined by the formula

$$C_{vd}^{ave} = a + 3,6 \cdot 10^{-4} \cdot \beta \cdot \frac{v-15}{f_{st}}, \quad (6)$$

where  $a$  – coefficient for the body elements, as required by [11] was assumed to be 0.05;

$v$  – construction speed, km/h;

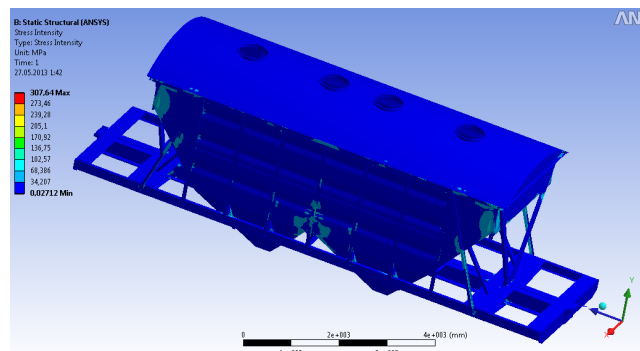
$\beta$  – coefficient taking into account the effect of  $n$  axes in the truck at one end of the crew;

$f_{st}$  – static deflection of spring suspension, m.

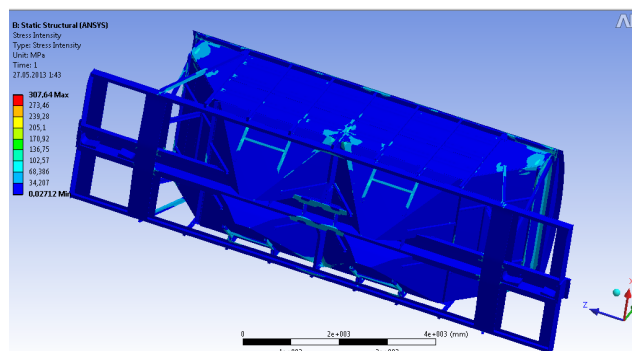
Inserting data into the formula (5), we received  $C_{vd} = 0.35$ .

As a result of the calculation, the equivalent stresses were obtained, resulting in the elements of the body of a hopper car on the first and third rated regimes.

Assessment of strength in accordance with the requirements [11] was performed on equivalent stresses calculated by the Mises theory. Distribution fields of maximum equivalent stress elements of the body of a hopper car considered for calculation modes are shown in Figures 5–6.

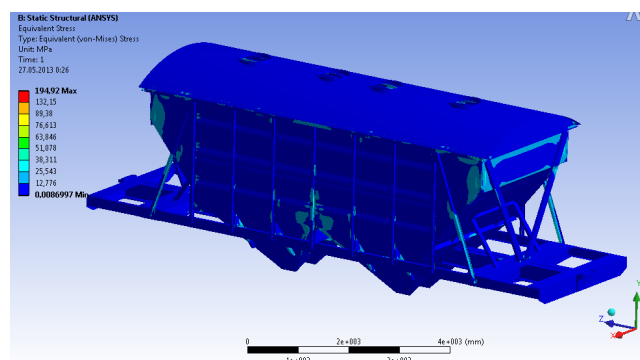


a) general view

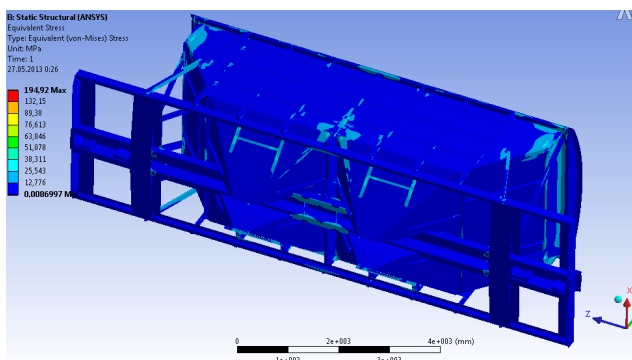


b) view from below

Figure 5. Fields of equivalent stress distribution in the hopper car elements (under dynamic compressive forces on the car according to I design mode (stroke)), MPa



a) general view



b) view from below

Figure 6. Fields of equivalent stress distribution in the hopper car elements (under the compressive forces on the car dynamic according to III design mode (stroke)), MPa

### Conclusion

As a result of evaluation of the strength of the car body — hopper for transportation of cement model 19–9596 established that the strength of the structural elements of the body satisfies the requirements [6–7; 11]. In this case the following values are taken:

1) When I design mode the maximum equivalent stress in the body elements are as follows:

– in the end and side walls and frame elements (impact) 308 MPa (89.3% of the allowable stress).

2) In design mode III, the maximum equivalent stress in the body elements are as follows:

– in the end and the side wall elements (impact) 195 MPa (88.6% of the allowable stress).

The new hopper car design for the transportation of cement with improved technical and economic performance will significantly reduce transport costs for the carriage of cement by rail. Operation of modern hopper cars in the future will provide economic benefits both for carrier and cement manufacturer.

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## Section 5. Medical science

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### Selection of the optimal composition and rational technology of core tablets of Aksaritmin

**Abstract:** Improving the provision of health care needs is directly related to the creation of drugs with targeted action and low toxicity. From this point of view, medicines with natural origination play a huge role in the pharmaceutical industry. The development of the aksaritmin tablet obtained on the basis of the northern fighter provides an opportunity to increase a number of antiarrhythmic drugs with high efficiency and low toxicity.

**Keywords:** Aksaritmin, Northern fighter, wet granulation, technological properties, pressing, residual moisture.

Improving the provision of health care needs is directly related to the development of medicines with high efficiency. From this point of view, purposeful search for medicinal products from plant raw materials is carried out at the Institute of Chemistry of Plant Substances of the Academy of Sciences of Uzbekistan, and as a one of the results of these researches a sum of alkaloid bases was extracted from rhizomes with roots of *A.septentrionale* (Northern fighter), an aksaritmin with antiarrhythmic action [1; 2; 3].

The selection of the optimal composition and development of a rational technology of the tablets of an aksaritmin is a very important stage in the tablet technology.

At the stage of developing a solid dosage form of aksaritmin, the physicochemical and technological characteristics of the active substance were studied in advance and displayed in the table 1 [4; 5; 6].

Table 1. – Characteristics of aksaritmin substance

Properties	Characteristics
Appearance of powder	Bright-yellow powder with creamy shade and specific odor
Form of substance particles	Anizodiametric polycrystals in the form of prism
Bulk density, kg/m <sup>3</sup>	429 ± 0,015
Flowability, kg/s	1,47 x 10 <sup>-3</sup> ± 0,03
Moisture content, %	3,14 + 0,1
Fractional composition, %	
– 2000 + 1000	11,09
– 1000 + 500	15,16
– 500 + 250	40,13
– 250 + 135	26,92
– 135	6,70

**Results of the study.** It has been established that the substance of aksaritmin is practically not flowable (1.47–10<sup>-3</sup> kg) and has a small bulk density (429 kg/m<sup>3</sup>). According to the results of the test on physicochemical and technological characteristics of the substance, it was evident that it is impossible to receive core tablets without the usage of the excipients.

In our previous studies, the selection process of auxiliary substances in various combinations for obtaining core tablets by the direct compression method was carried out [7].

On the basis of the conducted studies, it was found that the method of direct pressing with auxiliary substances in various combinations for the production of aksaritmin tablets significantly improves



the technological properties of the compressed mass and allows the carrying out of a normal pressing act. However, the quality of these tablets was comparatively low, the indexes like strengths to break and friction didn't meet the requirements, which caused to the doubt on the possibility of obtaining tablets in large-scale production.

In addition, during the research tablets of the aksaritmin the homogeneity of active substance did not meet the requirements due to the small amount of aksaritmin. The uniformity of dosage is a characteristic of the distribution of the active substance per unit of the dosage of the drug. During the operation of the tablet machine, the pressed mass in the batcher was stratified due to vibration of the machine. The stratification of the compressed mass occurred due to the difference in the bulk density of the ingredients, as well as the spread of the particles in size. It can lead to uneven dosing of the active ingredient in the tablets. In order to improve the technological properties of the tablet mass, the possibility of obtaining pellets with the method of moist granulation was studied. In the experiments we used compressed mass of 4 compositions with the subsequent study of the technological properties of the pressed mass and the physico-mechanical parameters of the tablets obtained from them. In this case, sucrose, glucose, lactose, ICC "Introcel", calcium carbonate and disubstituted calcium phosphate were used as fillers in various combinations. As a

disintegrant potato starch was used in amounts up to 1–5%, and as anti-friction agent — 1% calcium stearate was chosen. Unlike the method of direct pressing, the decisive factor that guarantees the high quality of the target product is the conditions for carrying out the moistening process [8]. The most effective technological method of increasing the compressibility of powdered medicinal substances is the input of auxiliary substances possessing a binding and moisturizing ability into the tablet mass. As a moisturizing and binding component, 96% ethyl alcohol, 1–5% starch paste and purified water were used. Four compositions of the tablets of an aksaritmin 0.025 g, were prepared by the wet granulation method and selected for further studies, the compositions presented in Table 2.

The content of the technology lies in the fact that the calculated amount of the substance of the aksaritmin, sifted through a sieve with a pore diameter of 160  $\mu\text{m}$ , is mixed with the required amount of filler and moistened with a solution of the binding substance until mass with optimal moist is formed. The essence of the technology lies in the fact that, the calculated amount of the substance of the ansarhythm, sifted through a sieve with a pore diameter of 160  $\mu\text{m}$ , is mixed with the required amount of filler and moistened with a solution of the binding substance until an optimally moist mass is formed.

Table 2. – Compositions for making core tablet aksaritmin 0.025 g by the method of moist granulation

Ingredients	Compositions			
	№ 1	№ 2	№ 3	№ 4
Aksaritmin	0,025	0,025	0,025	0,025
Lactose	0,022	0,045	0,0458	
Sucrose	0,021	0,0458		0,0908
Glucose	0,0208		0,045	
Starch	0,03	0,003	0,003	0,003
Calcium stearate	0,0012	0,0012	0,0012	0,0012
5% paste of starch	Needed amount	Needed amount	Needed amount	Needed amount
Average mass	0,12	0,12	0,12	0,12

The wet mass is passed through a sieve with a hole diameter of 2500  $\mu\text{m}$ , the granules are laid out in a thin layer on a sheet of parchment paper and dried in an oven at 40–50 °C until getting the optimum residual moisture ( $1.6 \pm 0.4$ ). The dried mass is re-granulated by passing through a sieve with a hole diameter of 1000  $\mu\text{m}$ , the granules are blended with a mixture of potato starch and calcium

stearate that previously sieved through a sieve with a hole diameter of 100  $\mu\text{m}$  [4; 5]. To assess the quality of the prepared granules which is obtained by the wet granulation method and will be used for making tablet drug form of axarhythm 0.025 g, their technological properties were determined and the results are shown in Table 3.

Table 3. – Technological properties of the pressed mass obtained by the wet granulation method

Technological properties	Unit of measurement	№ 1	№ 2	№ 3	№ 4
Fractional composition: – 1000 + 500 $\mu\text{m}$	%	7,04	5,35	6,17	7,21
– 500 + 250 $\mu\text{m}$	%	43,17	39,94	45,46	38,21
– 250 + 160 $\mu\text{m}$	%	47,25	52,84	45,16	51,50
– 160 $\mu\text{m}$	%	2,54	1,87	3,21	3,08
Flowability	$10^{-3}\text{kg/s}$	3,11	4,26	3,87	5,74
Compressibility	H	45,4	35,34	39,85	45,82
Angle of repose	°	52,6	44,18	49,92	27,85
Bulk density	$\text{g/m}^3$	735	558,23	549,82	637,48
Compression coefficient	K	1,98	1,56	1,62	1,17
Moisture content	%	3,2	2,76	2,11	4,6

The evaluation of the technological characteristics of tablets showed that, by using the wet granulation method for tablet making granules with necessary technological properties were obtained and the 4<sup>th</sup> composition for tablets was meet the requirements of GP XI [6].

**Conclusion.** Obtained tablets met the requirements of normative documents and wet granulation was chosen as a main method of obtaining tablet drug forms of aksaritmin.

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## Modern methods of pharmacotherapy of generalized forms of epilepsy

**Abstract:** epilepsy is a chronic poli-etiological disease, manifested by repeated unprovoked, seizures or other seizures, loss of consciousness and is accompanied by changes in personality [8]. Among the forms of epilepsy is one of the most common and dangerous forms of generalized seizures [1]. In recent years, ideas about generalized epilepsy have undergone significant changes: the features of focality in generalized epilepsy and the typical features of idiopathic generalized epilepsy with focal seizures. The relevance lies in the fact that the affinity of these forms is confirmed by genetic studies when one genetic disease, there are a variety of focal and generalized phenotypes in different members of the same family. This, of course, requires the search of new anticonvulsant agents for the successful treatment of various forms of epilepsy, including generalized, contributing to improve the quality of life.

**Keywords:** epilepsy, generalized seizures, focal seizures, quality of life, drug with wide spectrum of action.

**Purpose:** to analyze the literature of the modern methods of pharmacotherapy in generalized forms of epilepsy.

**Material and methods:** analysis of data on the incidence of epilepsy among adult population of the Stavropol territory on 2010–2016. Using data on the number of patients in percentage, we can observe maximum growth by 2015, and begin decline by 2016.

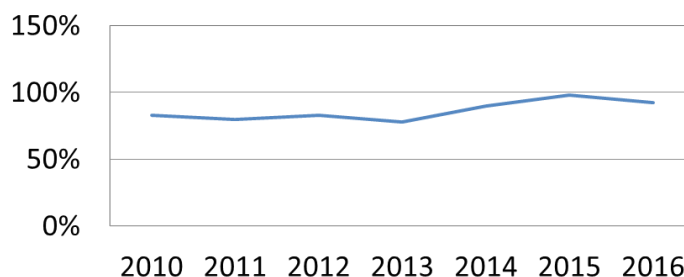


Figure 1.

Using data from diagnoses that were first installed, we can observe the wave-like change of the data, with maximum values in 2014, a downward trend in 2015 and 2016.

**Results:** the incidence of epilepsy is between 50 and 70 per 100 000 population, the prevalence is 5–10 cases per 1000 people. It is believed that 1 or more seizures in the course of life carry about

5% of the population. The prevalence of epilepsy among children is high and in different age populations from 0.3% to 2% (average of 0.7–1.0%) [1; 2]. Generalized seizures – seizures initial clinical and electrophysiological symptoms may indicate involvement in the pathological process of both brain hemispheres. Generalized epi-

leptic seizures in most cases are characterized by loss of consciousness. For generalized seizures include typical and atypical absence seizures, clonic, tonic, klonico-tonic and atonic seizures, as well as mioclonii [5].

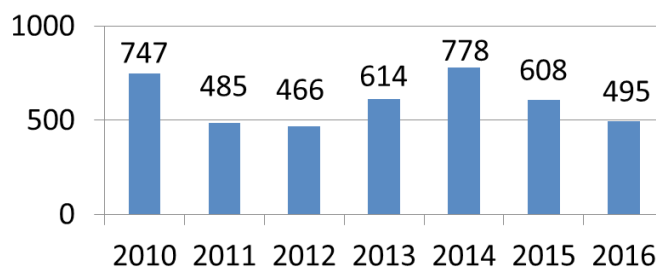


Figure 2.

Basic principles of therapy of epilepsy: individual approach; continuity and duration of treatment; complexity of treatment (etiological, pathogenetic and symptomatic); the continuity of treatment [7]. Treatment should begin with monotherapy; the treatment begins with small dose and gradually increase it until cessation of seizures or symptoms of overdose. In case of insufficient clinical effect of treatment to clarify diagnosis, to check the regularity of drug intake (compliance), and achieving the maximum tolerated dose. As a rule, 70% of patients properly selected monotherapy provides adequate control of seizures [5; 6]. Only in cases of ineffectiveness of properly selected monotherapy (after at least two consecutive times of use of drugs in monotherapy), you can use rational polytherapy (we are talking about drugs of first choice, which is adequate for a specific type of epileptic seizures). In its implementation it is necessary to follow certain rules. Rational polytherapy comes from the concepts of pharmacodynamics, i. e. drug interactions with a substrate of neurons, at the level of neuronal membranes and synaptic formations, which give it its particular therapeutic effect or side effects. It is theoretically feasible to combine drugs with the same mechanism of action, it is advisable to use drugs with complementary properties [10]. With continued seizures monotherapy appropriate timely administration of the second drug. Long-term treatment with two drugs is carried out exclusively at failing an adequate monotherapy. Treatment with three drugs is recommended only after failure of two adequate therapy drugs.

If not precisely defined form of treatment of epilepsy start with a drug with wide spectrum of action — Depakine-Chrono, Depakine chronosphere [3]. Success and drug-free remission for 2–5 years can be questioned on the gradual abolition of the drug. The ineffectiveness of valproate to specify the form of epilepsy and find a more specific drug. Valproate are the drugs of broad-spectrum, i. e. they have high clinical efficacy in various forms of epileptic seizures [6; 7]. At the same time, the maximum effect is seen when exposed to generalized tonic-clonic seizures and absence seizures. The most commonly used derivative of valproic acid in the treatment of epilepsy are sodium valproate (Depakine, Depakine-Chrono), valproic acid (konvuleks) in the form of the calcium salt of valproic acid (convulsofin).

The mechanism of action of valproate is associated with GABA inhibition and increased postsynaptic inhibition, and blockade of the PA – and SA-channels T-type. Depakine is well absorbed. Its bioavailability exceeds 90%. To increase the drug accumulates in plasma within 2–4 h. At the same time, it is noticed that the absorption of valproate when taken after a meal, especially after copious consumption of fatty foods, slows down somewhat. Depakine 70–90% bound to plasma proteins. The half-life is 8–20 hours, Frequen-

cy of administration 1–3 times daily (depending on the release forms of the drug). The time to reach a stable concentration in 5–7 days. Therapeutic concentration in blood corresponds to 50–150 µg/ml. The Average daily dose is 20–30 mg/kg of body weight. The benefit of valproate compared with other traditional antiepileptic drugs (AEDs) is a less pronounced effect on cognitive function. Treatment of valproate patients to keep mental performance, professional activity, the children will not worsen indicators of learning. Scientific Committee on drugs at the American Academy of Pediatrics also confirm the absence of negative impact of valproate used in the medium therapeutic doses on cognitive function and school performance. To dose-dependent side effects include drowsiness, nystagmus, vertigo, ataxia, tremor, headache, hallucinations, increase or loss of weight, increased or decreased appetite, hair loss, menstrual irregularities (oligo – or amenorrhea). In most cases, these symptoms regress when the dose of valproate. Interesting is the fact that weight gain often occurs if the valproate treatment starts at the age of 20 years than after that age, regardless of the length of treatment. Valproate can inhibit hematopoiesis, causing thrombocytopenia, leukopenia, inhibit platelet aggregation, increasing bleeding. In this regard, care should be taken to appoint valproate with anticoagulants or acetylsalicylic acid. They include acute effects develop in a few weeks or months of starting treatment. Symptoms of acute and chronic poisonings are myasthenia gravis, Hypo – or areflexia, convulsions, cardiovascular and respiratory disorders, cerebral edema, metabolic acidosis, hypernatremia, confusion, coma. Treatment is aimed at eliminating hypovolemia. For the relief of the depressive effects of valproate on the nervous system can be used naloxone [3; 6; 9]. Perampanel (Ticona, “eisai”) is the latest antiepileptic drug (AEDs) Registered for use in the adjunctive treatment in patients 12 years and older with focal and secondary generalized seizures. Perampanel was licensed in the US and Europe in 2012 [4; 11]; registered in 2013 and in 2014 entered the Russian pharmaceutical market. Perampanel is a fundamentally different mechanism of action antiepileptic, unlike other AEDs: non-competitive inhibition of the receptor ionotropic AMPA (α-amino-3-hydroxy-5-methyl-4-isoxazolidinone acid) glutamate (major stimulating neurotransmitter in the Central nervous system (CNS)) the drug leads to a decrease in the excitability of neurons. Perampanel is a potent highly selective non-competitive inhibitor of ionotropic AMPA receptors in postsynaptic membranes of neurons at the level of the neocortex and hippocampus [11]. According to many authors, perampanel is the first aed with a specific action on the metabolism of glutamate (glutamate-mediated excitation in CNS) efficacy and tolerability for refractory focal seizures were proven in clinical phase III studies [4]. Today, there are a number of empirical studies that have examined

the use of perampanel in clinical practice as adjunctive treatment for patients with refractory partial epilepsy. The data indicate that perampanel is effective and well tolerated, including in patients with resistant epilepsy and other diseases. Major adverse events perampanel applications include drowsiness and dizziness, rarely-ataxia, aggressiveness, nausea and irritability. Better tolerability, in patients receiving 1 or 2 main probes [11].

In generalized seizures primary generalized tonic-clonic, absence seizures (especially in combination with generalized seizures within the syndromes of idiopathic generalized epilepsy), myoclonic drugs of choice are valproate; carbamazepine and phenytoin contraindicated in absence seizures and myoclonic seizures [5]. Simple absence seizures drugs of choice are valproate and ethosuximide. Atypical absence seizures atonic and tonic seizures often resistant to treatment. In some cases, it may be effective one of the following drugs: phenytoin, valproate, lamotrigine, clonazepam, ethosuximide, phenobarbital, acetazolamide and corticosteroids or their combination. In myoclonic seizures the drug of choice is sodium valproate, also used clonazepam, lamotrigine. In case of insufficient efficacy or poor tolerability traditional AEDs the use of new anti-convulsants (e. g., lamotrigine or topiramate).

Cancellation of PEP should be gradual with regard to mandatory forms of epilepsy and its prognosis, the possibility of recurrence of seizures, individual and age characteristics of the patient (to take into account both medical and social factors). Abolition of anti-epileptic therapy is conducted, as a rule, not less than 2–3 years after the complete cessation of seizures (recommended up to 5 years), under the control of EEG studies [9].

**Conclusions:** Modern approach makes it the preferred choice of drug with wide spectrum of action (help for all types of seizures and forms of epilepsy) taking into account its efficiency, speed of titration, dosage forms, side effects and cost. Among drugs with broad spectrum of activity (valproate, VPA, levetiracetam, lamotrigine, topiramate) as first choice for the initial treatment of generalized epilepsies of priority are the original form of WPA with controlled release of active substance is Depakine Chrono and Depakine chronosphere. Thus, valproate are currently the most used and effective antiepileptic drugs for the treatment of epilepsy, as well as on the basis of available published data sovremenik perampanel is a promising drug for the treatment of partial and secondary generalized seizures with high efficacy and favorable tolerability.

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## Coronary CT angiography and conventional coronary angiography: Comparative analysis of diagnostic capabilities

**Abstract:** Coronary CT angiography is an upcoming alternative for the direct non-invasive assessment of coronary arteries with a fair overall accuracy for diagnosis of coronary artery disease.

**Rationale:** Cardiovascular diseases including coronary heart disease (CHD) remain the leading cause of mortality and disability of population. This matter requires development of early non-invasive methods of atherosclerotic lesions diagnostics. The coronary computed tomography angiography (CCTA) is among these methods. Continual improvement of the CCTA technologies requires data correlation between CCTA and coronary angiography (CA) at each new stage; the fact served as a trigger for the research.

**Materials and Methods:** the study involved 31 patients with clinical signs of CHD and indications for coronary angiography. All patients underwent evaluation of coronary bed by radiological methods: CCTA and classic invasive CA. Diagnostic accuracy of CCTA was assessed using the CA results as a "gold standard".

**Results:** sensitivity of CCTA compared to CA was 80.4% and specificity was 88%. Predictive value of positive test was 80% and predictive value of negative test made 96%. The accuracy made 93%.

**Conclusion:** thus the CCTA has higher accuracy in detection of coronary arteries lesions compared to CA, along with especially significant predictive value of negative result.

**Keywords:** coronary computed tomography angiography (CCTA), coronary arteries, atherosclerotic plaque, invasive coronary angiography.

### Introduction

The achievements of modern medicine resulted in changing of a "leader" among principal reasons of death rate. Cardiovascular diseases (CVD) displaced infectious diseases from a "pedestal" and continue to occupy the first place [1, 5–9]. So the CHD and its complications represent one of the major reasons of morbidity and mortality of population.

Routine methods of CHD diagnostics (clinical examination, ECG, echocardiogram, Holter monitor) make it possible to confirm the diagnosis, evaluate the disease functional class, to determine presence and severity of cardiovascular lesions. However, the ef-

forts to apply the methods for determination of precise location and extent of affection of the coronary arteries by atherosclerosis, and nature and constriction due to soft plaques and calcific plaques, failed [2, 4–9]. It is possible to obtain such data in direct CA study only, up to the present time performed using CA.

This study is the "gold standard", however due to its invasive nature it is accompanied by a risk of complications. The CA is an invasive intervention, therefore the patients and physicians typically deny it [2, 4–9]. In this connection the interest of physicians as well as public opinion in the methods of non-invasive coronary arteries evaluation is very high.



The emergence of possibility to apply coronary computed tomography angiography (CCTA) for non-invasive detection of coronary arteries lesions and determination of stenosis degree created new opportunities for diagnostics of atherosclerotic process. The diagnostic accuracy of the method increases significantly with increase in X-ray tube rotation rate, with reduction of section thickness, increase in number of CT detectors [2, 4–9; 3, 61–65]. Use of 64–320 slice [4, 2485–2490] CT scanners transferred the CCTA from the field of research to the sphere of clinical practice. Today using the procedure it is possible to assess coronary arteries condition non-invasively to identify and characterize atherosclerotic plaques, to determine stenosis degree and to clarify indications for selection of a method for CHD prevention or treatment. CCTA may be performed on an outpatient basis (without anesthesia and sedation), it takes less than 10 minutes and ensures high information capability of diagnostics of coronary arteries lesions [3, 61–65].

A direct comparison of the exercise tolerance test and a 16-slice CCTA conducted by Dewey et al [4, 2485–2490] in 2006 on 80 patients showed significant advantage of CCTA in detection of the coronary heart disease: sensitivity was 73% versus 91%, specificity: 31% vs. 83%;  $p = 0.039$  (CA was used as a reference method). The findings demonstrated that even 16-slice CCTA had a higher diagnostic value than the exercise tolerance tests for detection of coronary artery disease [3, 61–65].

Pugliese F. et al [5, 384–393] comparing results of CCTA on a 4-slice CT scanner and finishing the comparison on a 64-slice CT scanner have noted sensitization of the study from 57% to 99% and increase of specificity from 91% to 96% [2, 4–9].

The current generation of CT scanners enables performance of about 64–320 consecutive cross-sectional images of half-millimeter sections covering from 4 to 16 cm in one x-ray tube turnover (about 227–420 ms). Duration of scanning in one breath-holding spell reduced to 3–7 seconds enabling the examination in almost all patients. Reduction of the time resolution of the method up to 165–210 ms reduces artifacts from movements associated with arrhythmias [3, 61–65; 5, 384–393].

Most studies have shown that 64-slice CT of coronary arteries in the diagnostics of hemodynamically significant stenotic lesion in comparison with CAG has sensitivity of 94–100% and specificity of 95–97%, positive predictive value of 87–97%, and negative predictive value of 99–100% [6, 564–571; 7, 373–379; 8, 797–806; 9, 64–72; 10, 911–916].

Continuous improvement of CCTA technologies requires comparison of CCTA coronary angiography and CT data at each new stage that was the reason of our work.

**Objective.** To compare capabilities of CCTA in evaluation of coronary bed of stents, shunts and their viability compared with CA.

**Materials and methods.** The study included patients undergoing examination in the CT and MRI department of JSC “RSCS named after Academician V. Vahidov” with suspected coronary arteries abnormal changes and the proven CHD.

Diagnostic coronary angiography was performed with ECG monitoring. A puncture of an artery by the Seldinger technique was performed under local anesthesia. Left and right coronary arteries were sequentially catheterized by a diagnostic catheter with injected contrast medium in volume of 5–10 ml at the rate of 5 ml per second. Total amount of contrast agent administered to a patient was 50–70 ml. The study was performed in standard projections.

The CA findings were accepted as the standard definition of significant stenosis. In the segments with more than one stenosis the diagnostic accuracy was determined by more pronounced

reduction in the diameter. Stenosis exceeding 75% was considered as significant stenosis.

CCTA was conducted on 128-slice scanner GE Optima 660 with bolus injection of 60–100 ml of nonionic contrast agent (350 mg/ml) using an injector Missouri Ulrich at a rate of 4–6 ml/sec. Software Auto Coronary Analysis, Auto Ejection Fraction in AWS was used for data processing.

Stenosis exceeding 75% were determined in CCTA as significant ones and were isolated as a separate borderline group of 50–75% (in general calculations these data were considered as significant results); stenosis less than 50% were determined as non-significant ones. In analysis of CCTA significance in diagnostics and degree of stenosis, we proceeded from comparison of these values with the results of coronary angiography. The following segments of the coronary arteries were evaluated: left main coronary artery (LCA), anterior interventricular artery (AIVA), circumflex artery (Cx), right coronary artery (RCA).

Software Statistica 6 (Stat Soft, USA) was used for statistical processing of results.

Assessment of significance of differences between quality indicators of the compared groups was performed using a criterion  $\chi^2$  (chi-square) to compare binary trait frequencies in two unrelated groups of paired comparisons.

Student's t-test for independent samples (after checking the distribution of features against normal distribution by Kolmogorov-Smirnov test) or non-parametric Mann – Whitney U-test were used for evaluation of differences in the values of quantitative indicators.

The critical confidence level of statistical null hypothesis is accepted as equal to 0.05.

Quantitative evaluation of the CCTA method effectiveness in examination of vessels was conducted by calculation of sensitivity and specificity indicators, and the method accuracy using generally accepted formulas:

$$\text{Sensitivity} = \text{TP} / (\text{TP} + \text{FN}) \cdot 100\%, \quad (1)$$

$$\text{Specificity} = \text{TN} / (\text{TN} + \text{FP}) \cdot 100\%, \quad (2)$$

$$\text{Accuracy} = (\text{TN} + \text{TP}) / (\text{TN} + \text{FN} + \text{TP} + \text{FP}) \cdot 100\%, \quad (3)$$

$$\text{PPV} = \text{TP} / (\text{TP} + \text{FP}) \cdot 100\%, \quad (4)$$

$$\text{NPV} = \text{TN} / (\text{FN} + \text{TN}) \cdot 100\%, \quad (5)$$

where: TP — true positive result; TN — true negative result; FP — false positive result; FN — false negative result, PPV — positive predictive value, NPV — negative predictive value.

## Results

The study involved 31 patients, including: 22 men (71%), 9 women (29%). Average age was 58.6 (36–81) (fig.1). The majority of the patients 18 (58%) was under 60 and 1 patient (3%) was over-80.

Average height was 168.7 cm (131–182), average weight – 77.8 kg (52–105), average body mass index: 27.9 (20.8–39.6) (Fig. 2).

Figure 2 shows that the majority of patients: 18 (58%) had overweight; including: 6 patients (19%) had first degree obesity, 3 (10%) – second degree obesity.

The average value of systolic blood pressure (BP) was 135.2 mmHg (110–180), diastolic blood pressure was 82 mmHg (60–110). Average heart rate (HR) – 72.5 beats per minute (60–86).

The analysis of patients by a degree of coronary bed lesion demonstrated that 5 (16%) patients showed single vessel disease, 13 (42%) patients showed two vessel disease, and 12 (39%) patients had multi-vessel disease. Figure 3 shows that women (33.3%) predominate among patients with multi-vessel disease; and men (45.5%) predominate in patients with single vessel disease.

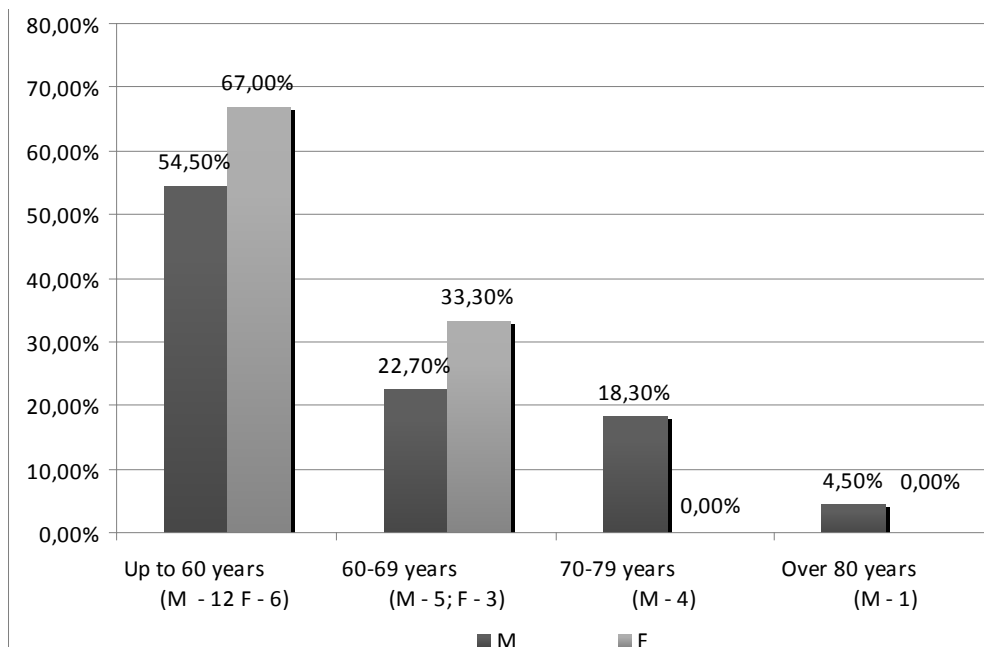


Figure 1. Patients by gender and age (n = 31)

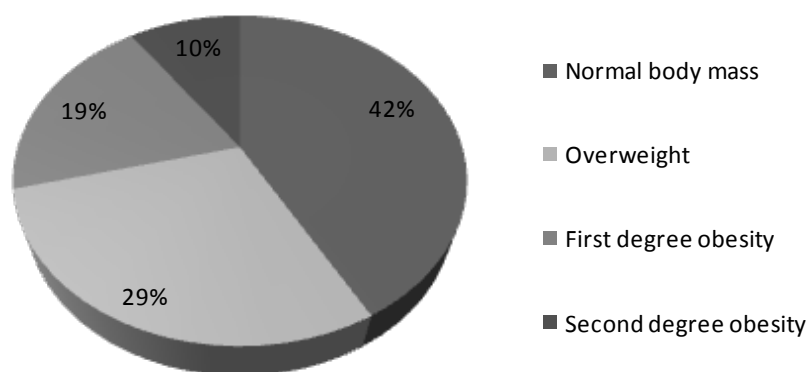


Figure 2. Patients by body mass index (n = 31)

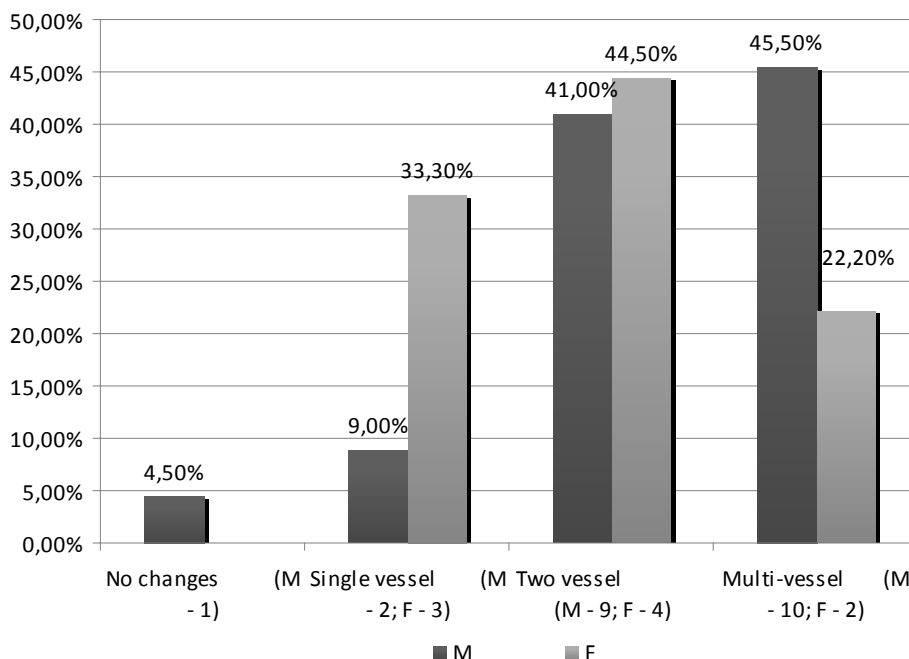
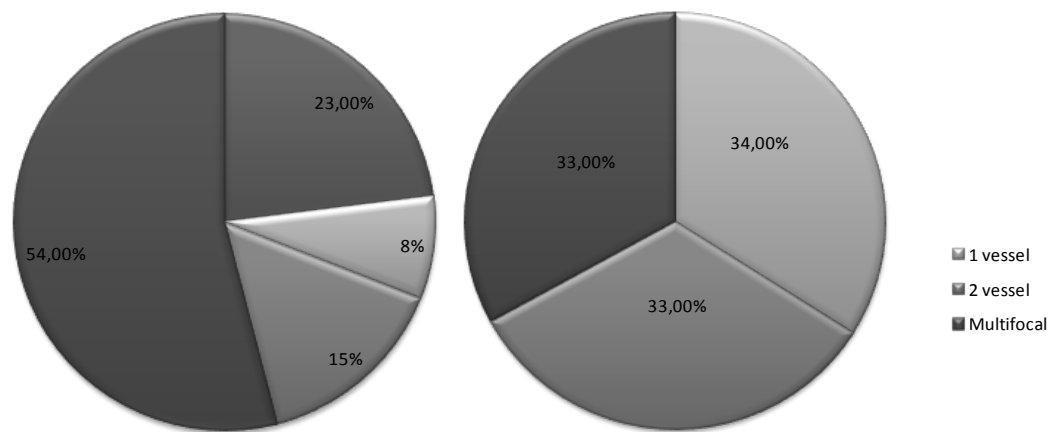


Figure 3. Patients by degree of coronary bed lesion based on gender (n = 31)

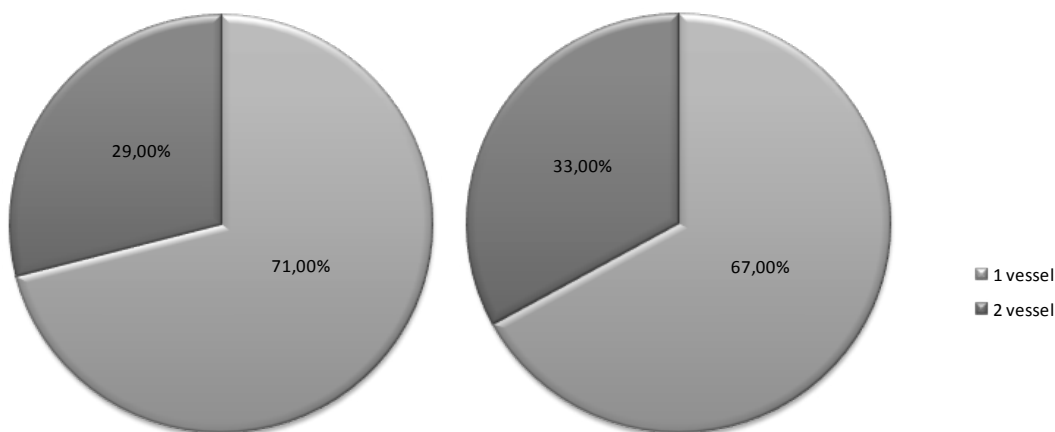
Evaluation of dependence of a degree of the coronary bed lesion on BMI revealed that the higher the BMI, the greater probability of multi-vessel disease, the absence of pathological changes in CA was

observed only in the group with normal BMI (Fig. 4). Dependence of degree of the coronary bed lesion on age is shown in Figure 5.



A Normal body weight (n = 12)

B Overweight (n = 9)



C Obesity I (n = 7)

D Obesity II (n = 3)

Figure 4. Patients by degree of coronary bed lesion based on gender (n = 31)

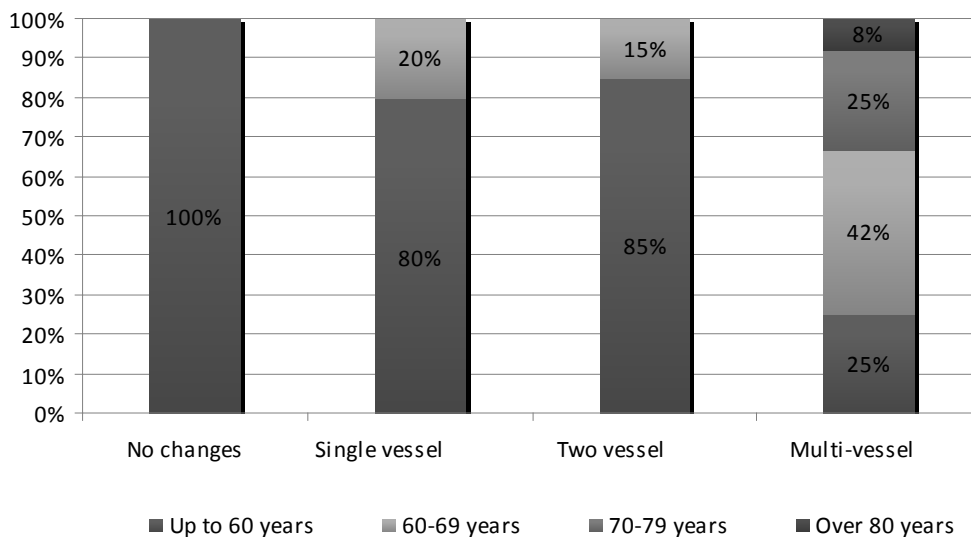


Figure 5. Dependence of degree of the coronary bed lesion on age (n = 31)

Analysis of patients by type of blood supply showed that a left type occurred in 10 (32%) patients, right type – in 6 (19%) patients, a mixed type occurred in almost half of patients 15 (49%). Distribution of patients by type of blood supply based on gender is represented in Figure 6, where no significant differences in the type of blood supply of the myocardium between men and women were detected.

An important advantage of CCTA is an opportunity not only to detect a vessel lumen, but also visualize an artery wall, examine a structure of atherosclerotic plaques: soft – lipid, mixed – fibrous

(soft tissue density), and calcified. The CCTA enables revealing not only significant stenosis and occlusions, but even insignificant plaques. It is believed that the majority of acute coronary syndromes are associated with rupture of soft plaques. Exposure of a plaque to rupture is the higher the greater the amount of lipids. At the same time, high calcium content ensures stability of the plaque. These data give an opportunity to predict the disease development and stability in course of the disease in an individual patient [2, 4–9].

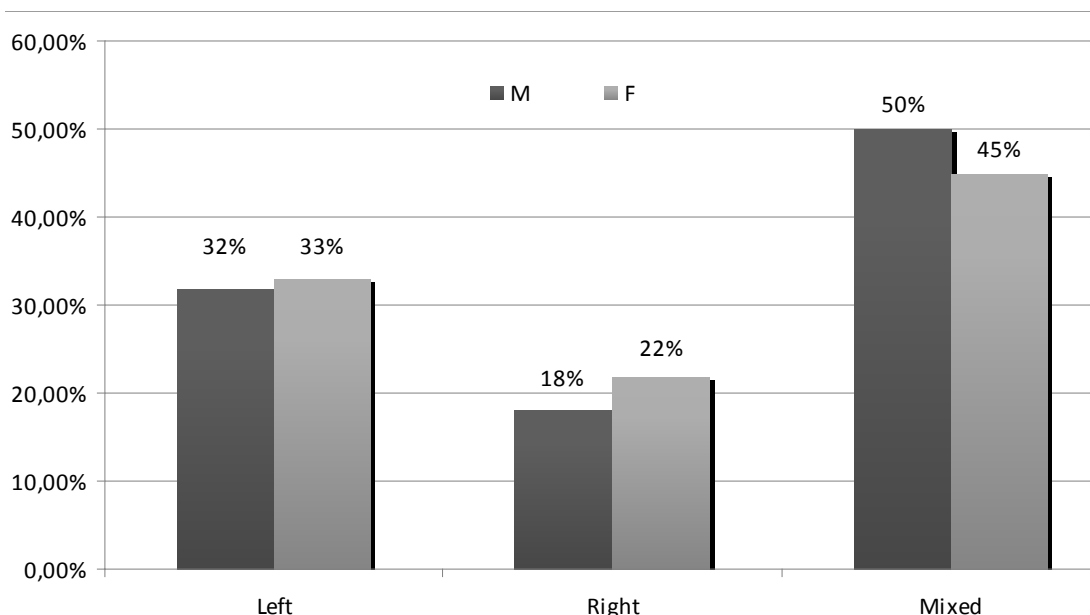


Figure 6. Distribution of patients by of blood supply based on gender (n = 31)

In this connection, in the process of CCTA data analysis attention was paid to a type of atherosclerotic plaques. The plaques were classified as follows:

- 1) a soft plaque: plaque density is less than density of contrasted lumen of the vessel and/or there is no “coronary” calcium;
- 2) mixed plaques: there are calcined and non-calcined elements; calcination is less than 50% of the total plaque area;

3) calcified plaques: calcifications is more than 50% of the plaque area.

Analysis of plaques type showed that mixed plaques 20 (67%) occurred in more than half of patients: 20 (67%); soft plaques occurred in 7 (23%) patients, and calcified plaques occurred in 3 (10%) patients. Patients by type of plaques according based on gender are shown in Figure 7.

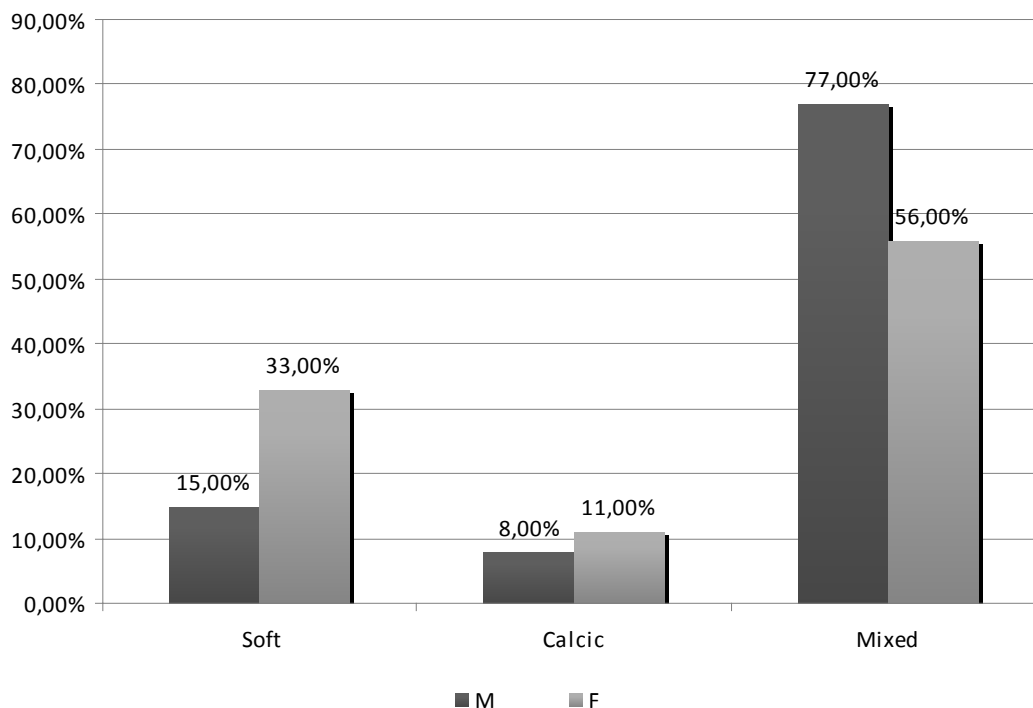


Figure 6. Distribution of patients by blood supply based on gender (n = 31)

Comparison of the data obtained using CCTA and CA based on calculation of number of arteries examined showed that according to the CCTA data the intermediate coronary lesions were detected in 15 cases (12.6%); CA data: 14 patients (11.7%). At the same time, according to CAG data subtotal stenosis was observed more often (in 9 cases (7.5%)), whereas in CCTA this value made 7 (5.8%) cases. CAG also showed a higher proportion of patients with no changes in the coronary arteries: 67 (55.8%) ver-

sus 54 (45%) (Fig. 8). This abnormality was detected in evaluation of coronary arteries occlusion using CCTA in 7 (5.8%) cases, whereas CA data showed 3 (2.5%) cases. Also, hemodynamically not significant stenosis were detected more often in CCTA data: in 30 segments (25%), whereas the CA data revealed this type of stenosis in 21 (17.5%) cases. However, not significant differences in indicators in the process of evaluation of the state of arteries by different methods were noted.



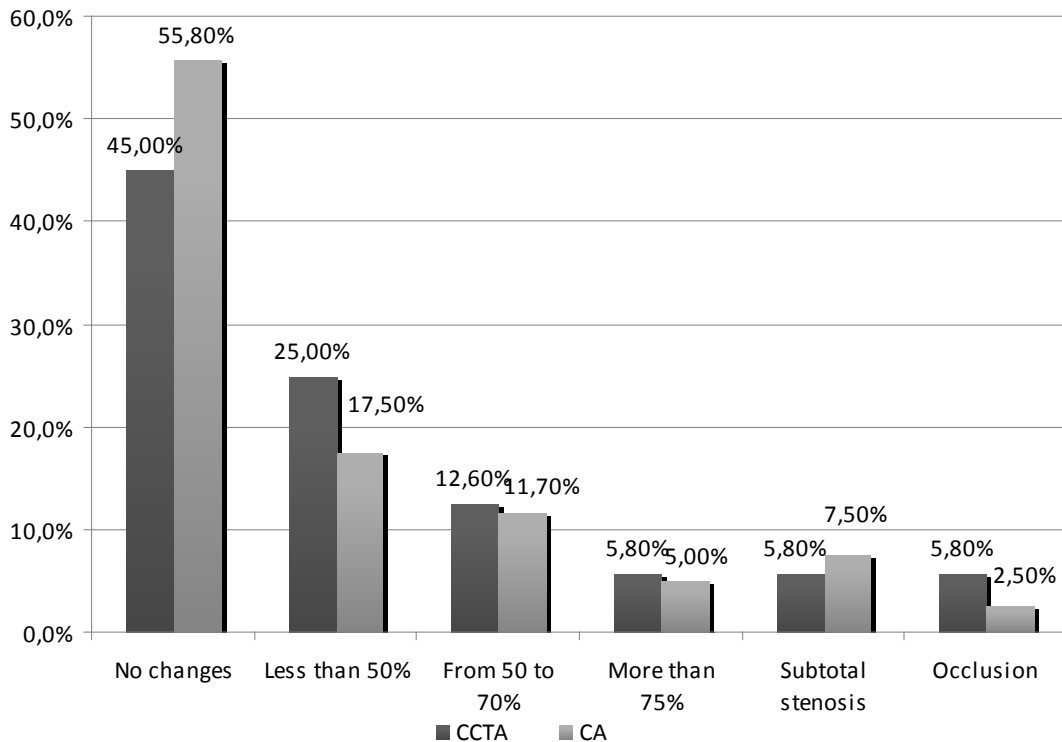


Figure 8. Comparison of coronary arteries study results according to CCTA and CA data based on the total number of arteries (n = 120)

Comparison of CCTA and CA data on LCA state showed that HDN stenosis were identified more often in CCTA data: in 3 cases (9.7%); according to CA data: 2 cases (6.5%); and intermediate stenosis were detected in 2 (6.5%) and 1 (3.2%) cases, respectively. CA results showed no changes in this artery a bit more often: in 25 (80.6%) patients, while CCTA showed 23 (74.1%) of these cases

(Fig. 9). One patient was diagnosed calcification of LCA mouth in CA; the CCTA did not identify the change. Also, no changes were found in one patient in evaluation of LCA stent state using CA and CCTA. Values of other indicators in evaluation of coronary arteries states by various methods in examined patients were identical. No significant cross-sectional differences in the indicators were identified.

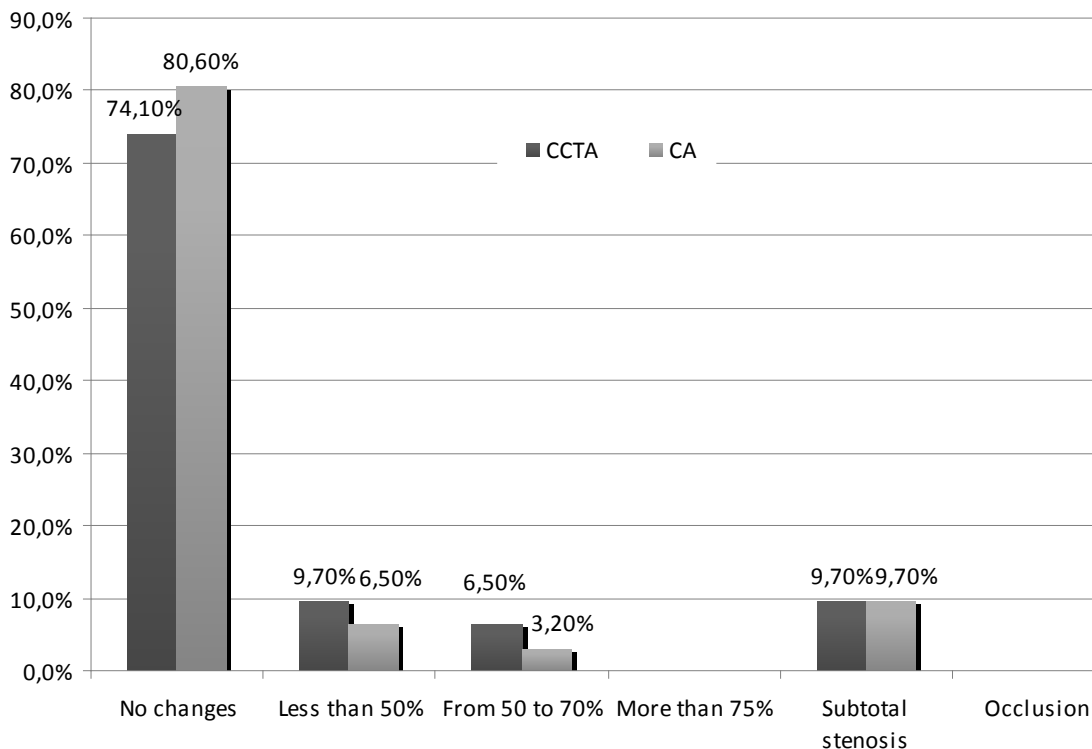


Figure 9. Comparison of LCA study results according to CCTA and CA data in examined patients (n = 31)

Comparison of data on RCA state indicated that one patient (3.1%) showed HDS stenosis per the CCTA data; and according to CA data the pathology was not identified; also in CCTA a RCA

occlusion was detected in 4 (13%) cases; and in CA: 2 (6.4%) cases (Fig. 10). At the same time, according to CA, there were 3 cases (9.6%) of subtotal stenosis of a vessel, whereas only 2 cases

were showed by CCTA (6.4%). CA results showed no changes in this artery a bit more often: 12 (38.9%) patients; whereas CCTA showed no changes in 9 (29%) cases. The incidence of hemo-

dynamically insignificant stenosis was the same. Not significant cross-sectional differences in the indicators were identified.

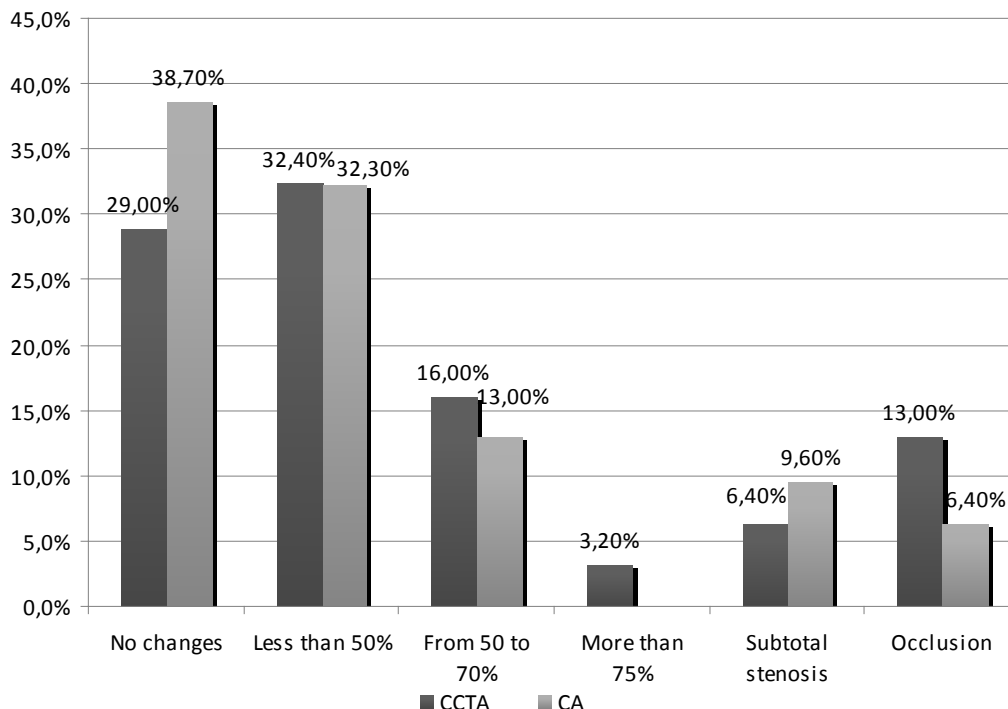


Figure 10. Comparison of RCA study results according to CCTA and CA data in examined patients (n = 31)

Comparison of evaluation of the AIVA state showed that according to the CCTA data the hemodynamically significant stenosis were identified rather less frequently: in 4 segments (14.9%), whereas in CA it was more often: in 5 cases (18.5%). According to the CCTA data hemodynamically not significant stenosis were identified more often as well: in 10 segments (37%), whereas in CA

this type of stenosis was identified in 6 (22.2%) cases. No cases of subtotal stenosis in these segments were detected by CCTA, versus 1 (3.7%) in CA. The incidence of occlusion was 3 (11.1%) in CCTA, when CA it was 1 (3.7%). No changes were identified in 3 patients in evaluation of AIVA stents using CA and CCTA. Not significant cross-sectional differences in the indicators were identified.

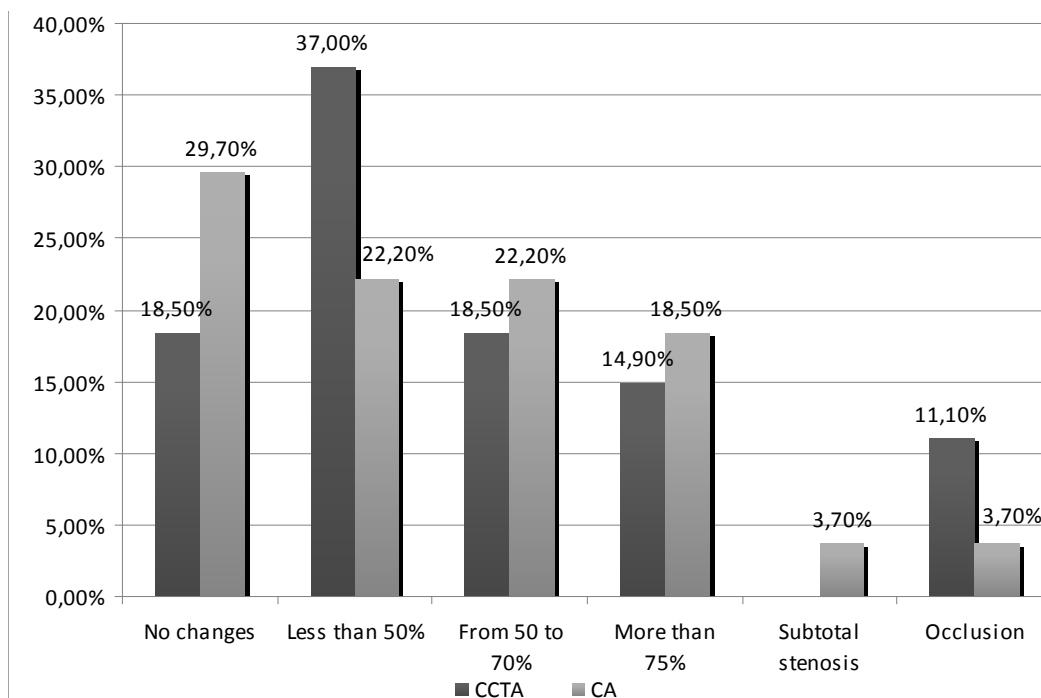


Figure 11. Comparison of AIVA study results based on CCTA and CA data in examined patients (n = 31)

Analysis of results of evaluation of the BA proximal segments state showed that in accordance with the CCTA data hemodynamically significant stenosis were detected in 2 (6.5%) cases, in CA: in 1 case (3.2%). Also, hemodynamically not significant stenosis

were detected more often according to CCTA data: in 7 segments (22.6%), while this type of stenosis was observed in 3 (9.7%) cases in CA. There were no cases of occlusion in these segments, frequency of detection of subtotal stenosis was 2 (6.5%) cases in

evaluation using both methods. No changes were identified using CCTA and CA in one patient in evaluation of BA stent state. CA showed higher incidence of lack of changes in these segments of

the coronary arteries – 22 (70.9%) compared with the results of CCTA: 17 cases (54.7%) (Fig. 12). Not significant differences in indicators in evaluation of BA proximal segments state were noted.

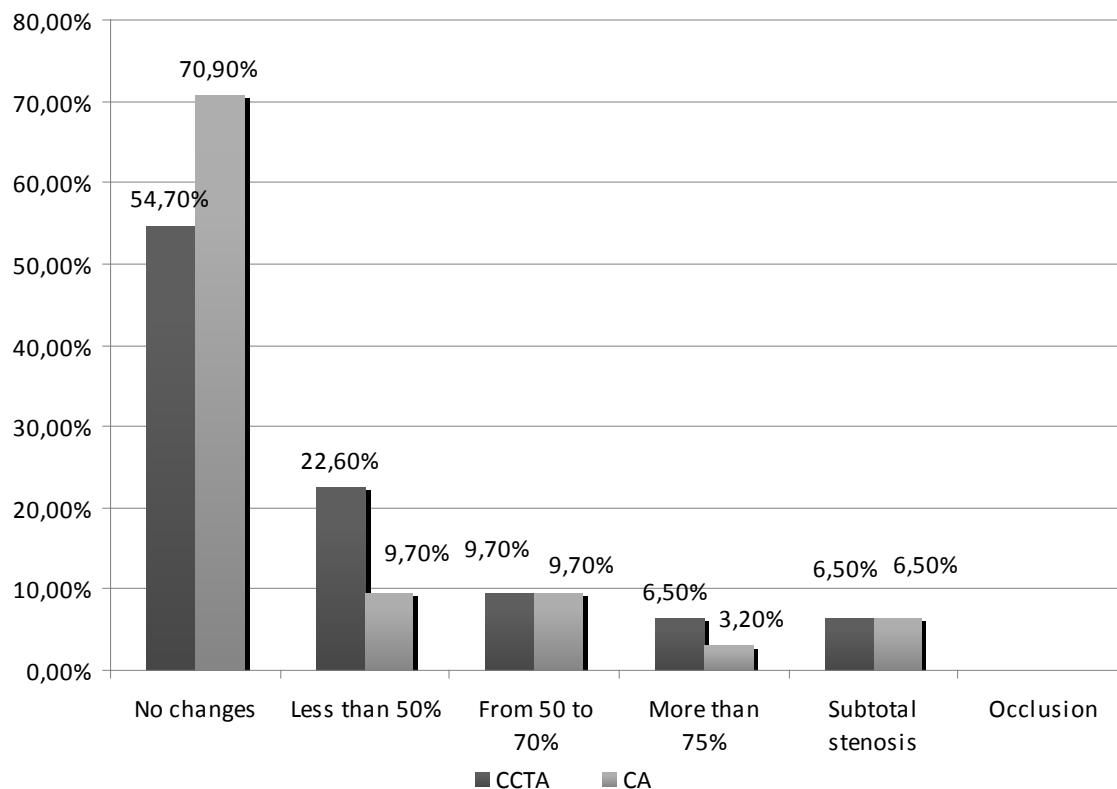


Figure 12. Comparison of BA study results based on CCTA and CAG data in examined patients (n = 31)

Table 1. – Comparison of CCTA results with coronarography data

Total	TP	TN	FP	FN	Total
CCTA	45 (12,4%)	297 (81,6%)	11 (3%)	11 (3%)	364 (100%)
CAG	302 (83%)		62 (17%)		364 (100%)

TP – true positive result; TN – true negative result; FP – false positive result; FN – false negative result

According to our data, CCTA sensitivity compared to coronary angiography was 80.4%, specificity – 88%. Predictive value of a positive test (probability that a patient does have significant coronary artery disease with a positive result of examination) was 80%. The predictive value of a negative test (probability that a patient does not have significant coronary artery lesions with a negative result of examination) was 96%.

The general accuracy was 93%.

#### Discussion

Today, CA is the most informative method in diagnostics of coronary artery stenosis. However, modern CCTA is already acknowledged to be an accessible, highly informative, non-invasive method of coronary artery evaluation [9, 64–72].

The CCTA reliably excludes presence of coronary artery stenosis, and in case of atherosclerotic plaques it helps to determine a treatment strategy.

According to data given in the literature, the CCTA sensitivity is 57–99%, value of a positive predictive test is 87%, value of a negative predictive test is up to 100%; all of these indicators increase with the use of more modern CCTA units and accumulation of lessons learned from the studies [2, 4–9; 11, 1413–1419]. The similar results were obtained in our work.

#### Conclusion

Thus the CCTA has a high diagnostic value in detection of coronary artery lesions. The advantages of the method are its non-invasive nature and an opportunity to evaluate not only a lumen of the coronary artery, patency of coronary artery bypasses and stents, but also condition of vessel wall and structure of atherosclerotic plaque. Considerable reduction in radiation dose on a patient (less than 2 mSv) shall be an additional incentive for development of CCTA in the coming years that will give a chance to use the method as CHD screening.

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## Pathogenic course of general conservative treatment of patients with juvenile glaucoma occurring on the base of progressive myopia

**Abstract:** we observed 44 patients, aged from 11 to 18 years, with progressive myopia, juvenile glaucoma, juvenile glaucoma on the base of progressive myopia. All patients were investigated by biochemical methods to the level of oxyproline in blood serum and on the base of this method there were prescribed the conservative treatment.

**Keywords:** progressive myopia, juvenile glaucoma.

**Introduction.** One of the major pathogenetic links of myopia's progression is a weakening of the supporting properties of the sclera on the base of damage its metabolism and structure [7]. With the progression of myopia in the sclera there occur biochemical, bio-mechanical and structural changes in the anterior segment of the eyeball and then in the rear section of the zone. The collagen framework changes, the fibrils split and as a result of it there the collagen's disaggregation occurs, which leads to the weakening and stretching of the sclera. In the posterior part the eyeball takes elongated shape, there occurs a tendency to increase the intraocular pressure, which further leads to the progression of myopia [1; 3].

In recent years, we study the connection between myopia and glaucoma. In addition, currently myopia has been regarded as one of the risk factors of appearing glaucoma [3,4]. Epidemiological data indicate a high risk of glaucoma in patients mainly with high and middle degrees of myopia [5]. A common feature of the analyzed diseases (myopia and glaucoma) are expressed by trophic changes, celebrated not only in the posterior of the eyeball, but also by the presence of the imbalance of contenting microelements in the sclera [2].

The study of the fractional composition of collagen gives an indication of changes in the catabolic processes, namely the content of the free oxyproline and decreasing total collagen in the tissues. The major metabolite of characterizing the rate of collagen decay is oxyproline. Increasing its content in blood plasma indicates disorders of collagen maturation. Since the free oxyproline is not included in the new chains of collagen biosynthesis, its content in the blood reflects the rate of collagen's decay [6].

**The aim of the research:** set the effectiveness of the general pathogenetic conservative treatment in patients with juvenile glaucoma occurring on the base of progressive myopia

**The materials and methods.** This study presents the results of surveys of 44 patients, aged from 11 to 18 years (mean age 16,8 ± 2,4 years), there are 14 boys and 30 girls. Patients were divided into 3 groups. The 1st group is of 16 patients with JG on the base PM, the 2nd group is of 17 patients with PM and the third group is of 11 patients with JG. Control data of biochemical results were 9 healthy subjects of different ages. Each patient is examined with the use of traditional ophthalmological methods (visometry, tonometry, tonography, static and kinetic perimetry, biomicroscopy, Gonioscopy using a three-mirror Goldmann gonioscopy). The daily tonometry of patients received every two hours, starting from 6–00 to 22–00 for a more detailed study of the IOP fluctuations. Also there were carried ultrasound echobiometry (Oftascan mini-B «Alcon»), computerized perimetry (Peritest-300, Russia) and also on the testimony the Doppler of brachiocephalic vessels and vessels of the eyeball. In the blood serum there were determined the total index of connective tissue metabolism of oxyproline. To determine the amount of oxyproline in the blood serum the work was divided into two stages. In the preparatory phase proteins of collagen of various fractions subjected to alkaline hydrolysis in sealed glass ampoules. Hydrolysis was carried out daily, 3, 5, 10 and 15 days of a complete hydrolysis time. Further, hydrolysates of proteins were evaporated in a ceramic dish at water bath. The dry residue was dissolved in a precise volume of water. The resulting solutions were



taken to determine the amount of oxyproline. The second stage used a method based on oxidation of Oxyproline by chloramine B and by condensation of products of oxidation with Ehrlich's reagent to produce a product colored red with further determination of the optical density on the photoelectric colorimeter concentration of PCC-2 with a wavelength of 590 nm. This is the most simple and fairly accurate method of determining the oxyproline by Bergman and Loxley, which modifies the method of Stegeman.

All studied patients received general conservative treatment to stimulate collagen formation, which was conducted with the use

of drugs such as aktovegin 200 mg pro injectionibus or solkoseril 2.0 ml № 10 in muscular with cofactors of collagen synthesis — the solution for injection 5% ascorbic acid C № 10, zinc-containing drug — komplivit by 1 tab. per 1 time a day for 4 weeks, Magne B6 per os by 1 tab. 3 times a day for two months and glycinum by 1 tab. 3 times a day under the tongue for 2 months.

#### The results and discussion.

We studied the level of oxyproline in the blood serum of patients which reflects the breakdown of proteins of the extracellular matrix, the results of which are shown in table 1.

Table 1. — The content of oxyproline (mmol/l) in blood serum (M±m)

Groups	Number of patients	Content of oxyproline (mmol/l)	P
Juvenile glaucoma on the base of progressive myopia	16	30,68±0,96	<0,001
Progressive myopia	17	26,03±1,05	<0,05
Juvenile glaucoma	11	24,98±0,17	<0,01
Control group	9	18,61±0,68	

Studies have shown a significant increase in the level of oxyproline in patients with PM 1.4 times and 1.34 times with JG and with combined pathology (JG on the base PM) is of 1.65 times relatively to healthy individuals.

Analysis of oxyproline level, depending on the stage of glaucoma and myopia showed the presence of a certain relationship. Thus, patients with PM, we observed differences depending on the degree of myopia in a significant increase of 1.4 (up to 26.03 ± 1.05 mmol/l) and 1.48 times (up to 27.02 ± 1.10 mmol/l), respectively, for medium and high degrees of myopia relatively to the values of healthy individuals.

In patients with combined pathology (JG on the base PM), as the progressing of disease, we observed an increase the levels of oxyproline in blood serum. If the level of oxyproline at the developed stage of JG significantly increased in 1.54 times, accounting for 28,65 ± 0,67 mmol/l, then at the far-advanced stage — in 1.89 times, accounting for 35,14 ± 1,10 mmol/l.

In patients with combined pathology (JG on the base PM) at the developed stage, raising the level of the oxyproline was 1.46 and 1.57 times, and in far-advanced stage — 1.75 and 1.87 times, respectively to the middle and high myopia. As can be seen from the data, the presence of the accelerated catabolism of collagen at the PM leads to increase connective tissue of dysplasia, as it was setting the stage for the rapid progression of the juvenile glaucoma.

Researched results are consistent with the clinical data of patients in groups. Thus, during the initial examination of patients with

JG and installed combined JG on the base PM, the typical complaints were visual discomfort (27%) and fatigue, especially when working near (45%) and the deterioration of twilight vision (61%). In the group with combined pathology (JG on the base PM) there was reported a more rapid progression of myopia (82%) in patients relatively with PM.

On the basis of researches of the level of oxyproline pointing to lack of collagen in the ECM system, in general conservative treatment of patients with combined pathology (JG on the base PM) were included the drugs of replacement therapy and drugs, which stimulate collagen formation along with local antihypertensive drugs. This treatment was carried out to all researched patients. We have not noted the above-mentioned side effects of medicines which would lead to stop the treatment.

Analysis of achieved results of the level of oxyproline in the blood serum in patients after treatment showed that the therapy helped to a significant decrease in the level of oxyproline in patients with combined pathology (JG on the base PM) and PM. Moreover, a significant reduction of oxyproline levels in patients with developed stages of glaucoma and far-advanced stage is statistically significant when compared with the results of researched patients with the comparison group regardless of the degree of myopia. Consequently, there achieved conditions for the suspension and reduction of collagen decay in ECM system (Table 2).

Table 2. — Data of the oxyproline level (mmol/l) in combined pathology (JG on the base PM) and PM before and after treatment.

Stages of glaucoma	Degrees of myopia			
	Middle		High	
	Before treatment (mmol/l)	After treatment (mmol/l)	Before treatment (mmol/l)	After treatment (mmol/l)
Developed	27,23 ± 1,13	24,42 ± 1,08	29,19 ± 1,28	25,02 ± 1,23
Far-advanced	32,57 ± 0,77	25,49 ± 0,79	36,68 ± 1,15	27,63 ± 1,16
Progressive myopia	25,03 ± 1,05	23,91 ± 0,86	27,02 ± 1,10	25,01 ± 1,10
Control group	18,61±0,68 mmol/l			

So a decrease of oxyproline in blood serum of patients with combined pathology (JG on the base PM) was observed more at the developed (on average, 4,17 ± 0,05) and far-advanced (on average, 9,05 ± 0,09) stages of glaucoma with high degree of myopia comparing the data of combined with the developed (an average of 2,18 ± 0,03) and far-advanced (an average of 7,08 ± 0,04) stages of glaucoma. Relatively these changes have been identified in patients of comparison group with PM downward at middle (an average of

1,12 ± 0,02) and high degree of myopia (an average of 2,01 ± 0,04) relatively on the data before treatment ( $p \leq 0.05$ ). In the control group of healthy individuals observed changes regarding the reduction were not statistically significant.

#### Conclusion

In our opinion, the accelerated disintegration of the extracellular matrix components, especially collagen, the severity of which depended combined on the stage of JG and on the degree

of myopia, is one of the pathogenetic mechanisms of the myopia progression.

Conservative general therapy of patients with juvenile glaucoma occurring on the base of progressive myopia, regardless of the stage of development of glaucomatous process, requires

the inclusion of pathogenetically directed treatment, the purpose of which is to slow and/or stabilization of the intensity of the destruction of collagen ECM system, prescribing substitution therapy and stimulating collagen formation on the base of antihypertensive therapy.

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## Morphological and functional features of thyroid gland of posterity under in utero and early postnatal exposure to pesticides

**Abstract:** The effect of prenatal and early postnatal exposure to pesticides of new generation (cyhalothrin and fipronil) on the postnatal dynamics of the formation of pituitary-thyroid system of offspring has been studied. It was found that the impact of pesticides through the mother's body slows down the rate of formation of thyroid follicles offspring. Violation of the pituitary-thyroid system is manifested in the form of hypothyroidism. All this leads to a thorough monitoring of thyroid function in pregnant women and newborns at increased risk of environmental pollution by pesticides.

**Keywords:** pesticides, thyroid gland, pituitary-thyroid system, postnatal ontogenesis.

**Introduction.** Many chemicals that are widely used in households, agriculture and industry have a negative effect on the endocrine system. They are now united under the name of "endocrine-disrupting substances, EDs or endocrine disruptors, ED" [5; 6]. This term together those chemicals that in humans and animals change the processes of synthesis, secretion, transport, metabolism of natural hormones and thus lead to a breach of the hormonal homeostasis [5]. That action has a number of pesticides, including the latest generation, household chemicals, some drugs [3; 4; 5]. The high sensitivity of the thyroid to the EDs has caused the need for a separate group of chemical substances (thyroid-disrupting chemicals), which predominantly inhibit the processes of synthesis, transport and receptor function of thyroid hormones [7; 9]. To date, can be considered a proven role of EDs in the pathogenesis of several diseases, such as obesity, atherosclerosis, hypertension and coronary disease, some of reproductive dysfunction and other related metabolic disorders and hormonal homeostasis [5; 6; 9]. Analysis of the literature shows that the majority of studies on the mechanisms and effects of EDs on the endocrine system, unfortunately, animals and adults carried out on mature individuals [3; 4]. There are only a

few reports that such ED substances have a more pronounced pathogenic effect in childhood and adolescence, disrupting the growth and formation of the body in the postnatal period [8]. However, many questions of adverse effects of environmental chemicals on the developing human body and animals remain unsolved.

The purpose of research is identifying the structural and functional features of postnatal growth and the formation of the thyroid gland in the offspring in terms of pesticide exposure via the mother's body.

**Materials and methods.** Experiments were performed on nulliparous, white adult female rats, which were divided into 3 groups of 30 animals each. Two groups of animals for 30 days daily per os obtained respectively pesticides cyhalothrin or fipronil. The third group receiving only the same volume of sterile saline served as a control. The following day, the females were coupled with healthy males for fertilization. Exposure of pesticides was continued incessantly during pregnancy and until the end of the lactation period. Pregnancy was monitored for the presence of sperm in vaginal smears. Offspring obtained from the experimental and control females were examined in dynamics on days 3,7,14, 21 and 30 after

birth. Thyroid gland (TG) was studied by morphometric and electron microscopic techniques [1; 2]. Furthermore, in the offspring was determined level of thyroxine ( $T_4$ ), triiodothyronine ( $T_3$ ) and thyroid stimulating hormone (TSH) of pituitary. All figures are statistically processed using the software package with the calculation criteria Student, reliable differences were considered satisfying  $P < 0.05$ .

**Results and discussion.** It was revealed that chronic intoxication the mother's body significantly reduces the growth rate and the formation of the thyroid in a postnatal ontogenesis. Starting from 1–3 days after birth, the average total number of follicles on the cut area in the experimental animals was significantly lower compared with the control. The areas of follicles were also significantly lower than the control. In the dynamics of postnatal growth the formation of morphometric parameters of thyroid in all studied groups, respectively, increased. However, the rate of growth of the thyroid as a whole, the formation of new follicles in the gland in the experimental animals lagged significantly from the control. Of particular note is the low specific indicators thyrocytes in all terms of the study, indicating a decrease in the secretory activity of the cells. The resulting morphometric data were fully confirmed by the results of electron microscopic studies.

Under the electron microscope the thyroid follicles of control animals at all stages of observation were typical structure. Thyrocytes of control animals were in various stages of the secretory cycle and generally characterized by ultrastructural signs of high activity and lysosomal synthetic devices. The cytoplasm of individual thyrocytes contained a considerable amount of granular endoplasmic reticulum cisterns. The nuclei of cells in the heart or were slightly shifted to the basal part of thyrocytes. The results of electron microscopic studies of thyroid in progeny derived from experimental animals, revealed the existence of certain submicroscopic changes in general reveal a violation of certain phases of the secretory cycle thyrocytes. Along with thyrocytes with intact ultrastructure, they are often in the wall of the follicle cells were found with obvious signs of disorganization profiles granular endoplasmic reticulum in the form of excessive expansion and reduce the density of the internal content.

Sometimes the cytoplasm of individual thyrocytes looked like a giant vacuole with a light content, the kernel and a few organelles were pushed to the cell periphery. Often detected thyrocytes with

marked swelling of mitochondria with enlightenment of their matrix and disorganization of the cristae or with their complete vacuolization. Much less in some thyrocytes failed to note the emergence of a few lipid droplets of different sizes, which hardly occurred in the control group. Finally, in the progeny of the experimental animals more frequently in comparison with the control were determined thyrocytes with clear signs of apoptosis and destruction of cytoplasmic organelles. It can be concluded on the basis of electron microscopy data, and in the formation of thyroid growth in chronic intoxications, along with a reduction in the proliferation of thyrocytes, there is a strong upset their differentiation process. This is indicated by the signs of destruction submicroscopic organelles responsible for synthesis, transport and cleavage of thyroglobulin. All of this eventually leads to thyroid dysfunction and disruption of metabolic processes in the developing offspring. Functional disorders in the pituitary-thyroid system offspring have been confirmed by determining the level of  $T_4$ ,  $T_3$  and TSH in the offspring in the dynamics of postnatal development. It was shown, that in the offspring, subjected to the pesticide through the mother (in utero and through breast milk) developing thyroid dysfunction, it appears as hypothyroidism, despite the fact that the concentration of pituitary TSH significantly exceeds the control group. Comparative evaluation of the negative effect of the studied pesticides showed that fipronil has a stronger negative impact on the structure and function of the thyroid gland offspring compared to cyhalothrin.

#### Conclusions:

1. The impact of the new generation of pesticides (cyhalothrin and fipronil) through the mother's body leads to structural and functional impairment of formation of the pituitary-thyroid system offspring. This significantly slowed down the pace of the formation of thyroid follicles offspring.
2. Identified disorganization granular endoplasmic reticulum and mitochondria destruction of thyrocytes represent morphological substrate of developing thyroid dysfunction.
3. Violation of the functions of the authority manifests itself in the form of hypothyroidism with decreased levels of thyroid hormones  $T_4$  and  $T_3$ , in spite of the increase in the concentration of thyroid-stimulating hormone pituitary.
4. All this necessitates careful monitoring of thyroid function in pregnant women and newborns in a high risk of environmental pollution by pesticides.

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## Association of extracellular DNA concentration with efficacy of treatment of patients with fibroids of uterus

**Abstract:** Despite considerable progress in studying of various myomas of a uterus, a number of key questions remain insufficiently studied, such as identification of genetic factors and the primary molecular defects leading to development and evolution of changes of a uterus, early diagnostics. It is now established that small amounts of DNA found outside the cells and, especially in the human blood plasma. The quantity of extracellular DNA (ecDNA) can essentially increase at a number of diseases what probably to consider as an early sign of corresponding pathologies. In this article the analysis of quantitative violations of ecDNA, exposure of genotypes of patients, is conducted with different hysteromyomas. The results showed that ecDNA can be used in practical gynecology solutions for early diagnosis of problems, and predicting the course of monitoring the effectiveness of treatment of this disease.

**Keywords:** extracellular DNA; genetic factors; early diagnostics; prognostication; efficiency of treatment.

Myoma of uterus is benign tumor, growing from immature immaturity of vascular walls of uterus [1]. This pathology is on the first step among benign tumors of genital organs, at the same time each tenth patient of gynecology suffers from myoma of uterus [2; 3]. Numerous hypotheses, explaining development and course of different fibroids of uterus, are under discussion and have not been studied enough, that gives difficulties in the designing of new organ-preserving methods of treatment and decreases the efficacy of treatment of this disease [4; 5].

At present, the issue of treatment of uterus myoma is the most difficult and debatable [6]. The choice of treatment method is determined by many factors such as features of pathogenesis, form and grow rate of tumor, age, absence or presence of children in woman and etc. [7].

Till the certain time it has been considered that DNA has been only in cellular structures: especially in nuclei of cells and some amounts in mitochondria, where it performs function of carrier of genetic information. The possibility of using of extracellular DNA in medicine is conditioned by changes of its concentration, changes in structure and molecule sizes of extracellular DNA of blood plasma, appearance of different mutations. The interest to extracellular DNA (ecDNA) immeasurably increased after it was revealed that a number of it might increase in several diseases, which can be taken into account as early sign of corresponding pathologies [8]. It gave the real practical meaning for the studying of circulating nucleic acids.

**The aim of this work:** To study efficacy of treatment of patients with uterus fibroids according to concentration of extracellular DNA.

### Materials and methods of investigation:

As the materials of investigation it was used the blood of women with varies fibroids of uterus. The blood in volume 1 ml was taken with the help of catheter from ulnar vein into vacuum tubes from 0,5 M EDTA. It was studied 40 blood samples of women of different ages.

**Extracellular DNA** was revealed by method described in previous work [9].

**Analysis of molecular mass** of extracellular DNA has been done by method of electrophoresis in 2% of agarose gel. The gel has been painted with ethidium bromide and taken the photo on trans-lyuminator through passing beams of UV. As markers of length it was used gidrolizatrestriktaza of phage DNA  $\lambda$  (HindII/EcoRI) and DNA ladder 100.

### Results and discussion.

Early and timely diagnostic of fibroids of uterus may completely replace the surgical intervention, to determine tactics of conservative way in treatment and plan the forms of prevention. At present, it was established that the content of ecDNA changed in diabetes, myocardial infarction, system lupus erythematosus, rheumatoid arthritis, glomerulonephritis, hepatitis and other pathological conditions [10,11]. Pathogenic processes, leading to the increasing of ecDNA rate in blood in diseases, almost have not been studied. But it was received preliminary data about presence of correlation between concentration of ecDNA in blood and developing of some pathology. Qualitative and quantitative composition of ecDNA, detected in blood plasma, is system indication which can characterize the course of pathological processes in organism. The most interest is aroused by dynamics of changes in content of ecDNA, rather than single meaning of their concentration in blood. In order to determine of informational content of qualitative and quantitative changes of ecDNA for estimation of treatment efficacy it was made comparative analysis on change of ecDNA concentration, in the course of treatment one can make conclusion about efficacy of treatment.

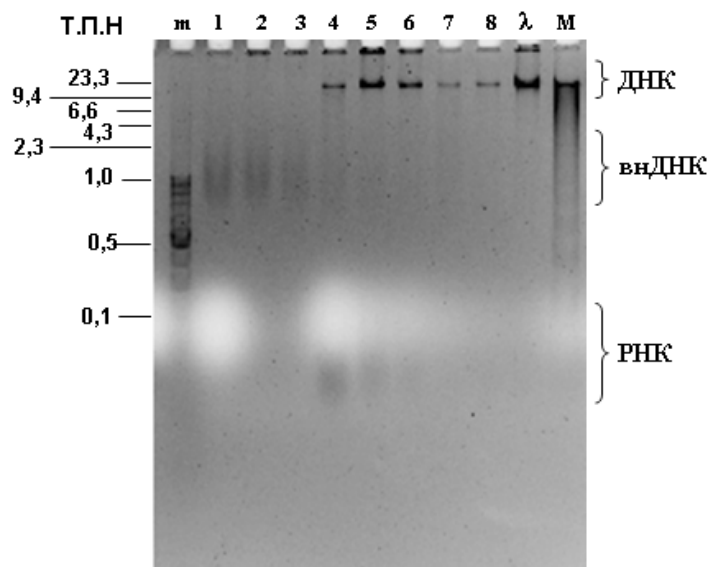
It was observed 30 patients of different age category with various forms of fibroids of uterus. Patients were divided into 3 groups: 1<sup>st</sup> – simple myoma of uterus (8 patients); 2<sup>nd</sup> – progressive (fast growing) myoma of uterus (10 patients); 3<sup>rd</sup> – symptomatic myoma – disturbance of menstrual cycle, symptom of bleeding (12 patients). As a control there were healthy donors (10 donors). From plasma samples of peripheral blood of women with fibroids of uterus it was revealed ecDNA. It was decided to get blood plasma, free from cellular elements, with the help of centrifugation of the whole blood on low speeds (3000 sp/min, 800g). Centrifugation of blood on high speeds leads to destruction of part of cells and hit of nucleic acids in plasma. Besides it, high speed centrifugation may result the distortion of qualitative and quantitative composition of extracellular nucleic acids. On the 1<sup>st</sup> picture it was given the electrophoresis of revealed ecDNA.

Concentration of ecDNA was determined with spectrophotometry and PCHR method in real time, as the using of this method is thought to give more detailed results. On the 2<sup>nd</sup> picture it was presented data of PCHR analysis in real time. By data of PCHR analysis the quantity of ecDNA in blood plasma of patients with fibroids of



uterus increases in comparison with healthy donors. With the help of PCHR to polymorphic marker C3435 T of MDR1 gene it was determined reliable differences in quantity of ecDNA. Analysis of

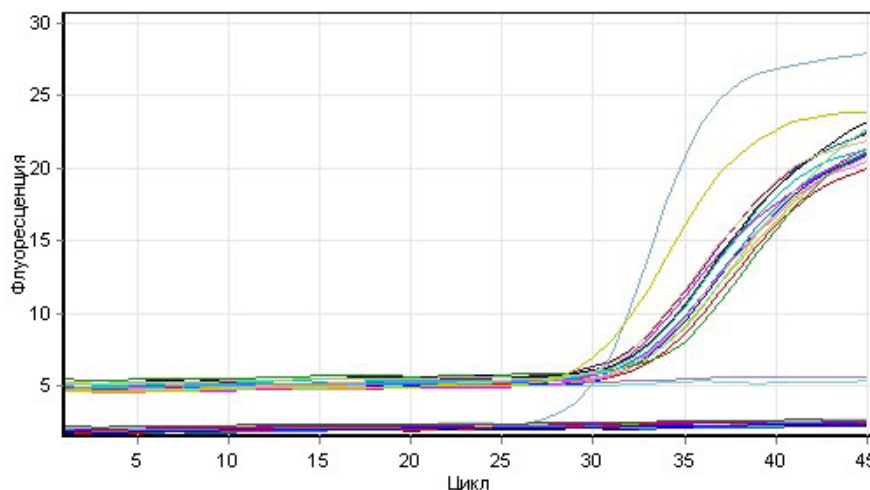
concentration of ecDNA of blood plasma may serve as effective indication in differentiation of patients with fibroids of uterus and may be used for monitoring of treatment.



Picture 1. Electrophoresis of ecDNA in 1,5% of agarose gel

Qualitative changes of ecDNA of blood plasma as well as quantitative are system indications, capable to characterize the course of pathological processes. In fibroids of uterus it has happened not only quantitative changes in ecDNA of plasma, but also qualitative

changes, i. e. happening of DNA fragmentation and appearing of low molecular nucleosome DNA. Determination of nucleosome in circulating blood may be used for diagnostics, stage of disease and monitoring of treatment of various fibroids.



Picture 2. Quantitative estimation of ecDNA concentration in blood plasma of patients with fibroids of uterus by polymorphic marker C3435 T of MDR1 gene, with the help of PCHR method in real time

In the table 1 it was given data of quantitative and qualitative composition of ecDNA in blood plasma of women in different fibroids of uterus.

Table 1. – Content of ecDNA in blood serum in fibroids of uterus

№	Group	Pathology	ecDNA, ng/ml	Size of fragments
1	n = 5	Control healthy donors	29,00 ± 1,07	20–23
2	n = 5	Simple myoma	85,0 ± 0,91	10; 6; 3,5; 1,5; 0,8
3	n = 9	Progressive myoma (fast growing)	148,6 ± 1,0	4,2; 1,2; 0,9; 0,8; 0,7; 0,6; 0,5; 0,4
4	n = 5	Symptomatic myoma (DMC, bleeding)	65,8 ± 1,55	21; 6; 4,2; 0,2

$P < 0,05$  in comparison with control

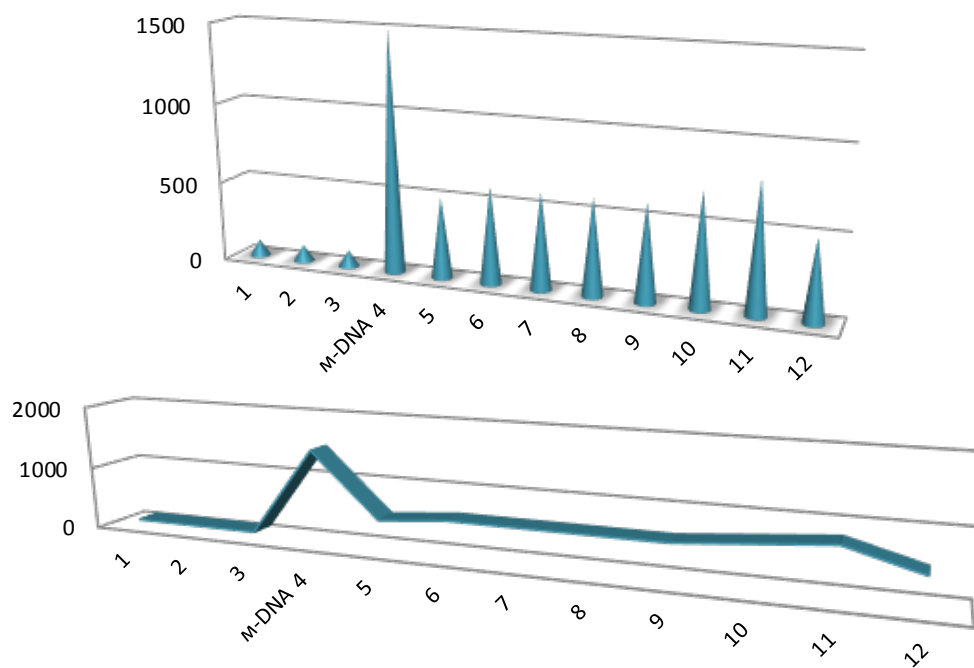
Presented results have showed that reliable increasing of concentration of ecDNA in blood plasma of women happens in different fibroids of uterus. It should be noted that the greatest emission of ecDNA in blood plasma happens in progressive myoma of uterus (148,6 ng/ml). Increasing of concentration of ecDNA allows making a conclusion about progressing of disease and about possibility

of using of this factor as biomarker of treatment efficacy. The data of table show that in healthy donors ecDNA has been presented with high molecular fragments of DNA, and in fibroids of uterus with fragments of degraded DNA.

For determination of treatment efficacy of patients with fibroids of uterus it was performed comparative analysis of concentration

of ecDNA in blood plasma of patients in dynamics. We presented that increased concentration of ecDNA of blood plasma was associated with efficacy of treatment and unfavorable outcome, which showed progressing of disease and potential importance of ecDNA as biomarker of forecast of clinical course of disease. After performing of conservative treatment in some patients with fibroids there have been decreasing of concentration of ecDNA, which shows the efficacy of making treatment. Rising of concentration of ecDNA indicates on clinical manifestations of progressing of disease and non-effective treatment, i. e. there are not results of performing therapy in patients. On the 3<sup>rd</sup> picture it was presented data about

changes of concentration of ecDNA in patients in dynamics. This picture shows that patients with symptomatic myoma have good results in the treatment (1, 2, 3). In patients with fast growing progressing myoma of uterus the concentration of ecDNA does not decrease after the treatment, i. e. the treatment is not effective (6–11). On the basis of received data we came to conclusion that the change of concentration of ecDNA in patients with fibroids of uterus may be used as marker of efficacy of treatment. Estimation of content of extracellular DNA in plasma of patients in fibroids of uterus may help for the prediction of disease course and in the monitoring of efficacy of treatment.



Picture 3. Dependence of treatment efficacy of patients with fibroids of uterus on concentration of ecDNA

Using of ecDNA, taken from plasma samples or **serums** of patients' blood with fibroids of uterus, may have important role in the improvement of methods of **diagnostics, monitoring** and forecast of disease course, increasing of treatment efficacy in patients with fibroids of uterus.

On the basis of received data one may make a conclusion that increased content of ecDNA in blood plasma of patients with fibroids of uterus is associated with the stage of disease, unfavorable outcome, inefficacy of treatment and genotype of patient.

#### Conclusions:

1. It has been established the correlation between concentration of ecDNA of blood plasma and developing of different forms of fibroids of uterus.

2. It has been shown that analysis of ecDNA concentration of blood plasma of patients with fibroids of uterus may be used as biomarker of efficacy of performed treatment in the observing of patients in dynamics and early diagnostics.

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## Studying of influence of patients' genotype on content of extracellular DNA in treatment process of fibroids of uterus

**Abstract:** Despite considerable progress in studying of various myomas of a uterus, a number of key questions remain insufficiently studied, such as identification of genetic factors and the primary molecular defects leading to development and evolution of changes of a uterus, early diagnostics. It is now established that small amounts of DNA found outside the cells and, especially in the human blood plasma. The quantity of extracellular DNA (ecDNA) can essentially increase at a number of diseases what probably to consider as an early sign of corresponding pathologies. In this article the analysis of quantitative violations of ecDNA, exposure of genotypes of patients, is conducted with different hysteromyomas. The results showed that ecDNA can be used in practical gynecology solutions for early diagnosis of problems, and predicting the course of monitoring the effectiveness of treatment of this disease.

**Keywords:** extracellular DNA; genetic factors; early diagnostics; prognostication; efficiency of treatment.

Myoma of uterus is benign, well delimited capsulated tumor, which develops from smooth muscle cells of cervix and body of uterus [1]. This pathology is on the first step among benign tumors of genital organs, at the same time each tenth patient of gynecology suffers from myoma of uterus [2; 3]. Studying of genetic factors of developing of uterus myoma in women of all age groups is actual problem of modern medicine. It is due to the myoma of uterus and its complications remain one of the main reasons of radical operations in modern gynecology practice. Myoma of uterus is a cause of infertility, uterine bleeding, and disturbance of functions of pelvic organs [4]. In spite of significant progress in the studying of this pathology, a number of issues such as identification of genetic factors and primary molecular defects, leading to the development and evolution of myoma changes of uterus, and early diagnostics have not been studied enough.

The most difficult problem is treatment efficacy of fibroids of uterus. At present, the issue of treatment of this pathology is most difficult and under discussion [6]. Selection of treatment method is determined by many factors such as features of pathogenesis, forms and grow rate of tumor, age, absence and presence of children in woman and etc. [7].

In spite of significant progress in the studying of fibroids of uterus, the issue of treatment efficacy of this pathology is the most actual. One of the obstacles for successful and effective treatment of fibroids of myoma is developing of drug resistance of myoma cells to the action of medications. Making of genetic test before the therapy, which, with high reliability, will predict the probability of developing and severity of side effects in each patients is the solution of this situation. As fundamental information it will be used the genotype of patients resistance to therapy, which will be determined by us with the help of PCHR methods. For the performing of effective treat-

ment of fibroids of uterus it will be considered individual reaction of organism on the action of medications.

**The aim of this work:** The studying of influence of individual peculiarities of the organism of patients with fibroids of uterus on the content of excDNA.

### **Materials and methods of investigation:**

As the material it was used the blood of women with different fibroids of uterus. Blood in volume 1 ml was taken with the help of catheter from ulnar vein into vacuum tube with 0,5 M EDTA. It was studied 40 blood samples of women of different age.

**Extracellular DNA** was revealed from 1 ml of peripheral blood, taken from ulnar vein and transferred in plastic tubes deposited with EDTA – Na<sub>2</sub>. Blood was centrifuged in 4° C consistently 1,5 thousands revolutions per minute (rpm) – 10 minutes, in 3 thousands rpm – 15 minutes, in 5 thousands rpm – 15 minutes. After centrifuge, 400ml of blood serum were taken from tubes in new sterile tubes. It was added previously 100mkg/ml of RNase A to the serum and incubated during 1 hour in 37° C, then it was processed with proteinase K (50 mkg/ml), incubation was 1 hour in 37° C. After enzymatic treatment, it was added to the blood serum 200ml of lysis buffer [100mM TrisHCl, pH 8,0; 25mM EDTA, pH 8,0; 0,15 M NaCl; 0,7 M β-mercaptoethanol; SDS (final concentration 2%). Lysis was performed on the cold 3 minutes (over ice). Then aliquots were deproteinized 15 minutes in 1,5ml of mixture of phenol/chloroform [1:2] with followed by centrifugation in 5 thousands rpm, 15 minutes in 4° C. Supernatant was transferred into new tubes. It was completed 1/10 volume of 3 M of sodium acetate, pH 5,2 and 2,5 volume of cooled 96% ethanol, then the tubes were left on the night in –20° C. Denatured preparations of excDNA were centrifuged in 5 thousands rpm – 30 minutes, 4° C. Sediment of excDNA preparations was washed in 1ml of cooled 70% ethanol with followed by centri-



fuge in 13 thousands rpm during 15 minutes in 4 °C. Preparations of excDNA were kept in -20 °C. They were dissolved in 100mcl of DNA – binding fluorescent dye (DBFD), comprising 10mM trisHCl, pH 8,0; 1mM EDTA, pH 8,0; ethidium bromide 0,5mkg/ml. Solutions of excDNA were measured on spectrophotometer at wavelength 350 nm. The intensity of fluorescence was increasing linearly with concentration of excDNA.

**Genotyping on polymorphic marker C3435 T of MDR1 gene** was performed by method of PCHR–PLRF with the using follow markers:

**Primers:**

Primer MDR1–C3435 T for: 5' – GAT CTG TGA ACT CTT GTT TCT A – 3'

Primer MDR1–C3435 T rev: 5' –GAA GAG AGA CTT ACA TTA GGC – 3'

Primer, control: IS711: 5' – TGCCGATCACTTAAGGGC–CTTCAT – 3'

**Performing of PCHR**

At work it was used primers for MDR1 gene encoding protein of drug resistance P–glycoprotein. As control it was used primers of reference gene GAPDH. PCHR was performed on the cycler «BioRad» USA. Before performing RCHR, products of PCHR were kept in -20 °C.

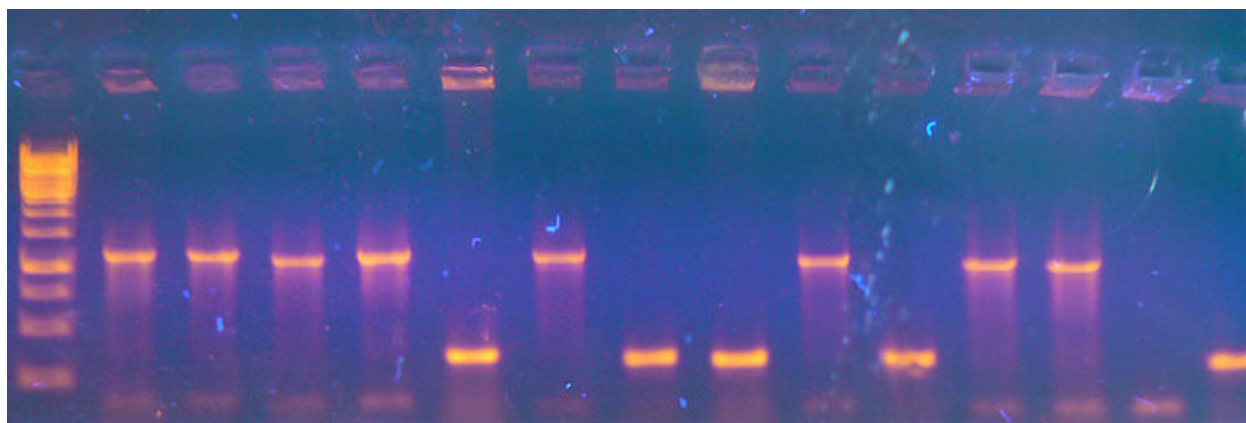
**Electrophoresis of PCHR products** was performed in 2% agarose in TAE buffer, 100 B, 1h. Then agarose gel was painted during 15 minutes in the solution of ethidium bromide (0,5mkg/ml). Results of electrophoretic analysis in gel were observed visually

through passing beams of UV on cycler «Bio–Rad». Agarose gel has been scanned after electrophoresis on densitometer, which analyzes intensity of glow of PCHR–products. Received bands image was processed with the help of computer densitometer (Gel–Pro–Analyzer 4.0).

**Results and their discussions**

In spite of significant progress in the studying of fibroids of uterus, the issue of treatment efficacy of this pathology today is the most actual. One of the obstacles for successful and effective therapy of fibroids of uterus is developing of drug resistance of myoma cells to the action of medications. Making genetic test before the therapy, which, with high reliability, will predict the probability of developing and severity of side effects in each patients is the solution of this situation. As fundamental information it will be used the genotype of patients resistance to therapy, which will be determined by us with the help of PCHR methods. For the performing of effective treatment of fibroids of uterus it will be considered individual reaction of organism on the action of medications.

It was carried out the determination of genotype of patients with fibroids of uterus. With the help of PCHR method it was synthesized excDNA with using of specific primers for MDR1 gene. Synthesizing of excDNA was processed by restriction enzyme Sau3A. After amplification and restriction it was performed electrophoresis in 2% agarose gel with the adding of ethidium bromide. Restriction fragments were visualized in ultraviolet translyuminator. Genotyping was made on the base of analysis of polymorphism of restriction fragments length.



Picture 1. Electrophoregram of genotypes by polymorphic marker C3435 T of MDR1 gene

Tracks: 2, 3, 4, 5, 7, 10, 12, 13 – TT genotype; tracs:6,8,9,11,15 – CC genotype PCHR product was split by restriction enzyme Sau-3AI. Electrophoretic separation of genotypes of PCHR products was performed in 2,0% agarose gel 2,5% agarose, 100V, 3h. M – marker of DNA ladder, 100kb.

Polymorphic marker C3435T of MDR1 gene, representing itself replacement in nucleotide sequence in the position of 3435 cytosine to thymine, is most clinically informative. Therefore, we made investigation using only this marker. Genotypes were determined on the criterion of presence of restriction site in the position 3435. On the 1<sup>st</sup> picture it was presented electrophoregram of genotypes on polymorphic marker C3435 T of MDR1 gene. It was revealed genotypes TT – resistance and CC – sensitive to the action of medications. Results of genotyping have shown that heterozygous genotype CT – medium sensitivity to the action of medications has not been revealed among patients of this group. It is known from literature data that in carriers of TT – genotype the disturbance of expression of MDR1 gene has been noted at the level of transcription, which leads to increasing of amount of glycoprotein–P and

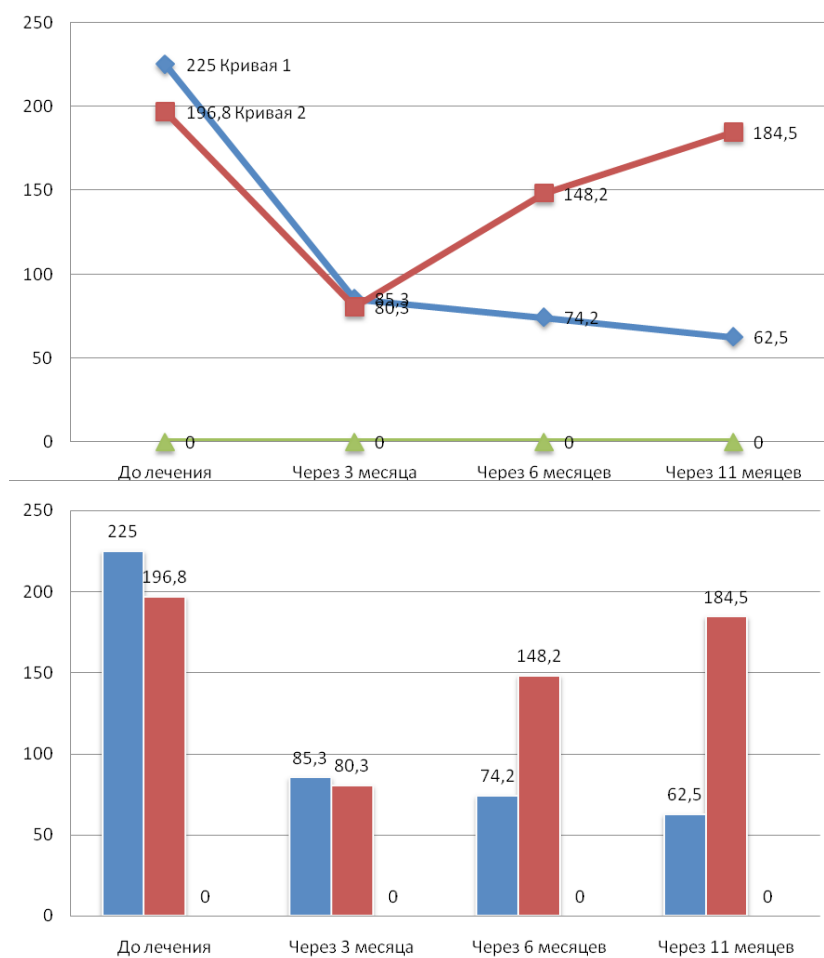
rapid removal of medications from organism. As a result, the carriers of TT – genotype have probably significant decreasing of concentrations of medicines in blood, which leads to the developing of undesirable drug reactions, side effects and decreasing of treatment effect [11, 12].

It was interesting to study how genotype of patient influenced on concentration of DNA. On the 2<sup>nd</sup> picture it was presented data about changes of concentration of excDNA depending on the genotype of patient in progressing myoma of uterus. From the data, it is seen that in patient with genotype CC (curve 2), i. e. sensitivity to the treatment the concentration of excDNA decreases and gains normal level. In patient, who has homozygous genotype (curve 1), i. e. resistance to therapy the concentration of excDNA does not decrease and after 3 courses of treatment stays almost on the same level as before the treatment. On the basis of received data one may come to conclusion that identification of genetic features in patients on polymorphic marker C3435 T of MDR1 gene allows to predict the character pharmacological response. Genotyping, i. e. identification of individual responsible reaction of patient organism on the



action of medications gives possibility to increase efficacy and safety of applying of medications dose, multiplicity of the introduction,

replacement of medicines and real opportunity to individualization of pharmacotherapy in patients with fibroids of uterus.



Picture 2. Concentration of excDNA depending on the genotype of patient in progressing myoma of uterus

Thus, our studies, aimed to the analysis of quantitative disorders of excDNA and identification of genotype of patients with different fibroids of uterus, may be used in gynecology practice for the solving

of problem of early diagnostics, prediction of course and monitoring of treatment efficacy of this disease.

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## Microflora of biotopes as a leading etiological factor at oral diseases in children

**Abstract:** Being a source of foreign genetic information, microbes and viruses regardless of the exact place of the invasion during their life damage tissues' integrity and as a result provoke the development of disease of various severity. Oral cavity stands on the second place by the number of microbes with different level of virulence. Dysbiotic abnormalities cause biofilms formation in various oral biotopes. The associated links within biofilms facilitate the increase of microflora virulence. Poor oral hygiene stimulates microbes' growth and reproduction. Oral cavity is not homogeneous by the number of microbes' settlements. Most of microbes concentrate in areas with special anatomical features. Stomatitis, dental caries, parodontitis and periodontitis are the most frequent clinical manifestations of high active microflora. Monitoring of oral biocenoses allows to perform the analysis of their variety and structural adjustments, which is vital for optimal treatment and prevention of oral diseases.

**Keywords:** Microbes, Anaerobe, dental caries, oral hygiene, children, stomatitis.

The most frequently spread somatic diseases are stomatological ones. Every child knows what stomatitis or dental caries is. The main factor, which causes stomatitis in children is the oral bacterial flora [1]. Normally *the inflammatory response* is prevented by specific and nonspecific factors of antimicrobial resistance of *oral mucous membrane, as well as biochemical and immunological features of saliva. The forming of oral micro-biocenosis is a multilevel process, closely linked with the regularities of dento-facial system development. Transient microbes constantly getting into the children's mouth by dirty hands, toys and kisses of relatives damage micro-ecological and adaptive microbes' interrelations with both environment and each other.*

Clinical picture of inflammation in the particular patient depends on the factor, causing it as well as on the individual conditions of the patient, complementing this pathological process [2].

Understanding of the oral pathological processes in children requires knowledge of topographic, anatomic, histological and histochemical processes, often sharply changing depending on age.

There are distinguished 3 periods of age, which significantly differ by constitution and characterize the dynamic of main mucous structures development: the infants – a period of age from 10 days to 1 year, early childhood – the children from 1 to 3 years old and childhood – primary (4–7 years old children) and postprimary (8–12 years old children). With age the factors of local mucous protec-

tion improve [3; 4]. And, in spite of quality changes of oral mucous membrane structures during childhood, characterized by principally new ways of defence building, stomatitis is remains a very frequent disease among the children.

Catarrhal, acute and aphthous stomatitis are very similar by their symptoms among the children, therefore inadequate complex treatment of a trivial form of stomatitis often provokes its shifting into aphthous stomatitis [4; 5; 6]. Up to now, the etiology of stomatitis, specifically which factors are dominant and which propose the development of the disease remains open to discussion.

The identification of the exact etiology of stomatitis in each particular case defines the system of medications and preventive measures as well as the prognosis of the disease recurrence.

**The aim of investigation** is to enhance the effectiveness of stomatitis diagnostics among the children and specify biocenotic interrelations of staphylococci and streptococci, colonizing biotopes of cheek, interdental gingiva and sublingual area.

**Materials and methods.** The study included the analysis of 60 kids from 7 to 10 years old from the first and second health groups with negative allergic anamnesis. Parents of children, who took part in the analysis, gave their informed agreement. At the moment of investigation 50 kids had no complaints typical for oral inflammatory diseases. 10 kids had from 2 to 5 elements of inflammation of various oral locations.

The children were divided into 3 groups by the frequency of stomatitis occurrence. The first group included healthy kids with no complaints specific for stomatitis in anamnesis in any period of oral system development (20 patients). The second group included 20 kids having a single visit to the doctor related to stomatitis in anamnesis.

20 kids visiting stomatologist once a year with complaints on painful aphthae in the mouth formed the third group. Investigation included various methods of analysis such as questioning, oral examination, probing, percussion, hygiene state identification and microbiological analysis of oral biotopes.

During oral examination, probing and percussion there were identified oral cavity and tooth lines conditions, carious and noncarious changes of hard tooth tissues. The oral hygienic state was estimated by Green-Vermillion (OHI-S) method. Dentobacterial plaque was colored by «Dinal» tablets due to their simple use and no emotional impact on children. Dentobacterial plaque was esti-

mated on teeth, belonging to different groups, on surfaces, the most effected by dental deposits. Numeric representation of diagnostic criteria in this method of analysis [7] characterized the area of dental deposit. The intensity of caries at this stage of mixed dentition was estimated by KP and KPU analysis [8].

The bacteriological analysis was conducted according to general rules of clinical microbiology with definition of aerobic and facultative anaerobic microbes and quantitative estimates of the results (primary seeding was done from  $10^{-1}$ – $10^{-5}$  dilutions of analyzed tissues (material)), required to extract conditionally-pathogenic bacteria [9]. Clear cultures of facultative anaerobic bacteria were grown using five-percent blood agar in exsiccators. The extracted cultures were identified after the number of isolated colonies on solid mediums counting. For bacteria identification a complex of morphological, cultural and biochemical patterns according to Berdgi classification (1980) was used. Biochemical identification of clear streptococcus, enterococcus and staphylococcus cultures was fulfilled by Lachema test systems.

Density of microbes' population was expressed in colony-forming units (CFU). The material for bacteriological analysis was taken from surfaces of buccal mucosa, interdental gingival mucosa within the teeth used for hygiene index analysis, oral floor mucosa and aphthae.

Based on the analysis of caries intensity patients in groups were divided as following: the first group was characterized by low active caries and good oral hygiene, satisfactory structure of hard tooth tissues, correct forms and sizes of the erupting permanent teeth, oral mucosa of standard rose-pink color without any pathological changes. In the second group 8 patients from 20 had medium intensive caries, 4 had high intensive caries and 8 had low intensive caries, oral hygiene in the group was mainly satisfactory. No changes of hard tooth tissue structure, no pathological changes of oral mucosa were revealed within the investigation. The third group included 10 patients having oral aphthae at the moment of the investigation. Aphthae were located mostly on buccal mucosa within the necks of teeth, covered by soft dental deposits, and were covered by fibrinous pellicle, tender to palpation. Average value of OHI-S index in this group was equal to 0,5, which corresponded to good oral hygiene level, 2 patients had OHI-S index equal to 1,2. 12 patients had caries of high intensity and 8 patients had caries of medium intensity.

Table 1. – Average values of identified microbial CFU and corresponding frequency of occurrence in gingival margin among the patients of the 1<sup>st</sup>, 2<sup>nd</sup> and 3<sup>rd</sup> groups at  $10^{-4}$  dilution

Microobes	1 <sup>st</sup> group (20 patients)		2 <sup>nd</sup> group (20 patients)		3 <sup>rd</sup> group (20 patients)	
	Average, m (CFU)	Occurrence rate ( $0 < p < 1$ )	Average, m (CFU)	Occurrence rate ( $0 < p < 1$ )	Среднее, m (CFU)	Occurrence rate ( $0 < p < 1$ )
S. salivarius	9,57	0,7*	13,57	0,7	16,33	0,9
S. sanguis	10,55	0,9	12,25	0,8	15,7	1,0
S. mitis	9	0,7	16,14	0,7	12,0	0,9
S. mutans	12,33	0,6	13,5	0,8	19,0	1,0
S. viridans	0	0	0	0	4,75	0,4
S. aureus	3	0,1	4	0,1	4,28	0,7
S.haemolyticus	0	0	0	0,1	3,2	0,5
Lactobacter	7,66	0,3	17,13	0,8	16,75	0,8
Enterococcus	9,0	0,5	14,71	0,7	8,7	1
Candida spp.	3	0,1	4	0,5	5,75	0,8

\*The occurrence rate characterizes the number of patients in a group which have a particular microbe (0,7 corresponds to 70% of patients, namely 14 from 20 analyzed patients of the 1st group with S. Salivarius revealed).

**The results of investigation** demonstrated low caries intensity and good oral hygiene in 100 per cent cases among the patients of

the first group, as well as chronicity of the existing pathological sites on hard tissues. Patients of the second group had caries of low and

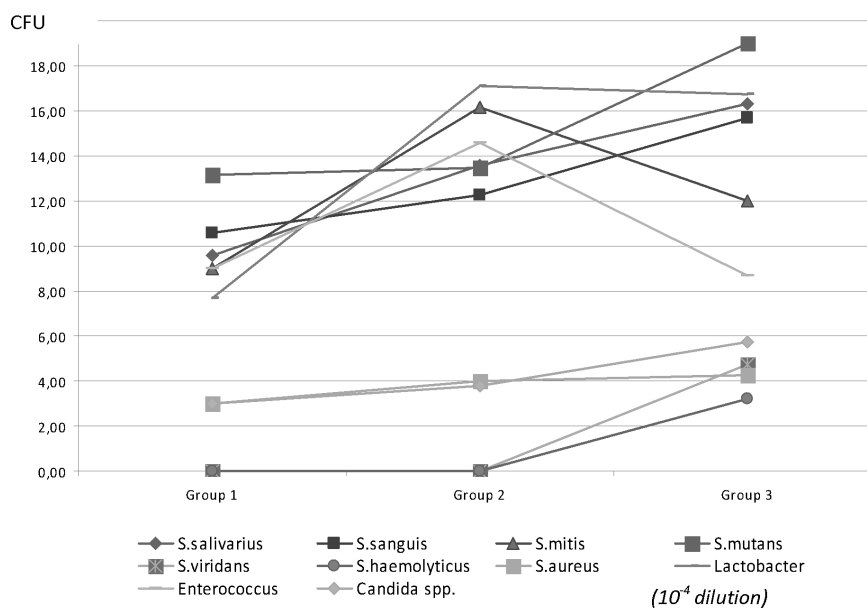
medium intensity in 80% of cases and caries of high intensity in 20% of cases. Hygienic index was low in 100% cases. Among the patients of the third group poor hygiene was shown in 20% cases, 80% of patients demonstrated satisfactory hygiene level. However, together with good oral hygiene 40% of children in this group had caries of medium intensity and 60% of patients – caries of high intensity. Pathological processes on hard teeth tissues revealed acute development in 90% cases.

The conducted bacteriological analysis revealed a multiple variety and high density of CPU in all analyzed biotopes at primary inoculation. Streptococci appeared to be the most representative microbes.

High CFU density of streptococci remained up to  $10^{-4}$  dilution of biomaterial, taken from interdental gingival mucosa and gingival margin in all 3 groups of patients (table 1, pic.1). Among streptococ-

ci there were identified *Streptococcus mutans*, *S. sanguis*, *S. salivarius*, *S. mitis* and *S. viridans* with index of dominance equal to 100%.

At  $10^{-4}$  dilution *S. salivarius* and *S. Mitis* were identified in 70% cases among the patients of the 1<sup>st</sup> and the 2<sup>nd</sup> groups, in the 3<sup>rd</sup> group *S. salivarius* and *S. mitis* were detected in 90% cases. *S. Sanguis* and *S. Mutans* were found in all patients of the 3<sup>rd</sup> group and 80% patients of the 2<sup>nd</sup> group at  $10^{-4}$  dilution. Data analysis based on parametrical criteria of Dannel with the 1<sup>st</sup> group used as control revealed a significant difference of the 1<sup>st</sup> and 3<sup>rd</sup> groups by *S. salivarius* (test significance level  $\alpha = 0,05$ , number of degrees of freedom  $v = 29$ , number of compared groups  $l = 3$ ), *S. Sanguis* ( $\alpha = 0,05$ ,  $v = 35$ ,  $l = 3$ ) and *S. mutans* ( $\alpha = 0,05$ ,  $v = 29$ ,  $l = 3$ ) indexes. The revealed difference was also proved by nonparametric criteria Kruskall-Wallis and Dann.



Picture 1. Average values of identified microbial CFUs in analyzed biotopes of gingival area ( $10^{-4}$  dilution)

Analysis of biomass in first inoculation demonstrated high density of staphylococcus. Typing allowed to extract *Staphylococcus aureus* and *S. haemolyticus*. The highest frequency of occurrence of these microbes appeared in the 3<sup>rd</sup> group of patients (pic.2a) at all dilutions. 95% confidence intervals for frequency estimates in the 1<sup>st</sup> and 3<sup>rd</sup> groups at  $10^{-4}$  dilution built with the use of binomial distribution with regard to small samples allowed to reveal the significant differences of groups by given microbes and consider these indexes as essential for pathological process prognosis. High CFU density of lactic bacteria and enterococcus in the 3<sup>rd</sup> group remained up to  $10^{-5}$  concentration with average lactic bacteria CFU density within gingival margin equal to 5,25 and enterococcus CFU density equal to 7,5.

Frequency index of *S. viridans*, extracted from aphthae surfaces, made 100%. This alpha-hemolytic streptococcus was distinguished in 40% patients of the 3<sup>rd</sup> group within gingival margin at  $10^{-4}$  dilution (average density equal to 4,75 CFU). It also appeared as 5 CFU among 20% patients at  $10^{-5}$  dilution. Aerobic microflora of this biotope in analyzed groups appeared to be dynamic and changeable.

The comparative study of bacteria population in biotopes of buccal, sublingual and gingival areas revealed the highest bacterial number in gingival margin. Gingival biotopes of conditionally healthy patients in all three groups significantly differed by both quantitative and qualitative indexes at maximum dilution (pic. 2a, 2b). The highest CPU density of identified streptococci, staphylococci, enterococci and lactic bacteria appeared in the 3<sup>rd</sup> group. Microbial density was lower in buccal mucosa and the lowest in sublingual area.

High number of residential bacteria at buccal mucous areas remaining at  $10^{-4}$  and  $10^{-5}$  dilutions contributes to local immune depression and, therefore, creates favorable conditions for transient microbial contamination, which increase biotope virulence.

The study revealed modifications and adjustments of aphthae micro-biocenosis, characterized by both the decrease of dominance and environmental significance of the leading symbiotes and the increase of transient microflora frequency.

Transient microbes, been inoculated at stomatitis, have distinctive pathogenicity, which is clinically expressed by pathological formations on buccal mucous membrane. *S. Haemolyticus* in aphthae's biotope saves dominance up to maximum dilution.

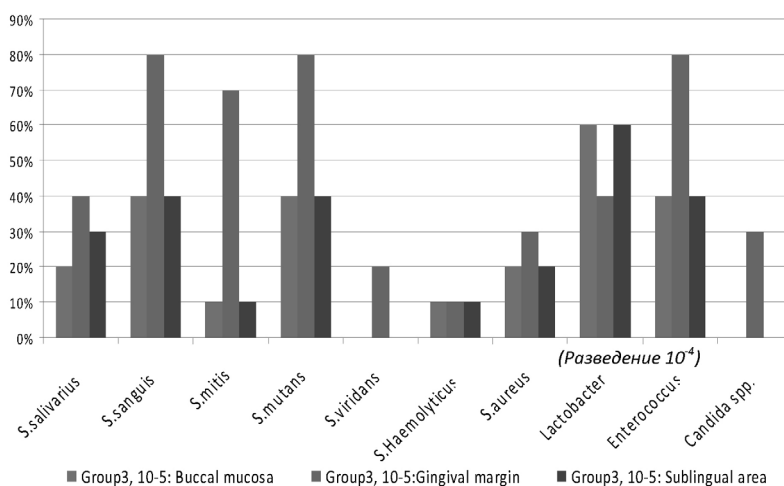
Different degree of various biotopes' contamination in the particular patient is linked with anatomic features of these surfaces and immunological background. Constant sublingual and submaxillary salivatory secretions support high concentration of immune protective factors in sublingual area, which allows controlling the bacteria and preventing possible inflammation in this area. However, the diagnosed dysbiotic disorders in biotopes of buccal and interdental gingival areas prove the failure of local oral immunity in general.

In summary, the type of staphylococcus bacteria-carrying and *S. viridans* in oral diseases becomes a way of microbiological monitoring and detection of high risk groups at a particular oral pathology in compliance with identification of the disease structure, as well as clinical and microbiological factors.

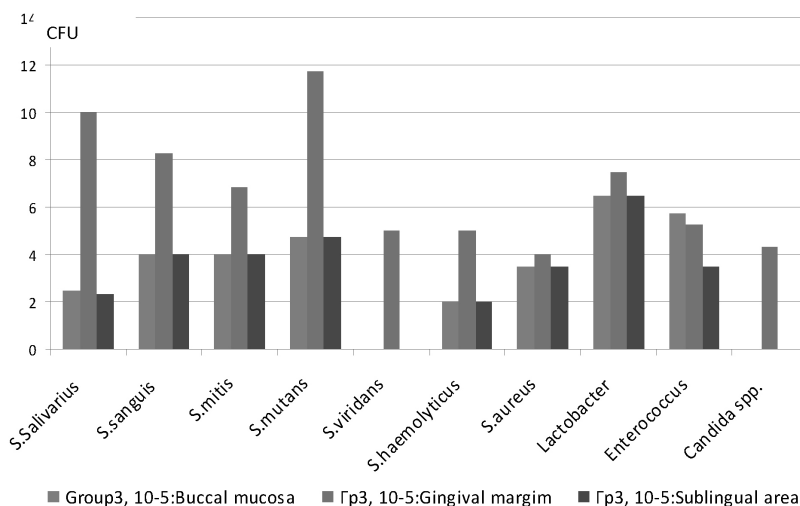


The analyses of ecosystem anaerobic structure demonstrated different contributions of microbes to oral biocenoses and allowed to define dysbiotic changes in biotopes. It was proved that dominant

microbes critical for microflora of microbiocenosis were streptococci with different type ratios in analyzed biotopes.



Picture 2 a. Frequency of occurrence (%) of aerobes and facultative anaerobes in analyzed biotopes at  $10^{-5}$  dilution among the patients of the 3<sup>rd</sup> group



Picture 2 b. The bacterial number (CFU) of analyzed biotopes at  $10^{-5}$  dilution among the patients of the 3<sup>rd</sup> group

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## **The effect of low-dose drospirenone and 17 $\beta$ -estradiol for correction of the manifestations of climacteric syndrome in postmenopausal women**

**Abstract:** vasomotor symptoms are the most common symptoms of menopause, requiring treatment with estrogen or with progestogen. Recent international guidelines recognize the need to use the lowest effective dose of hormone replacement therapy. Drospirenone (DR) in combination with 17 $\beta$ -estradiol (E) is used as hormone therapy (HT) for relief the symptoms and prevention of postmenopausal osteoporosis. The review presents data of 2 large randomized controlled studies that evaluated the lowest effective dose combination of DR/E, the safety of this dose for endometrium, identified features of its pharmacodynamics and pharmacokinetics, depending on various factors. The minimum effective dose for the relief of HF without causing any significant impact on the endometrium is DR of 0,25 mg/E of 0,5 mg. According to the results of the pharmacokinetic study a correlation between effectiveness of low dose DR/E with DR and E exposure levels was showed, and smoking reduces the effectiveness of hormonal therapy. This drug not only copes with moderate to severe hot flashes, but also reduces the incidence of symptoms of vulvovaginal atrophy, improving quality of life.

**Keywords:** menopause, drospirenone, 17 $\beta$ -estradiol, hot flashes, endometrial hyperplasia.

Climacteric syndrome — a complex of vegetative-vascular, mental and metabolic and endocrine disorders, occurring in women on hormone background with fading of ovarian function and the overall age involution of the body — are observed, according to the literature, in 30–60% of women. In the pathogenesis of climacteric syndrome, the main role belongs to the mismatch of the activity of hypothalamic brain structures to ensure coordination of the cardiovascular, respiratory and temperature reactions with emotional and behavioral reactions. The earliest and specific manifestations of the climacteric syndrome, the so-called hot flashes, reflecting disruption in the central mechanisms controlling the synthesis and pulsatile release of neuropeptides hypothalamus (lyuliberina, thyrotropin-releasing hormone, corticotropin, and others.), which are involved in regulating the secretion of tropic pituitary hormones, cardiovascular activity and respiratory systems, as well as in the regulation of the formation of emotional-behavioral reactions. When menopause syndrome manifested that took place earlier, in violation of higher regulatory centers, as evidenced by the presence of a significant number of women burdened heredity, concomitant extragenital diseases and paroxysmal autonomic disorders.

These violations, together with changes in cognitive function and mood changes reduce the quality of life of both the patient and the next of kin, making the problem even more significant.

To this day, the only method of treatment of climacteric syndrome (CS) having evidence base remains MGT, whose efficiency reaches 95%. Medical intervention is required in approximately 1/3 of women with vasomotor symptoms of menopausal syndrome. Latest international clinical guidelines recognize the need to use the lowest effective dose of HT in accordance with the objectives of the treatment for each woman. The Endocrine Society in 2010 undertook a review of the existing data in order to assess the benefits and risks of HT in postmenopausal women.

Of all the natural estrogen estradiol it is the most active and has the highest affinity for the estrogen receptors. Target organs for estrogens include, inter alia, the uterus, the hypothalamus, the pituitary gland, vagina, mammary glands, bone (osteoclasts).

Other effects of estrogens include: reducing insulin and glucose concentrations in the blood, mediated by receptors vasoactive effects and independent effect on the receptors of the smooth muscle cells of the vessel walls. Estrogen receptors have been identified in the heart and coronary arteries.

Oral administration of natural estrogens has advantages in cases of hypercholesterolemia due to more favorable effects on lipid metabolism in the liver. Monotherapy estrogen has a dose dependent stimulatory effect on mitosis and proliferation of the endometrium, and thus, increases the incidence of endometrial hyperplasia and

therefore the risk of endometrial cancer. To avoid endometrial hyperplasia, need combination with progestogen. According to the analysis, Endocrine Society concluded: the minimum effective dose of estrogen used in postmenopausal symptomatic treatment provides and maintains bone mineral density. In addition, standard or low dose of hormones used in healthy postmenopausal women did not significantly increase the risk of cardiovascular diseases.

Also, to facilitate postmenopausal symptoms and prevention of osteoporosis as HT in combination with 17 $\beta$ -estradiol effectively used drospirenone. Drospirenone pharmacological profile similar to endogenous progesterone, in addition, it has antiminerocorticoid and antiandrogenic effects, which makes it leader programs antiaging therapies. Drospirenone is a potent progestogen with a central system inhibitory action on the hypothalamic-pituitary-gonad. In women of reproductive age drospirenone has a contraceptive effect; when administered as a single agent in drospirenone, ovulation is suppressed. The threshold dose of drospirenone for the suppression of ovulation is 2 mg/day. Complete transformation subjected previously exposed endometrial estrogen dosing occurs after 4 or 6 mg/day for 10 days. Drospirenone is capable of competitive antagonism with aldosterone. Women who are in the clinical study were obtained in addition to estradiol, drospirenone, rarely mentioned peripheral edema than those taking only estradiol [10].

It should also be emphasized that drospirenone has neither the glucocorticoid or antiglucocorticoid activity and has no effect on glucose tolerance and insulin resistance. In 2007–2008. in the US was a randomized, double-blind, placebo-controlled study of the lowest effective dose of drospirenone/estradiol for the treatment of moderate to severe vasomotor symptoms of menopausal syndrome in women in post-menopause. Its purpose was to identify the lowest effective dose of drospirenone/estradiol for their leveling [11].

The study enrolled women aged 40 years and older who developed spontaneous amenorrhea for 12 months or more, or spontaneous amenorrhea with the level of follicle-stimulating hormone in the blood is higher than 40 mIU/mL within 6 months or more, or patients after bilateral oophorectomy with/without a hysterectomy within 6 weeks previously conducted after surgery. Patients experiencing hot flashes per day 7–8 moderate-to-severe hot flashes or 50–60 week of moderate to severe manifestations of climacteric syndrome for at least 7 consecutive days during the study. The results of mammography data transvaginal ultrasound (TSS) in women with preserved uterus and endometrial biopsies corresponded to the reference values.

Exclusion criteria were: use of any hormones (progestogens, estrogens or combinations thereof in any form of steroid hormones), anticoagulants, antibiotics, anti-epileptic drugs and CYP3A4-inhibitors and inducers of selective serotonin reuptake inhibitors, norepinephrine or monoamine, raloxifene or tamoxifen for last 8–24 weeks. 735 partitioned into groups of women depending on the preparation obtained in a ratio of 1: 1: 1–0.25 mg drospirenone/estradiol 0.5 mg, 0.5 mg drospirenone/estradiol 0.5 mg or 0.3 mg oestradiol placebo. The women were asked to record the daily frequency and severity of hot flashes during the entire period of observation in the diaries of self-control. Evaluates the primary indicators: frequency weekly dynamics of the tides from baseline to the current rate to 4 and 12 weeks, and the average weekly rate of frequency of hot flashes and 4 and 12 weeks of observation. Scale of severity varied from 0 (no symptoms), 1 (mild symptoms, sensation of heat without perspiration), 2 (moderate symptoms, sensation of heat through sweat may continue the current activities), 3 (severe symptoms, sensation of heat with sweating, causing termination of current activity), in accordance with the recommendations of the GT acceptance [12].

Also monitor the secondary indicators: changes in vaginal pH and vaginal maturation index of discharge; the ratio of participants to vulvovaginal atrophy and urogenital symptoms.

The average daily level of tidal gravity calculated by the formula:  $[(2 \times \text{number of moderate hot flashes}) + (3 \times \text{number of severe hot flashes})] / \text{the total number of hot flashes}$  Average weekly rate of frequency of hot flashes was calculated by calculating the average value of the daily severity of hot flashes In addition to clinical assessment indices performed.. laboratory tests (general clinical and biochemical blood tests, urinalysis), evaluation of endometrial thickness (ultrasound), immunohistochemistry (endometrial biopsy), physical examination, Pap test, identification of adverse effects of treatment, were a record degree of blood loss (in women with preserved uterus).

The mean age of subjects was 53.5 years. Time elapsed from the date of last menstrual period, amounted to an average of 9.36 years. Patients with hysterectomy accounted for 54.4%, ovariectomy – 34.4% (including 77.1% with bilateral ovariectomy). The most common co-morbidities were hypertension (20% of participants) and dyslipidemia (13.5%). The frequency of these states was comparable in all groups. Fully completed the study (12 weeks), only 635 (86.4%) participants. The remaining 100 (13.6%) patients had never taken or prematurely discontinued use of the drug that has been associated with non-participation, adverse effects (NOE) or the loss of contact with the test. Average weekly frequency of hot flashes in patients of all 4 groups was similar and ranged between 73.25 (group estradiol 0.3 mg) to 74.64 (0.25 mg drospirenone/estradiol 0.5 mg). The average daily level of severity of hot flashes was similar between groups: 2.52 (placebo group) – 2.58 (0.25 mg drospirenone/estradiol 0.5 mg).

In the group of patients receiving drugs registered more significant decrease in average weekly frequency of hot flashes and the mean daily severity of hot flashes compared with placebo at 4 and 12 weeks of the study. The frequency and severity of hot flashes were significantly different in the drospirenone group compared with the placebo group. Averages of frequency and severity of hot flashes by 12-week study were significantly different in the group of 0.5 mg of drospirenone/estradiol 0.5 mg group as compared to 0.25 mg of drospirenone/estradiol 0.5 mg, with estradiol group 0.3 mg were much smaller. Reducing vaginal pH at the end of the study it was more pronounced in all treatment groups compared to placebo: 0.63 (0.94) 0.63 (0.87) 0.66 (0.97) and 0.06 (0,7) group drospirenone 0.25 mg/estradiol 0.5 mg, 0.5 mg drospirenone/estradiol 0.5 mg Estradiol 0.3 mg and placebo, respectively ( $p < 0,0001$ ). Reducing the percentage of parabasal cells and an increase in surface epithelial cells counted using the maturation index of the vaginal fluid were much more significant in all treatment groups compared with placebo ( $p \leq 0,0028$ ). Only a few women complained of symptoms of vulvovaginal atrophy or urogenital complaints in addition to the tides (the statistical analysis of this group has not been done).

Therefore, the combination of drospirenone 0.25 mg/estradiol 0.5 mg is the lowest effective dose. Reducing vaginal pH and increase the maturation index of the vaginal fluid in all the studied groups treated compared to placebo demonstrate the beneficial effect in the treatment of symptoms of vulvovaginal atrophy, increasing compliance in patients older age group.

The second important aspect of this study was to evaluate the pharmacokinetics (PK) and pharmacodynamics (PD) of drospirenone and estradiol, as well as the influence of factors such as body weight, body mass index (BMI) and smoking. Also demonstrated the relationship between exposure to estradiol and drospirenone

and efficiency, based on the measured decrease in the number of hot flashes.

Equilibrium concentrations of estradiol were described using a one-compartment model with first-order elimination, and absorption of the zero order, which showed that the elimination of estradiol concentration dependent, whereas the absorption is not dependent. The initial concentration of estradiol increased with BMI ( $p < 0,001$ ), which was confirmed by other researchers [13]. The clearance (CL/F) of estradiol at steady state was 39%, which is significantly higher in smokers than non-smokers (1,559 l/h against 1,120 l/h;  $p < 0,001$ ). The effect of smoking on CL/F can be explained estradiol complicated complex metabolic effects, including the induction of CYP1A1, which is involved in the metabolism of estradiol [14; 15]. Other indicators, such as age, height, body mass, muscle mass, body surface area, body fat mass, race, dose, and treatment of alcohol use, no significant influence, in addition to BMI and smoking, the concentration of estradiol.

FC drospirenone is described by a linear two-compartment open model with first-order elimination from the central chamber and sustained absorption of the first order orally administered dose. Individual variability described for CL/F drospirenone. CL/F increases linearly with an increase in body weight ( $p < 0,001$ ), but this ratio is not preserved when 5% were excluded women weighing 110 kg or more. This was not found other factors that have a significant impact on the FC drospirenone.

A generalized linear model with a negative binomial distribution was used to model the changes in the frequency of hot flashes from baseline to week 12 according to the area under the curve of concentration vs. time to estradiol, and other factors. In addition to the expected strong relation ( $p = 0,02$ ) between the exposure of estradiol and a relative reduction in the incidence of moderate to severe hot flashes degree, it was awarded an additional pharmacodynamic effect of smoking on the effectiveness of treatment ( $p < 0,01$ ).

According to the data, smoking reduces the effectiveness of HT estradiolnezavisimly through a mechanism that leads to the lower level of estradiol in the blood, which complements the previous findings about the effects of smoking on the metabolism of estradiol [10].

Consequently, this study demonstrated that the efficacy of low doses of drospirenone/estradiol to reduce vasomotor symptoms correlates with an exposure of drospirenone and estradiol in the serum, while smoking adversely affects the effectiveness of treatment.

Another large study focused on assessing the risks of endometrial hyperplasia and characteristics of bleeding in patients receiving 0.25 mg drospirenone/estradiol 0.5 mg for 12 months. The objective was to characterize the changes of the endometrium and bleeding pattern during continuous, long-term therapy of 0.25 mg drospirenone/estradiol 0.5 mg compared to treatment norethisterone acetate (NETA) 0.5 mg/1.0 mg estradiol (a preparation containing a double dose of estradiol, unlike drospirenone 0.25 mg/estradiol 0.5 mg), [16].

Inclusion criteria: women with an intact uterus between the ages of 40 and 65 years, who developed spontaneous amenorrhea for 12 months or more, or spontaneous amenorrhea with the level of follicle-stimulating hormone in the blood is higher than 40 mIU/mL within 6 months or more, or the patient after bilateral oophorectomy without a hysterectomy (6 weeks after surgery). Women had to have indications for induction of menopausal hormone therapy confirmed by researchers, with no evidence of endometrial hyperplasia or cancer, according to the screening endometrial biopsy.

Exclusion criteria were: use of vaginal hormone preparations or estradiol in the form of nasal sprays for 1 week, transdermal estrogen or estrogen-progestin drugs for 4 weeks, oral estrogen and/or

progestogen, or intrauterine forms of progestogen for 8 weeks to provide informed consent. Progestogen implants and injectable forms of estrogen for 3 months, estrogens tablets or injectable forms of progestogen for 6 months and have been banned. The presence of clinically significant disease (including contraindications to HT) or laboratory abnormalities were additional exclusion criteria. supplementation was expelled the following drugs: steroids, anticoagulants, antiepileptic drugs, antibiotics, inhibitors of CYP3A4-inducers, and selective estrogen receptor modulators (raloxifene or tamoxifen).

The primary measure of efficacy was the proportion of women with histological conclusion endometrial biopsy "hyperplasia or transition typical form in atypical" ("hyperplasia, or atypia") at any time during the trial or after the 13 cycles of treatment, which was evaluated by three independent pathologists [17; 18].

The secondary measure of effectiveness was the rate of amenorrhea (defined as no bleeding or spotting) for 1–3, and 10–12 months of treatment, according to the self-monitoring diaries, fills patients. Also assessed the frequency of urogenital symptoms, the symptoms of vulvovaginal atrophy, emotional and physical symptoms with the help of women's health profiles [19].

According to the study of any one patient in the group drospirenone/estradiol have been reported histological conclusion "hyperplasia, or atypia." The ratio of women with urogenital symptoms was similar in both treatment groups at baseline. General urogenital symptoms at the beginning of the study included urinary frequency (36.6% in the drospirenone/estradiol, 35.7% of NETA/estradiol group) and urinary incontinence (30.3 and 33.3%, respectively). Among the women who complained of frequent urination in the beginning of the study, about 56% reported relief of this symptom in both groups by the end of the study. Similarly, women complaining of urinary incontinence in beginning of the study, more than 50% longer observe this phenomenon in both groups at endpoint.

The proportion of participants who have had vaginal dryness, decreased from 64% at baseline to 37% at the end of the study in both groups, and the proportion of women with vulvovaginal atrophy – from 27 to 13%. dyspareunia rate decreased from 40.3 to 18.2% in the drospirenone/estradiol and from 36.8 to 16.0% in the NETA/estradiol. NE were reported in 386 (58.4%) women in the study, including 279 (57.1%) – a group of drospirenone/estradiol and 107 (62.2%) – a group of NETA/estradiol. NEs that are considered as side effects of the treatment have been reported in 90 (18.4%) and 44 (25.6%) women groups drospirenone/estradiol and NETA/estradiol, respectively. Serious adverse events were reported in one patient treated with drospirenone/estradiol (acute pancreatitis), and 1 – in the group of NETA/estradiol (thrombosis of retinal vessels).

Accordingly, this 12-month double-blind, randomized, active drug use as a control study, the first opportunity to assess and confirm the safety of the endometrium and bleeding profile characterized allowed in patients receiving low-dose combination of drospirenone (0.25 mg) and estradiol (0.5 mg) in women with an intact uterus in postmenopausal women.

A meta-analysis of randomized controlled trials found that the lowest effective doses of the combination of HT in postmenopausal women are drospirenone 0.25 mg/0.5 mg of estradiol. This therapy can successfully arrest vasomotor symptoms, not providing, at the same time, a significant effect on the endometrium. According to a randomized controlled trial on the therapy with drospirenone 0.25 mg/0.5 mg estradiol fixed very low risk of developing endometrial hyperplasia, or atypia, while as the number of episodes of bleeding or spotting decreases with continued dosing. In the appointment



of HT should be considered comorbid conditions such as obesity and smoking. The study of PK and PD was discovered that the effectiveness of low doses of drospirenone/estradiol correlated with exposure estradiol and drospirenone in serum, and a significant factor as smoking, reduces the efficiency of HT through estradiol-*nezavisimy* mechanism which leads to a lower level of estradiol in the blood.

Receiving drospirenone 0.25 mg/estradiol 0.5 mg contributes to the prevention of cardiovascular disease and osteoporosis, which is most important in terms of anti-aging prevention. Combination of 0.25 mg drospirenone/estradiol 0.5 mg is effective in reducing moderate to severe vasomotor symptoms of menopausal syndrome, can reduce the frequency of symptoms of vulvovaginal atrophy, significantly improving compliance and quality of life of patients.

Currently, the Russian market registered the first ultranizkodoz-irovanny drug for menopausal hormone therapy (MHT) Anzhelik® Micro (17β-estradiol 0.5 mg/0.25 mg drospirenone).

Anzhelik® Micro is fully consistent with modern strategies MGT application in the lowest effective dose and extends the capa-

bilities of hormone replacement therapy in postmenopausal women. Most warranted Anzhelik® appointment in early postmenopausal women, and then transition to Anzhelik® Micro, while maintaining the indication for treatment. This is because in the early postmenopausal required dose of 1 mg estradiol for rapid and more effective relief of menopausal syndrome, the patient can then go to the ultra-low dose estradiol.

Keep in mind that more than one third of women vasomotor symptoms persist for more than 10 years of menopause and when you try to stop the MHT renewed. MGT combined continuous mode capable of ultra-low dose empower patients individualization of treatment in postmenopausal women with vasomotor symptoms, as MGT efficacy against these symptoms fully retained, while side effects are minimized.

Now two drugs presented in the Russian market with the same composition of the hormonal components, but in different doses: a well-established low-dose Anzhelik® (17β-estradiol 1 mg/2 mg drospirenone) and Anzhelik® Micro (17β-estradiol 0.5 mg/drospirenone 0,25 mg).

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## General combined anesthesia on the basis of spinal-epidural blockade during oncurologic and oncogynecological surgeries

**Abstract:** The results of the study showed that the use of general combined anesthesia based on regional blockades justifies for anesthetic supply of long and traumatic surgeries in oncurology and oncogynecology.

**Keywords:** Extended oncurological and oncogynecological surgeries, general combined anesthesia on the basis of SEB, general multicomponent anesthesia.

**Introduction:** In recent years, in the surgery of pelvis organs, the indications for over-aggressive, multi-organ and long-term surgeries have expanded. The most typical of these should be considered extended cystectomy and hysterectomy for cancer, followed by broad removal of regional lymphatic collectors. The high traumaticity and duration of such operations with the coverage of the vast reflexogenic zones of small pelvis and surrounding tissues dictates the need for highly effective anesthetic protection capable of reliably blocking the flow of powerful nociceptive stimulation from extensive surgical lesions, both during surgery and in immediate postoperative period. The variants of the general combined anesthesia on the basis of regional blockades meet the most complete requirements [5; 6; 7; 8]. Among them, our attention was drawn to the spinal-epidural block (SEB), which allows to combine the advantages of spinal and epidural anesthesia, to reduce the number of complications and to provide long and highly effective postoperative analgesia [2; 3; 8; 9; 10; 11].

**The aim of the study** was to evaluate the efficacy and safety of combined anesthesia on the basis of SEB for extended surgeries in oncurology and oncogynecology.

**Materials and methods.** To evaluate the efficacy of the approved method, 2 groups of patients aged 42 to 74 years, 63 women and 31 men, whose physical status corresponded to ASA classes II–IV, were formed. In all patients, in the order of examination and preparation for surgery by the method of echocardiography, CI, HR, and reserve capacity of left ventricle were determined before and after passive orthostatic test [10]. The criterion for preserving the reserve abilities of cardiovascular system was the increase in RV intensity index, CI, and HR in response to orthostatic test. The study groups included only the patients with preservation of reserve capacities of the cardiovascular system.

The main group consisted of 50 patients operated under conditions of general combined anesthesia on the basis of SEB, the control group – 44 patients operated under general multidivision anesthesia. All patients were operated routinely. The volume and nature of surgical interventions were distributed as follows: extended hysterectomy – 24, expanded cystectomy with bilateral ureterocutaneostomy – 70. The duration of surgery ranged from 2 to 3.5 hours, the average blood loss was  $550.4 \pm 230$  ml. By age, sex, nature and extent of surgical interventions, both groups of patients were identical, which allowed to make their objective comparative evaluation.

Method of general combined anesthesia based on SEA. Pre-medication included phenazepam (1–2 mg) the night before the operation, 0.2–0.25 mg/kg sibazone intramuscularly on the day of surgery 40 to 50 minutes before transportation to the operating room. Dexamethasone (0.07 mg/kg), dimedrol (0.2 mg/kg), atropine according to indications were intravenously administered on the operating table. Before anesthesia, for 15–20 minutes, 8–10 ml/kg crystalloid solutions were intravenously administered. All patients were used two-segment variant of SEA. The first moment under local infiltration anesthesia in the lateral position at  $L_1-T_{10}$  was conducted the puncture – catheterization of epidural space with catheter in the cranial direction for 4–5 cm followed by introduction of “test dose” (2% – lidocaine solution). The second moment at the  $L_2-L_4$  level subarachnoid space was punctured and 2.5–3.0 ml of 0.5% hyperbaric bupivacaine solution in combination with fentanyl (0.7 µg/kg) was injected. Patients were turned on their backs and laid in strictly horizontal position. With the appearance of the first clinical signs of subarachnoidal blockade, induction was conducted in anesthesia (ketamine 1.5 mg/kg), precurarization (1 mg pancuronium), dithiline (2 mg/kg), trachea was intubated. Before intubation, the voice gap was treated with 10% lidocaine aerosol and 1.4 µg/kg fentanyl was administered intravenously. Ventilation in the mode of moderate hyperventilation was performed by air — oxygen mixture (1:1); the total curarization was provided with pancuronium, consciousness was turned off with propofol [(1.2 mg/(kg·h<sup>-1</sup>)). After 110–120 minutes from the moment of subarachnoidal administration of local epidural anesthetic they introduced 14–16 ml of 0.5% solution of bupivacaine with an interval of 120 minutes as needed. The extubation of trachea was carried out after the complete restoration of reflex-muscle activity, consciousness, adequate independent breathing, against the background of stable hemodynamics and compensated hemorrhage. Medicinal decurarization was not used, giving preference to spontaneous. The intraoperative infusion-transfusion program was based primarily on the introduction of crystalloids and hydroxyethylated starches, and with a blood loss of 10 ml/kg and more it corresponded to the conventional protocol. For postoperative analgesia, morphine (0.05–0.07 mg/kg) was used which was dissolved in 10 ml of 9% isotonic sodium chloride solution and was administered epidurally.

For the patients of the control group, it used general multicomponent anesthesia with AVL based on ketamine, propofol, fentanyl and benzodiazepines. Pre-medication, the nature and volume

of intraoperative infusion-transfusion therapy did not differ from those in the patients of the main group. Postoperative analgesia was carried out with traditional way (narcotic and non-narcotic analgesics, antispasmodics).

The effectiveness of anesthesia was evaluated according to generally accepted clinical signs. Central hemodynamics was assessed by echocardiography using the SA-600 apparatus of MEDISON. They studied: stroke index (SI), cardiac index (CI), general peripheral vascular resistance (GPVR). The average dynamic pressure (ADP), heart rate (HR), and saturation ( $SpO_2$ ) were monitored by the monitor (BMP 300 "Biosis") continuously, throughout the surgery. The rate of urination in oncogynecologic patients was assessed using Foley catheter installed in the bladder, and in oncological patients only at the end of the surgery. The state of autonomic nervous system (ANS) was estimated according to cardiointervalography, using mathematical analysis of heart rhythm [1]. The mode (Mo), the mode amplitude (AMo), the variation range ( $\Delta x$ ) were calculated, the voltage index (VI) was calculated. The response of the sympathetic adrenal system was assessed by the rate of excretion of noradrenaline (NA) in the urine [4], the functional state of the hypothalamo-pituitary-adrenocortical system — by the level of total cortisol (TC) in blood plasma (radioimmunoassay).

The studies were performed in 6 stages: I – the day before the surgery, II – before the cutaneous incision, III – in 10–15 minutes after the cutaneous incision, IV – in the most traumatic stage of the surgery, V – in 3–3,5 hours from the beginning of the surgery, VI – after the end of the surgery. All the numerical values obtained during the study were statistically processed using the Student's test (using the Microsoft Excel program) and are represented in the form  $M \pm m$ , where  $M$  is the arithmetic mean value,  $m$  is the standard error. Statistically significant differences were considered for  $p < 0.05$ . The results are presented in the table.

**Results of the study and their discussion.** The initial state of hemodynamics of patients of both groups was characterized by eukinetic circulation (see Table). There was moderate activation of the sympathetic divisions of ANS, VI was  $236.3 \pm 9.1$  and  $229.3 \pm 8.4$  conv. units. The concentration of TC in blood approximated to the upper limits of physiological oscillations, the excretion of NA in the urine was  $7.9 \pm 0.7$  nmol/l in the main group, and in the control group –  $7.4 \pm 0.5$  nmol/l.

Immediately, before starting the surgery, the patients of the main group were registered significant decrease in the rate of ADP and GPVR by 14.8% and 19.9%, which we regarded as a classic manifestation of segmental sympathetic blockade. The changes in the other indicators studied were insignificant and did not have a reliable character (see Table). The  $SpO_2$  index corresponded to  $98.9 \pm 0.5\%$ , VI –  $282.8 \pm 12.1$  conv. units.

At the same terms in the control group of patients, the significant increase in heart rate was registered by 10.7%. At that, ADP, GPVR, SI and CI remained without reliable dynamics. VI increased by 76.9%, amounting to  $405.7 \pm 15.4$  conv. units in the autonomic balance, the tone of the sympathetic division of ANS dominated. This indicates the more pronounced tension in the regulatory systems of the heart rhythm in comparison with the main group of patients. The  $SpO_2$  index at that time corresponded to  $99.1 \pm 0.6\%$ .

Ten to fifteen minutes after the cutaneous incision, hemodynamic stability persisted in the patients of the main group. The hemodynamic parameters studied did not differ significantly from the previous stage of the study (see Table). ADP was  $90.1 \pm 2.7$  mm Hg, HR –  $78.4 \pm 2.2$  per min, GPVR –  $1302.2 \pm 52$  dyne-centimeter  $cm^{-5}$ , CI –  $3.34 \pm 0.17$  l/ $m^2$ /min. From the side of ANS, there was still mod-

erate increase in the activity of the sympathetic division of ANS with a minimal degree of stress in the regulatory systems of the heart rhythm. At that stage of the study VI was  $313.9 \pm 13.8$  conv. units.

At the same time the control group of patients, in spite of stable indicators of single and minute cardiac output and trends towards normalization of ADP and GPVR (see Table), there was a significant increase in VI, respectively, relative to the previous stage of the study and initial preoperative values, by 101, 2% and 256%, which indicates the significant strain of regulatory systems of heart rate. At the same time, it should be noted that the absolute value of VI ( $816.4 \pm 21.7$  conv. units) did not exceed the limits of the "stress norm".

In the most traumatic stage of the surgery, the hemodynamic parameters studied remained stable in patients operated under conditions of general combined anesthesia on the basis of SEB, did not differ significantly from the previous stage of the study (see Table). ADP was  $92.1 \pm 1.8$  mmHg, HR- $80.2 \pm 1.6$  beats per min, CI –  $3,38 \pm 0,14$  l/min/ $m^2$ , GPVR –  $1320,6 \pm 60$  dyn.c- $cm^{-5}$ . The value of VI was  $529,3 \pm 12,6$  conv. units, and TC of blood plasma was  $427,6 \pm 42,3$  nmol/l.

In patients operated under GMA conditions, the studied hemodynamic parameters also remained relatively stable, did not differ significantly from the initial preoperative values and the previous stage of the study (see Table). However, they differed to a great extent from those in the patients of the main group. Thus, ADP was  $104.2 \pm 13.6$  mm Hg, HR was  $86.8 \pm 1.4$  per min, GPVR –  $1563.4 \pm 51$  dyn.c- $cm^{-5}$ . At this stage of the study VI corresponded to  $1256.4 \pm 19.8$  conv. units, and blood plasma TC was  $749.3 \pm 39.1$  nmol/l, which indicates the more pronounced activation of sympathetic division of the ANS in comparison with the main group of patients, the degree of tension of the regulatory systems of heart rhythm, activation of the hypothalamic-pituitary-adrenal system.

After 3–3.5 hours from the beginning of the surgery, the hemodynamic stability (see Table), the decrease in the activity of sympathetic division of the ANS and the degree of stress of the regulatory systems of heart rhythm were still registered in the patients of the main group. VI was  $324.6 \pm 8.4$  conv. units.

Patients of the control group had clear tendency to decrease in the ADP and GPVR, reduction in HR, increase in CI (see Table). VI, in comparison with the previous stage of the study, significantly decreased from  $1256.4 \pm 19.8$  st. units up to  $850.4 \pm 9.5$  standard units. However, significant differences remained between the studied parameters of hemodynamics and the degree of stress of heart rhythm regulatory systems between the main and control groups of patients (see Table).

The end of the surgery in patients of the main group was characterized by hemodynamic stability. HR was reduced to  $72.8 \pm 1.4$  b/min. ADP and GPVR were, respectively,  $86.6 \pm 2.7$  mm Hg and  $1236 \pm 63$  dyne c- $cm^{-5}$ , CI –  $3.36 \pm 0.16$  l/min/ $m^2$ . VI corresponded to  $356.0 \pm 9.4$  conv. units, TC of blood plasma –  $513.4 \pm 48.4$  nmol/l, and the rate of excretion of NA in urine for the surgery period was  $9.1 \pm 1.2$  nmol/l and significantly was not different from the day before surgery (see Table). The hourly diuresis during the surgery was 40.6 ml/h, which indirectly indicates the preservation of peripheral blood flow and kidney function as a whole. In those terms, normalization of the hemodynamic parameters studied was also recorded in the control group. ADP was  $95.4 \pm 2.7$  mm Hg. HR –  $80.3 \pm 2.6$  per min. GPVR –  $1385.1 \pm 54.3$  dyne c- $cm^{-5}$ . However, all of the above indicators were significantly different from those in the main group of patients (see Table). VI was  $718.2 \pm 41.2$  conv. units, the concentration in blood plasma TC –  $718.2 \pm 41.4$  nmol/l, and the

excretion of NA in the urine during the surgery – 17,9±1,6 nmol/l, which indicates the more pronounced, in comparison with the main group, activation of sympathoadrenal and hypothalamic-pituitary-adrenocortical systems in response to operational trauma. Comparative characteristics of the course of anesthesia and the nearest postoperative period in patients of the main and control groups revealed significant advantages of the method we tested, which lead to:

- minimal consumption of narcotic drugs and muscle relaxants;
- rapid recovery and restoration of reflex-muscle activity, allowing to make trachea extubation at an earlier time;
- the possibility of using epidural catheter to obtain long-term postoperative analgesia;
- early activation of patients and restoration of motor-evacuation function of gastrointestinal tract.

Table 1. – Some indicators of hemodynamics, sympathoadrenal and hypothalamo – pituitary – adrenocortical systems during the stages of anesthesia and surgery in patients of the main and control groups.

Indicators studied	Groups	Stages of the study					
		I	II	III	IV	V	VI
Mean dynamic pressure, mmHg	Main	108.4±3.1	92.4±4.3 * Δ	90.1±2.7 * Δ	92.1±1.8 * Δ	90.2±1.6 * Δ	86.6±2.7 * Δ
	Control	106.1±2.8	110.8±2.4	102.8±2.1	104.2±3.6	98.8±1.9 *	95.4±2.7 *
Heart rate, in 1 minutes	Main	81.5±2.1	78,1±1,1Δ	78,4±2,2Δ	80,2±1,6Δ	74,6±2,1 * Δ•	72,8±1.4 * Δ
	Control	82.6±2.3	91.4±2.2 *	88.5±3.1	86.8±1.4	82.2±1.6 •	80.3±2.6
Voltage index, conv. units	Main	236.3±9.1	282.8±12.1Δ	313.9±13.8 * Δ	529.3±12.6 * Δ •	324.6±8.4 * Δ •	356.0±9.4 * Δ •
	Control	229.3±8.4	405.7±15.4 *	816.4±21.7 * •	1256.4±19.8 * •	850.4±9.5 * •	584.1±10.1 * •
Cardiac index, l/m <sup>2</sup> /min	Main	3.26±0.17	3.36±0.15	3.34±0.17	3.38±0.14	3.44±0.12	3.36±0.16
	Control	3.12±0.18	3.28 ±0.14	3.29±0.16	3.36±0.16	3.41±0.18	3.41±0.13
General peripheral vascular resistance, dyne/(c.cm <sup>-5</sup> )	Main	1610±78	1290±39 * Δ	1302±52 * Δ	1320±60 * Δ	1252±58 * Δ	1236±63 *
	Control	1608±61	1649±48	1514±74	1564±51	1407±43 * •	1385±54 *
Total cortizol (blood plasma), nmol/l	Main	369.8±32.2			427.6±42.3Δ		513.9±48.4 *Δ
	Control	396.3±36.4			749.3±39.1 *		718.2 ±41.2 *
Noradrenalin in urine, nmol/l	Main	0.73±0.06	0.88±0.03 *				9.1±1.2Δ
	Control	0.74±0.04	0.86±0.04 *				17.9±1.6 *
Hourly diuresis, ml/hour	Main	62.4±5.2					40.6±4.3 * Δ
	Control	60.9±4.8					21.4±1.2 *

Note: \* – statistically significant differences ( $p < 0.05$ ) relative to the initial preoperative values; • - statistically significant differences ( $p < 0.05$ ) relative to the previous stage of the study; Δ – statistically significant differences ( $p < 0,05$ ) between the groups studied.

The data obtained make it possible to assert that the general combined anesthesia on the basis of SEB provides reliable antinociceptive protection of the organism from surgical aggression, provides smooth course of anesthesia and the nearest postoperative period, and, therefore, has a clear advantage over the traditional variant of general multicomponent anesthesia.

**Conclusions:**

1. The use of general combined anesthesia based on spinal-epidural blockade is justified for anesthetic supply of long-term and traumatic oncological operations on pelvis organs.
2. The tested variant of balanced anesthesia on the basis of regional blockades provides reliable antinociceptive protection of the organism from surgical aggression, hemodynamic stability and smooth course of the nearest postoperative period.

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## Personalized medicine: new or well-forgotten old?

**Abstract:** The aim is to try to Dana Article demonstrate the essence of the contradictions between the fundamental philosophical principles of medicine and modern medical science and practice; identify the causes of conflict, identify the causes contributing to the fact that this contradiction is in the area of “blind spot” for many professionals, as well as to expose the fallacy of the essence of a selective approach in that now appears as “personalized medicine.” Finally, describes the new trend brings us back to basic principles of medicine. And propose solutions based on current and future technologies.

**Keywords:** Personal medicine, allostas, new technologies.

*If we do not deviate from the chosen path, it is likely to arrive at where we are going  
 (Chinese proverb)*

*The concept of personalized medicine is known to people since the time of Hippocrates, who is credited with saying:  
 “It is more important to know what kind of person has a disease than what disease a person has.”*

Modern medical education is focused on illness, namely students learn nosology and characteristic symptoms of their syndromes, an objective clinical and laboratory parameters. Information on the life history, family history and medical history are also classified in the context of nosology. The task of the modern physician, so – it is possible to more accurately determine the diagnosis (“what a person has the disease?”) And for this purpose we study the man, which is a direct contradiction of the above-described principle of Hippocrates.

It is noteworthy that many clinicians and medical scientists overlooked the essence description contradictions, even when faced with a reality in practice. Moreover, accumulated to date experience, knowledge and understanding, allow bare-sided sword, the reverse side of which affects those who currently is positioning itself as a supporter of “personalization of medicine” in while almost still further deviates from the original principle Hippocrates.

Among the scientific papers there are not a few, where logic and mathematics are impeccable, but who nevertheless do not stand because the assumptions and hypothesis on which they rest impeccable logic and mathematics does not correspond to reality [1].

Consider the essence of the “problem” of medicine focus on the diagnosis of a central target of medical science and practice?

Medical science since the industrial revolution has made considerable progress in the elimination of certain nosology, and great progress in the treatment and control of many diseases, improving the quality and length of life. Great dostozheniya medical science and practice in comparison with past centuries is still for many an occasion the conviction that “we are on the right track, and that is how we develop, is an evolution of the Hippocratic principles.” Nevertheless, progress in the study of the dynamics becomes more and more obvious its sharp slowdown in decades. At the same time, paradoxical and ironic, it is that progress is becoming less and less noticeable as the acceleration of technological development. The concept of personalized medicine is known to people since the time of Hippocrates, who is credited with saying: “It is more important to know what kind of person has a disease than what disease a person has.”

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Due to the accumulation of the arsenal of modern tools in the diagnosis of Diseases and the development of specialization, at this time the vast majority of patients that fall to the doctor are not detectable one nosology and individual combination of several Diseases, which in the context of specialized agencies are classified as “primary” diagnosis and pathology. Individual sensitivity to treatment (in particular pharmacological), as well as individual side effects in each case lead to different outcomes and the development of “adverse” effects, complications and for subsequent violations in the form of other, or relapse. Thus, despite the familiarity of the current



situation, if the result is to evaluate objectively, the modern approach to medical practice is not optimally effective in the diagnosis or treatment of any. This situation dictated by the progress of technology now pushes the development of “personalization of therapy”, which claims to be a more “individual-focus» approach through the study of human genetic diversity. While a great number of scientists and clinicians around the world at this time to spend trillions of dollars on the identification and validation of genetic markers, it becomes clear that most of the genetic variants are outside the coding genome and function they are not clear, and therefore can not yet be no question of possible therapeutic use of this information.

The concept that we are a product of our DNA leads to fantasies that through manipulation of [it], we could avoid or cure all diseases and even prevent death. It is really fantastic. All flesh is mortal (Lewontin). One of seeing “O” is the direction of the use of genetic markers as diagnostic. But in fact, this approach also relies on nosologically-oriented paradigm. Owned A statistical significance of genetic markers is determined in groups of people classified according to nosology, that does not solve the above-described problems of practical medicine. Parallel developing directions of studying the global gene expression (transcriptomics) and epigenetics (the study of non-genetic markers of gene expression regulation) as well go to the beaten path nosologically centering approach. In addition, the fact that more than 90% of the genome is not kodiruyushie protein sequence, and the resulting data on the role of non-coding RNA, micro RNA, transposons and endogenous viruses in gene expression regulation, points out that the traditional approach of epigenetics (focusing on modification and histone methylation/acetylation DNA) does not reflect the complexity of the regulation of gene expression mechanisms. Another growing branch of science: mikro-biomic already reveals details about the incredible complexity of the composition of the microbiome of the individual, his dynamic relationship with environmental factors on the one hand and the role of the human genome regulation of expression, on the other hand. Thus, it becomes evident the need for not only an integrative approach to the study of the individual person but also the revision of its application paradigm.

Namely, we must learn not what markers define nosology, as well as markers of the nosology and express the individual characteristics of a particular person as integrated unit dynamically adapts to conditions definid its dynamic environment [15].

The reason that the experts are not able to see the essence of the contradictions in the developing dynamics inherent in the very basis of specialization system, which leads to difficulty or inability to

explore the details and combining them with practice. This is clearly reflected in the inherent tensions of modern physics in the form of incompatibility at its Apparently, the principles of quantum mechanics, the principles of Newtonian mechanics [2; 4]. The problem of the traditional scientific approach, is in a linear-reductional approach in thinking on the principle of “the whole is the sum of its components». [16] The second, more important problem is the reluctance of scientists to go beyond the standard thinking that but in fact contrary to the very principles of science as a discipline that distinguishes its religious system based on dogma [2; 4] Nevertheless, the exponentially growing number of receiving information about the components of the human body and the inability to equip them in the “traditional framework” nosology calls for a qualitatively new way of thinking.

#### Perspective of new technologies

Chance for correcting the trajectory of further development of medical practice and science is the application of modern information technologies and the use of mobile non-invasive sensors, allowing a dynamic collection of information on the functioning of the body’s systems in real time. This will set an individual rate for each individual in the context of his individual perception and the way to respond to the environment and the search for individual correction methods an managementt these deviations. [19,20,21] Thus, the next logical step will be to study the dynamics of adaptive Sustainability Index organism as an integrated unit reflecting the cumulative construction of the previous adaptive reactions in the context of current environmental conditions in which it operates. One of the parameters that on the one hand reflects the degree of adaptive resistance of the organism, on the other hand is an option available for non-invasive dynamic monitoring is heart rate variability [3].

Heart rate variability is the most convenient indicator by which you can assess the effectiveness of the interaction of the cardiovascular and other systems of the body. This analysis is becoming popular due to its simplicity, because it is not invasive. This test is beginning to be used in functional diagnosis, as the index of heart rate variability allows us to give an overall assessment of the patient’s condition, as they reflect management’s vital indicators of physiological functions, these include functional reserves its control mechanisms and autonomic balance [3; 6; 11; 12; 21].

Effect of sympathetic nerve leads to an increase in heart rate due to stimulation of beta-adrenergic receptors of the sinus node. In turn, the vagusnerve stimulates cholinergic receptors of the sinus node and lead to bradycardia. The sympathetic system has greater influence over the ventricles, while the vagus nerve has an effect on the sinoatrial and atrioventricular nodes [5; 7; 8; 10; 17].



Figure 1. Stairs of states

In the heart rate affect the phase of respiration. During inhalation inhibited vagal influence (the influence of the vagus nerve) and the accelerated rhythm. During exhalation heart activity slows as the vagus nerve is irritated. We can say that the heart rate is a reaction to the stimulus of internal and external environment. Therefore, the change rate is a response to changes in some factors and regulated by sympathetic and parasympathetic divisions of the nervous system.

For example Russian project Kardi.Ru, offers its clients monitor the performance of the cardiovascular system, which is based on heart rate variability indices for assessing the adaptive capacity of the organism and its functional reserves. On the state of the cardiovascular system can be judged by the degree of tension of regulatory systems, the effect of which affects the heart rhythm [13; 14; 15; 16].

In a study of people receiving the conclusion, which is a graph of “Stairway states”, where you can see the approximate functional state of regulatory systems.

The physiological norm – hence the regulation of heart on the part of the autonomic nervous system is normal. Psycho-emotional state, and the energy supply of the body are also within the normal range.

Prenosological state – a decrease of adaptation options are possible signs of fatigue.

Premorbid state – indicates overstrain of regulatory systems.

Failure to adapt – in overvoltage is the autonomic nervous system, drastically reduced the energy resources of the organism. In humans, there are signs of accumulated fatigue and nervous overstrain. Patients are advised to visit a specialist.

The analysis of heart rate variability allows to evaluate the overall condition of the person to identify the adaptive capacity of the body, to analyze the psycho-emotional state [14]. Heart rate variability can be used in therapeutic practice for the detection prenosological signs of adaptation failure, and is already beginning to widely applied in sports medicine for dispensing individual loads.

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## Absence: modern methods of diagnostics and treatment

**Actuality.** Absences are states with sudden short loss of consciousness. Patients stop and stay in the pose that they were when the absence caused and when the absence is finished they continue doing action. During such attack patients may turn pale (seldom they may flush), roll their eyes and throw their heads. Attacks are springing up in groups several times in the day, mainly after sleeping in the morning. Such a difficult problem requires further research of modern methods of diagnostics and treatment to improve patient's life. It is one of the most widespread types of children and teenagers epilepsy attacks. There are 6,13 cases of new diagnosed absence attacks in the year among 100 000 children under 16 years [1; 2; 11]. Absences make 50% through all generalized seizures [3]. Girls preponderate in 1,5–2 times. First appearance of children absence epilepsy (CAE) takes place in the age of 1 to 9 years, averages  $5,3 \pm 0,31$  years [1]. Effectiveness of treatment of epilepsy depends on accurate diagnostics of every form of epilepsy or epileptic syndrome. Epilepsy form influences as prognosis of disease's tendency (intellect saving, sensitivity to anticonvulsants) as treatment tactics. That's exactly diagnosis determines when the anticonvulsant therapy should be started, what medicine should be given, what dose of anticonvulsant a patient requires and how long should the treatment last [12].

**The objective of research.** To analyses modern methods of diagnostics and treatment of absence with the aid of literature information.

**Results.** During an absence (a small fit), the patient interrupts the conversation or some action, his gaze stops or wanders, and after a few seconds he continues the interrupted conversation or action. In some cases, the deactivation of consciousness is accompanied by a change in the tone of individual muscle groups (more often the muscles of the face, neck, upper limbs), bilateral light muscle twitching or vegetative disorders. Diagnostics of absences in many cases is difficult. Outside the attack, most often there are no signs of neurologic pathology. There may be a gap in mental development. The main method of diagnosing epilepsy is the EEG, at which typical specific absences reveal a specific generalized pattern-peak — a slow wave at a frequency of 3 Hz. For the detection of absences, a standard clinical record and an EEG background record are required, in which the bioelectric activity of the brain during the interstitial period can be quite normal, but discharges of generalized bilateral synchronous complexes of 3 Hz peak-wave can be recorded for various periods on background of normal basal rhythms [2]. Moreover, functional tests can be used: eye opening has a blocking effect on epileptiform activity; rhythmic photostimulation provokes the appearance of peak-wave activity in a small number of patients with CAE (not more than 10% of cases); hyperventilation — the main provoking factor for the

appearance of absences [1; 5; 3]. If necessary, they use EEG-video monitoring, positron emission tomography (PET), as well as a number of biochemical, immunological and other special methods of investigation.

In the treatment of epilepsy with typical absences, the base drug is sodium valproate, as was shown in many studies. The advantage is given to monotherapy. For example, in one of the studies, clinical systematization was carried out and the principles of therapy for the absence of children epilepsy were developed. At the same time, all variants of absence seizures were isolated into separate epileptic syndromes: child's absence-epilepsy (CAE); Juvenile absences-epilepsy (UAE); Juvenile myoclonic epilepsy (UME); Epilepsy with myoclonic absences (OMA). The main criteria for differential diagnosis were the age of the debut of absences, their nature, the presence of concomitant seizures, EEG data and response to therapy. The drugs of choice in the treatment of all forms of absence epilepsy were the derivatives of valproic acid. The initial treatment was carried out with monotherapy with depakin in the initial dose of 15 g/kg/day with a gradual increase to 30–50 mg/kg/day and higher to obtain a pronounced therapeutic effect. When the monotherapy was ineffective, a combination of valproate + lamotrigine (lamictal) or valproate + succinimide (suxilep) was used. The starting dose of lamictal was 0.2 mg/kg/day in one dose, with a gradual increase to 25 mg/kg/day in 2 divided doses. In comparison, lamictal was more effective than suxylep in cupping absences and had significantly better tolerability. The therapeutic prognosis varied significantly depending on the form of absence epilepsy. The best prognosis was observed in CAE and JME with achievement of complete remission in 70% and 71% of cases, respectively. In the case of JAE, the prognosis was significantly dependent on the adherence of generalized convulsive seizures, and remission was noted in 56% of patients. With EMA, remission was achieved in 33% of cases, solely with polytherapy (combination of depakin and lamictal). The study shows the need to identify different forms of absent epilepsy due to different prognosis and therapeutic approaches [4; 9; 10].

Initial treatment of absences is carried out with monotherapy with valproic acid derivatives. If it is inefficient, there is optimal the combination of valproate with lamotrigine. The prognosis of various forms of epilepsy with atypical absences is much worse and requires, as a rule, the use of polytherapy with antiepileptic drugs (AEP). In this case, the combination of valproates with succinimides is optimal. In addition, the psychotherapeutic methods used at different stages of the disease acquire special significance. Their effectiveness depends on a complex of factors, including qualitative characteristics of the pathological process, as well

as individual personality characteristics, the level of its compensatory capabilities. General and special psychotherapeutic measures contribute to a higher level of rehabilitation of patients, which is reflected in more orderly behavior, fixes the achieved reduction of convulsive disorders, and in some cases, causes a transfer to a stable decrease in the doses of anticonvulsants [5; 6; 7; 8]. Resistance to AED, the presence of neurological and cognitive impairment in patients with absence forms of epilepsy require careful examination (including high-resolution neuroimaging and modern methods of molecular genetic diagnosis) to exclude the symptomatic genesis of epilepsy [3]

**Conclusion.** All types of small seizures occur mainly in childhood, but, disappearing in adolescence, can be transformed into polymorphic convulsive and large epileptic seizures. In connection with this, the treatment of small forms of epilepsy must be combined with the use of anticonvulsants to prevent large seizures. The leading method of diagnosis at present with small forms of epilepsy is the EEG using provocative samples, especially hyperventilation; the leading method of therapy is still the use of valproic acid and ethosuximide. Therefore, the diagnosis and treatment of small forms of epilepsy are one of the most difficult problems in medicine, which requires further study.

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## The influence of in utero and early postnatal exposure to pesticides on the process of cells apoptosis and proliferation in immune and endocrine organs of the offspring

### Abstract

**Objective:** Immunohistochemical evaluation of apoptosis and cells proliferation in the thyroid and thymus of offspring in a prenatal and early postnatal exposure to pesticides.

**Material and methods:** Experiments were performed on white adult female rats, which were divided into 3 groups of 30 animals each. Two groups of animals for 30 days daily per os obtained respectively pesticides cyhalothrin (8 mg/kg), or fipronil (3.6 mg/kg). The third group receives only the same volume of sterile saline served as control. Apoptotic and proliferating cells of the thyroid gland and thymus were determined by immunohistochemistry method using monoclonal antibodies (Thermo Scientific, USA).

**Results:** It was found that both fipronil and cyhalothrin under the influence through the mother causes a marked induction of apoptosis in the offspring thyroid and thymus. Simultaneously, these pesticides cause inhibition of proliferative activity of cells in these organs.

**Conclusions:** Intrauterine and early postnatal exposure of pesticides to cause the induction of apoptosis, but the inhibition of proliferative activity of cells in the thyroid and thymus of offspring. In the mechanism of induction of apoptosis, besides the direct toxic effects of drugs are important hypothyroidism and oxidative stress observed in the offspring. These data contributes to the development of a new method of prevention and treatment of hidden toxic effects in pregnant women and their newborns.

**Keywords:** pesticides; postnatal ontogenesis; thyroid; thymus; cells apoptosis; cells proliferation; immunohistochemistry.

**Introduction.** Programmed cell death (PCD), or apoptosis, is the mechanism which is crucial to the body under the control of cell proliferation and the maintenance of tissue homeostasis [2; 3; 5]. Under physiological conditions, between the processes of apoptosis and cell proliferation there is a balance that allows you to maintain tissue homeostasis [2; 7]. Defects in apoptosis physiological mechanisms can lead to a variety of human diseases, including the development of malignancy and cancer process [2; 5]. This explains the great interest in the in-depth study of the mechanisms of apoptosis and effector proteins, as well as genes involved in apoptosis. The results of these studies have opened great possibilities to control the process of apoptosis and to develop new methods for treating various diseases, including cancer [2]. In recent years, it revealed that many environmental contaminants, including pesticides of new generations, act as apoptotic cells triggers [3; 4; 6; 7]. It is found that one of the most widespread and effective insecticide Fipronil (F) substantially induces apoptosis in line SH-SY5Y and *Drosophila* S2 cells under in vitro [12; 13]. Another, no less common, pesticide of pyrethroid class lambda-cyhalothrin (C) led to an increase in fragmentation of rat bone marrow of human lymphocyte cell nuclei, indicating the induction of apoptosis [1; 6]. Most authors believe that the induction of apoptosis under the influence of pesticides associated with the development of oxidative stress and the subsequent activation of the caspase family enzymes and apoptosis-stimulating p 53-family proteins [3; 4; 6; 12; 13]. However, it should be noted that all of these studies were conducted on cell lines or on adult individuals of experimental animals. We have previously shown that in utero and early postnatal exposure to pesticides through the mother's body has a negative effect on the organs of the endocrine and immune progeny systems, leading to

their structural and functional impairment of growth and formation in the dynamics of postnatal ontogenesis [10; 11]. However, the value of cells apoptosis and proliferation in the mechanism of these disorders remains unclear.

**The purpose** of the study was a immunohistochemical assessment of cells proliferation and apoptosis in the thymus and thyroid of offspring in conditions of in utero and early postnatal exposure to pesticides.

**Material and methods.** Experiments were performed on nulliparous, white adult female rats, which were divided into 3 groups of 30 animals each. Two groups of animals for 30 days daily per os obtained respectively pesticides cyhalothrin (8 mg/kg), or fipronil (3.6 mg/kg). The third group receiving only the same volume of sterile saline served as a control. The following day, the females were coupled to healthy males for fertilization. Pregnancy was monitored for the presence of sperm in vaginal smears. Exposure of pesticides was continued incessantly during pregnancy and after delivery until the end of lactation. Offspring obtained from the experimental and control females were studied in dynamics on days 7, 14, 21 and 30 after birth. For immunohistochemical studies of proliferation and apoptotic cells paraffin sections of thymus and thyroid have been used. Apoptotic cells were detected using a rabbit monoclonal antibody to fragments of caspase – 3 proteins and the family of p – 53 (manufactured by Thermo Scientific, USA). Proliferation cells have been detected using a rabbit monoclonal antibody to protein Ki – 67 (manufactured by Thermo Scientific, USA). Further procedures for visualization of proliferation and apoptotic cells by labeled with horseradish peroxidase were carried out by the standard procedure using reagents Ultra-Vision complex (manufactured by Thermo Scientific, USA). Further sections have been stained

methylene blue and neutral red. Further the numbers of labeled proliferating and apoptotic cells counted on 1000–5000 total cells and calculated an index of proliferation and apoptosis, that is expressed in parts per thousand. All digital data were processed by the method of variation statistics. Statistical significance between control and experimental groups was compared using the Student's *t* test and *P* values < 0.05 were considered significant.

**Results and discussion.** Apoptotic and proliferating cells on sections after carrying out immunohistochemical reaction looked dark brown due to visualization of horseradish peroxidase-labeled secondary antibodies. They were easily identified from unlabeled cells. Differences between the levels of proliferation and apoptosis of the cells of the studied organs were most clearly manifested in the quantitative calculation of the indices of proliferating and apoptotic cells. The cell proliferation index of both thymus and thyroid gland was highest on day 7 after birth. In the future, it gradually decreased and on the 30 th day after birth was about 55–60% of the baseline. Similar dynamics was characteristic for both control and experimental groups of rats. The effect of pesticides led to inhibition of the proliferative activity of cells of both thymus and thyroid gland. On the 7th day after birth, the index of thymus cells proliferation under the action of cyhalothrin in 1,5 times, and when exposed to fipronil 1.8 times decreased in comparison with the control (*P* < 0.05). A similar decrease in the proliferation index was found in the thyroid gland. A significant decrease in the cell proliferation index in both organs persisted up to 21 days after birth. At 30 days after birth, the decrease in the cell proliferation index in both organs was statistically unreliable (*P* > 0.05). Thus, exposure to pesticides led to inhibition of proliferative activity of cells in both the immune and endocrine organs of the offspring. In this case, the negative effect of fipronil was more pronounced in comparison with cyhalothrin.

Data of a different nature were obtained when calculating the apoptosis index of cells in the thymus and thyroid gland. The level of apoptosis in the thyroid gland of control animals was very low and at the dynamic of postnatal development the apoptosis index gradually increased. In contrast, in the thymus, apoptosis was initially high and increased significantly in the dynamics of postnatal growth of animals. Intrauterine and early postnatal exposure to pesticides led to a significant increase in the degree of apoptosis of cells of the thyroid gland and thymus. In the thyroid gland of the offspring, under the influence of cyhalothrin, the apoptosis index was 3.5–4 times, and when fipronil was 4.5–5 times higher than the control group in all periods of the study (*P* < 0.05). A similar significant increase in the apoptosis index at all times of the study was observed in the thymus of the experimental animals. Thus, exposure to pesticides led to a significant increase in the degree of apoptosis of cells of both the thyroid gland and thymus. Un-

der the influence of fipronil, the induction of apoptosis of the cells was manifested to a higher degree as compared with cyhalothrin.

Thus, both fipronil and cyhalothrin when exposed through the mother's organism cause a marked induction of apoptosis in the thyroid and thymus glands of the offspring. Simultaneously, these pesticides cause inhibition of proliferative activity of cells in these organs. Thus, there is an imbalance between the processes of proliferation and apoptosis in organs and tissues. Our previous studies have shown that both pesticides in conditions of prenatal and early postnatal expose cause a slowdown in the growth and formation of the thyroid gland, a decrease in organ function in the offspring in the form of hypothyroidism [10; 11]. In this case, hypothyroidism was more pronounced when exposed to fipronil compared with cyhalothrin. It has long been known that the thyroid hormones, along with the growth hormone, regulate the proliferation of cells in virtually all tissues. Recent data show that thyroid hormones also have a high anti-apoptotic effect, which opens great prospects for the regulation of apoptosis in various diseases [5]. All this makes it possible to consider that the intensity of induction of apoptosis in our experiments is to a certain extent determined by the degree of thyroid dysfunction and the weakening of the proliferation-stimulating and anti-apoptotic effects of its hormones. This is confirmed by our data indicating a more pronounced induction of apoptosis when exposed to fipronil. On the other hand, an important role in the induction of apoptosis is played by oxidative stress, caused by an increase in the production of free radicals [3; 7]. Earlier, we showed that both pesticides in prenatal and early postnatal conditions cause pronounced oxidative stress in offspring [8; 9]. Consequently, the induction of apoptosis in the experimental progeny is caused not only by the direct toxic effect of pesticides, but also largely mediated by the weakening of the anti-apoptotic function of thyroid hormones due to hypothyroidism and the resulting oxidative stress in the form of an increase in the number of free radicals.

#### Conclusions:

1. Pesticides of the new generation of cyhalothrin and fipronil in conditions of *in utero* and early postnatal expose cause induction of apoptosis in the thyroid and thymus glands of the offspring.
2. In the mechanism of induction of apoptosis of cells, along with direct toxic effects of drugs, an important role is played by hypothyroidism and oxidative stress observed in offspring.
3. Induction of apoptosis and inhibition of cells proliferation are more pronounced when exposed to fipronil compared with cyhalothrin.
4. Disclosure of mechanisms of apoptosis induction under the influence of pesticides contributes to the development of a new methods for the prevention and treatment of latent toxic effects in pregnant women and their newborn children.

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## The role of adipokines, triglycerides and free fatty acids in the development of insulin resistance in the presence of metabolic syndrome

**Abstract:** The objective of the study was to investigate the possible role of adipokines (leptin, adiponectin), triglycerides (TG) and free fatty acids (FFA) in the development of insulin resistance (IR) in patients with metabolic syndrome (MS).

The study included 170 patients with MS (67 men and 103 women) at the age of  $51,5 \pm 3,93$  years. It was determined that the increase of TG, FFA, leptin and the decrease of adiponectin were observed in the patients with MS with high HOMA index. However, the analysis of data in the groups of patients with different body mass demonstrated that the development of IR in patients with obesity may be influenced by the increase of TG, FFA and leptin concentrations, while in patients without significant obesity — by the increase of TG, FFA levels and the decrease of adiponectin.

Thus, it is possible to assume that leptin, adiponectin, TG and FFA may influence the development of IR, however, their role depends on the severity of obesity.

**Keywords:** adipokines, leptin, adiponectin, triglycerides, free fatty acids, insulin resistance, metabolic syndrome.

Insulin resistance is an important pathogenic factor in the number of diseases and disorders such as diabetes mellitus of the 2<sup>nd</sup> type, atherosclerosis, arterial hypertension (AH), atherogenic dislipoproteinemia [1; 2; 3; 14]. Insulin resistance (IR) means the reduction in the response of insulin-sensitive tissues to insulin in the case of its sufficient concentration [3; 12; 13; 17]. In this case, these disorders are combined into a single complex called “metabolic syndrome”.

In the pathogenesis of metabolic syndrome (MS) the special role is assigned to obesity or abdominal fat distribution, which con-

tribute to the development of IR [1; 2; 8; 9; 13]. Therefore, with regard to the mechanisms of development of IR with MS a special attention is paid to the change of adipokine levels in the blood — biologically active proteins that are produced by fatty tissue (leptin, adiponectin, visfatin, resistin, interleukin-6, tumor necrosis factor alpha) [5; 7; 8; 15]. Moreover, an important role in the development of IR can be assigned to triglycerides (TG) and free fatty acids (FFA) that are produced in the course of lipolysis by fatty tissue and in the blood stream by lipoproteins, which contain a great amount of



TG [9, 18]. However, the role of each of these substances in the development of IR is still not clarified; and also it is not clear how the change in their concentrations is connected with the presence of obesity and pathogenesis of IR in the case of MS [4; 12; 20].

The objective of the study was to investigate the role of fatty tissue hormones – adipokines (leptin, adiponectin), triglycerides and free fatty acids – in the development of insulin resistance in patients with metabolic syndrome.

#### Material and methods

170 patients with MS (67 men and 103 women) at the age of 35–70 years (on average –  $51,5 \pm 3,93$  years) were examined. The control group (volunteers) included 58 people of similar sex and age.

Metabolic syndrome was diagnosed according to the criteria, which were proposed by the Expert Panel of the National Cholesterol Education Program of USA (2005). The criteria of MS were as follows: waist circumference – over 94 cm in men and over 80 cm in women; blood pressure – 130/85 mm Hg and higher, the glucose level in blood plasma on an empty stomach – 5,6 mmol/l and higher. The body mass index (BMI, Quetelet index) was calculated using BMI formula = body mass (kg)/height (m<sup>2</sup>).

Glucose-insulin homeostasis was determined according to the fasting blood glucose level, the insulin level in blood by immunoenzyme method in radio-immune laboratory of the Republican Endocrinology Center (Tashkent city), using the kits of the firm “Beckman Coulter” (Czech Republic). HOMA index was calculated (insulin on an empty stomach microunits/ml x fasting blood glucose mmol/l:22,5). Hyperinsulinemia was diagnosed, if the insulin level on an empty stomach was higher than 12,5 microunits/ml. The patients were considered to be insulin-resistant, if HOMA index was above 2,77.

The values of lipid blood composition (total cholesterol (TC), HDL cholesterol and TG) were determined using the express-analyzer “Reflotron plus” of the firm “Roshe” (Germany), with the help of reagents kits “Biocon” (Germany). The levels of LDL cholesterol, VLDL cholesterol were calculated using W. Friedwald formula. Integral index – atherogenic coefficient (AC) – was calculated using the following formula:  $AC = (TC - HDL \text{ cholesterol}) / HDL \text{ cholesterol}$ .

The concentration of FFA in the blood serum was determined with the help of NEFAFS test-system of the firm “Disus” (Germany) in the laboratory of the Department of Biochemistry of Tashkent Medical Academy.

The levels of leptin and adiponectin were estimated through a competitive immune-enzyme analysis, using the kits of the firm “Bio Vender-Laboratorni medicina E. S.” (Czech Republic), in the laboratory “Immunogen-test” at the Institute of Immunology of the Uzbekistan Academy of Sciences.

Statistical data processing was performed by the variational method with the use of Student’s t-tests. The results were processed with the help of the program package “Statistica-6”. Correlation and regression analyses were performed in order to identify the connections between HOMA index and different parameters. The level of significance was considered to be reliable at  $p < 0.05$ .

#### Results and their discussion

The results of the study have shown that patients with MS with reduced insulin sensitivity (the 2<sup>nd</sup> and 3<sup>rd</sup> groups according to HOMA index) have a higher body mass index and a more pronounced abdominal fat distribution. In addition, the increase of TG, FFA, TC levels and the decrease of HDL cholesterol were observed in these patients (Table 1).

Correlation analysis confirms these relationships and denotes the connection of HOMA index with abdominal obesity and atherogenic changes of lipid spectrum, which does not depend from BMI. These changes are consistent with the well-known notions about the close relationship between abdominal obesity and IR, as well as about the important role of IR in the development of atherogenic dislipoproteinemia in the case of obesity with MS [4; 6; 16]. However, the mechanisms of the development of IR with MS are still insufficiently studied. One of the approaches in the study of this issue is to research the role of substances, which are produced by fatty tissue, such as adipokines, TG and FFA. The results have shown that the decrease of insulin sensitivity of the tissue was accompanied by the increase of TG, FFA, leptin levels in the blood and the decrease of adiponectin concentration.

Table 1. – Clinical and metabolic parameters in the patients with MS with different values of HOMA index

Parameters	Values of HOMA index		
	1 group (n=37)	2 group (n=65)	3 group (n=68)
HOMA index	1,22±0,28 (0,81–1,54)	2,32±0,54 (1,55–2,99)	6,85±2,13 (3,00–12,88)
Men/women	15/22	25/40	27/41
Age/years	54,7±10,42	50,8±8,02	52,3±9,18
Body mass index kg/m <sup>2</sup>	26,2±3,93	33,6±4,71***	38,6±6,04***
Waist circumference, cm	94,0±10,21	98,1±11,0*	104,2±12,6**
Leptin, ng/ml	18,6±3,68	23,5±4,16**	30,9±6,42***
Adiponectin, µg/ml	7,6±3,52	6,15±3,11*	5,75±2,77**
Glucose on an empty stomach, mmol/l	5,9±1,13	6,6±1,32*	8,7±2,78***
Insulin, microunits/ml	7,1±2,06	11,3±4,41**	18,13±9,41***
Total cholesterol, mmol/l	6,21±1,64	6,90±1,93*	7,51±2,56**
TG, mmol/l	1,94±1,03	2,18±1,97*	2,43±1,34**
HDL cholesterol, mmol/l	1,02±0,16	0,94±0,13*	0,84±0,10**
LDL cholesterol, mmol/l	4,32±1,85	4,85±2,03*	5,33±2,71**
Atherogenic index	4,91±1,78	5,41±2,21*	6,8±2,96**
FFA, mmol/l	0,60±0,35	0,75±0,42*	0,86±0,69**

Note: \* – The values of significance of differences between the groups: the differences are reliable in comparison with the 1<sup>st</sup> group at: \* –  $p < 0,05$ ; \*\* –  $p < 0,01$ ; \*\*\* –  $p < 0,001$ .



According to correlation analysis, each of these factors has connections with IR, which do not depend from BMI (Table 2).

The literature also provides information on the connection of IR with FFA, leptin and adiponectin concentrations, which does not depend from BMI [4; 10; 12]. In other words, we can say that the change in the levels of TG, FFA and adipokines reflects not only obesity, but also IR, and therefore, we can assume that these substances may be involved in the development of IR [12]. However, it is still insufficiently studied, whether these substances may be involved in the pathogenesis of IR in individuals with normal and excessive body mass, or the change of their concentration has a greater importance for the development of IR in the case of obesity with MS [15; 17; 20].

Table 2. – The connection of HOMA index with clinical and metabolic parameters in patients with MS

Parameter	Correlation
Age, years	-0,22*
Body mass index, kg/m <sup>2</sup>	0,45*
Waist circumference, cm	0,43*
Leptin, ng/ml	0,33*
Adiponectin, µg/ml	-0,37*
TG, mmol/l	0,39*
FFA, mmol/l	0,44*
Total cholesterol, mmol/l	0,23*
HDL cholesterol, mmol/l	-0,36*
Atherogenic index	0,30*

Note: \* – the significance of correlation at  $p < 0,05$

Table 3. – The blood levels of TG, FFA, leptin and adiponectin in patients with MS with different values of BMI and HOMA index

Parameters	Patients with MS with normal and excessive body mass (BMI < 28kg/m <sup>2</sup> )		Patients with obesity (BMI ≥ 28kg/m <sup>2</sup> )	
	HOMA < 1,5	HOMA > 2,77	HOMA < 1,5	HOMA > 2,77
Number of patients	20	17	12	40
Men/women	8/12	7/10	5/7	17/23
Age, years	53,7±9,2	51,9±8,51*	50,7±8,04	52,9±9,36
Body mass index, kg/m <sup>2</sup>	24,4±2,67	26,9±3,96*	33,1±4,80###	37,7±5,73*###
HOMA index	1,14±0,31	4,85±1,49***	1,31±0,49	5,76±2,08*###
TG, mmol/l	1,93±1,03	2,11±1,83**	2,04±1,62	2,42±1,61#
FFA, mmol/l	0,60±0,35	0,72±0,39**	0,71±0,43	0,85±0,17*#
Leptin, ng/ml	12,6±3,09	16,7±5,03**	21,5±4,04###	28,5±5,87*###
Adiponectin, µg/ml	7,5±3,58	6,11±3,42**	6,03±3,41	5,75±2,93*#

Note: 1. The differences are reliable in comparison with individuals without obesity in HOMA category at: \* –  $p < 0,05$ ; \*\* –  $p < 0,01$ ; \*\*\* –  $p < 0,001$ .

2. The differences are reliable in comparison with the insulin sensitive individuals in BMI category at: # –  $p < 0,05$ ; ## –  $p < 0,01$ ; ### –  $p < 0,001$ .

Table 3 provides information on TG, FFA, leptin and adiponectin levels in patients with different values of body mass and HOMA index. As shown, TG, FFA and leptin levels in the presence of IR change only in patients with obesity (BMI ≥ 28kg/m<sup>2</sup>), while the adiponectin concentrations change in the examined individuals without pronounced obesity (BMI < 28kg/m<sup>2</sup>).

According to the correlation analysis, the TG and FFA levels are still connected with IR in patients with BMI < 28kg/m<sup>2</sup>,

although this correlation is less pronounced in comparison with the group of patients, who suffer from MS with obesity (Table 4). Therefore, we can assume that TG, FFA and adiponectin may be involved in the development of IR in patients with MS without pronounced obesity; however adiponectin, in contrast to FFA and leptin, is not connected with the development of IR in patients with obesity.

Table 4. – The connection of HOMA index with TG, FFA, leptin and adiponectin levels in patients with MS with different BMI

Parameter	Patients with excessive body mass (BMI < 28 kg/m <sup>2</sup> )	Patients with obesity (BMI ≥ 28 kg/m <sup>2</sup> )
TG, mmol/l	0,30*	0,41*
FFA, mmol/l	0,29*	0,40*
Leptin, ng/ml	0,27	0,33*
Adiponectin, µg/ml	-0,29*	-0,16*

Note: \* – correlation is reliable at  $p < 0,05$

The reasons of the detected differences in the connection between TG, FFA, adipokines levels and IR under different degrees of body mass excess remain unknown. However, it is possible to assume that these differences may be caused by the differences in the production of other substances by fatty tissue (for example, other adipokines, which, influencing the insulin sensitivity, may decrease the impacts of leptin and adiponectin on IR) [6; 10; 11]. However, another study shows that adiponectin levels decrease in the presence of IR in persons with normal and excessive body mass, as well as in patients with obesity [5; 16; 19]. Apparently, this was due to the fact that the adiponectin concentration in patients with obesity and without IR was as high as in patients with normal and excessive

body mass without IR [4; 9; 20]. Adiponectin level with normal insulin sensitivity and obesity reduced considerably. Thus, apparently, an important reason for the lack of impact of adiponectin on IR in patients with MS and obesity is a low dispersion of its concentrations in this group and respectively a low degree of its impact.

Regression analysis revealed that HOMA index was influenced by the levels of adiponectin ( $\beta = -0,30$ ,  $p < 0,01$ ), leptin ( $\beta = 0,22$ ,  $p < 0,01$ ), TG ( $\beta = 0,25$ ,  $p < 0,01$ ), FFA ( $\beta = 0,24$ ,  $p < 0,01$ ).

In the course of analysis of the literature review we did not reveal any studies that simultaneously investigate the impact of TG, FFA and different adipokines on the development of IR in the case of MS. However, there are works, which also show that adiponectin

and leptin are independent predictors of IR [5; 6; 14]. However, there are still many ambiguities with regard to the influence of adiponectin and TG on insulin sensitivity. It is assumed that adiponectin exerts this impact through stimulating influence on TG and FFA oxidation through the decrease of the glucose production by hepatocytes [18; 20]. These effects are not connected with the impact of adipokine on the insulin signal transduction [4; 20]. Signal pathways of influence of adiponectin remain unknown [4; 20]. However, the connection between adiponectin and IR in patients with MS, which we detected in our study, makes us suggest that the decrease of adiponectin level plays an important role in the development of IR in patients with MS.

### Conclusions

1. The levels of leptin, adiponectin, TG, FFA in patients with MS change not only in the case of obesity, but also in the case of insulin resistance.
2. The independent role of leptin, adiponectin, TG and FFA in the development of insulin resistance in patients with MS was identified.
3. The development of insulin resistance in persons with MS and obesity is influenced by the increase of leptin, TG and FFA concentrations, while in persons with MS without pronounced obesity – by the decrease of adiponectin and the increase of TG, FFA levels.

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## Noninvasive topical diagnostics and radiofrequency ablation of ventricular arrhythmia

**Abstract:** The article provides data on 35 patients with ventricular arrhythmias of non-ischemic etiology, who underwent radiofrequency ablation. Topical diagnostics was performed on the basis of 12-lead electrocardiogram according to algorithms, which again confirmed their rapid response. The effect of RFA was full except for the ventricular arrhythmia that was caused by organic pathology.

**Keywords:** ventricular tachycardia, radiofrequency ablation, electrophysiological study.

Patients with non-coronary ventricular tachycardia (VT) represent a fairly heterogeneous group and constitute about 10% of all ventricular heart rhythm disturbances (HRD) [1]. It is believed that non-coronary ventricular arrhythmias, especially idiopathic, which occur in perfectly healthy people, are safer and have a favorable prognosis [2]. However, even really idiopathic ventricular arrhythmias subjectively are often poorly tolerated by patients, significantly deteriorating their quality of life, disturb hemodynamics and may lead to myocardial remodeling and formation of the so-called arrhythmogenic cardiomyopathy and ultimately to the development of heart failure. Often solely the factor of presence of arrhythmia deteriorates significantly the patients' quality of life, leads to the work decrement and social maladjustment. Therefore, it is very important to develop and improve the methods for timely diagnostics and treatment of heart rhythm disturbances [3; 4; 5]. It should be noted that drug therapy in patients with ventricular HRD is often inefficient or completely inefficient. In addition, for many patients, especially young, who consider themselves to be healthy, it is psychologically difficult to tolerate the need for daily consumption of medicines. Modern approaches to the treatment of cardiac arrhythmias are associated with active introduction of new methods of electrophysiological diagnostics and interventional treatment options into clinical practice. In recent years it was demonstrated that catheter ablation of non-coronary ventricular arrhythmias is an effective and rather safe method of treatment [6]. At the present time the Republican Specialized Center of Cardiology of Uzbekistan (RSCC) has an experience of using the radiofrequency ablation (RFA) of various HRD. Temporary absence of navigation system for a more accurate topical diagnostics reduces the possibilities for surgical treatment of HRD. However, as shown in the studies, adherence to the algorithms of ECG-diagnostics of the arrhythmogenic focus location allows to make a differentiated approach to the selection of patients for RFA.

**Objective:** assessment of effectiveness of RFA in the patients with VT, depending on their topography (based on the analysis of standard 12-lead ECG) without use of navigation system.

**Materials and methods:** 35 patients at the age from 18 to 48 years (average age  $30 \pm 12,6$  years) were examined in the department for surgical treatment of HRD at RSCC. Strongly pronounced symptoms of arrhythmia were observed in all patients: 18 persons had past syncopal conditions in anamnesis, 20 persons complained

of dizziness, 33 patients felt cardiac malfunctions; all patients experienced the shortness of breath on exertion. Thus, no case of asymptomatic course of ventricular HRD was observed. 9 patients had the signs of past myocarditis, 26 patients were diagnosed with "idiopathic VA". The selection of anti-arrhythmic therapy was performed for all patients at the prehospital stage, which included cordarone, a combination of several anti-arrhythmic drugs of different classes, which turned out to be ineffective. All patients underwent: analysis of the morphology of ectopic ventricular complexes, which were recorded by the body-surface 12-lead ECG; daily ECG monitoring by Holter; blood test for thyroid hormones; echocardiography; coronarography (on indications); endocardial electrophysiological study (EPS). Under daily ECG monitoring by Holter, a significant number of extrasystoles was marked in all patients: from 8000 and more within 24 hours. In 29 patients the frequent monomorphic ventricular extrasystole (VE) was the main manifestation of ventricular arrhythmia (VA).

The conventional algorithms of ECG were used as a criterion for location of VE [7; 8].

After conduct of electrophysiological study and receipt of criteria concerning this type of arrhythmia, RFA of the arrhythmogenic zone was performed. The criterion for arrhythmia from the right ventricular outflow tract (RVOT) was the outrunning of early activity by 30-55 ms as to QRS-complex on the body-surface ECG, for the fascicular left ventricular tachycardia (FLVT) x – spike of the Purkinje fibers in the posterior branch of the His bundle in 2 cases and in the anterior branch in 3 cases on the attack of tachycardia. The average procedure time amounted to 60 minutes. The average number of RFA-exposure was 3; the intensity of exposure amounted to 35-40W, the average effective temperature was 50-57 degrees. The criteria for effective ablation were as follows: elimination of the existing arrhythmia, impossibility for induction of arrhythmia affected by stimulation under re-entry tachycardias and the absence of focal activity under ectopic arrhythmias. Repeated Holter monitoring was performed a month after RFA.

### Results and their discussion:

Studies have shown that arrhythmogenic focus in the case of non-coronary ventricular extrasystole is detected in more than half of the cases in the region of the right ventricular outflow tract, which corresponds to our data, when this localization of arrhythmogenic focus was revealed in more than half of the patients.

This zone is a complex three-dimensional structure, and the conduct of intraoperative mapping takes time [9]. In this regard, it is important to develop non-invasive methods of pre-surgical topical diagnostics of non-coronary extrasystole. The use of such methods would allow to narrow the search area of the arrhythmogenic focus, to reduce the time of intraoperative fluoroscopy. At the present time several algorithms for topical diagnostics of ventricular extrasystole have been suggested based on the standard 12-leads ECG [7; 8]. These algorithms show a fairly high specificity and sensitivity in the terms of defining the belonging of arrhythmogenic focus to different anatomic zones of the ventricles (the front wall of RVOT, antero-septal region of the right ventricle, etc.). Comparison of the data of ECG-analysis and intracardiac electrophysiology study showed a coincidence of arrhythmogenic focus localization in all cases.

So, according to the obtained data the localization of VA from RVOT was detected in 21 patients (60%), in the projection of the right sinus of Valsalva – in 5 patients (14,2%), para-Hisian localization was diagnosed in 1 patient (2%), fascicular VT – in 5 patients (14,2%), localization from the region of the interventricular septum – in 1 case (2,8%), from the right ventricular basal segment – in 2 cases (5,7%).

According to the summarized data of numerous literature sources, the efficiency of catheter ablation for VA totally amounted to 75-95%. With structurally normal heart, especially in the case of RVOT tachycardia, the efficiency of RFA may be up to 97% according to some reports, but more often it amounts to about 80%, with recurrences in 5% of the cases [10; 11].

As the analysis of our own results has shown, if VA was localized in RVOT, the efficiency was observed in 20 cases (95%).

We did not manage to obtain positive results in the case when the arrhythmogenic focus was localized in the sidewalls and in the region of moderator band, which corresponds to the data of other authors [3]. This is explained by the presence of structural pathology (past myocarditis) in patients. According to the classification of ventricular HRD there is a special group of fascicular VT. As a rule, a benign arrhythmia is observed in such patients [3]. In our case, the effect in the case of fascicular VT with the absence of organic cardiac pathology was full. When the arrhythmogenic focus was localized in the projection of the Valsalva sinus and in para-Hisian region, the effect of RFA was absolute immediately after surgery and a month after RFA. It should be noted that the procedure in the latter case was complicated by the development of complete right bundle branch block.

#### Conclusion

The results of our analysis confirmed once again that RFA of VHRD is a highly effective and relatively safe method of arrhythmia treatment. We demonstrated the specificity and sensitivity of ECG algorithms for topical diagnostics of arrhythmia. On the basis of accurate localization of arrhythmogenic focus it is possible in advance to predict the outcome of RFA. The presence of structural pathology does not allow to obtain the absolute effect from the procedure of RFA.

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## The characteristics of articular manifestations systemic lupus erythematosus

**Abstract:** A typical pattern of articular syndrome in systemic lupus erythematosus was manifested in the form of arthritis of small joints, which was characterized by symmetry, slight swelling and soreness of medium intensity. Arthralgia without signs of inflammation were often detected in large joints, had a migratory character, and was accompanied by symptoms of muscle damage.

**Keywords:** systemic lupus erythematosus, arthralgia, arthritis.

Joint damage is an important clinical picture of systemic lupus erythematosus (SLE). Arthritis that affects two or more peripheral joints, manifested by pain, swelling and effusion is one of the main ACR criteria of SLE (1997), the severity of arthritis (heavy, medium, light – activity index on a scale of BILAG (2004) and SELENA-SLE-DAI (2005) [1, 186–189; 6, 410–416; 7, 31 P.; 10, 720 P.; 12, 53–58].

E. L. Luchikhina (1998) [8, 15 p.] on the basis of retrospective analysis of medical records (containing 80 parameters) in 228 patients with SLE in 80.5% of cases showed joint damage. In studies of T. A. Lisitsina (2014) [9, 32 p.] in patients with SLE compared to other diagnostic criteria that were most commonly diagnosed with arthritis (67.8%). However, in the works of E. A. Filatova et al. (2012) [13, 15 p.] a complex of symptoms, designated under conventional names “systemic inflammation”, “the defeat of the cardiovascular system”, “reno-parenchymal lesions” and “skin change” frequently (8–23%) than the defeat of the musculoskeletal system (6%). For Zhorniyak, A. P., Ivanova M. M. (2005), Antipova, O. V. et al. (2007) in inflammatory lesions of SLE are very often localized in the interphalangeal, metacarpophalangeal and wrist joints, shoulder and knee joints are rarely affected, hip joints, spine and joints are caroleanne “with the exception of the joints” [3, 115–116; 5, 42–46].

Despite the large number of studies of joint damage in SLE, many questions to this problem to date remain controversial and require further study. In particular, very little is known about the destruction of medium and large joints in SLE, the role of the immune system affects the development of disorders of phosphorus-calcium metabolism, osteoporosis inter connection of lupus arthritis with other clinical and musculoskeletal manifestations of the disease.

**The purpose of the study.** To study the frequency and characteristics of articular manifestations in SLE, depending on the variant of its course and degree of disease activity.

**Materials and methods.** The study involved 80 patients with SLE (75 females, 5 males) were treated at Republican rheumatologic center at clinic No. 3 of Tashkent medical Academy, in rheumatology department of the hospital № 1 of Samarkand state medical institute and in the therapeutic department of the clinic of Andijan state medical institute. All patients were residents of the indigenous population.

Diagnosis of SLE is based on the presence of clinical manifestations and laboratory data. For confirmation of the diagnosis requires at least 4 of the 11 criteria of the ACR (1997) and SLICC criteria (2012), according to which the diagnosis of SLE must be 4 criteria, one of which must be immunological (any of: a-DNA, ANF, Sm, a-CL, C3, C4).

Examination of patients was carried out according to the Federal clinical recommendations on diagnostics and treatment of systemic lupus erythematosus FSBU “SRIR named after V. A. Nasonova” of RAMS (2014). A retrospective analysis of medical records in accor-

dance with specially designed research card. Onset of the disease is determined at the time of the onset of symptoms, significantly might be related to SLE. Disease activity was assessed using the scale SLEDAI-1 (Systemic Lupus Erythematosus Disease Activity Index, 1992).

All patients were indigenous (100%), dominated by females (1:9) employed in agriculture (30%) and with secondary education (75%). The average age of patients at the beginning of the disease was equal to  $23.0 \pm 0.6$  years, at the time of diagnosis was  $25.3 \pm 0.8$  years, currently to  $32.1 \pm 0.9$  years. Disease activity on a scale ECLAM at the time of the first and last hospital stay was, respectively, to  $19.4 \pm 0.7$  a  $14.4 \pm 0.8$  points. The frequency of skin lesions was detected in 100%, kidney – 85,0%, CNS – 33,8%, pneumonitis, pleurisy, pericarditis and vasculitis, respectively – 45,0%, 30,0%, 22.5% and 20.0% of patients. The acute course of SLE was detected in 30%, subacute – 48,8%, chronic – in 21.2% of patients.

The study of articular syndrome included determining the severity of the joint pain assessment by the patient (visual analogue scale – VAS), the index of exudation, manipulation ability of hands, the number of swollen and painful joints, the degree of functional insufficiency. Status of bone metabolism was judged by the concentration of serum total calcium (CA, mmol/l), phosphorus (P, Inmmol/l) and the activity of alkaline and acid phosphatase (ALP and KF, e/l).

To determine the bone density was used the method of computer tomography (CT), densitometry. The measurements were carried out with the use of CT apparatus of the American company “General electric”, model bright Speed 16 of the Treasury, with application programs created on the basis of studies of bone density in the United States. The program of examination of patients included osteodensitometry of vertebral bodies of the lumbar spine. Bone density was determined in units of Hounsfield (HU). The data obtained were compared to standard age and sex data. The degree of loss of bone density was calculated in arbitrary units in connection with the age and gender norm.

All patients underwent x-ray examination. If you suspect damage to the knee joints (35 patients) was performed by ultrasonography (US). With this survey, activlessons contours of the joint, of the joint space, cartilage, soft tissues (partial), cortical bone, capsules, volume of liquid in the joints and the joint capsule.

Statistical data processing was performed using software package statistica 6.0. The use of simple descriptive statistics, non-parametric correlation analysis by Spearman method.

**Results and their discussion.** SLE patients are the main forms of joint syndrome – arthralgia and arthritis was detected in 86.3% of patients.

In addition to activity stage and the duration of SLE nature of articular syndrome depends on the size of the affected joints. Inflammation is often detected in patients with moderate and high

disease activity, in acute and subacute SLE. Arthralgia without signs of active inflammation with low activity or chronic.

Bu localization arthritis more often developed symmetrically in small-metacarpophalangeal, proximal interphalangeal, talus-calcaneal, tarsal, metatarsophalangeal and wrist joints (ratio of arthritis/arthralgia, respectively, amounted to – 1/9, 1/8, 1/8, 1/2 1/04). Migratory joint pain is often detected in large joints, mainly of the hip (ratio of arthralgia/arthritis – 5/9), shoulder joint (the ratio of arthralgia/arthritis – 2/6), spine, sternoclavicular (ratio of arthralgia/arthritis – 2/6) and sacroiliac joint. In the middle joints (elbow, knee, ankle) the nature of the defeat was mixed, where there is arthritis and arthralgia (ratio of arthralgia/arthritis, respectively, 2/7 and 1/6 and 1/2).

Swelling, arthritis of small joints were unstable and were accompanied by moderate pain (for VAS  $4.5 \pm 0.5$  cm), slight limitation of motion. Arthritis of small joints of the indicators the patients age ( $36.3 \pm 4.6$  years) and disease duration ( $135.6 \pm 7.6$  months) was significantly higher than in patients with arthralgia ( $27.6 \pm 3.8$  years;  $102 \pm 5.2$  month,  $P_{12} < 0.05$ ). Quantitative indicators of joint syndrome: the pain intensity for VAS was  $3.5 \pm 0.8$  cm, the number of swollen joints  $4.6 \pm 1.2$ , number of painful joints –  $6.4 \pm 1.4$  points, figure manipulation the ability brush –  $85.5 \pm 7.8\%$ , morning stiffness is  $40.5 \pm 5.4$  min.

The defeat of small joints is accompanied by other symptoms of SLE: Raynaud's syndrome (22.5%), "clean livedev" (17.5%) and erythema in the region of the joints (16.3%). In 11.3% of patients lose interphalangeal and metacarpophalangeal joints, especially the severity of atrophy of the interosseous muscles, severe pain, tendon and ligaments, the formation of pronounced deformations and fixed flexion of the fingers. There was a sharp decline in manipulative ability of the hands (on average  $35.5 \pm 4.8\%$ ). This type of lesion met the criteria for D. Allarcon Segovia (1988) deforming arthropathy of the hands Jakku syndrome [3, 115–116; 5, 42–46; 11]. Arthropathic index Jakku (JAI, was calculated according to the severity of the deformation of the brush and the number of affected joints) in 6.3% of patients were less than 5 points (JAI  $\leq 5$ , moderate arthropathy), 5.0% — more than 5 points (JAI  $> 5$ , severe arthropathy). The average age of patients with deforming arthropathy of brushes made up of  $30.6 \pm 3.2$  years, duration of SLE –  $98.4 \pm 8.4$  months.

The degree of arthralgia of the shoulder, elbow and knee joints (22.5, 30.0 and 27.5%) were respectively 2.5 and 2.6 and 1,6 times higher the degree of arthritis (of 8.8, 11.3 and 17.5%). At patients with arthralgia of the knee was observed and a slight uniform thickening of the joint capsule (37.1%) and a moderate increase in the number of joint fluid (14.3%). Arthritis was visualized the uneven contours of the joint, the presence of free fluid in the cavity, considerable thickening of the joint capsule and irregularity of the cortical layer of the bone (34.3%). In 14.2% of cases, while ultrasound examination of the contours of the joints was smooth, the echogenicity of the cortical layer of the bones of the front and rear horns of the medial and lateral meniscus of the knee and joint fluid was homogeneous (normal levels).

In 3.8% of patients (all women, age was  $26.3 \pm 3.2$  years, the duration is  $3.2 \pm 1.8$  years) had severe SLE complications – aseptic necrosis of the femoral head. The characteristic symptoms of aseptic necrosis was a pain, uncertain localization and penchant for wide irradiation: in the lower back and buttocks, calves, groin and often into the region of the knee joint, as well as significant restriction of movement (patients avoiding active movements of the leg). When radiographic study of the femoral head was homogeneously darkened, the structure of the head lubricated. Height compared to the healthy side was reduced. The surface of the joint in places had the appearance of compacted

facets. There was a slight expansion of the joint space. For magnetic tomography study in the anterior part subchondral department heads have identified areas of osteonecrosis (1 to 3 pieces) of varying intensity, size 5–8 mm, limited by the periphery of the Crescent-shaped band of low intensity (symptoms of the II stage).

Articular syndrome in SLE was accompanied by signs of defeat of the muscles – myalgia, myositis, atrophy (43.8% of patients). Muscle pain was migratory in nature and often noted in the neck muscles, shoulder girdle, upper arm, forearm, interosseous muscles of the hands, the pelvic girdle and thighs. Atrophic changes occurred gradually and they had systemic character. At 66.3% of the detected failure of body mass index (calculated according to the formula: body mass index = body weight in kilograms/height in  $m^2$ ): in 37.5% within 16.0–18.5 (insufficiency of body weight), 28.8% of less of 16.0 (significant deficiency).

To date there is no unified approach to the clinical interpretation of lesions of medium and large joints, spine, sedentary joints in SLE. This is probably due to the lack of diagnostic landmarks to the pain syndrome, the origin of which is with the activity of systemic inflammation is important to reduce mineral bone density and osteoporosis. An in-depth study of the mechanisms of decrease in mineral density of bone tissue, the timely diagnosis of osteoporosis in SLE will help early appointment of adequate therapy.

Diagnosis of osteoporosis was carried out according to the methodical recommendations of the Health Department of the city of Moscow (2007). Screening was conducted using the questionnaire of the International osteoporosis Foundation (all patients). A positive response to two or more questions was the reason for laboratory-instrumental investigations (second stage).

One survey question is positively answered to 17.5%, and two questions – 27.5%, on three – 35.0%, four – 20.0% of patients. Of laboratory tests at 18.8% of patients, the calcium content was in the range of 2.2 to 2.8 mmol/l (normal level), in 65.0% of patients were below 2.2 mmol/l (low content) and 16.2% were above 2.8 mmol/l (high levels). In patients with normal calcium content, a marker of bone resorption activity of KF was in the range of 5.5 and 6.4 IU/l, at low and high levels of calcium there was an increase in its activity – 6.0–7.8 IU/L. At normal calcium concentrations, the age of the patients amounted to  $27.3 \pm 1.9$  years, duration of illness from 2 to 68 weeks. At low and high concentrations of calcium the age of the patients amounted to an average of  $27.3 \pm 1.9$  years, duration of illness, from 26 to 960 weeks.

Computer tomographic intentionally (studied 30 patients) contributed to the identification of characteristics characterizing the I degree of osteoporosis in 40.0%, II degree – in 26.7%, III degree – in 33.3% of patients. The increase in the duration of the disease contributed to the increase in the frequency and worsening of osteoporosis. The degree of disease activity had an inverse correlation with the degree of decrease in density of a bone tissue: at low activity bone density amounted to  $145.0 \pm 15.2$ , with an average –  $129.0 \pm 10.1$  and in high –  $112.0 \pm 9.3$  HU/cm<sup>2</sup>.

Assessment of the impact of therapy on the degree of reduction of bone mineral density showed that in patients treated with corticosteroids in supporting a dose of 10 mg/day (from 6 months to 8 years) bone mineral density averaged  $132.0 \pm 12.9$  HU/cm<sup>2</sup>, which is significantly higher than in patients treated with glucocorticosteroids (GC) in a dose of 20–40 mg/day. Statistically significant differences in mineral density of bone tissue in patients receiving and not treated with pulse therapy is not marked. These data confirm the relative safety of low-dose corticosteroids and pulse therapy in the development of osteoporosis.

It is known that the genetic predisposition to SLE (genotypic) stage becomes clinically expressed (phenotypic) under the influence of adverse environmental factors and climate [2, 21–24; 4, 57–62]. The climate of the greater part of Uzbekistan, where the research was conducted is sharply continental, there is a big range between day and night, summer and winter temperatures. The nature of arid, rainfall is not enough, the relative humidity is low (<http://www.svali.ru:8101>; <http://www.advantour>; <http://www.poedem.ru>). Most patients with SLE, in our study, the disease was associated with insolation (43.7%). While 13.8% of the cause of the disease was abnormal hot days in late spring, early or late summer when daytime temperatures exceed 40° C. On other climate change and weather are warming in the winter, the lack of «spring and autumn rainy days» and «snow winter days», as factors of SLE, indicated by 8.8% of patients. From 13.8% the onset was associated with hypothermia (especially at night when there is a sharp decrease in temperature).

As the triggers of SLE, premature birth, abortion and held obstetric manipulations indicated 11.3% of the patients. Lupus has also provoked by psycho-emotional factors (7.5%), physical strain (5.0%), medications (3.8%) – TB (isoniazid), antifungal drugs (fluna) and antibiotics (tetracycline). 6.3% of patients were unable to indicate the cause of the disease.

Have 40.0% of patients arthralgia (ossalgia, myalgia) was observed before the development of SLE. The main part of this group of patients indicated that prodromal pain was intermittent. When the weather changes, especially in the summer and in the evening (26.3%) had increased pain. 16.3% of patients in anamnesis took place alarming symptoms of SLE, such as general weakness, wanton periodic low-grade fever (non-specific), pain in lymph nodes.

Thus, according to our data, in 86.3% of patients with SLE occurred articular syndrome, and in the pathological process involved all joints, particularly small joints of hands and feet. The frequency of arthritis was higher among patients with medium and high activity of the pathological process in acute and subacute, the frequency of arthralgia — chronic disease course, with medium to low activity of the pathological process.

A typical pattern of articular syndrome in systemic lupus erythematosus was manifested in the form of arthritis of small joints, which was characterized by symmetry, slight swelling and soreness of medium intensity. Severe involvement of the small joints, deforming arthropathy Jakku were not registered often (11.3%), but in all cases contributed to the failure of joint function and permanent disability of patients.

Arthralgia without signs of inflammation were often detected in large joints, had a migratory character, and was accompanied by symptoms of muscle damage. Degenerative and atrophic changes in the muscles was gradually built, had system character, has led to general exhaustion and emaciation of the patients. Arthralgia and myalgia were the prodromal signs of SLE, as, pain and stiffness in bones and muscles were observed long before the development of the disease. Hypothermia, a change in the weather, sun exposure, physical activity, mental exposure provoked the appearance of prodromal signs.

In addition to the factors of SLE, pain in the middle and large joints were due to the violation of calcium-phosphorus metabolism and osteoporosis. In a laboratory study in 81.6% of patients discovered a change in the content of calcium and increased activity of KF (markers of bone resorption), 60.0% of CT densitometry have contributed to identifying symptoms II and III degree of osteoporosis. The increase in the duration of the disease and increase in the degree of its activity had a direct correlation with the degree of decrease in density of a bone fabric. To prevent osteoporosis, along with observance of rules of healthy lifestyle, you must eat enough calcium and vitamin D, the desire to reduce the dose of GK by optimizing treatment of the underlying disease (in the morning, once in 1 dose).

The clinical picture of SLE also had a severe complication of arthritis of the hip — avascular necrosis of the femoral head, which contributed to a significant deterioration of the general condition of the patients. Therefore, examination of the patient with SLE, in addition to the general descriptive characteristics of the musculoskeletal and other systems should include quantitative and objective criteria of articular syndrome, radiographic, ultrasonic and densitometric studies to assess the nature of the lesion and the functionality of the joints.

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## Combined treatment of unresectable primary cancer of the liver by using intraoperative intratumoral destruction by ethanol

**Abstract:** in this article discusses the results of treatment of unresectable forms of primary liver cancer and using intraoperative minimally invasive sclerotherapy of the tumor with 96% ethanol. The study was conducted with 33 patients who were in Andijan regional oncologic dispensary.

**Keywords:** Unresectable liver cancer.

In recent years, along with the increasing of cancer incidence has increased and the number of patients with primary and metastatic liver cancer, and mortality from them. According to WHO, every year around the world recorded a quarter of a million new cases of primary liver tumors and their relation all other tumors is 5–11% [1].

According to the International Agency for Research on Cancer, age-standardized incidence rate of HCC among men in developing countries is 17,4/100000 and 8,7/100000 in developed countries [7].

The morbidity of primary liver cancer is 8,7% of the total morbidity of the malignant tumors. Among men, liver cancer is in 5<sup>th</sup> place after cancer of the lung, stomach, prostate and colorectal cancer and is 13,06/100 000, at women on 8<sup>th</sup>, and makes 5,25 per 100 000 people [5].

In Uzbekistan in recent years increased incidence of liver cancer in cities and rural areas. Thus, in the structure of total cancer incidence in the Republic the liver cancer in 2000 year was 4,0%, in 2006 year 4,3% and in 2009 year 4,6%. For example, the intensive incidence rate increased from 18,99 in 2003 year to 22,84 in 2006y.

### Materials and methods:

The study is based on clinical and laboratory examination of 33 patients with primary unresectable liver cancer, who were on treatment in thoracoabdominal department of the Andijan regional Oncology dispensary over the period from 2011 to 2016.

### Results and discussion:

When ethanol is injected into tumor, the maximum intensity changes of the liver tissue was observed throughout the tumor. To determine the effectiveness of alcohol exposure determines the ratio of the volume of the edema to tumor volume and volume index, in the calculation of which the formation of an edema zone exceeding the diameter of the tumor node by 1 cm was taken into account. Data showing the relationship between exposure conditions and treatment efficacy indicators are shown in table 1.

The volume index was calculated as the ratio of the volume of the edema area to the volume of the conditional formation, the diameter of which was taken as the diameter of the tumor node, increased by 1 cm. The effect was considered effective at values of the volume index greater than 1 (i. e. edema > 100,0% of the tumor volume). From the results given in table it is seen that the magnitude of the volume index exceeds 1, than the effect is effective.

The index of hepatotoxicity were evaluated before the operation 1–2, 3–4, 7–10 days after and at discharge. Comparison of hepatotoxicity indexes before and after DED operation showed a short-term worsening of liver function during the first several days after the intervention. Index of hepatotoxicity in all patients before surgery did not exceed 0–3 points through 1–4 days after the operation, the level of 0–3 points was observed in six, 3–8 points – twenty-four and 9 to 14 points – in three patients.

Table 1. – The relationship between the quantity of ethanol injected into the tumor and the characteristics of the edema area

Indicators	Patients (n = 33)
Tumor volume before treatment (cm <sup>3</sup> )	185,3 ± 30,8
The volume of the edema area (cm <sup>3</sup> )	232,4 ± 28,4
Volumetric index	1,54 ± 0,22
The ratio of the volume of the tumor to edema area	0,79 ± 0,02

As you can see, soon after surgery (1–4 days) in 78,5% of patients were observed I degree and a 3,6% – II degree of hepatotoxicity. However, in subsequent days in the postoperative period and on the day of discharge, the hepatotoxicity was normalized in almost all patients.

From these data it follows that there are no significant changes in liver function under the influence of local alcoholic destruction.

After destruction by ethanol and a full course of treatment in patients observed reduction of initial tumor volume on 81,5% (table 2).

Table 2. – The dynamics of reducing the volume of tumor sites in patients with primary liver cancer

Size of the tumor	Patients (n = 33)
Before treatment	185,3 ± 30,8
After treatment	102,1 ± 15,6*

The effectiveness of the treatment was also evaluated in accordance with WHO recommendations after treatment (Table 3).

Complete regression was observed in 2 patients (6,1%), partial regression was observed in 42,4%, and the stabilization process was observed in 54,5% of cases progression was observed in only 15,2%.

Ultrasound examination of the liver was carried out according to standard methods not less than 1 times a week during the



course of the combined treatment and after 2, 4, 8 and 12 weeks at the end.

Echsonography signs of therapeutic pathomorphism, we considered the change of the texture pattern in the area of influence of ethanol, increased echogenicity of both – the tumors and its surrounding liver parenchyma, the disappearance of texture elements “granularity”, dopplerographic signs of the reduction of pathological blood flow.

Table 3. – The effectiveness of chemotherapy according to WHO, patients with unresectable forms of primary liver cancer

Condition	Patients (n = 33)	
	Number of patients	%
Complete regression	2	6,1
Partial regression	14	42,4
Stabilization process	12	54,5
Progression	5	15,2

Treatment was considered effective in the presence of ultrasonographic signs of development fibrosis in the area of influence of ethanol. In all cases, effective local effects were accompanied by no evidence of increase in tumor size. The appearance of additional nodes considered as evidence of the ineffectiveness of the treatment.

Local destruction by ethanol of unresectable malignant primary tumors of the liver does not affect the functional state of the organism as a whole and the liver, in particular, as well as damage to large vessels and bile ducts.

**Conclusions:**

1. Our experience of using local injection therapy with ethanol for malignant liver tumors testifies to the safety of the method and does not require expensive equipment.

2. The use of intraoperative local destruction by ethanol in combination with adjuvant chemotherapy and immunotherapy in unresectable forms of primary cancer has led to a partial regression 42,4%, and the stabilization of the process of 54.5%.

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## Rehabilitation of children after repeated surgical interventions regarding anorectal malformations

**Abstract:** aim of our investigation was elaboration of complex step-by-step rehabilitation before and after surgical operations in repeated surgical interventions regarding anorectal malformations. For the period from 1990 to 2015 inclusive 140 children with different recurrent complications after previous surgical correction of anorectal malformations were treated. Boys were 77 (52,4%) and girls were 63 (47,6%). Due to the age children in the age category before 3 years old were predominated. During abdominal-perineum decumuoization good results have observed in 10%, satisfactory results in 25% and unsatisfactory results have been observed in 65% of patients. In the basic group good results have observed in 57,1% of cases, satisfactory results have observed in 35,8% of cases and unsatisfactory results have been observed in 1 (7,1%) patients.

**Keywords:** Anorectal malformations, rehabilitation, children.

**Introduction.** Step-by-step complex rehabilitation has a big importance after repeated surgical interventions for the restoration of retentive function of sphincter apparatus and anal sphincter. Treatment of congenital anorectal malformations in children is a complex objective. Anorectal malformations (AM) are included a wide spectrum of congenital abnormalities affecting anus, rectum and urogenital tract. Anorectal malformations is one the most frequent pathologies amongst congenital abnormalities [1]. According to the data of different authors frequency of such pathology is varies from 1:2000 to 1:9000 [2; 3; 4]. In the structure of congenital abnormalities the share of anorectal malformations are approximately 7%, besides they are on the 9 place amongst all abnormalities due to the data of international register [5]. According to the opinion of the number of foreign specialists mortality from anorectal malformations is from 16–19% and high [6]. In spite of the many achievements of the last two decades in the diagnostic and treatment of anorectal malformations, this pathology is left one of the most unsolved problems in pediatric surgery [7; 8; 9; 10]. Rehabilitation of patients after surgical operations remains very debatable problem. The significant rehabilitation component is control of the treatment effectiveness and concrete assessment of the results. We should regret to say that proctologic patients not

always and not in sufficient volume receive restoral treatment, especially after surgical operations. The above mentioned gives us the reason to develop the complex restoral rehabilitation scheme after repeated corrections of AM. This was prerequisite to carry out of the presented work.

**The aim of investigation** was to elaborate complex step-by-step before and after operational rehabilitation in repeated surgical interventions regarding anorectal malformations.

**Materials and methods.** For the period from 1990 to 2015 inclusive 62 (44,3%) patients with different recurrent complications after previous surgical correction of anorectal malformations were treated in the Second clinic of Samarkand State Medical Institute and 78 (55,7%) sick children with the same pathology were treated in the surgical department of Scientific Center of Pediatric and Pediatric Surgery of Alma-Ata city (Republic of Kazakhstan). These 140 children have been included in investigation for the explanation of basic terms of tis work. Boys were 77 (52,4%) and girls were 63 (47,6%). Due to the age children in the age category before 3 years old were predominated.

Diagnosis of anorectal malformation has been classified due to the last consensus of diagnostic standards of anorectal malformations of International Crackenback's classification (2005).

Distribution of patients according to the diagnostic standards with recurrent types of anorectal malformations according to the Inter-

national Crackenback's classification (2005) have been presented in table 1 below.

Table 1. – Distribution of patients with recurrent types of anorectal malformations according to the International Crackenback's classification (abs/%)

Types of anorectal malformations	Groups of patients		
	I	II	In general
<b>Big clinical groups</b>			
Perineal fistula	18 (69,2)	6 (30,8)	24 (18,6%)
Recto-urethral fistula in the bulbar part of urethra	9 (64,3)	5 (35,7)	14 (10,0%)
Recto-urethral fistula in the prostate part of urethra	1 (100)	–	1 (0,7%)
Recto-vesicular fistula	1 (100)		1 (0,7%)
Vestibular fistula	35 (89,7)	4 (10,3)	39 (28,8%)
Cloaca with general segment less than 3 cm.	1 (50)	1 (50)	2 (1,4%)
Atresia without fistula	23 (82,1)	5 (17,3)	28 (23,6%)
Stenosis of anus	8 (100)		8 (5,7%)
<b>Rare/local types</b>			
Atresia/stenosis of rectum		1 (100)	1 (0,7%)
Recto-vaginal fistula	1 (50)	1 (50)	2 (1,4%)
Recto-urethral H-fistula with perineal syrxinx	1 (100)	–	1 (0,7%)
Vestibular H-fistula	5 (83,3)	1 (16,7)	6 (4,3%)
Vaginal H-fistula	1 (100)	–	1 (0,7%)
Other	1 (100)		1 (0,7%)
In general	107 (82,3%)	23 (17,7%)	130 (100%)

**Results and discussion.** The level of rectum atresia or anus towards to puborectal muscle has determined the height and type of anorectal malformation. In our series all children were observed lower and intermediate types of anorectal malformations.

1. Lower types of anorectal malformations (perineal, vestibular fistulas, H-fistula, imperforated anus) were observed in 108 (83,1%) of children.

2. Intermediate types of anorectal malformations (recto-urethral fistulas in bulbar, cloaca with general segment less than 3 cm) were observed in 22 (16,9%) of children.

Functional disorders of the restrained function of the sphincter apparatus of rectum in all cases have been presented by stool incontinence of the different severity degrees. The degree of stool incontinence was determined according to International Crackenback's classification (2005) [10]. According to which the first degree of

stool incontinence is established during periodic (one or two times per week) episodes of stool smearing in our series of investigations have not been determined. The second degree – every days episodes of stool smearing are not caused any social problems for patients have been observed in 56 (43,1%) children. The third degree – persistent episodes of stool smearing which create social problems for patient have been observed in 74 (56,9%) children.

By the character of the performed reanorectoplastic all children were divided into two groups. The first (basic) group was consisted of 107 children (82,3%) who had different reanorectoplastic from perineal and posterior sagittal approaches with remained mucosal membrane of rectum. The second (control) group were consisted of 23 (17,7%) children who had abdominal-perineal reanorectoplastic with intrarectal demucosation of rectum due to Romualdy-Rebein (table 2).

Table 2. – The results of investigation due to the character of the performed reanorectoplastic (abs/%)

Name of surgical operation	Basic group	Control group
Amount of patients	107 (82,3)	23 (17,7)

All patients from the basic group before and after operation period were carried out two-step complex rehabilitation. At the same time with generally accepted methods of rehabilitation diagrammatic bougienage, electro-stimulation of rectum and sphincter and also tonic procedures of sphincter apparatus have been included.

All children before radical operation it has been carried out rehabilitation treatment which included aperient diet, cleansing enemas, drug treatment (lactulose, magnesium, wheat brans and others); physiotherapy (electro-stimulation of large intestine, electrophoresis with prozerine on the stomach area).

The II stage of rehabilitation has been started in the post operational period. Besides it has been carried out the individual approach to patients. The course of complex rehabilitation was lasted from 1 to

1,5 years depending on restoration of retentive function sphincter apparatus and anal sphincter.

Simulation has been carried out on "Ultraton – AMP-2INT" apparatus with rectal detector sweeping form of which supplies effective exposure to the walls of rectum during performing proctoplastic operations. The work principle of apparatus (in the ultratono-therapeutic regime) is based on transformation of system voltage into high sinusoidal voltage (0,5–3 kW) of supersonic (22 kHz) frequency applying to the gas-discharge electrode. Under the impact of high voltage in the balloon of electrode inert gas ionized and gained features of conductor by processing into it glow discharge.

Also we followed the bougienage scheme which has been used in the leading coloproctological clinics. The sizes of bougies were corresponded to the patient's age.

Table 3. – Bougienage schemes in compliance with patient's age

Age	Number of Gagar's bougie
1–4 months	12
4–8 months	13
8–12 months	14
1–3 years old	15
3–12 years old	16
Older than 12 years old	17

## Bougienage scheme

1. No more than 1 time per day during a month.
2. Once per 3 days during a month.
3. Twice per week during a month.
4. Once per week during a month.
5. Once per month during 3 months.

Special importance we attach to the tonic procedures of sphincter apparatus in the form of exercise with tube by diameter of 2,0 cm

and length of 4–5 cm. in the lumen of rectum it has been put this tube patient is explained procedure which increases the tone of sphincter. Procedure is carried out during the year which begins from 3–5 times. In dynamic these exercises are led to 25–30 times. Also with inserted tube into the rectum in the walking position the child has to hold it during 3–5 minutes. Besides that it has been carried out therapeutic enemas in the concentration of 100–150 ml and child held water in the walking position during 5–7 minutes.

The long-term results have been showed that in abdomino-perineal proctoplastics with intrarectal demucosation the good results have observed in 10% of cases, satisfactory results in 25% of cases and unsatisfactory results have registered in 65% of cases. In the basic group the good results have observed in 57,1% of cases, satisfactory results in 35,8% of cases and unsatisfactory results have registered in 1 patient (7,1%).

**Conclusions.** Thus, intrarectal demucosation cannot in full carry out proprioceptive function of rectum, thereby dictate reasonability of preservation of the mucous membrane of rectum, and also step-by-step rehabilitation after surgical operation is obligatory in the complex treatment.

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## Special features of clinical and functional disorders in patients with undifferentiated connective tissue dysplasia

**Abstract:** The objective of the study was to investigate the special features of clinical and functional disorders in patients with undifferentiated connective tissue dysplasia (UCTD) with primary mitral valve prolapse (MVP). The patients were divided into 2 groups depending on the degree of MVP: the 1<sup>st</sup> group included 97 patients with the 1<sup>st</sup> degree of MVP and the second group – 111 patients with the 2<sup>nd</sup> degree of MVP. In the patients, who have UCTD with MVP, the external and internal phenes are clinically observed, a heart rhythm disturbance is noted, and the cardiac hemodynamics indicators undergo statistically significant deterioration in the course of the disease development.

**Keywords:** undifferentiated connective tissue dysplasia, mitral valve prolapse, external and internal phenes of dysplasia, ECG and EchoCG.

The problem of early diagnostics in modern medicine of undifferentiated connective tissue dysplasia (UCTD) in the patients with

congenital mitral valve prolapse (MVP) determines the necessity for advanced study of propagation mechanisms of this disease, which



occurs in 5–20% of cases. It was established that the patients with MVP have an increased risk for development of mitral insufficiency, infective endocarditis, cerebral embolisms, arrhythmias and sudden death [5]. The objective of the study was to examine the special features of clinical and functional disorders in patients with undifferentiated connective tissue dysplasia with primary mitral valve prolapse.

**Materials and methods of research.** 208 patients at the age from 15 to 25 years ( $19,5 \pm 1,42$ ) with etiological signs of primary MVP were observed. The diagnosis was established on the basis of T. I. Kadurina's classification [4] and was confirmed by the data of EchoCG and ECG. The research groups did not include individuals with secondary MVP, cardiovascular diseases, rheumatism, chronic pathology of liver, kidneys and lungs. The indicators of clinical manifestations were central hemodynamic parameters, which were assessed with EchoCG aloka [2]. The patients were divided into 2 groups. The 1<sup>st</sup> research group included 97 patients (46,6%) with MVP with regurgitation of the 1<sup>st</sup> degree, and the 2<sup>nd</sup> group – 111 patients (53,4%) with the 2<sup>nd</sup> degree of regurgitation. The data from 20 relatively healthy individuals of comparable age without signs of EchoCG disturbances served as verification for both comparison groups.

**The results of research and discussion.** The studies, which were conducted in this regard, showed that UCTD is mainly typical for young people. Research of sex characteristics demonstrated a predominance of females in the 1<sup>st</sup> group (60,8%), whereas the 2<sup>nd</sup> group included a bit more males, but these differences were statistically insignificant. Our results are slightly different from literature ones, which show the predominance of females; these differences may be due to ethnic and regional peculiarities, as the patients of Uzbek population prevailed in our studies. Research of probands showed a certain dependence of genetic factors in UCTD formation from development of MVP and its intensity. So, if in the 1<sup>st</sup> group of patients the frequency of occurrence of UCTD-signs in the 1<sup>st</sup>, 2<sup>nd</sup> and 3<sup>rd</sup> lines of consanguinity is revealed in 6 (8,5%), 9 (13%) and 5 (7%) patients out of 71 examined persons, then in the 2<sup>nd</sup> group they were detected in 13 (18,3%,  $P < 0.01$ ), 14 (20%,  $P < 0.05$ ) and 11 (15,5%,  $P < 0.01$ ) examined persons.

The first stage of our research was to study the external manifestations of UCTD in patients with MVP of various intensities. The analysis of frequency of bone-skeletal external phenes in patients of both groups showed that spinal deformity was revealed in 43 patients (44,3%) of the 1<sup>st</sup> group. It manifested itself through formation of scoliosis of the 1<sup>st</sup> and 2<sup>nd</sup> degree in 19 (19,6%) and 12 (12,4%) patients, kyphoscoliosis of the 1<sup>st</sup> and 2<sup>nd</sup> degree in 7 (7,2%) and 2 (2,1%) examined persons, hyperlordosis – in 3 patients (3,1%). The frequency analysis of spinal deformity in patients of the 2<sup>nd</sup> group showed that it was detected in 48 patients (43,6%). Furthermore, scoliosis of the 1<sup>st</sup> and 2<sup>nd</sup> degree was diagnosed in 22 (20,0%) and 9 (8,2%) patients, kyphoscoliosis of the 1<sup>st</sup> and 2<sup>nd</sup> degree – in 8 (7,3%) and 3 (2,7%) patients, hyperlordosis – in 6 patients (5,5%). The frequency analysis of thoracic cage deformities in patients of the 1<sup>st</sup> group showed their occurrence in 50 examined persons (51,5%). Basically, they manifested themselves through a funnel-shaped form of the 1<sup>st</sup> and 2<sup>nd</sup> degree in 20 (20,6%) and 11 (11,4%) patients, through asthenic form – in 11 patients (11,4%), through carinate form of the 1<sup>st</sup> and 2<sup>nd</sup> degree – in 6 (6,2%) and 2 examined persons (2,1%). Among the patients of the 2<sup>nd</sup> group the thoracic cage deformities were diagnosed in 40 examined persons (36,1%), which was statistically less significant than in the first group ( $P < 0.05$ ). Basically, they manifested themselves through a funnel-shaped form of the 1<sup>st</sup> and 2<sup>nd</sup> degree in 14 (12,6%,  $P < 0.05$ ) and 7 (6,3%) patients, through asthenic form – in 4 patients (3,6%,  $P < 0.05$ ), through a

carinate form of the 1<sup>st</sup> and 2<sup>nd</sup> degree – in 10 (9%) and 5 (4,5%) examined persons.

Skin manifestations of UCTD in patients with MVP in the form of skin extensibility of various intensity were observed in 37 (38,1%) and 43 (38,7%) patients of the 1<sup>st</sup> and 2<sup>nd</sup> groups. So, if among the patients of the 1<sup>st</sup> group they manifested themselves mainly through skin extensibility of the 1<sup>st</sup> and 2<sup>nd</sup> degree in 16 (16,5%) and 11 (11,4%) examined persons, then among the patients of the 2<sup>nd</sup> group the skin extensibility of the 1<sup>st</sup>, 2<sup>nd</sup> and 3<sup>rd</sup> degree was diagnosed in 27 (24,3%), 10 (19,8%) and 6 (5,4%) patients, respectively. Muscular hypotonia was observed in 21 (21,6%) and 32 (28,8%) patients of the 1<sup>st</sup> and 2<sup>nd</sup> groups, respectively.

Articular manifestations of UCTD are platypodia and hypermobility of joints. The frequency analysis of platypodia revealed its occurrence in 20 (20,6%) and 22 (19,8%) patients of the 1<sup>st</sup> and 2<sup>nd</sup> groups. Moreover, transverse platypodia was detected in 4 (4,1%) and 10 (9%) patients, longitudinal platypodia – in 16 (16,5%) and 12 (10,8%) examined persons. Hypermobility of various intensities was detected in all examined patients. So, if among the patients of the 1<sup>st</sup> group hypermobility of joints of the 1<sup>st</sup>, 2<sup>nd</sup>, 3<sup>rd</sup> and 4<sup>th</sup> degree was observed in 56 (57,7%), 17 (17,5%), 18 (18,6%) and 6 (6,2%) patients, then among the patients of the 2<sup>nd</sup> group it was detected in 47 (42,3%), 28 (25,2%), 24 (21,6%) and 12 (10,8%) examined persons; we did not reveal any significant differences between the groups.

Another external phenes in the patients with UCTD are minor development abnormalities, which manifest themselves through large protrudent ears and accreted earlobe. These signs were observed in 20 (20,6%) and 16 (16,5%) patients of the 1<sup>st</sup> group and in 24 (21,6%) and 18 (16,2%) examined persons of the 2<sup>nd</sup> group. As can be seen from the abovementioned data, the external phenes of UCTD in patients with MVP manifested themselves through bone-skeletal, skin, articular forms and the occurrence of minor development abnormalities. According to the degree of intensity they manifested themselves through hypermobility of joints (100%), change of the shape of spine (44%) and thoracic cage (43,8%), skin extensibility of various intensity (38,8%), minor development abnormalities (21,1%) and platypodia (20,4%). The frequency of combinations of various phenes in patients was different. So, if among the patients of the 1<sup>st</sup> group the frequency of combination of 6 external phenes was detected in 3 patients (3,1%), combination of 5 phenes – in 5 patients (5,1%), combination of 4 phenes – in 28 patients (28,9%), combination of 3 phenes – in 27 patients (27,8%), combination of 2 phenes – in 25 examined persons (25,8%) and combination of 1 phene was observed in 9 patients (9,3%). Among the patients of the 2<sup>nd</sup> group the frequency of combination of 6 external phenes were detected in 5 cases (4,5%), combination of 5 phenes – in 11 cases (10%), combination of 4 phenes – in 22 cases (20%), combination of 3 phenes – in 27 cases (24,3%), combination of 2 phenes in 34 examined persons (30,6%) and combination of 1 phenes was detected in 11 patients (10%). We did not reveal any significant differences in both examined groups, however it should be noted that more severe manifestations of external phenes were mainly revealed in the patients with MVP of the 2<sup>nd</sup> degree.

Analysis of internal phenes in patients with UCTD and MVP depending on its intensity showed that ocular manifestations were characterized by development of myopia of various degrees in 26 patients of the 1<sup>st</sup> and 2<sup>nd</sup> groups. However, the degree of myopia precisely concurred with the intensity of MVP. So, in the 1<sup>st</sup> group the 1<sup>st</sup> degree of myopia was detected in 23 patients (23,7%), the 2<sup>nd</sup> degree – in 3 patients (3,1%); and in patients of the 2<sup>nd</sup> group the 1<sup>st</sup> degree of

myopia was detected in 3 patients (2,7%,  $P < 0.01$ ), the 2<sup>nd</sup> degree – in 23 examined patients (20,7%,  $P < 0.01$ ). Furthermore, in the 2<sup>nd</sup> group astigmatism was revealed in 20 patients (18%), anisometropia – in 34 patients (30,6%,  $P < 0.05$ ) and degenerative changes in the retina – in 30 patients (27%). As can be seen from the abovementioned data, the frequency of lesions of ocular organs was reliably highest in the patients with MVP of the 2<sup>nd</sup> degree, which indicates a severe course of main disease. We did not reveal any significant differences in both examined groups, however it should be noted that more severe manifestations of external phenes were revealed in a greater degree in the patients with MVP of the 2<sup>nd</sup> degree.

The next stage of the research was to study clinical symptoms, heart condition and ECG indicators depending on the degree of regurgitation. In the subjective status the cardiovascular complaints were predominant according to the frequency of occurrence and intensity: cardialgia (34,8–76,4%), feeling of “heart discomfort” (22,8–55,1%), palpitation (17,4–52,8%), cardiac malfunction (17,4–43,8%), dizziness, general weakness with a sharp decrease in blood pressure under the conditions of orthopnoea (13–38,2%). The frequency of occurrence of these clinical symptoms was in direct relationship to the degree of MVP and regurgitation, and it was detected significantly more often in patients of the 2<sup>nd</sup> group. These symptoms were not confirmed electrocardiographically approximately in 50% of cases. Holter monitoring allows to reconfirm the existence of heart rhythm disturbances and cardiac conduction defects in persons with various degree of connective tissue dysplasia. The studies, which were conducted in this regard, have shown that MVP is accompanied by certain ECG changes. The cardiac rate of the patients examined by us varied widely: from 56 to 96 beats per minute in patients of the 1<sup>st</sup> subgroup, from 75 to 100 beats per minute in patients of the 2<sup>nd</sup> subgroup A. On average, these values amounted to  $82,78 \pm 3,53$  and  $87,67 \pm 0,65$  beats per minute according to the groups. In our research we observed a tendency towards cardiac rate increase as the pathological process aggravated. It should be noted that patients often complained about episodes of cardiac rate acceleration within 24 hours, especially under active physical loads, which affected the patients’ quality of life. Sinus arrhythmia was found in 5% of the examined patients, sinus bradycardia – in 3% of the patients, and sinus tachycardia – in 24,6% of the patients. According to the literature data, atrial and ventricular extrasystole is the most common heart rhythm disturbance in patients with UCTD and was found in 28% of the examined patients. According to our observations, atrial extrasystole at rest increases under physical loads by 1,5–2 times in the patients with pronounced manifestations of UCTD. In rare cases we observed the phenomenon of ventricular preexcitation (4,7%) in the examined patients; and paroxysmal heart rhythm disturbances in the form of atrioventricular paroxysmal tachycardia were detected in these patients. Moreover, attacks occurred both during exercise activities and at rest or during sleep. AV blockade of I and II degree was also detected in 24,8% of the patients. According to ECG data, changes in the terminal part

of ventricular complex were detected in 15.7% of the patients, which we interpreted in terms of metabolic disturbances in the myocardium under metabolic cardiomyopathy.

The next stage of the research was to detect changes in cardiac hemodynamics, so in the patients with MVP of the 1<sup>st</sup> degree the values of EDD (end-diastolic dimension) and ESD (end-systolic dimension) had a tendency only towards increase, remaining within the upper normal limits. At the same time we observed excess of the normative values in 23,7 and 26,1% of the examined patients. The values of ejection fraction had a tendency towards decrease in relation to the control group, which was observed in 21,2%; the values of stroke volume had a tendency towards increase and the excess of normative values was detected in 23,7% of the patients with MVP of the 1<sup>st</sup> degree. The values of left ventricular posterior wall and interventricular septum remained within upper normal limits. Excess of normative values of these indicators was observed in 26,1% of the patients. It should be noted that the values of SBP (systolic blood pressure) and DBP (diastolic blood pressure) remained within the age norm. However, heartbeat acceleration in the course of leaflet prolapse was observed in all patients. As may be seen from the given data, changes in the values of cardiac hemodynamics are detected not in all patients with MVP of the 1<sup>st</sup> degree, determining less pronounced changes of their average values. At the same time it should be noted that deviation in the values of cardiac hemodynamics was noted in the patients with regurgitation of the 2<sup>nd</sup> degree, which is, in our opinion, associated with a more pronounced leaflet prolapse and the increase of blood regurgitation backwards to the left atrium. So, the values of EDD (end-diastolic dimension) and ESD (end-systolic dimension) exceeded the values of the age norm in 53,7 and 58,8% of patients. The average values of these indicators increased; however, such deviations were statistically insignificant. The values of ejection fraction had a tendency towards decrease, which was observed in 74,2% of the patients; the values of stroke volume had a tendency towards increase, which was detected in 42,3% of patients with MVP of the 2<sup>nd</sup> degree. The excess of normative values of the sizes of left ventricular posterior wall and interventricular septum was observed in 48,1% of the patients with MVP of the 2<sup>nd</sup> degree. It should be noted that the values of SBP (systolic blood pressure) and DBP (diastolic blood pressure) remained within the age norm. Higher values of SBP and DBP were detected more often in the 2<sup>nd</sup> group.

Thus, the indicators of cardiac hemodynamics statistically deteriorate a lot against the control group in the course of mitral valve prolapse progression. It is known that in response to volume overload, in order to maintain an adequate pumping function the local (myocardial) neurohumoral systems, stimulating development of tachycardia and subsequently the risk for development of myocardial hypertrophy of the left atrium and ventricle become more intense. Myocardial hypertrophy leads to the increase of diastolic rigidity of the left ventricular myocardium and consequently to systolic dysfunction. Constant tachycardia increases the cardiac energy consumption, reduces its functional activity.

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## Section 6. Mechanics

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### Mathematical modeling of transfer of the moment from the engine to the executive mechanism

**Abstract:** Dynamic loading of hubs of motor-transmission and power gears of the traction vehicle are analysed. Made mathematical model of transfer of the moment from the engine to the executive mechanism which allows to learn working conditions of each main knot of the car. The moments of resistance of driving wheels and a shaft of selection of power are analytically defined, taking into account the moment of friction it is elastic the pneumatichydraulic drive.

**Keywords:** the engine, the executive mechanism, the car, a driving wheel, a powertake-off, a motor and transmission and power gears, the traction vehicle, it is elastic the pneumatichydraulic drive, dynamic loading, the friction moment.

Progress in autotractor building is characterized by continuous increase of requirements as to functional indicators of cars — productivities, universality, rapidity, dynamism, a power saturation, and to consumer — reliability, durability, non-failure operation, noiselessness and small vibroactivity. All indicators of cars depends on quality and loading of their main working hubs.

One of the most important elements of the traction vehicle is the complex of hubs of motor-transmission, or power gears.

Loading of motor and transmission and power gears of the traction vehicle has dynamic character. It is formulated as a result of action of both external, and internal perturbations. Loading of motor and transmission and power gears of the traction vehicle has dynamic character. It is formulated as a result of action of both external, and internal perturbations. Among external fluctuations of traction resistance and engine torque, perturbation from fluctuations of skeleton on the suspender, and also influences from control system are considered as the main. Among internal kinematic and power perturbations from regears engagement, misalignment of shaft, not uniformity of rotation of cardan, deformations and shifts of case shaped parts are considered as the main.

Numerous researches demonstrate that on loading of transfer from internal perturbations decisive impact is exerted by correctness of the choice of its own dynamic characteristics determined by set of elastic and inertial and dissipative parameters of elements [4].

In this regard, more and more the importance is got by problem of purposeful forming at design stage of dynamic characteristics of power gears on the basis of the analysis of influence on their loading of dynamic parameters of elements of transfers and the external and internal loading factors.

In view of the fact that now there are no methods allowing at design stage that is in the conditions of incompleteness of information on dynamic parameters of elements, adequately to consider influence on loading of transfers of internal perturbations, the specified problem has not received the full decision. Meanwhile at design stage there are possibilities of purposeful forming of set of dynamic parameters for ensuring the required loading in elements of transfers of operation. Therefore, creation of the methods allowing to estimate dynamic loading of each element of the power gear at change of parameters and certain ranges is necessary.

Emergence of irregularity of thrust effort, its unsteady character and excessive fluctuation in PTO negatively influences dynamic, fuel and economic and ergonomic indicators of the tractor and transport and machine and tractor unit.

Considering start-off and dispersal, M. M. Schukin in pile to work has defined that elastic communication influences nature of process of start-off and dispersal. The elastic hitch allows the tractor at start-off from the place to make preliminary dispersal within deformation of elastic element. Energy of dispersal is implemented in the



form of additional effort on hook. At the same time traction properties and passability of the traction and transport unit increases. At very small rigidity of the traction coupling device or sharp start-off from the place the tractor with elastic hitch is theoretically capable to shift the trailer having weight twice big than the tractor with rigid hitch. Besides, elastic communication in comparison with rigid hitch can provide start-off of the machine and tractor unit from the place at much smaller coefficient of coupling with the soil. For decrease in dynamic shock loads in the course of start-off and the size of slipping of clutch coupling it is necessary to install the elastic damping drive (EDD).

The analysis of the developed mathematical models of machine and tractor units which is carried out by B. P. Fedorov has shown that cardinal way of decrease in dynamic loading of tractor — application of the elastic elements reducing danger of impact on health of the operator of low-frequency fluctuations.

Number of scientists believe that one of ways of improvement of traction and economic indicators of the tractor and transport unit (TTU) at the unsteady loading is creation of such transmission which will allow the engine not to feel influences of variable nature of traction efforts in certain conditions.

However use in point of hook of the tractor and trailer of elastic communication — the traction coupling device with the elastic damping element [1, 2] is most acceptable for stabilization of the thrust effort improving operating and ergonomic characteristics of TTU. Use of such device will improve operational properties and as a result — will positively influence productivity and fuel efficiency.

Forming of the machine and tractor unit (MTU) on the basis of power saturated tractors has led to development of the truck tractor into the mobile power means (MPM) now [3]. The analysis of MTU on the basis of MPM shows that the “excess” part of power of the tractor engine removed from PTO appears opportunity unitization of the perspective wide and combined farm vehicles. It unitizations allows uses of weight of all MTU for creation of thrust effort that to lower costs of self-movement of tractor and consolidation of the soil with simultaneous increase in productivity of MTU and decrease in specific power consumption of works. At it unitizations appears excessive fluctuations of driving wheels and in PTO.

The exception of adverse effect of alternating load is possible improvement of operational receptions, or improvement of design of the making MTU. One of constructive solutions of partial, or full isolation of the engine from the excessive shifting jerks caused by change of drag torque is application of the transmissions possessing the high damping qualities. In transmission comes two third-party excessive fluctuation, from the moving mechanisms and from external influences. And external influences appears from excessive fluctuations of axis of driving wheels and in PTO.

For removal of excessive fluctuations of axis of driving wheels and PTO the elastic damping drive of different design is usually used. EDD repays excessive fluctuations easier and to provide standard duties of work.

We accept dynamic rated system such view: “engine” – “transmission” – “axis of driving wheels with EDD” – “PTO with EDD” – “the mass of the rotating mechanisms of the unit given to the cardan shaft”. Let’s model this rated scheme.

Mathematically process of inclusion of friction coupling is described by system of the differential equations of dynamic balance (1) considering position forces (elastic forces) and resistance forces (damping, friction force). The formula for calculation of the moment of friction includes two functional dependences: specific pressure upon friction surfaces, time-dependent, and friction coef-

ficient as function from the relative speed of sliding of the interfaced surfaces. The second and third equations of this system describe power communication between leaders and the conducted parts of friction coupling. Thanks to such option of drawing up mathematical model it is possible to consider nature of change of friction coefficient for different models of friction, and also to consider behavior of system at different laws of change of pressure in the booster of friction coupling.

$$\left\{ \begin{array}{l} J_1 \ddot{\varphi}_1 + k_1 (\dot{\varphi}_1 - \dot{\varphi}_2) + c_1 (\varphi_1 - \varphi_2) = M_d \\ J_2 \ddot{\varphi}_2 + c_1 (\varphi_1 - \varphi_2) = M_{m11} \\ J_3 \ddot{\varphi}_3 + c_2 (\varphi_3 - \varphi_4) = M_{m12} \\ J_4 \ddot{\varphi}_4 + k_4 (\dot{\varphi}_3 - \dot{\varphi}_4) + c_4 (\varphi_3 - \varphi_4) = M_{tr} \\ J_5 \ddot{\varphi}_5 + k_4 (\dot{\varphi}_4 - \dot{\varphi}_5) + c_4 (\varphi_4 - \varphi_5) = M_{s.v.k.} \pm M_{udps.v.k} \\ J_6 \ddot{\varphi}_6 + k_6 (\dot{\varphi}_4 - \dot{\varphi}_6) + c_6 (\varphi_4 - \varphi_6) = M_{vom} \pm M_{udpvom} \\ J_7 \ddot{\varphi}_7 + k_7 (\dot{\varphi}_6 - \dot{\varphi}_7) + c_7 (\varphi_6 - \varphi_7) = M_{s.vrash.m.a.} \end{array} \right. \quad (1)$$

here  $M_d$  – the torsion torque developed by the engine;  $M_{m11}$  – moment of drive disk of clutch coupling;  $M_{m12}$  – moment of driven disk of clutch;  $M_{tr}$  – the moment on transmission;  $M_{s.v.k.}$  – drag torque of driving wheels;  $M_{udps.v.k}$  – the moment of the elastic damping drive to resistance of driving wheels;  $M_{vom}$  – the moment on PTO;  $M_{udpvom}$  – the moment of the elastic damping drive in PTO;  $M_{s.vrash.m.a.}$  – drag torque of the rotating unit mechanisms.

$$\left\{ \begin{array}{l} J_1 \delta \ddot{\varphi}_{d1} + k_1 (\delta \dot{\varphi}_{d1} - \delta \dot{\varphi}_{d2}) + c_1 (\varphi_{01} + \delta \varphi_{d1} - \varphi_{02} - \delta \varphi_{d2}) = M_d + \delta M_d \\ J_2 \delta \ddot{\varphi}_{d2} + c_1 (\varphi_{01} + \delta \varphi_{d1} - \varphi_{02} - \delta \varphi_{d2}) = M_{m11} \\ J_3 \delta \ddot{\varphi}_{d3} + c_2 (\varphi_{03} + \delta \varphi_{d3} - \varphi_{04} - \delta \varphi_{d4}) = M_{m12} \\ J_4 \delta \ddot{\varphi}_{d4} + k_4 (\delta \dot{\varphi}_{d3} - \delta \dot{\varphi}_{d4}) + c_4 (\varphi_{03} + \delta \varphi_{d3} - \varphi_{04} - \delta \varphi_{d4}) = M_{tr} \\ J_5 \delta \ddot{\varphi}_{d5} + k_5 (\delta \dot{\varphi}_{d4} - \delta \dot{\varphi}_{d5}) + c_5 (\varphi_{04} + \delta \varphi_{d4} - \varphi_{05} - \delta \varphi_{d5}) = M_{s.v.k.} \pm M_{udps.v.k} \\ J_6 \delta \ddot{\varphi}_{d6} + k_6 (\delta \dot{\varphi}_{d4} - \delta \dot{\varphi}_{d6}) + c_6 (\varphi_{04} + \delta \varphi_{d4} - \varphi_{06} - \delta \varphi_{d6}) = M_{vom} \pm M_{udpvom} \\ J_7 \delta \ddot{\varphi}_{d7} + k_7 (\delta \dot{\varphi}_{d4} - \delta \dot{\varphi}_{d7}) + c_7 (\varphi_{06} + \delta \varphi_{d6} - \varphi_{07} - \delta \varphi_{d7}) = M_{s.vrash.m.a.} \end{array} \right. \quad (2)$$

here  $\delta \varphi_{d1}$ ,  $\delta \varphi_{d2}$ ,  $\delta \varphi_{d3}$ ,  $\delta \varphi_{d4}$ ,  $\delta \varphi_{d5}$ ,  $\delta \varphi_{d6}$ ,  $\delta \varphi_{d7}$  – deviations angles of rotation from equilibrium state by the form impacts on system of the variable moment from the engine;  $\varphi_{01}$ ,  $\varphi_{02}$ ,  $\varphi_{03}$ ,  $\varphi_{04}$ ,  $\varphi_{05}$ ,  $\varphi_{06}$ ,  $\varphi_{07}$  – angles of rotation, caused by static load.

$$\left\{ \begin{array}{l} J_5 \delta \ddot{\varphi}_5 + k_5 (\delta \dot{\varphi}_4 - \delta \dot{\varphi}_5) + c_5 (\delta \varphi_4 - \delta \varphi_5) = M_{s.v.k.} \pm M_{udps.v.k} \\ J_6 \delta \ddot{\varphi}_6 + k_6 (\delta \dot{\varphi}_4 - \delta \dot{\varphi}_6) + c_6 (\delta \varphi_4 - \delta \varphi_6) = M_{s.vrash.m.a.} \pm M_{udpvom} \end{array} \right. \quad (3)$$

here  $\delta \varphi_1$ ,  $\delta \varphi_2$ ,  $\delta \varphi_3$ ,  $\delta \varphi_4$ ,  $\delta \varphi_5$ ,  $\delta \varphi_6$ ,  $\delta \varphi_7$  – fluctuations of instant angle of rotation rather equilibrium state.

From fluctuations of turning angles we will pass to fluctuations of the moments into transmissions  $\delta M_{tr}$ , resistance of back driving wheels  $\delta M_{s.v.k.}$ , PTO  $\delta M_{vom}$  and resistance of the rotating unit mechanisms  $\delta M_{s.vrash.m.a.}$ .  $\delta M_{s.v.k.} = c_5 (\delta \varphi_4 - \delta \varphi_5)$ ,  $\delta \dot{M}_{s.v.k.} = c_5 (\delta \dot{\varphi}_4 - \delta \dot{\varphi}_5)$ ,  $\delta \ddot{M}_{s.v.k.} = c_5 (\delta \ddot{\varphi}_4 - \delta \ddot{\varphi}_5)$ ;  $\delta M_{vom} = c_6 (\delta \varphi_4 - \delta \varphi_6)$ ,  $\delta \dot{M}_{vom} = c_6 (\delta \dot{\varphi}_4 - \delta \dot{\varphi}_6)$ ,  $\delta \ddot{M}_{vom} = c_6 (\delta \ddot{\varphi}_4 - \delta \ddot{\varphi}_6)$ . (4)

Having substituted the equations (4) in (3) and having transformed the turned-out equations, we will receive, in it value of size  $\delta \varphi_4$  does not influence system, we consider their values are equal to zero

$$\left\{ \begin{array}{l} J_5 \delta \ddot{M}_{s.v.k.} / c_5 + \delta \dot{M}_{s.v.k.} k_5 / c_5 + \delta M_{s.v.k.} = M_{s.v.k.} \pm M_{udps.v.k} \\ J_6 \delta \ddot{M}_{vom} / c_6 + \delta \dot{M}_{vom} k_6 / c_6 + \delta M_{vom} = M_{s.vrash.m.a.} \pm M_{udpvom} \end{array} \right. \quad (5)$$

$$\left\{ \begin{array}{l} \delta \ddot{M}_{s.v.k.} + \delta \dot{M}_{s.v.k.} k_5 / J_5 + \delta M_{s.v.k.} c_5 / J_5 = M_{s.v.k.} c_5 / J_5 \pm M_{udps.v.k.} c_5 / J_5 \\ \delta \ddot{M}_{vom} + \delta \dot{M}_{vom} k_6 / J_6 + \delta M_{vom} c_6 / J_6 = M_{s.vrash.m.a.} c_6 / J_6 \pm M_{udpvom} c_6 / J_6 \end{array} \right. \quad (6)$$

$$\begin{aligned} M_{s.v.k.} &= M_{udps.v.k} \frac{a_1 (S^2 + b_1 S + b_2) - b_2 (a_1 S + a_2)}{\delta}, \\ M_{vom} &= M_{udpvom} \frac{b_1 (S^2 + a_1 S + a_2) - a_2 (b_1 S + b_2)}{\delta}. \end{aligned} \quad (7)$$



here  $\delta = (S^2 + a_1 S + a_2)(S^2 + b_1 S + b_2) - (b_1 S + b_2)(a_1 S + a_2)$ .

$a_1, a_2, b_1, b_2$  – coefficients of dynamic system.

$a_1 = k_3 / J_3, a_2 = c_3 / J_3, b_1 = k_6 / J_6, b_2 = c_6 / J_6$ .

**Conclusion.** The analysis of dynamic loading of nodes motor and transmission or power gears of the traction vehicle, has given the chance to find the existing problems of elementstraction vehicle.

– mathematically modeling transfer of the moment from the engine to the executive mechanism which allows to learn operating condition of each main nodes of the car. This model will help clerks and designers for creation new designs of TTU and MTU.

– have analytically defined drag torques of driving wheels and shaft of selection of power taking into account the moment of friction it is elastic the pneumatichydraulic drive.

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## Section 7. Pedagogy

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### Psychology and pedagogical escort of rural school students at the stage of the professional choice

**Abstract:** In this work the problem of psychology and pedagogical escort of rural school students in professional orientation work and in development of personal and professional self-determination, and also feature of system of maintenance in the conditions of rural school is considered. Various points of view in the theory and practice of modern researchers are analyzed.

**Keywords:** maintenance, development, system of maintenance, rural school students.

At the present stage of development of the state by the defining factors of its sustained economic growth high technologies and the knowledge-intensive production which innovation depends on quality of scientific and intellectual potential of society, level of professional competence of experts, their creativity and development of research skills act. In this regard formation of professional competence has paramount value, as one of the main ways of the decision of which personal professional self-determination of future experts during school training acts. It is confirmed by the directions of educational policy reflected in the new Education law, the Federal target program of development of education for the period till 2020, a national educational initiative "Our new school".

In the Russian Federation the school psychological service exists nearly two decades. The board of the Ministry of Education of the Russian Federation summed up on March 29, 1995 some results of activity of psychological services in education. The board noted that development of practical psychology promoted a humanization of all system and led to creation of psychological service in an education system. The humanistic aspect of appearance of psychologists at school is expressed in gradual transition from "pedagogics of knowledge, skills" to development pedagogics:

- orientation of school personnel to each child separately, but not on group of pupils in general;
- understanding by teachers of need of emergence at schools of psychologists, development of the developing, correctional programs for the children promoting optimum development of their mental potential.

Process of the professional choice — long process, completeness can be stated only when at the person the positive attitude towards itself as to the subject of professional activity is created. Therefore choice of profession is only an indicator that process of the professional choice passes into a new phase of the development.

According to E. A. Klimov [2, 132–134], there are 8 corners of a situation of choice of profession. The senior takes into account data not only on features of various professions, but also the mass of other information.

1) Position of the senior family members. Of course, care of seniors of future profession of the child is clear; they bear responsibility for how there is his life. Very often parents give to the child liberty of choice, demanding thereby from him independence, responsibility, an initiative. Sometimes, that parents do not agree with the choice of the child, suggesting to revise the plans and to make other choice, considering that it still small. Often interfere with a right choice of a profession installations of parents who aspire that children compensated their shortcomings of the future, of that activity in which they could not prove completely.

2) Position of companions, girlfriends (peers). The friendly relations of seniors are already very strong and influence them on choice of profession is not excluded as the attention of the professional future of peers also increases. The position of microgroup can become decisive in professional self-determination.

3) Position of teachers, school teachers, class teacher. Each teacher, watching behavior of the pupil only in educational activity, all the time "gets a thought for a facade of external manifestations of the person, makes some kind of diagnoses concerning interests, tendencies, thoughts, character, abilities, readiness of the pupil". The teacher knows a set of that information which is unknown even to the pupil.

4) Personal professional plans. In behavior and human life of idea of the near and long-term future play very important role.

5) Abilities. Abilities, talents of the pupil of the senior classes need to be considered not only in study, but also to all other types of socially valuable activity. 6) Level of claims on public recognition. Realness of claims of the senior — the first step of vocational training.

7) Knowledge — important, undistorted information — an important factor of choice of profession.

8) Tendencies are shown and formed in activity. Consciously joining in different types of activity, the person can change the hobbies, so and the directions. It is important for the senior as preprofessional hobbies — a way to the future [2, 134–139].

For a right choice of a profession control of this process which is exercised of the teacher is necessary. In narrower plan in relation

to a problem of choice of profession studying the teacher it is extremely important to know the objective and subjective factors making the content of management. Treat objective factors: system of objectively operating regularities, living conditions of the subject, Wednesday, education, an economic environment and others. Treat subjective factors: possibilities of the subject, tendency, interests, abilities, intentions, motives, character, temperament, inclinations and other parties of the personality. That management of choice of profession was really effective, it is extremely important to understand in effect the composed parties of a subject of management stated above two. Management of choice of profession is impossible without knowledge of the personality, its structure.

Search of new solutions of the problem of psychology and pedagogical maintenance of self-determination of the studying youth in the conditions of vocational guidance of training assumes:

- strengthening of integration of content of education with nonlearning practice of social and professional self-determination of school students;
- orientation to consolidation of resources and efforts of schools with other educational institutions (interschool educational plants, schools, colleges, lyceums, higher education institutions);
- ensuring profile training of school students on the basis of variability, taking into account the individual educational trajectories chosen by them corresponding to interests, tendencies, abilities of pupils and inquiries of labor market;
- ensuring the obligatory preprofile training of pupils including mastering school students idea of an image of the “I” about the world of professions, about labor market; acquisition of practical experience for the reasonable choice of a profile of training;
- rendering the psychology and pedagogical help to the teacher in reorientation of his activity of the creator, mentor to the activity directed to empathy; providing school student with support in the choice of a profile of training and further professional activity.

In the conditions of educational institution an effective type of the help to seniors in the professional choice are psychological and pedagogical support which are defined in world and domestic science and practice as the most effective. Fundamental in questions of the theory and practice of professional self-determination

of seniors in the context of vital self-determination V. I. Zhuravlev [1], V. A. Polyakov [3], N. S. Pryazhnikov [4] works, etc. are defined.

The rural school needs to provide the conditions stimulating human height therefore he could take the responsibility for the professional choice. Inner world at youthful age is autonomous and independent. It complicates process of psychology and pedagogical maintenance, children of this age do not wish to accept the help from the persuasive adult. Much more effective remedy for the solution of many psychological problems of rural school students are special methods of group work when the help proceeds not from the adult, and from children whose opinion for them is more significant. As an optimum method psychological trainings on development of consciousness of seniors, and also psychology and pedagogical and role-playing games in our opinion can serve. Also to a solution of the problem of choice of profession and a further educational route the course personally — professional self-determination, developed for pupils of 9–10 classes can promote. This course is complex according to contents as consists of two programs: 1) “Self-knowledge psychology” for the 10th classes; 2) “I and my professional choice” for the 9th classes. The course is offered to pupils for choice to create individual educational inquiry at the teenager, to develop ability to analyze and understand external circumstances.

Thus, psychology and pedagogical maintenance at rural school gains new quality. It is not only the most important component of education, but also its priority purpose. Also still serious easing of attention to questions personally — professional self-determination of pupils in all types of educational institutions, weak communication between an education system and labor market takes place. All this demonstrates that only the coordinated and purposeful work of pedagogical staff of Tarasinsky school positively affects the general improvement of quality of psychological and practical training of school students for conscious choice of profession.

Thus, the system of psychology and pedagogical maintenance at a stage of the professional choice has to be directed to activation of internal psychological resources of the personality, joining in professional activity, the person could fully realize himself in the chosen profession.

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## Joint analysis of Unified State Exam results and academic performance of technical university students by methods of nonparametric statistics

**Abstract:** The results of statistical data processing of the Unified State Exam (USE) scores, outcomes of university entrance control of school knowledge and academic performance of the first- and second-year students are analyzed in the article.

Methods of nonparametric statistics are used to assess the relationship between variables and the capacity of USE scores to predict the academic performance at university.

**Keywords:** engineering education, Unified State Exam, academic performance, nonparametric statistics.

### 1. Introduction.

Problems of modern engineering education in Russia have been studied in many papers [3; 11; 14]. It is noted not only a decrease in the number of students in technical specialties [2], but also a deterioration in the quality of engineering education [1]. The quality of engineering education is related not only to the quality of teaching and knowledge control at university, but also with the level of students' preparation to the study of technical disciplines. Students of technical universities should have a basic knowledge of physics and mathematics and be able to use it actively. Accumulated data on students admitted to universities by USE results allows answer the question whether Unified State Exam an adequate assess of the student's academic potential. Various mathematical methods are used for processing and analysis of large data samples on USE scores, results of entrance control of knowledge and academic performance of students at technical universities [9; 10]. The study [8] has shown that USE scores explain an average of 25–30% on the higher education progress scale, which is a rather high indicator, since academic progress is determined by a great number of factors apart from preliminary examinations. As applicants are ranked and selected by their USE scores, it is implied that students with higher scores are more talented and thus should demonstrate higher academic achievements after enrollment. Besides, the system is designed to select high school graduates based on their total USE scores in specific subjects required for admission. Therefore, it is expected that further performance is predicted equally in all subjects. The research using methods of regression analysis to assess how preliminary examinations (both composite USE scores and scores in specific subjects) affect academic performance in higher education have been provided at for about 19,000 students enrolled at five Russian universities of different profiles. The obtained results allow conclude the predictive capacity of composite USE scores is high enough to accept this examination as a valid applicant selection tool. In the same time it has been found that USE scores in mathematics and Russian are better predictors of grades in almost all of the academic fields and, conversely, USE scores in field-specific subjects often appear to be poorly related to performance at university. The results of econometric study on predicting first-year average grades and dropout probability with USE scores are also presented in the paper [12]. Regression methods allow to conclude that using a sum of four exams — math, social studies, Russian language and foreign language — gives less accurate predictions than a sum of three exams, excluding foreign language. In models with separate exams as predictors, the greatest effect on dependent variable provides math grades. It should be noted that according to [16] 100-point scales for different subjects are inherently inconsistent. USE scores can be compared directly neither across subjects nor within one subject across different years. As regard to how long the impact of USE scores on the academic success is preserved, data on students of the first, second and third years has been analyzed and significance of USE results for prediction of academic performance and dropout probability after 2 or 3 years of study has been proved [17]. Analysis of changing correlation strength between USE scores and academic performance of first-year students through 2010 to 2014 has shown the decreasing of correlation in 2010–2012 and increasing in 2013–2014 [7]. With regard to decrease of correlation, new techniques of bypassing the requirements of the USE were created and developed every year. The violations include disseminating exam questions before the examination, using mobile phones (for Internet searches or SMS), receiving help from the onsite proctors, and reopening sealed test en-

velopes to correct mistakes [5]. Video cameras used during the USE from 2013 and control over Internet resources from 2014 have resulted the increase of the correlation. The statistically significant correlation between the USE results and academic performance allows identify groups “at risk” among first-year students [13]. Timely identification of first-year students that may potentially have low academic performance enables to organize early tutoring, counseling, training for these students. Monitoring academic performance and USE scores allows solve the problems of educational process associated with a varied approach to different groups of students, identifying violations and abuses, or, on the contrary, the positive effect of initiatives and interventions.

### 2. Methods and data.

Outcomes of a joint statistical analysis of USE scores, results of entrance control of school knowledge and students' academic performance are presented in this study. The analysis requires processing of large data sets taking into account the character of collected data. The raw data are often encoded in an ordinal or a nominal scale and their distribution significantly differs from the normality. Statistical techniques known as nonparametric statistics (or distribution free statistics because they make no assumptions about the distribution of the data) has been applied [4; 6; 15]. The methods include: computing Kolmogorov-Smirnov statistics to test whether the data fits a normal distribution; estimating quartiles of distributions; calculating Wilcoxon rank sum test and Kruskal-Wallis H test for testing the hypothesis that several groups have the same median; measuring the correlation with Spearman's rank-order coefficient; drawing histograms and box plots. With regard to the regression analysis, the method of logistic regression has been used for a prediction of a binary dependent variable and for capacity estimation of ordinal variables.

Data on USE scores on Physics, Mathematics and Russian language; results of Entrance Control of school knowledge on Physics and Academic Performance on Physics and Mathematics in the first and second semesters had been collected; Data Bases were created and the data has been processed. Data Base DB1 contains information about students of Mechanical Engineering Faculty. It contains six ordinal variables: USE scores on Physics, Mathematics and Russian language; Semester Rating, Examine Rating and Grade on Physics in the first semester. There are three nominal variables in DB1: Specialty, Gender and Admission to the Exam on Physics in the first semester. Semester Rating is the result of knowledge control during the semester coded from 0 to 60 via 1. Exam Rating is coded from 0 to 40 via 1. Variable “Rating” obtained as a sum of Semester Rating and Exam Rating is used as the key Academic Performance indicator. Variable “Grade” is obtained from Rating according to the rule: from 0 to 49 – “fail”, from 50 to 69 – “satisfactory”, from 70 to 84 – “good”, from 85 to 100 – “excellent”. Admission to the Exam (0 – fail, 1 – success) is depended on the Semester Rating and results of laboratory works.

Data Base DB2 contains the information about students of six engineering Faculties: Petroleum Geology and Geophysics (Geology); Reservoir Engineering (Reservoir); Pipeline Engineering, Construction and Operation (Pipeline); Mechanical Engineering (Mechanical); Chemical and Environmental Engineering (Chemical); Automation and Computing Engineering (Computing). DB2 contains seven ordinal variables: USE scores in Physics and Mathematics; results of Entrance Control of school knowledge on Physics; Rating on Physics and Mathematics in the first and the second semesters. Entrance Control of school knowledge on Physics is



carried out for students of all engineering faculties except Chemical and requires resolving five simple problems from school program. There are four nominal variables in DB2: Faculty; Gender; Type of Admission (Budget – sponsored by State, Target – sponsored by Company, Contract – students pay tuition); Region of student's high school graduation (Central District, South District, Volga Region, Ural, Siberia, Far East, North Caucasus).

### 3. Results and discussion.

We have conducted a logistic regression analysis to predict the probability of getting the Admission to the Exam on Physics in the

first semester, using students' USE scores on Math, Physics and Russian language. The accuracy of prediction is estimated by a parameter "sensitivity" obtained through dividing the number of confirmed outcomes by the number of all observed outcomes in the control group. Maximum of sensitivity has been obtained in prediction model using a sum of two exams: Physics and Russian language. In models with separate exams as predictors, USE scores on Physics have the greatest effect on the dependent variable. The latter is confirmed by Spearman rank-order coefficient estimations (Table 1). Median values of distributions of USE scores on Russian language are presented in Table 2.

Table 1. – Spearman rank –order coefficients between USE scores and Rating on Physics in the first semester, Mechanical Engineering Faculty

	Unified State Exam			Rating on Physics
	Math	Physics	Russian	
USE Math	1			
USE Physics	0.4405	1		
USE Russian	0.3063	0.3164	1	
Rating on Physics	0.2759	0.5241	0.3214	1

Table 2. – Medians of distributions of USE scores on Russian language by categories of variable Grade on Physics in the first semester, Mechanical Engineering Faculty

USE scores on Russian language	Grade on Physics in the first semester			
	fail	satisfactory	good	excellent
min	73	65	71	70
median	87	84	84	82
max	100	98	100	90

Analysis of Table 2 and calculating the Kruskal-Wallis H test reveal that USE scores on Russian is significantly less for higher categories of variable "Grade". The share of students for whom the difference between the USE scores on Russian and on Physics is more than +20 points is about 40% of all students on the faculty. Most of these students had not been admitted or failed the exam on Physics in the first semester (Table 3). These results are confirmed by author's experience during teaching Physics at the Preparatory Courses of the University. Some students even had not attempted to solve problems of the second part of USE on Physics by declaring: "I find it easier to get high USE scores on Russian language than

to learn solving problems on physics". They were admitted to the university by the sum of three Unified State Exams (Math, Physics, Russian) and have not been able to perform the program on Physics in the first semester.

Results of Internal Control (IC) of students' knowledge in the university include Entrance Control and Academic Performance presented by variable "Rating" as a key indicator. In accordance with the generally accepted methodology for ordinal data, we assessed the relation between USE scores and results of Internal Control through measuring the correlation with Spearman's rank-order coefficient (Table 4).

Table 3. – Grades on Physics in the first semester and differences between USE scores on Russian language and Physics

Difference between USE scores in Russian language and Physics	Grade on Physics in the first semester		
	Failed or not admitted to exam	Satisfactory	Good or excellence
≥ 20	54%	34%	12%
< 20	35%	33%	32%

Table 4. – Spearman's rank-order coefficients for USE scores and Internal Control results on Physics for students of five engineering faculties

Physics	USE scores	Entrance Control	Rating 1 <sup>st</sup> semester	Rating 2 <sup>nd</sup> semester
Unified State Exam	1			
Entrance Control	0.482	1		
Rating 1 <sup>st</sup> semester	0.395	0.574	1	
Rating 2 <sup>nd</sup> semester	0.315	0.566	0.777	1

The calculations were made for five engineering faculties (except Chemical). With a level of 0.05 we rejected the null hypothesis that USE and Internal Control scores are unrelated. It has been found that there is the tight correlation (0.777) of the Academic Performances in the first and second semesters. The correlation of variables "Rating" with variable "Entrance Control" (0.574/0.566) is stronger than with variable "USE scores" (0.395/0.315). Using

Chaddock scale of correlation tightness, we could say that the correlation between USE scores and results of Entrance Control is moderate, the correlation between results of Entrance Control and Semester Rating is salient, and the correlation between Ratings in the first and the second semesters is high.

Thus, the Entrance Control results are evaluating student's potential to study physics at university better than USE scores. The strong

correlation between the variables Rating 1 and Rating 2 confirms the sustainability and the fairness of assessment of students' knowledge of physics at university. Wilcoxon rank sum test reveals zero's shift between the distributions of the two variables. Hereinafter we are using the variable Rating 1 with the name "Rating" as an assessment of academic performance. Box plots of USE scores and IC results for

engineering faculties are represented on Fig. 1. The most significant disagreement between USE and IC is obtained for Pipeline Faculty, the best agreement – for Computing Faculty (Fig. 2). Perhaps it is due to the geography of student's high school graduation – in this sample the majority of students on Computing Faculty are from Moscow, on Pipeline faculty – from various regions of Russia.

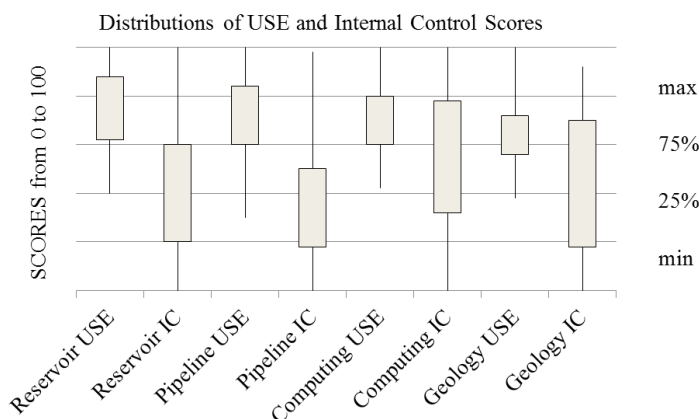


Figure 1. USE scores and Internal Control results (the first semester of studying Physics)

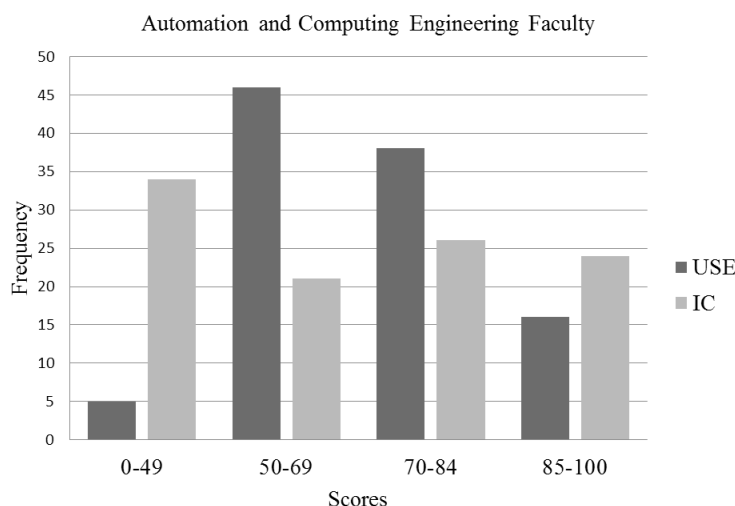


Figure 2. USE scores and Rating points on Physics in the first semester

Maybe the situation on Pipeline Faculty is due to the fact that students from other regions should be adapting to life in Moscow during the first semester and have additional difficulties in their study. Maybe students on the Computing Faculty better learn math, and by their choice of specialty, are more interested in getting knowledge and problem-solving skills on physics. The majority of engineering students had been studying physics at school only for successful passing USE. Their motivation for obtaining

deep knowledge and aspiration to learn solving problems, as a rule, are not great.

Contingency table (Table 5) with USE scores and Rating on Physics in the first semester reveals significant difference between the results of internal and external controls for students with the highest USE results: 40% of students with USE scores more than 80 got grades on Physics for the first semester "failed" or "satisfactory".

Table 5. – Contingency table of USE scores and Rating on Physics for Computing and Geological faculties

USE scores on Physics	Rating on Physics at the first semester			SUM
	0–59	60–79	80–100	
0–59	65%	31%	4%	100%
60–79	59%	23%	18%	100%
80–100	40%	26%	34%	100%

It is not always like the results associated with fraud or violations of the USE. The gap between technical universities requirements and skills acquired at school is great and it is growing every year. It does not apply to special physical and mathematical schools but regular schools deliver students having neither sufficient theoretical knowledge nor ability to solve practical problems. The majority of high school students are performing only the first part of USE on physics, which is

not focused on solving problems, but is consisted of simple questions. It is not preparing students for studying physics in technical universities. As an example, author's observations of students of Chemical faculty (not required passing USE on physics) and Mechanical faculty (required positive scores of USE on physics). In the first semester most students of Chemical faculty were confused and scared, but they regularly attended special additional classes, learned to solve problems and

as a result in the second semester they passed the exam in physics with average rating better than students of Mechanical faculty.

Additional difficulties in the process of studying physics are caused by a low level of mathematical knowledge and the lack of

basic mathematical skills of students. Tables 6, 7 show values of Spearman rank-order correlation coefficients calculated for USE scores and Rating in the first semester of mathematics and physics for Mechanical and Computing faculties.

Table 6. – Spearman’s rank-order correlation coefficients for USE scores and Rating on Physics and Mathematics for Mechanical faculty (N = 350 students)

N = 350	USE Physics	USE Math	Rating Physics	Rating Math
USE Physics	1			
USE Math	0.570 <sup>(2)</sup>	1		
Rating Physics	0.403 <sup>(1)</sup>	0.382 <sup>(1)</sup>	1	
Rating Math	0.379 <sup>(1)</sup>	0.411 <sup>(1)</sup>	0.793	1

Table 7. – Spearman’s rank-order correlation coefficients for USE scores and Rating on Physics and Mathematics for Computing faculty (N = 200 students)

N = 200	USE Physics	USE Math	Rating Physics	Rating Math
USE Physics	1			
USE Math	0.627 <sup>(2)</sup>	1		
Rating Physics	0.439 <sup>(1)</sup>	0.503 <sup>(1)</sup>	1	
Rating Math	0.450 <sup>(1)</sup>	0.438 <sup>(1)</sup>	0.593 <sup>(2)</sup>	1

Calculating the significance test for Spearman rank-order correlation coefficients reveals that the variables are truly related in the populations with a level of 0.05. Statistical significance of differences between the correlation coefficients was tested using z-statistics with a level of 0.05. Correlation coefficients not significantly different from each other are marked with the same indices in the tables. According to Chaddock scale, the correlation between Rating on Mathematics and Rating on Physics is high for Mechanical faculty (0.793) and salient for Computing faculty (0.579); the correlation between USE

scores on these subjects is salient (0.570 and 0.627 resp.); the correlation between USE scores and rating for both subjects and both faculties is moderate. So we can conclude that the academic performance in two subjects is in good agreement and the same could be said about USE scores in these subjects. But the relationship between USE scores and Rating on Physics and Mathematics is significantly weaker.

Table 8 shows values of medians of distributions of USE scores and Rating on physics by classes of variable “Type of Admission” for three engineering faculties (Reservoir, Mechanical, Pipeline).

Table 8. – Medians of distributions of USE scores and Rating on Physics in the first semester for various values of variable “Types of Admission”

TYPE of ADMIS- SION	FACULTY					
	Reservoir		Mechanical		Pipeline	
	USE	Rating	USE	Rating	USE	Rating
Budget	81	70	73	63	77	70
Target	57	64	52	53	61	56
Contract	54	54	53	50	50	50

Calculating Wilcoxon rank sum test, we have rejected the null hypothesis that the mean of the differences between the pairs is null. So, the medians have significantly different values for different types of admission. The largest gap between USE scores and Rating is observed for the Budget form of education, that is, for high USE scores. This is consistent with results of contingency tables (Table 5) and once again points to the need for careful checks to bad matching of high USE scores and poor academic performance at university.

With regard to the Regional factors, calculations show that students from Volga Federal District have the maximum median value for the USE scores (70) and Rating on physics in the first semester (70) and the minimal difference between them (0). The biggest difference (20) between the median values for the USE scores (70) and Rating on physics in the first semester (50) have students from the North Caucasus Federal District. These results are confirmed by the experience of author on Preparatory Courses for USE on physics in different regions of Russia including Volga Region and North Caucasus.

**Conclusion**

Nonparametric statistical methods take into account the specifics of the processed data — discrete variables encoded in an ordinal or a nominal scale; distribution does not fit the normal

law. Carried out with the help of these methods, data processing allows to:

1. test statistical significance for correlation and estimate the strength/direction of relationship between two variables;
2. calculate medians of the variable for different grades of factor;
3. compare medians of set of variables and test the hypothesis that several groups have the same median;
4. evaluate the predictive ability of individual variables and their combinations;
5. predict the value of a dependent dichotomous variable using a set of independent variables.

Data on the USE scores, results of entrance control of school knowledge and academic performance of the first- and second-year students were processed using these methods. The processing of the data included:

1. prediction of dichotomous variable “Admission to the Exam in Physics” with a method of binary logistic regression;
2. estimation of prediction capacity of variables: USE scores on Physics, Mathematics, Russian language and their combinations, — to predict the Grade on Physics in the first semester;
3. calculation of rank-order correlation coefficients between USE scores on Physics, Mathematics, Russian language and Rating on Physics in the first semester (table 1);

4. estimation of medians of USE scores on Russian language for different values of Grade on physics in the first semester (tables 2, 3);

5. calculation of rank-order correlation coefficients between the USE scores on Physics, results of Entrance Control on Physics and Rating on Physics in the first and second semesters (table 4);

6. calculation of a contingency table on USE scores on Physics and Rating on Physics in the first semester (table 5);

7. calculation of rank-order correlation coefficients between USE scores on Physics and Mathematics and Rating on Physics and Mathematics in the first semester (tables 6, 7);

8. calculation of medians of two variables: USE scores on Physics and Rating on Physics in the first semester, — for different grades of variable “Type of Admission to the university” (table 8) and variable “Region” (Federal District where student graduated high school).

The results of the calculations made it possible to draw the following conclusions:

1. Prediction of the dependent variable “Admission to Exam in Physics” lets to preselect the first-year students who could be not-admitted to the session because of their poor academic performance during the semester. It makes possible to arrange extra classes in advance to help these students in passing tests, doing laboratory works and preparing to exams.

2. Analysis of relationships between USE scores on Russian language and Rating on Physics in the first semester leads to the conclusion that this exam is not such a good tool for selection of technical university students. May be using of USE scores on Russian language with a weight less than weight of scores on Physics and

Mathematics will improve assessing of student’s academic potential for engineering university.

3. Compare of strength of correlation between results of internal and external knowledge control revealed that Entrance Control (which is performed in the form of a control work and requires problem solving skills) estimates student’s capacity to study physics at the university better than the USE.

4. Analysis of contingency tables for the USE scores on Physics and Rating on Physics in the first semester shows an unreliability of high scores (>80) for a large number of students. This may be due to violations of requirements of the USE or because currently the USE variants are not good enough to prepare student for the physics course in engineering university.

5. Analysis of the difference between the USE scores and Rating in the first semester for various factors (Type of Admission, Region) lets to reveal groups of freshmen who do have problems of the first-year studying (domestic, social, psychological). Solving these problems helps students adapt more quickly to their studies in the university and protects them from academic failures. Results of this analysis help to highlight areas where the school is successfully preparing students for studies at technical university (Volga Region), and areas where the USE is performed with violations (in our case, North Caucasus).

6. Monitoring of academic performances on Physics and Mathematics on the first and second courses and of their connection with USE scores in these subjects enables to answer the question of how long USE results have an impact to academic achievements of students.

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## Health protection activity of a teacher in formation of students' personality

**Abstract:** for the successful implementation of health-preserving activity of the teacher on formation of physically healthy, spiritually Mature and harmoniously developed generation, capable to take responsibility for the fate of the younger generation, it is necessary to consider: the students have the necessary medical and hygienic knowledge; professional and pedagogical knowledge and skills on health protection of students; the degree of adaptation to innovative endeavors in the practice of health care; the creative potential of the subject of health; skills student-centered learning; systematic knowledge and skills of health care; ability to form healthy life; knowledge and skills for health-exercise.

**Keywords:** health care, teacher, students, physical health, harmoniously developed generation, a healthy lifestyle.

The multifaceted activities of teachers involved in the system of continuous education, health protection occupies an important place, which is a part of educational programs aimed at the formation of students' personality. In this context, the insufficient competence of students in matters of preservation and strengthening of health of the younger generation is the cause of various diseases and personality neuroticism.

This raises the need to develop programs for the conservation and recovery of health of both students and teachers by means of psychological, medical and sports actions. This can be achieved in the case of the introduction of idea of a healthy lifestyle in educational institutions, which considers health as a personal, social and educational value of students. The implementation of this idea is possible in the case of planned management of pedagogical process for the purpose of health protection, on the one hand, at the level of teacher's activities control, on the other hand, on the level of trainees' activities control [1].

Teacher at all stages of lifelong education system is to implement active health activities of learners through the content, principles and forms of organizing the learning process, interactive methods of training and education, methods and communication styles.

This training should primarily focus on promotion of their health, excepting the presence of bad habits, exercising commitment to promote healthy lifestyles.

Many years of our research in the framework of education and character building activities in preschool educational institutions, secondary schools, vocational colleges and universities show that first of all teacher's activities on formation of students' motivation to health is an important factor of health protection of the younger generation.

The acquisition of a tutor and a teacher of knowledge about what the "health" is, the ability to implement health-saving technologies, taking into account individual psychological characteristics of students, providing health-saving environment to prevent occurrence of stress factors and etc., are key elements of health-professional competence of a teacher [2].

The scientific literature presents a number of definitions of "health", in particular, that the health is the most important condition of a person, the basis of his life, material wealth, labor activity, success and longevity. The training is designed to convince students that person's health reflects the standard of living and country welfare and it directly affects labor productivity, economy, defense, moral principles of the society,

mood of people, paying particular attention to the fact that the level of health depends on the socio-economic, material-technical, sanitation, environment, culture, health, science, lifestyle, food [3].

Currently, there has been a system of organization of educational and training process aimed at students' health protection, which includes the following subsystems: formation of knowledge and skills of health culture and healthy lifestyle (HLS), organization of health-protection educational process, improvement in educational and extracurricular time. Purposeful and consistent interaction between a tutor and a student contributes to health culture through health-protection education, including knowledge of laws of formation, preservation and strengthening of health, mastery of skills aimed at preservation of personal health, factors forming assessment, mastering knowledge of healthy lifestyle and skills of construction, as well as formation of health values, healthy lifestyle as common to humanity values. In order to develop students' skills in field of health preservation, including their personal health, a teacher uses a variety of modern health-saving technologies, forms and methods of teaching, such as lectures, video lectures, seminar workshop, management game, thematic sessions, conference and etc [4].

Health-saving activities of an educator can be successfully realized in the course of studying in small groups to develop specific health-saving topics and projects, followed by presentation of information technologies, organization of competitions of best works on health creative activities of students of schools, lyceums, colleges, supplementary education institutions, "Barkamol Avlod" students, promoting activation of educational, extracurricular work and activities of health-saving nature, outside educational institutions. Teamwork of a tutor and a student contributes to the development of students' interest in health protection issues, promotion of children and teenagers creativity in field of preservation, strengthening and expanding health reserves and formation of health culture.

In solving problems of preservation of the younger generation of health and diseases prevention, including the so-called "school diseases" of students, a lot of attention is paid to health-care measures, as well as the implementation of health protection policy at all stages of continuing education through creation of "health schools" on the basis of educational institutions. It should be noted that high efficiency of work is being done in this direction by tutors, psychologists, teachers, doctors and parents. Each

educational institution at the present stage of society development can become a “Health School” in which health protection environment is ensured by proper competence of health-medical and teaching staff, as well as implementation of health protection technologies achieved at all stages of training and education. In these “health schools”, working under the slogan “None of the students will be left without care and attention”, the goal was set to expand the scope of work in this direction, to increase the scope of students by constant attention to their physical, mental and spiritual health. In the context of the “Health School”, the implementation of our educational system is carried out through a variety of processes, such as management, training, educational, health as well as supportive processes (medical, psychological, social, valeological) development of students and tutors personality. The importance of such educational system component of “Health School” as pedagogical (teaching and educational) process has been mentioned above. Not least important is the fact that components of educational system of “Health School”, in our opinion, are the services that provide the educational process and ensure preservation, promotion of health and formation of healthy life style philosophy and personal development of students and teachers.

Work of medical, psychological, valeological, social and educational services appears to be as an essential condition for achieving goals of pedagogical process in “Healthy Schools”, in this regard, experts of these services take part in them as indirect participants.

The fact that the activities of the services are aimed at tracking and correction of qualitative changes in physical, mental and social development of students, introduction of psychological, physiological and valeological knowledge into practice, helps teacher to realize the greatest benefit of the content and ways of organizing health-saving pedagogical process. Accompanying the pedagogical process, the services of educational institutions largely determine their effectiveness in terms of ensuring health of students.

Thus, the backbone factor of “Healthy Schools” is the general goal in education, training and development of a healthy person,

which affects the final outcome of all subjects of the educational system.

Educational system of “School Health”, oriented towards personal development and ensuring health of children, accumulates flexible education, management, health-improving programs and technologies adapted to individual qualities of a tutor and a student. Therefore, “School health” compared with traditional educational institutions is adaptive, leaning to the type of tightly connected social and educational systems.

Among the factors contributing to low efficiency of health protection activity in modern educational institutions is the lack of competence of teachers in matters of protection and promotion of healthy lifestyle formation among students, because a teacher, who is conscious of the importance for targeted activities on conservation and strengthening his own health, will be able to contribute effectively to the normal physical and mental development of the younger generation. In this respect, it stands out from a specialist who is not able to mobilize students by his own example and who maintains healthy lifestyle not only in words.

In the development of teachers’ readiness criteria for health protection activity and application of health-saving technologies in educational process and extracurricular time, the following should be considered: presence of required medical and hygienic knowledge in students; professional and pedagogical knowledge and practical skills in health protection of students; degree of adaptation to innovative initiatives in health preservation practice; creativity potential in health protection of a person; ability to student-centered learning; systematicity of knowledge and skills of health preservation; the ability to generate healthy lifestyle; knowledge and skills of implementing health-saving exercises.

Only in case of provisions of the following aspects such as formation of healthy, spiritually mature and harmoniously developed rising generation that could take responsibility for the fate and future of the country, health-saving activity of a teacher can be successfully implemented.

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## Section 8. Political science

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### Some features of Armenian think tank industry

**Abstract:** The Article gives notion of some key results of the research which refers to Armenian think tanks. In particular according to data available as to April, 2017 number of think tanks functioning in Armenia dynamics of establishment, typology research priorities and other data characterizing the sphere.

**Keywords:** think tanks, Armenia, public policy, expert community.

#### Introduction

According to research since 1991 just after the independence of Armenia around 130 think tanks or organizations having some structural similarities with think tanks were established in Armenia. From the other hand research of activities of the above mentioned shows that majority of those organizations were just formal or were active in a very short period of time. After this active period those organizations both became very passive or just ceased their public activities and finally closed.

Nevertheless, according to carried research currently there are 50 think tanks or think tanks-like organizations in Armenia.

#### Overview of Armenian think tank industry

When we classify think tanks currently acting in Armenia it is expedient to divide those into four conditional types:

1. Independent/Autonomous think tanks;

2. Government affiliated or Quasi-governmental think tanks, which mainly are think tanks under state founding or in the structure of a state agency;

3. University affiliated think tanks;

4. Branches, representations of foreign think tanks, local organizations of associated or networking of international organization.

According to types and establishment dates list of current acting think tanks in Armenia is depicted in Table No. 1.

It is well know that the main mission of academic institutions is carrying of researches of basic academic nature. Nevertheless considering professional orientation among those global, regional and interior political researches carried on social, economic and current processes (in this case it is of applied nature) some institutes of National Academy of Sciences of the Republic of Armenia are also involved in the list.

Table 1. List of Armenian think tanks

N	Government affiliated/Quasi governmental think tanks	Established
1	2	3
1.	M. Kotanyan Institute of Economics of National Academy of Sciences	1955
2.	Institute of Philosophy, Sociology and Law of National Academy of Sciences	1969
3.	Institute of Oriental Studies of National Academy of Sciences	1971
4.	“Noravank” Scientific and Educational Foundation	2000
5.	Public Relations and Information Center of Staff of the President of the Rep. of Armenia	2008
6.	National Defense Research University of Ministry of Defence of the Rep. of Armenia	2016
<b>Independent/Auotonomous think tanks</b>		
1.	“Alternative” Analytical Center	1991
2.	Armenian Center for National and International Studies	1994
3.	“Modus Vivendi” Center	1999
4.	International Center for Human Development	2000
5.	“Spectrum” Center for Strategic Analysis	2001
6.	Economic Development and Research Center	2001
7.	Armenian Center for Political and International Studies	2001
8.	Institute for Civil Society and Regional Development	2001
9.	Analytical Centre on Globalization and Regional Cooperation	2002
10.	Caucasus Institute	2002
11.	Research Center for the Problem of the Non Proliferation of weapons of Mass Destruction	2003
12.	International Center for Intercultural Research, Learning and Dialogue	2003
13.	Institute for Political and Sociological Consulting	2006
14.	“Ararat” Center for Strategic Research	2006

1	2	3
15.	Institute of New Social Studies	2007
16.	“Region” Research Center	2008
17.	“Socioscope” Societal Research and Consultancy Center	2008
18.	“Progress of Gyumri” Civil Society Development Center	2008
19.	Regional Studies Center	2012
20.	Youth Studies Institute	2013
21.	“Arar” Foundation for Civilization Studies	2014
22.	“Euphrates” Middle Eastern Research Center	2014
23.	“Compass” Research, Training and Consultancy Center	2014
24.	“Insight” Analytical Center	2014
25.	ANI Armenian Research Center	2014
26.	Institute of Public Policy	2014
27.	Apella Institute for Policy Analysis and Dialogue	2014
28.	Armenian Institute of International and Security Affairs	2014
29.	Armenian Center for Society Research	2015
30.	Armenian Center for Young Analyst	2016
31.	International analytical center “Delta”	2017
<b>International think tanks</b>		
1.	The Open Society Foundations – Armenia	1997
2.	Caucasus Research Resource Center-Armenia	2003
3.	Eurasia Partnership Foundation – Armenia	2007
4.	Transparency International Anti-corruption Center – Armenia	2008
<b>University affiliated think tanks</b>		
1.	Paul Avedisian Center for Business Research and Development of American University of Armenia	1992
2.	The Turpanjian Center for Policy Analysis of American University of Armenia	1995
3.	Centre for European Studies of Yerevan State University	2006
4.	Center for Civilization and Cultural Studies of Yerevan State University	2007
5.	“Amberd” Research Center of Armenian State University of Economics	2013
6.	Center for Gender and Leadership Studies of Yerevan State University	2013
7.	Center for Regional Studies of The Public Administration Academy of the Rep. Armenia	2014
8.	“Center for Strategic Research” Lab. of Yerevan State University	2014
9.	Laboratory for Strategic Research in the Sphere of National Security of Russian-Armenian University	2015
<b>Total: 50 think tanks</b>		

It is obvious from the list that 31 out of 50 think tanks currently acting in Armenia are independent organizations. If consider those from the point of view of percentage it will be around 62% of overall. Besides there are 6 Government affiliated / Quasi governmental, 4 international and 9 University affiliated think tanks and share of above mentioned is accordingly 12%, 8% and 18%. Overcentralization fo think tanks in the capital city of the country is typical to Armenian think tanks. Around 96% of mentioned organizations are in Yerevan. Only two of Armenian think tanks – “Progress of Gyumri” Civil Society Development Center and “Compass” Research, Training and Consultancy Center out of 50 are in the second city of Armenia-Gyumri.

It is important to note that think tanks are registered in Armenia in different formats and have different juridical status. In particular those are established usually as state, non-state/non-governmental organizations or foundations and sometimes even have status of limited trade companies (LTD). Nevertheless, it is important to mention that establishment of think tanks with the status of LTDs somehow contradicts traditional perception and mission bearing in the public-political processes of think tanks as non-profit organization.

Around 60% of currently acting think tanks was established after 2005. This should be conditioned by the following factors:

- significant improvement of social and economic situation in the country, also local and foreign financial support towards science

and social sector, development of skills and culture to take part in different grant calls;

- establishment and development of state and democratic institutions;

- some increase of interest among the political elite towards expertise consultation and intellectual product of think tanks.

At the same time current research depicts the following below mentioned research priorities among Armenian think tanks:

- democratization, civil society, human rights;
- conflict, regional security issues: Southern Caucasus, Middle East;

- economy, political and economic integration processes (European Union, Eurasian Economic Union);

- Armenian diaspora and Armenian studies;

- sociological research;

- education, youth issues.

Also it is important to mention that unlike Government affiliated/Quasi-governmental and international think tanks, which have an opportunity to have larger resources of experts in case of sustainable financial provision, and in case of necessity they have more opportunities of implementing a concrete draft by involving external experts in majority cases of Armenian independent/autonomous think tanks number of experts does not exceed 10 and in many cases they are limited with one or two experts. Referring to University



affiliated think tanks we can highlight “Amberd” Research Center of Armenian State University of Economics. This center has around 10 researchers, plus expertise council consisting of 13 scholars [1], also Centre for European Studies of Yerevan State University which joins around 15 local and international experts [2].

Vast majority of Armenian think tanks has a web page, though updates are not very frequent. Facebook is the most popular social media among Armenian think tanks where 80% of the mentioned organizations have their official pages. Though it should be noted that many official pages are not very active reasons of which are a subject of another research. Nevertheless leading among mentioned organizations considering page likes (as to 21 April, 2017) are Institute for Political and Sociological Consulting, “Compass” Center and Armenian Center for Young Analysts, accordingly 11156, 6708 and 5314 Likes. In Twitter around 32% of Armenian think tanks are present but in general number of followers is not big in this social area.

### **Conclusion**

Concluding it is important to mention that given result is not comprehensively covering complete results of the research done which is of more comprehensive nature. It is obvious that in the frames of one article it is not possible to analyze framework of all questions regarding activities of the think tanks currently based in Armenia. In the frames of the current Article it was set a goal to outline current state of arts and processes regarding Armenian think tanks. At the same time this research is a good base for the next publication referring the same subject. A deep reflection will be given to more deep issues referring this sphere in particular peculiarities of Armenian think tanks, main issues of operations, impact on wider public and decision-making process, level of activeness in the media sphere, interaction between the political elite and expert community, and other key issues.

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## Section 9. Technical sciences

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### Methods of technological processes' intensification of in situ leaching of uranium from low-penetrating ores

**Abstract:** However, it is studied with electrical exposure to the leaching layer or passing to it working solutions in this work. Alternating and direct current are used. During electrical impact on to be leached ores various physic-chemical processes are followed: electrolysis, gas evolution, heat generation, electroosmosis, electrophoresis, strengthening, fastening, thixotropy, softening, dipolephores and so on. Depending on the mode of influence prevails one or another process. Impact with high frequency is used for worming up the massif which has low-penetrability and low-electro conductivity (oil, sulphur deposits). Thermal energy is generated thank to dielectric lose. The impact promotes lowering of oil viscosity, paraffin melting, well mudding, sulphur melting. Impact with direct current. First experiences of electrical impact were held by the institute of. The main effects are electrophoresis, ore-solution system's electrolysis, dissolution of chemical mud fillers. Disadvantages of this method are high speed corrosion of anodes and gaseous mudding of filtering zones. Externally, under direct electrostatic field ions of metal and leaching solution acquire ordered motion.

**Keywords:** uranium leaching, exposure to alternating electric current, electric action, filtration, filtration coefficient, diffusion rate, uranium content, preparation of ore deposits, productive solution, working solution.

Conception of "intensification methods" is practically respectful with the usage of various physical, hydrodynamical, chemical and other methods that accelerate mass exchange processes while solutions pass through orebody.

Nowadays, in situ leaching method of uranium mining, preparation of ore deposits is occurred in three directions: physical method (hydraulic rupture of the layer), chemical method (chemical interaction of leaching reagents with well-soluble uranium minerals) bacterial exposure on to be leached ores.

However, it is studied with electrical exposure to the leaching layer or passing to it working solutions in this work. Alternating and direct current are used.

During electrical impact on to be leached ores various physic-chemical processes are followed: electrolysis, gas evolution, heat generation, electroosmosis, electrophoresis, strengthening, fastening, thixotropy, softening, dipolephores and so on. Depending on the mode of influence prevails one or another process.

Impact with high frequency is used for worming up the massif which has low-penetrability and low-electro conductivity (oil, sulphur deposits). Thermal energy is generated thank to dielectric lose. The impact promotes lowering of oil viscosity, paraffin melting, well mudding, sulphur melting.

Impact with direct current. First experiences of electrical impact were held by the institute of. The main effects are electrophoresis, ore-solution system's electrolysis, dissolution of chemical mud fillers. Disadvantages of this method are high speed corrosion of anodes and gaseous mudding of filtering zones. Externally, under direct electrostatic field ions of metal and leaching solution acquire ordered motion.

The impact with alternating current is directed on desorption of friable connected water with surface of capillaries and on hardening

clayiness of admixture sandy-argillaceous ores with a purpose of prevention of its swelling and postponement in the form of mudding sediments; listed effects from electrical impact promote growth of ore's penetrability in filtering zones and rise of ell's average productivity to 25–30%.

An impact with high density current. At the expanse of intensive energy generation in narrow areas of capillaries their augmentation and cleaning-up take place as a result of which during short period irreversible effect of penetrability increase is created. Unlike listed above methods which rely on development in the sphere of electroosmosis, in this method energetic approach is used, theory of percolation and development in an area of rigid body physics.

On uranium administrations complex approach of electrical impact on strata that takes into account all main physical effects which promotes imposition of electricity current on ore.

It is evident from provided brief characteristics of methods that all of them figured on growth of penetrability of orebody. Sufficient reasons of theory electrical impact on speed of chemical reactions of leaching does not exist yet. If we stipulate intensification of leaching in the system of ore-solution in accordance with electro dialysis rules, then taking into account mineralization of solutions we will find that allocation of 1 kg metal on cathode in productive well requires a few thousands of kilowatt-hour electricity. Though, in experiments of and our studies it is followed that some increase of concentration of metals in solutions under electrical impact (about 20%) that points at necessity of accounting all diversity of factors while developing theory of chemical reactions' intensification of leaching metals with electrical power:

– reanimation of leaching solutions filtration in ore layers thank to selective growth of their penetrability;

- disclosure of capillaries that were unavailable for leaching solutions before;
- desorption of metals with electrical power from walls of capillaries along with friable connected water;
- prevention of postponement of metals on the front of leaching;
- improvement of structure of leaching solutions' stream in regions of production and injection lines (from radial to plane-parallel) thank to creation of zones with advanced penetrability between wells and lines. Other processes are also possible.

Positive results of laboratory experiments that show possibility of connected water cast and particles of clay binder which are components of hydrogen deposits, to bring into movement under impact on them with alternating current of low voltage, full-size experiments on sole wells, allowed to pass to industrial sampling and application of the method.

To establish an impact of alternating current exposure on solutions' movement in sandy-argillaceous ores preliminary connected (friable connected and adsorbed) waters and alteration of filtration coefficient in process of filtration 1% solution of sulfuric acid. Filtration studies were held on ore sands with mixture of clay (1,5 and 10%) montmorillonite and hydromica content.

Two similar trials were executed: first one was held on distilled water, another one was held on productive solutions from industrial field of ISL. Change of clay sand's humidity over length of columns. According to methodology, three zones were separated out from top to bottom: capillary humidity, maximal molecular humidity. Maximal molecular humidity in experiment with productive solutions 12% witnesses that some swelling of clay fractions of ores in solutions.

Results of experiments showed us that during filtration of leaching solutions by ores of specific mining field friable connected

water which accounts for certain poral volume, creates hydraulic resistance. Share of connected water in the volume of  $1\text{m}^3$  of soil with a humidity of 10% constitutes for:

$$V = \frac{w\gamma_n}{100\%\gamma_o} = \frac{10\% \cdot 1,7}{100\% \cdot 1,0} = 0,17\text{cm}^3$$

Where  $w$  – 10%-maximal molecular humidity,  $\gamma_n = 1,7\text{ g/sm}^3$  – relative density of dry sand;  $\gamma_o = 1,0\text{ g/sm}^3$  – relative density of water.

Taking into consideration that 40% of porosity in  $1\text{m}^3$  orebody occupies  $0,4\text{ m}^3$  volume, it is evident that huge role of connected water in filtration process (in this case it occupies 42,5% volume of pores):

$$100\% \cdot \frac{0,17}{0,40} = 42,5\%$$

In the process of filtration, we measured the discharge of solutions and its temperature. On the basis of measurements, we have calculated the coefficient of penetrability of ores with a formula

$$K_n = Ql\mu / (F\Delta P),$$

Where  $Q$  – solution's discharge,  $\text{sm}^3/\text{s}$ ;  $l$  – length of the sample,  $\text{sm}$ ;  $\mu$  – viscosity,  $\text{sP}$ ;  $F$  – net area of the sample,  $\text{sm}^2$ ;  $\Delta P$  – differential pressure,  $\text{kg/sm}^2$ .

Of the results of the experiments it can be concluded that rise of clay concentration considerably brings down penetrability of ores. Penetrability of ores that measured by acid solution, turns to be significantly lower than penetrability of distilled water. Notably, appearance of gaseous mudding was not determined in experiments.

Filtration experiments were held in two tubes simultaneously: in one – with application of electrical power, in another- without electrical power. The impact with alternating current on orebody was occurred periodically. Alteration of filtration coefficient and metal concentration in solution in dependence from correlation of S: L is demonstrated in figure 2.

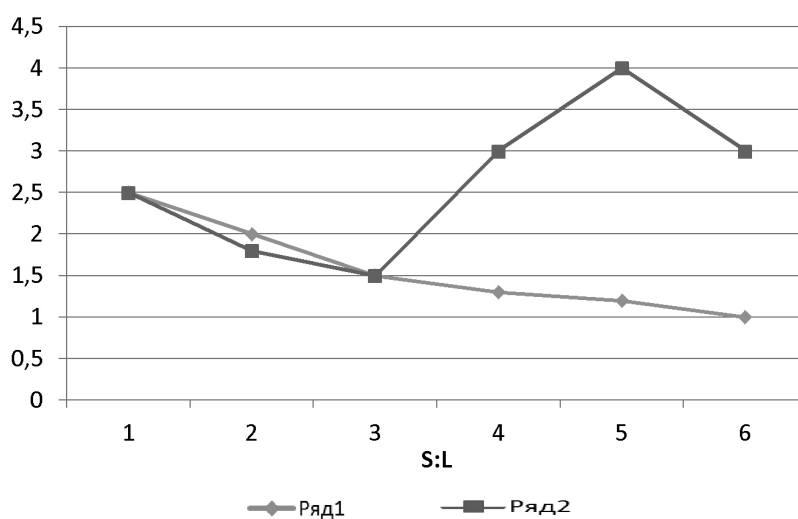


Figure 1. Dependence of filtration coefficient  $K_f$ , concentration of metal in solution from S: L during periodical impact with electrical power and without electrical power

As can be seen from the graph, during the impact with electrical power not only coefficient of filtration rises, speed of metal extraction is also increases. Improvement of filtration coefficient is interpreted by us as a result of solution's viscosity reduction in consequence of its warming up while impacting with electrical power and as a result of connected water's transmission into moving condition that brings an improvement of effective cross-section of pores and penetrability of ore.

From considered electro physical methods up to industrial application in in situ leaching of ores from hydrogen deposits it is carried out wells' processing by electro hydraulic impact that increases

penetrability of sand-clay layers direct or alternate currents of industrial part.

Filter processing and filtration zones with electrohydraulic hit in the administrations of ISL methods of regeneration of filters and filtration zones (high-pressure retreatment with water, pumping with compressed air, chemical mud fil cleaning) is characterized short time requirement and negligible increase of well productivity. More prospective is a method of electrohydraulic hit in combination with compressed air pump to the well. The research is accomplished by the electrohydraulic hit equipment with following technical characteristics:

Table 1.

Maximal depth of treatment, m	150
Tension, kV	50
Volume of impulsive condensator, mkF	0,5
The charge tension, V	220
Consuming power, kVt	1

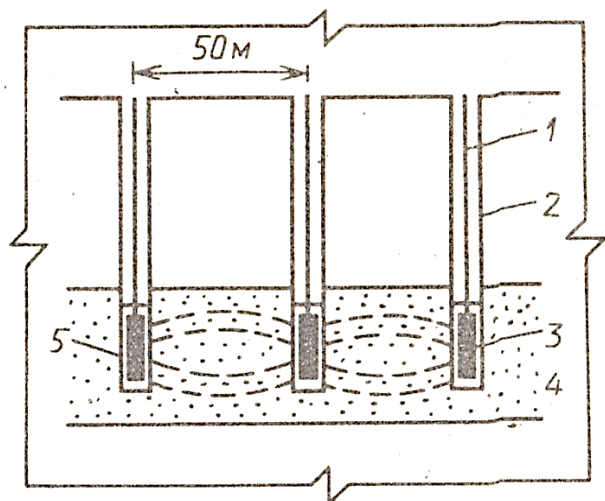


Figure 2. the scheme of cell with impact on layer with alternate current

An essence of the physical effect of sandy-argillaceous ores' promotion while transmission of electrical power in department of loamy fractions associated water, whereupon increases section of pores. Besides, unlike constant current, alternating current impacts on water too that immobilized by helium, mudding pores spaces. Thixotropic (helium like) structure is formed in contact with sulfuric acid and argillaceous fraction of the ore owing to crystallizational cement's solution and their softening. Helium even during negligible quantity of solid material (1–10%) accounts a big volume, that stipulated net structure in cells of which contains 90% and higher immobilized water. Immobilized water differs from water of diffusive layer with the first is not connected with cations and not pulled up surface charges of particles.

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## Waste from flotation enrichment of rocks — as a complex raw material for the cement industry

**Abstract:** Provides information about the possibility of obtaining an extension of the portlandcement with the use as additives-fillers secondary raw materials: recycled steel slags, waste, flotation of tungsten, and fluorite ores of Uzbekistan, “dry” and “wet” wastes of production of chrysotile-cement products.

**Keywords:** beneficiation of ores by flotation, secondary raw materials, additive in cement, portland cement additional, physical and chemical properties, structure, hardening, the formation of artificial conglomerate, strength, brand, environment, economy.

**Introduction.** The trend of development of the cement industry of Uzbekistan is aimed at reducing fuel and energy costs per unit of production and increasing the volume of cement production through maximum involvement in the production process local raw materials of natural and anthropogenic origin, not worsening the quality of cement. To do this, cement plants of the republic carried out a deliberate policy on the adoption of appropriate measures in the field of exploration of promising new sources of local cement raw materials. In this aspect, the most important is the question of finding new sources of mineral admixtures and additives — filling cement, clinker ensure maximum savings component while improving the physical and mechanical, construction and technical properties of the cement additive.

**Formulation of the problem.** Due to the fact that the flotation tailings tungsten (FTTO) and fluorite ores (FTFO) are aluminosilicate minerals with impurities of different oxides may be used as additives to cement. This requires a comprehensive study their properties in order to determine the possibility of using as an additive in the production of cements with additional optimization of their content in the composition of additional cement and to determine the physical and mechanical properties and compliance with the data requirements of the Interstate standard GOST 10178–85. At the same time, the development and application of technology for additional cement using waste flotation concentrators is not only technically feasible option saving energy and resources in the production of ce-

ment additive, in quality not inferior without additional cement and physico-mechanical properties meet the requirements for cement with mineral additives brand PC 400 D20, but the actual decision of environmental problems.

**Materials research methods, equipment and instruments.** During the experimental research as the starting materials used are Portland cement clinker of JSC “Kizilkumcement” and JSC “Akhangarancement”, gypsum, flotation tailings deposit Ingichka tungsten ores and fluorite ores (deposit Agatha — Chibirgata). Investigations were carried out in an accredited laboratory of the Research and Testing Centre “Strom” Institute of General and Inorganic Chemistry of the Academy of Sciences of Uzbekistan, which is equipped with the necessary tools and equipment to perform chemical analysis and physico-chemical and physical-mechanical source of raw materials and cement (analytical laboratory, DTA, IR, X-ray, electron microscope). Determination tails activity enrichment fluorite and tungsten ores in order to establish their application as active mineral or filler additive for Portland cement, carried out by determining their compressive strength and, then by calculation — by Student's test according to the procedure of GOST (State Standard) 25094.

**Results and its discussion.** Determination of the chemical composition of samples of the flotation tailings fluorite ores showed that its chemical composition is represented mainly by the content of silicon oxide, the presence of calcium oxide, aluminum,



iron, magnesium. The magnitude of mass loss on ignition, as well as the presence of calcium oxide and sulfur trioxide indicates the presence in the samples of the flotation waste carbonate and sulfate compounds (table 1). The composition of the flotation waste secondary enrichment of tungsten ores is characterized by the presence of oxides: silica  $\text{SiO}_2$ ;  $\text{Al}_2\text{O}_3$  aluminum;  $\text{Fe}_2\text{O}_3$  iron; calcium magnesium  $\text{CaO}$  and  $\text{MgO}$ . Based on the chemical composition of the forecasted made the conclusion about the possibility of the use of waste as a filler additive for cement production.

It is known that the main criterion for determining the use of a supplement, is an indicator of its activity, defined by its ability

to absorb  $\text{CaO}$  of saturated lime solution or compressive strength, determined by Student's criterion [1; 2].

As a result of testing and mathematical transformations of the results obtained by the method of GOST 25094 established that the value of the Student test for flotation tailings fluorite ores amounted to  $t = 4,18$ , and for the flotation waste secondary enrichment of tungsten ores –  $t = 4,54$ , which is greater than the standard value  $t > 2,07$ . Consequently, both the flotation considered to pass the test of strength and activity, in accordance with  $\text{Oz DSt}$  (National Standard of the Republic of Uzbekistan) 901–98 (p. 4.2), they can be used as additives for cements.

Table 1. – The chemical composition of the starting components

Material	The content of the mass fraction of oxides, %								
	LOI	$\text{SiO}_2$	$\text{Al}_2\text{O}_3$	$\text{Fe}_2\text{O}_3$	$\text{CaO}$	$\text{MgO}$	$\text{SO}_3$	other	$\Sigma$
Clinker	0,75	20,54	5,19	3,56	62,04	3,60	0,62	3,7	100,0
Gypsum stone	at 400 ° C, 19,10	1,52	0,13	0,14	33,04	0,20	43,46	2,41	100,0
FTFO	4,89	46,17	5,28	14,90	21,71	2,22	Ca.	4,83	100,0
FTFO	2,81	88,89	1,89	1,60	2,90	0,52	1,02	0,37	100,0

For use of a particular type of mineral cement admixture necessary to determine the efficiency of its use in accordance with GOST 25094 and set the optimum dosage of the cement additive. To this end, a study on the optimal dosage of flotation waste tungsten and fluorite ores in the cement and the optimal composition of Portland cement with the addition of these wastes. For this joint grinding of clinker and additives composite sample fluorite flotation tailings and tungsten ores in the presence of 5% gypsum was performed in a

laboratory ball mill. The amount of the admixture was (10, 15, 20)% by weight of clinker. As a basis for comparison, a cement composition in which no additives were manufactured by co-grinding of the clinker with 5% gypsum. The results show that the introduction of up to 15% fluorite flotation tailings tungsten ores and does not reduce the strength of cement, comprising an additive which has not (Table 2). The increase of flotation waste reduces the strength of cement on one brand [3–5].

Table 2. – The test results of additional portlandcement containing flotation tailings fluorite and tungsten ores

Designation of cements	Clutch time, hour – minute		the expansion cone, mm	Tensile strength after 28 days ( $\text{kgf/cm}^2$ )		
	Start	end		flexural	Compressive	Growth (+) or loss (–) strength
<i>Additional cements flotation tailings fluorite ores</i>						
PC D 0	2–18	3–34	115	<b>67,0</b>	<b>413</b>	–
PC D10	2–35	3–44	114	65,7	406	+7,0
PC D15	2–48	3–52	115	64,1	<b>403</b>	+10,0
PC D20	3–10	4–14	114	60,5	376	–27,0
<i>Additional cements flotation tailings tungsten ores</i>						
PC D 0	2–15	3–30	114	68,2	402	–
PC D10	2–55	3–40	114	76,1	410	+8,0
PC D15	2–45	3–35	116	75,4	<b>418</b>	+16,0
PC D20	2–55	4–00	115	59,6	367	–35,0

**Conclusion.** The possibility of using up to 15% of mineral technogenic waste — flotation tailings tungsten and fluorite ores as an additive filler in the production of common Portland cement without reducing their grade strength. Flotation waste concentrators, according to GOST 24640–91 “Additives for cements. Classification”, by the nature of the main effects on the properties of cement, can be attributed to the components of the material composition of cement. The main effect of

the impact of this type of additive is to save the clinker, and the main criterion for evaluating the properties of the additive — a greater decrease in the proportion of clinker than the decline in the cement activity. The use of these additives reduces energy costs for clinker grinding, increase production and reduce the cost of cement and at the expense of large-scale utilization of flotation waste – improving the environmental situation in the areas of mining and enrichment plants.

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## Application of Rnd () function in the process of question choice in electronic exams

**Abstract:** In the article, the advantages of application of RND () function to the algorithm of introducing the questions to the students in the electronic exams. As a result of research, it was known that the application of RND () function to the process of question choice in the electronic exams incites the students to study more. The work implies that as the selection of every question in this process is occasional, full hypothesis of dependence of the meeting level of credits on the subject on the volume of material read has been calculated for all cases, verity of the so-called ideas has been proved theoretically. Besides, the advantages of application of RND () function to the algorithm of introducing the questions to the students in the electronic exams have been proved theoretically and the results of researches carried out over 4000 students were demonstrated practically.

**Keywords:** electronic University, electronic exam, occasional process, hypothesis, irrelevant occurrence, RND.

It is known that major duty of high educational institution is to provide the society with citizens having a high scientific potential. And the rating of Universities is directly related to the achievements gained by the cadres in different fields of industry. That is why universities always search for innovative methods to bring up more educated cadres. The students' evaluation level of assimilating knowledge in the operational process of universities is one of the major conditions. Final assessment of students' assimilating the knowledge had been carried out in the exams before. In this case the students' education level was assessed incorrectly. So that the students who are active in seminars are not able to answer the questions properly in the exam because of psychological tension or vice-versa the students don't demonstrate any activity along the semester who rely on his or her memory and the ability of swotting. Only in the end, he or she could get the adequate mark by cramming up the material temporarily. Consequently, the students can't get success in their activities after becoming graduates and this caused to the emergence of negative ideas about Universities.

However, after 1999-Bolony declaration was accepted and more than 49 countries of the world joined this process, evaluation criteria changed in education as well [1].

Thus, the student's knowledge level is evaluated not only with exam points, but also for his or her daily activity, free work, précis work on the whole. This is, in its turn, a good case that the student is obliged to demonstrate good activity both in semesters and in the exams. But sometimes the students succeed in meeting the credits without full assimilation of teaching materials in this process. The passage to the electronizing the exam process is suggested in order to achieve the assimilation of teaching materials by the students in Bologna process. In this case the students are examined by means of tests. Meanwhile, there is an opportunity to ask the students more questions. As the evaluation performed by the computer, the mark is completely objective. Application of Rnd function in the process of question choice in such kind of exams gives better results. Let's

make comparison between traditional and electronic exams in order to specify all afore-said.

It is known that the student must perform minimum 51% result to have met the credit on the subject. Let's suppose that the student have demonstrated 47% result in semester. In this case his or her scoring the minimum point in the exam is sufficient to have met the credit. This point changes between 17–25 depending on the decision of Ministry of Education of every country.

In traditional exam the questions are prepared by the teacher in the form of tickets beforehand and are hung on the exam poster. As a rule, the tickets cover the questions of the materials had in this or that way. In case the student gets ready for 60% of the tickets perfectly, this time, hypothesis of his or her taking the tickets that he or she studied for the exam equals 0,6. So the hypothesis of student's getting an excellent mark equals 0,6, in other word 60%.

On the contrary, let's suppose that exam questions are not given to the students. If the student studies 60% of the material perfectly again, the student will answer 60% of the questions. And this means that the student will definitely get a satisfactory mark and it is even possible for him or her to get a good mark.

The questions between 500–1000 are prepared in the electronic exam. At this time the teacher who teaches the subject notes which theme it belongs to in relevant section in front of every question. While placing the questions in the system, they are arranged in the form of variants separating them to some definite numbers manually (for example, being 50 questions). This way is not so effective. That is why the student can get a grade without studying the material completely.

The most effective way in the choice of questions in the electronic exam is the application of Rnd () function to the algorithm selection.

It is known that Rnd () function is the most effective function generating occasional figures in two-number ambit shown [4].

In case Rnd () function is applied, the algorithm of question selection process can be formed shown as in figure 1.

In this case the student does not know which theme and how many questions of the very theme he will face. And this urges the student to learn most of the material on the subject.

To prove all these visually, let's calculate the occurrence supposition using the theory of hypothesis.

If we indicate the total number of test questions compiled on the subject –N, the number of questions relevant to the volume of material which the student studies – n, the number of questions to introduce to the student in the exam – m, the number of questions to be interesting for the student – k, we can calcu-

late the occurrence supposition of this process with the formula below [2].

$$P = \frac{C_n^k \cdot C_{N-n}^{M-k}}{C_N^m}$$

Before doing the sum with conventional value indicator, let's accept that the student has demonstrated such a result out of possible 50% indicator till the exam that he can meet the credit with the grades "satisfactory", "good", "excellent" depending on the results shown in the exam. (for example, as in the first case similar –47%).

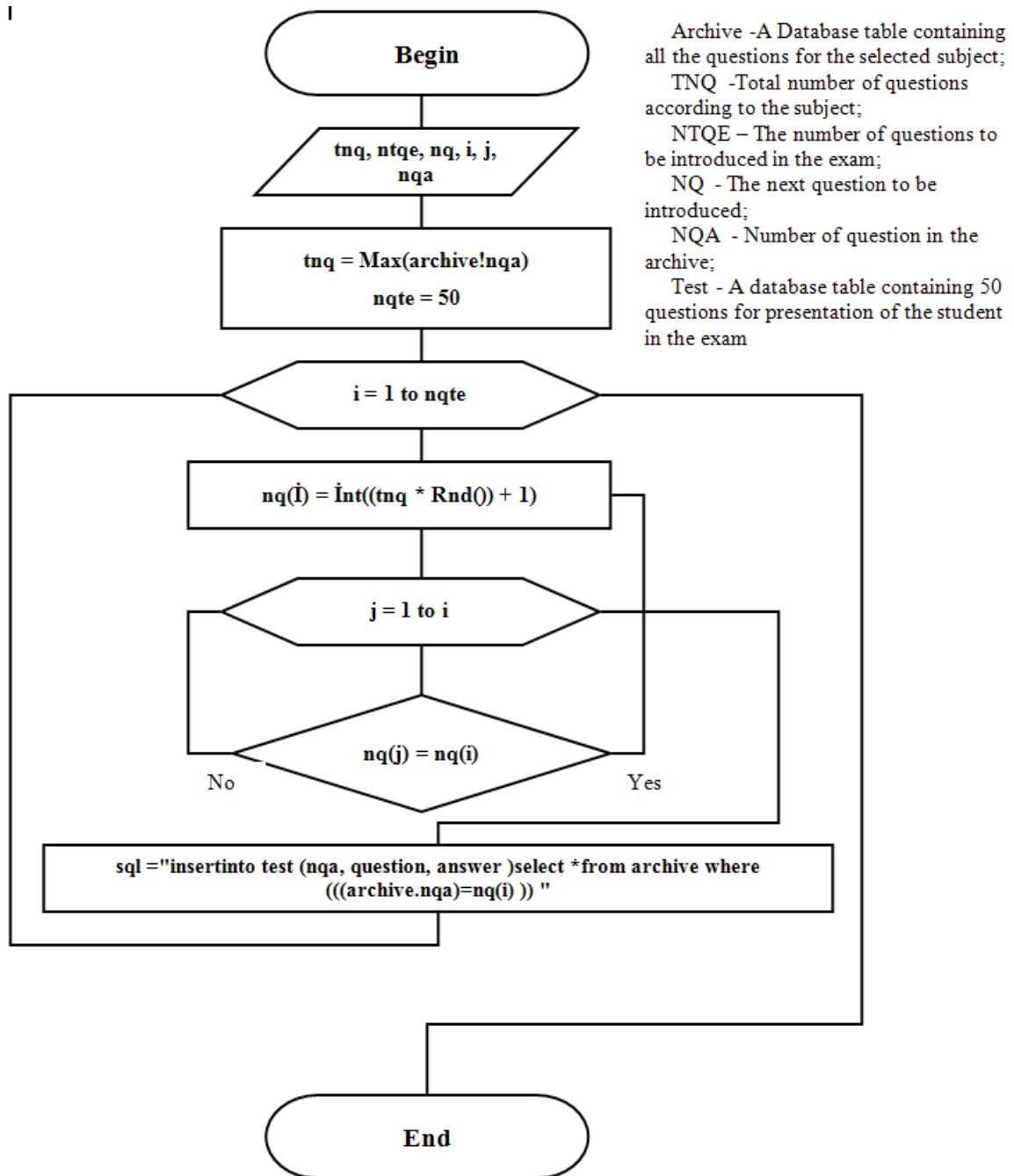


Figure 1. Algorithm of the question selection in electronic exam

In this case let's indicate the hypothesis of getting satisfactory grade as P (satisfactory), the hypothesis of getting good grade as P (good), the hypothesis of getting an excellent grade as P (excellent). Then let's conventionally accept that the number of test questions compiled on the subject N=1000, the number of the questions to be introduced in the exam m=50, the number of questions to be interesting for the student to get a satisfactory grade k=45, to get a

good grade k=35, and it is k=45 for an excellent grade. Let's do the sum taking the number of questions relevant to the volume of the material that the student studies as n=100, 200, ..., 900, 1000.

It is obvious that the process of question selection while introducing the questions to the student is irrelevant. At this time, using the addition theorem of the hypothesis, in case the student studies conventionally 40% of the material we can write the followings for

the realization of the process of getting satisfactory, good and excellent grades.

$$P(kafi) = \frac{C_{400}^{17} \cdot C_{600}^{33}}{C_{1000}^{50}} + \frac{C_{400}^{18} \cdot C_{600}^{32}}{C_{1000}^{50}} + \dots + \frac{C_{400}^{50}}{C_{1000}^{50}}$$

$$P(yaxsi) = \frac{C_{400}^{35} \cdot C_{600}^{15}}{C_{1000}^{50}} + \frac{C_{400}^{36} \cdot C_{600}^{14}}{C_{1000}^{50}} + \dots + \frac{C_{400}^{50}}{C_{1000}^{50}}$$

$$P(ela) = \frac{C_{400}^{45} \cdot C_{600}^5}{C_{1000}^{50}} + \frac{C_{400}^{46} \cdot C_{600}^4}{C_{1000}^{50}} + \dots + \frac{C_{400}^{50}}{C_{1000}^{50}}$$

The results for the case of application of all grades of -n of this formula can be written as in table 1. (K is a count of questions a student needs)

Table 1. – Dependence of the student’s satisfactory, good and excellent grades on the volume of the material read

The volume of the material read		10%	20%	30%	40%	50%	60%	70%	80%	90%	92%
k = 20	P (satisfac-tory)	6E-09	0,0007	0,0794	0,5553	0,9452	0,9989	1	1	1	1
k = 35	P (good)	2E-26	4E-15	2E-09	1E-05	0,0027	0,0898	0,5701	0,9726	1	1
k = 45	P (excellent)	3E-44	4E-28	1E-19	6E-14	9E-10	2E-06	0,0006	0,044	0,6166	0,7964

It seems from the obtained dependence, it is necessary for the student to learn 60% of the material taught to meet the credit with satisfactory grade, at least 80% to meet the credit with good grade

and more than 92% to meet the credit with excellent grade.

Graphical description of all the afore-said was presented in figure 2.

**Dependence of the level of success from the volume of prepared material on electronic exams**

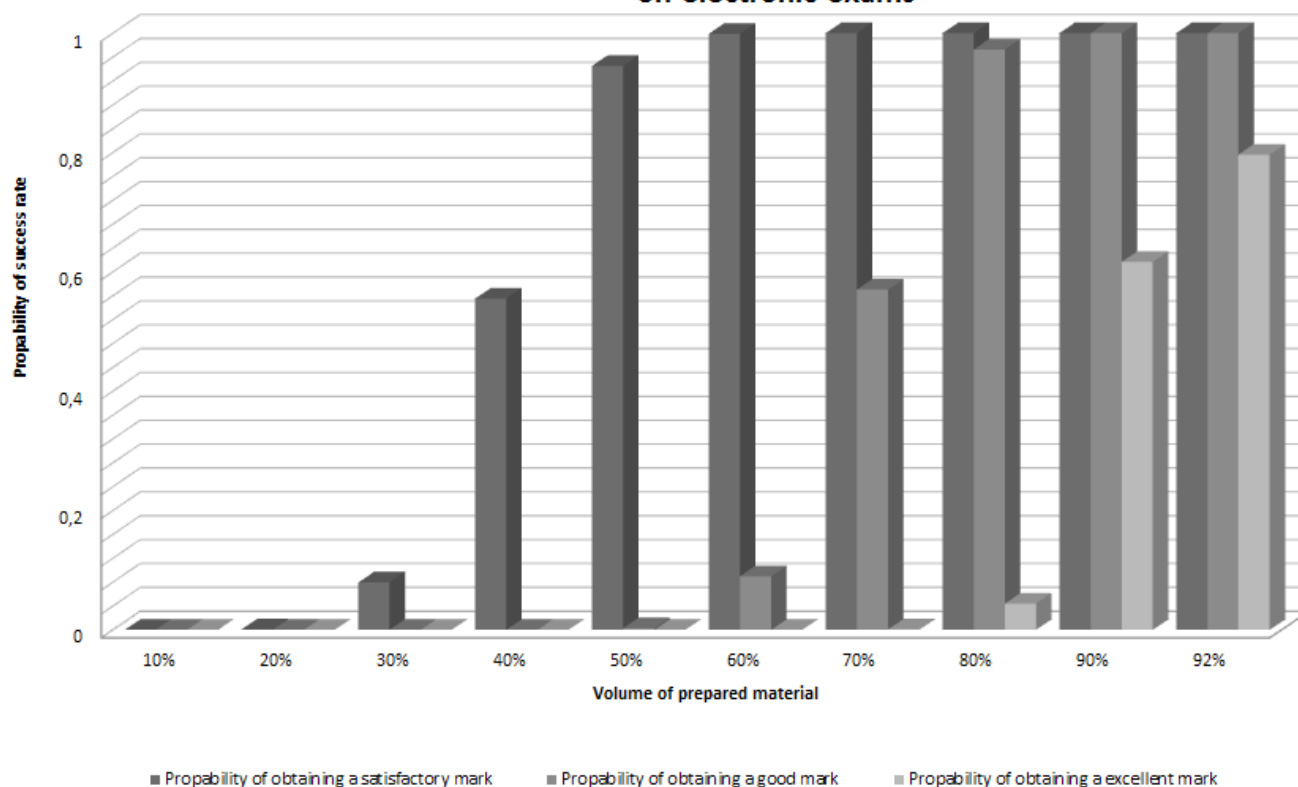


Figure 2. Dependence of success gained in the electronic exams on the volume of the material read

Besides, as the choice is chaotic two students can never meet the same questions with the same succession. Its accuracy may be proved with the formula of “combinasion” [3]

Let’s again accept that there are 1000 questions on the subject and every student will be presented 50 questions. In this case the numbers of possible variants are equal.

$$C_{1000}^{50} = 9,46046E + 84$$

All these proved themselves in practical researches. Thus, 1000 questions have been prepared for electronic exams that all University students have to meet the credit on any subject. These questions were chosen by application of algorithm indicated in Figure 1 and introduced to 4000 students being 50 questions for each of them. At the end of the exam during the investigation of the questions answered by students, it was known that more than 20 ques-

tions were introduced to 3677 students, more than 35 questions were given to 321 students while only 2 students faced more than 46 questions out of the first 600 questions.

In the succession of the questions introduced the case of overlapping was not registered in general.

Practical results of the so-called are demonstrated in the graphics given in Figure 3. The research was carried out for the civil protection subject in Nakhchivan State University. To realize the graphics clearly we consider only 10 results more expedient out of 4000 results.

It is possible to come to such a conclusion from all carried out investigations and calculations that the passage to the electronic exam and application of Rnd () function to the process of question selection are expedient as caused more assimilation of teaching materials by the students.



A variety of selected questions when applying RND functions

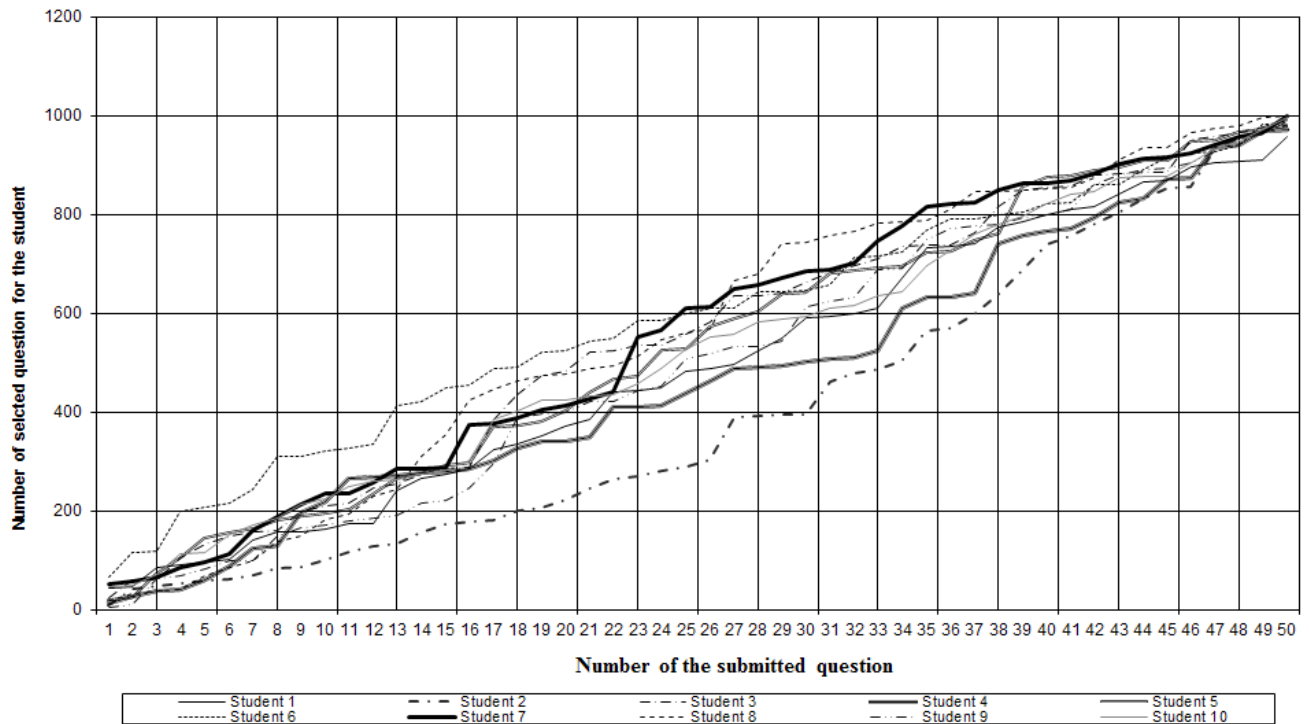


Figure 3. Variety of the selected questions during the application of Rnd () function

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**Increasing the reliability of the protection of electrical networks as a way to increase the reliability of power supply to consumers**

**Abstract:** Article is devoted to the research of reliability of systems of power supply. Results of introduction of the latest technical solutions realized in automatic Master pact breakers of the Schneider Electric company are given in it, for modernization of 0.4 kV of traditional devices of relay protection applied now in networks. With objective of reduction conformity to modern safety requirements under standards of International Electric-technical Commission it is offered to apply these achievements at the organization of a domestic production on release of power automatic breakers.

**Keywords:** Master pact, compact, low-voltage automatic breakers.

**I. Introduction**

For the reason adductions in correspondence to the modern requirements to safety on standard International Electric-

technical Commission (IEC) is offered use these achievements at organizations domestic production on issue of the power automatic breakers.

It agrees taken effect on January 1, 2003 (in Russia) to new requirements of Rules of device of electrical installations (RDEI) [1, 13–14], concerning an electrical security and the rules corresponding to the international norms, one of the major requirements to protective equipment in networks to 1000 V is the requirement for ensuring speed of shutdown of the damages connected with impact on the person. This time according to table 1.7.1 of RDEI, depends on value of a voltage and at the phase voltage 220 V should not exceed 0.4 sec.

At present the begun transition in abroad and in Russia to the next generation of microprocessor (digital) device of relay protection and automatics (DRPA) with integration within the limits of a uniform information complex of functions of relay protection, measurement and commercial account electric power, regulation and management of electrical installation it is directed on maintenance of increase of reliability of electrical supply of consumers and conformity to modern safety requirements on IEC [2, 22–25].

The spectrum of arrangements DRPA for networks of the low and average voltage, offered to the consumer the domestic and foreign companies, allows executing adequate systems of protection for various objects.

Digital terminals possess all standard functions of microprocessor protections: measurements, relay protection, system automatics, self-diagnostics, diagnostics of work of the breakers device and a network, digital oscillography and have communication with system of the MANAGEMENT information system on interface RS-485 c open report MODBUS. The given arrangements have a modular design and program formation of protection.

In descriptions on digital relays as well in standard IEEE, IEC time current characteristics current protection are set by mathematical formulas. For construction of these characteristics with objective of their coordination with characteristics of other protective devices (the relay and fuses) is necessary to know the basic traditional conditions of a choice maximal current protection (currents of operation, characteristics, time of operation).

The comparative analysis of different types independent current characteristics of digital relays and Russian analog relays PTB-I, II, III, PT-80 as well as current characteristics of the Russian fuses of type SDQCL (safety device quartz current limiting) has shown, that in the majority of cases the most suitable for Russia is «standard independent», or «normal» the characteristics and to it similar characteristics of standards IEEE (it is moderate independent) and IEC (independent). However there can be an indispensability of use and other types of characteristics.

The known electrical technical firm «Schneider Electric» lets out and delivers on the market various electric equipment and including microprocessor (digital) relays-terminals of set SEPAM, as well as low-voltage automatic breakers (AB) to set Compact and Master pact. Master pact is one of the best AB on greater currents in the world [3, 14–17]. Having improved base model, the company «Schneider Electric» has let out on the market breakers Master pact NT and NW under trade mark Merlin Gerin. To the basic dignity of power breakers of possibility enable, selectivity and to convenience service — the built in functions of communication and measurements have increased.

The block of the control and management of Micro logic A/P/H is equipped by the liquid crystal display and simple navigating keys. The user has a direct access to necessary parameters and set point. Navigation between screens is carried out intuitively; adjustment is simplified at maximum by direct reading from with display. The text information is displayed on chosen language (from possible 6 languages).

AB Master pact is integrated into the general system of scheduling that optimizes its operational service. The architecture of system of data transmission is characterized by openness and may be adapted for any reports.

Protection functions are independent of the measurement. These functions are controlled by the electronic element of the ASIC common to all units and control that ensures immunity to immunity to interference, as well as a very high reliability [4, 12–16].

The patented system «double regulation» system protection lets you give:

- upper threshold by means of breakers;
- more precise setting by using the keypad or remotely. Such accurate adjust set points (before 1 Ampere) and extracts the time (before 1 second) appears on the display.

Another difference is their environmental security, AB Master pact represent a potential danger to the environmental, factories producing this apparatus, do not pollute the environmental and are in accordance with ISO 14001.

Fig. 1 below shows the Master pact driver performance, AB established in cell developed by the author distributing device -DD-0.4 kV for complete transformer substation (CTS). In coordination with the Master pact (the regulation IDMTL) with protection of the average voltage or fuse is optimized by adjusting the curve of the overload protection. This regulation also provides better adapted this protection to some consumers.

In three-polar automatic breakers Masterpact are neutral protection setting with keyboard or remote (with additional function communication COM) and provides 4 positions: unsecure neutral (4P 3d), partially protected neutral (4P 3d+N/2), fully protected neutral (4P 4d), double protected neutral (4P 3d+2N). Dual neutral protection applies if the neutral section is twice cross-section of phases (a strong asymmetry of load, high late of third order harmonics).

In four pole automatic breakers Master pact are neutral protection setting with keyboard realized with three-terminal section switch and has three positions: unsecure neutral (4P 3d), partially protected neutral (4P 3d+N/2), fully protected neutral (4P 4d). Neutral protection not activated, if the curve overload protection is regulated by one of the protections IDMTL.

In accordance with the current setting and time adjustable from keypad or remotely if there are additional function communication COM, blocks of Micro logic P/H control current, voltage, power, frequency and phase rotation. If there are additional functions for each set point is exceeded COM remotely. Each exceeding the set points can be optionally unhooking (protection) or to the, alarm by additional programmable contact M2C, M6C when you unhooking the memorization is current, ten recent unhooking and emergency signals are recorded in two separate chronological reports. Three — service indicators (wear contact, number of contacts, etc.) are stored in the register.

The additional function communication COM provides:

- read data and remote parameter setting protection or emergency-preventive signaling;
- the transfer of all measurement data and calculated factors;
- the signaling of the reasons of the unhooking and emergency-preventive signaling;
- viewing chronological reports and indicator of the technical service;
- reset counters maximum values.

Some of the measured or calculated values are available only if you have additional function communication COM:

$$- I_{\text{shock}} / \sqrt{(I_1 + I_2 + I_3)} / 3, I_{\text{no balance}};$$

- load factor from  $I_r$ ;
- total power factor  $\cos \varphi$ . And with block Micro logic H further available:
  - total value of the phase and power factor  $\cos \varphi$ ;
  - the harmonic distortion on current and voltage;
  - coefficient of current  $K$  and average to  $K$ ;
  - intensified coefficients of current and voltage;
  - all basic components of harmonics on each phase;
  - phase shift the main components of the current and voltage harmonics;
  - power and distortion coefficients on each phase;
  - amplitude and phase shift 3–51 order harmonics current and voltage.

Access to all counters for the maximum and minimum values is provided if there are additional data transfer functions for COM dispatch system.

The Master pact circuit (2, 5, 6, 7-performances) to protect the mains leads are implemented:

- protection against overloading, triggered by the current value of the current. Thermal memory: thermal “image» before and after the trip.

- Protection against short circuits – selective circuits (MCP) and the instantaneous current cutoff. Select the state function  $I^2t$  (enabled or disabled) in setting time protection with low exposure time.

Blocks of the control and management Micro logic 6, 7<sup>th</sup> performance also include:

- protection against short-circuits- protection type “No balance” or “return of current in accordance with current earth lead” (fig.2). Select the State function  $I^2t$  (enabled or disabled) in the setting time;

- but block of the control and management Micro logic 7<sup>th</sup> performances:

- differential current protection of zero sequence (Vigi).

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## The Amudarya river basin water resources management issues: case study

**Abstract:** The Amudarya is one of the main water resources involving all Central Asian countries and playing a key role in their development. The most recent period of water scarcity is impacting negatively on the socio-economics of the region. Water deficit is bound to increase, especially in the light of climate change and by increases in the demand for food production. In the paper current water availability state is analyzed.

**Keywords:** River basin, water resources management, reservoir sedimentation, water loss

### Introduction

The Amudarya runoff is mainly generated within Tajikistan (72,8%) and partly in Afghanistan and Uzbekistan (Fig.1). However, water consumption by the riparians is not divided according to their share of generation which is a potential cause of conflict of interests for these countries.

The fate of the river runoff depends on human demands. In reality the entire hydrological cycle and water quality have been changed due to interaction between the river and the territories which is characterized, on the one hand, by water withdrawal for human consumption, industrial and irrigation water require-

ments all of which have a rising trend and, on the other, by the return of water to the river containing pollutants.

At the present time the runoff is controlled by two main reservoirs (the Nurek and the Tuyamuyun) and by several inter-system reservoirs which play an important role in seasonal water storage.

The problems arising in the basin are connected to the development of hydropower in the upper region, increasing water demands, pollution and water losses. The ecological crisis in the region is intensifying and increasing social problems in the Aral Sea region, mainly due to the imperfect water management.

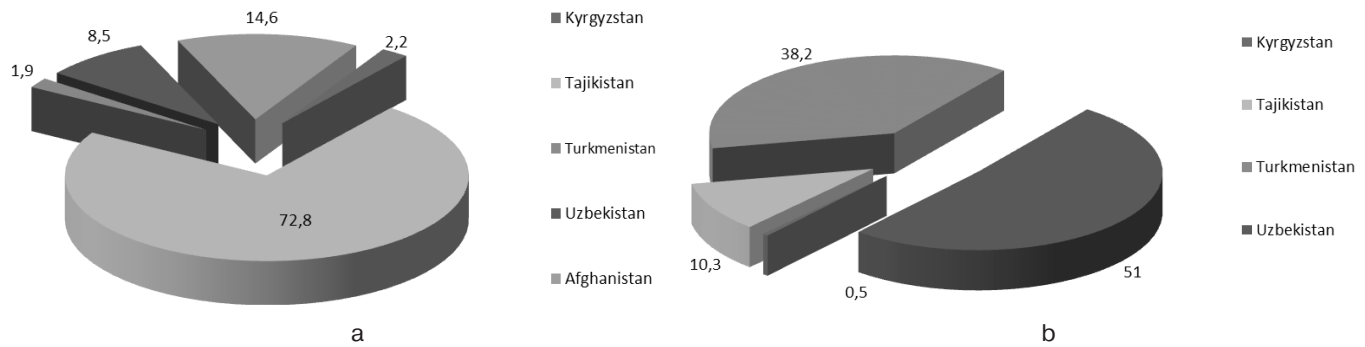


Figure 1. The division of Amudarya runoff (a) and water consumption by the riparian countries (b)

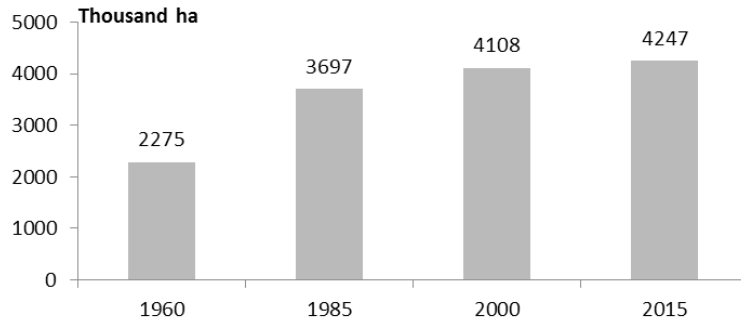


Figure 2. Increased irrigation in the basin

*Water loss and pollution.* Irrigation in the basin, based on well-developed irrigation and drainage systems with its inevitable return flows, is the main source of ecological pollution and water losses in the basin. Evaporation and seepage losses from the Amudarya and reservoirs also represent a significant contribution to losses. At present it is very difficult to identify these contributions. Estimated water losses in sections of the river can be accounted for as follows: upper stream to Kerki – 1,2 km<sup>3</sup> a year; middle stream from Kerki

to Tuyamuyun – 3,6 km<sup>3</sup> a year; lower stream – 1,4 km<sup>3</sup> a year. The most up to date investigations indicate that the losses vary between 7 and 13 km<sup>3</sup> a year which amounts to 20–40% of the total water withdrawal, i. e. there is a significant imbalance. Technical water loss in the system and on the irrigated fields is also significant due to low efficiency of the irrigation systems and technology. Annual average water delivered to the fields and consumed water amount is presented in Fig. 3.

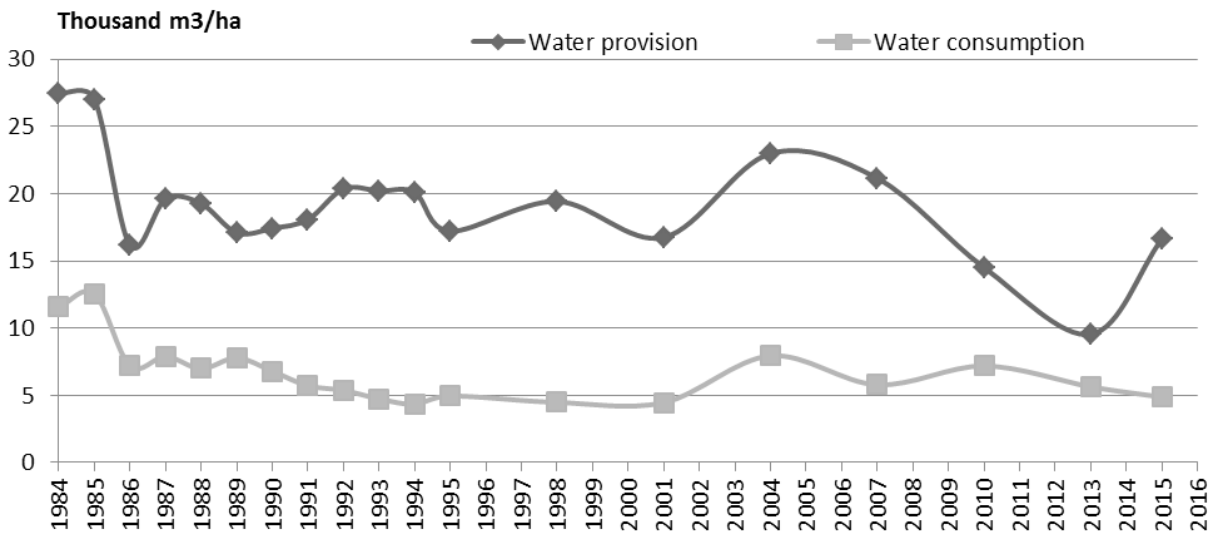


Figure 3. Comparison between the irrigation water delivered and actual consumption in the lower reaches of the Amudarya River

The total volume of salt transported by the river reaches is about 30–40 Million tons a year which negatively influences crop production as well as the environment. In the Vakhsh-Pyanj section of the river 7–9 Million Tons enter, whilst in the Kerki-Tuyamuyun section – 13–16.5 Million Tons of salt inflow to the river from the drain-collectors. Cotton loss due to this case varies from 20% to 60% depending on soil salinity. Due to this situation, the irrigated lands are in a poor condition. Over 20% of them are rated as being in a very bad condition due to high salinity and

high levels of ground water. Crop productivity in Karakalpakstan is 4–5 times lower than it is in the other regions; crop losses account for 15–20% of the productive capacity and, moreover, has a decreasing trend (Fig.4).

Water scarcity and pollution impact negatively on human activity, particularly in the lower reaches of the river where the main occupations are cropping and processing (40%). Ecological issues have brought to and social issues as unemployment and diseases, poverty and migration.



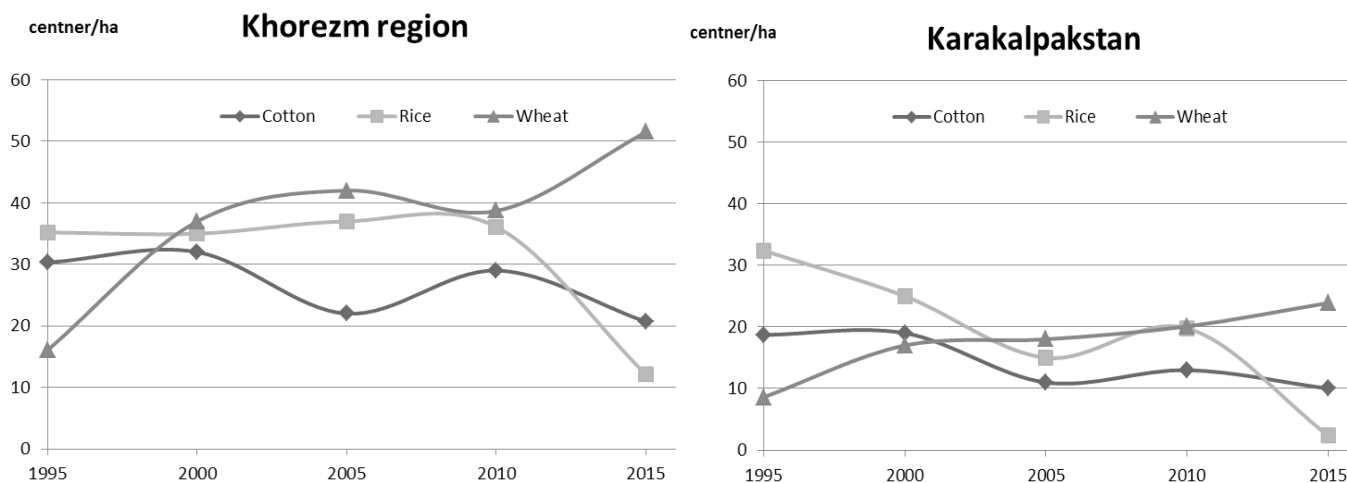


Figure 4. Crop productivity trends in Khorezm and Karakalpakstan regions

*Water accumulation capacity of THC reservoirs.* Irrigated agriculture in the Lower reaches of the Amudarya depends on reducing due to siltation capacity of the 4 reservoirs (Channel, Kaparas, Koshbulak and Sultansanjar) of the Tuyamuyun Hydro Complex (THC). The reservoirs filling was started in 1981. During 35 years' operation period the reservoirs have been deformed significantly and lost almost 40% of operational capacity. The field investigations of the reservoirs have been carried out regularly by Scientific Research Institute of Irrigation and Water Problems (ex.SANIIRI) and the last by the Bathometric Center of the MAWR in 2008. The field investigations and data provided by the THC Management Unit allowed analyzing of accumulation and removal processes in the Channel reservoir. Analysis of the measurement data has resulted that the total designed reservoir capacity loss dynamics for the period 1995–2015 show that average annual sedimentation volume for operation period consists of average 22.0 Mio m<sup>3</sup> a year. The most intensive accumulation of sediments took place in 1991–1992 (222 Mio m<sup>3</sup>) and in 1998 (108 Mio m<sup>3</sup>). Maximum removal of sediments has been observed in 1986 (135 Mio m<sup>3</sup>) at the 20,8km<sup>3</sup> runoff, 1997 (56 Mio m<sup>3</sup>) at the runoff of 18,3 km<sup>3</sup> and 2000–2001 (110 Mio m<sup>3</sup>) at the runoff of 18,7.

**Conclusion**

The above-mentioned issues are caused by major disadvantages in the system of management. Despite significant progress in the management of water resources, leading to positive experiences of economic cooperation, many organizational regulations still need to be improved in the basin. The following **technical issues** such as low data reliability and available water resources assessment, drought damage, inexact information about actual water withdrawal and water deficits, ineffective irrigation systems all contribute to a decline in the effective use of water resources.

The following actions must be taken to address these problems: introduce a reliable forecasting system; improve water accounting systems and the water metering status of the hydrological services; increase the efficiency of the irrigation systems and improve watering techniques and technologies.

Investigations, carried out by researchers of the Scientific Research Institute of Irrigation and Water Problems, present that the above-mentioned actions will provide significant positive economic, social and ecological benefits. The urgent and long-term actions list and expected efficiency of its application at the lower reaches of the Amudarya River is indicated in Table 1.

Table 1. – Expected efficiency gains and recoupment due to water loss reductions

Expected efficiency	Khorezm	Karakalpakstan
Irrigated land productivity increase due to a reduction of water salinity, USD/ha a year	56.33	49.40
Productivity increases due to the elimination of waterlogging: % of gross output	12	15
USD/ha a year	169.00	148,13
Collector-drainage system: operational cost reduction, USD/ha a year	12.50	12.50
Reduction in the costs of drinking and industrial water supply, USD/ha a year	24.46	31.02
Reduction in the cost of ecological and natural protection would be applied to the irrigated lands, water bodies and adjacent territories in the basin, USD/ha a year	10.19	10.34
Expected profit for an irrigation systems efficiency increase to 90%, USD/ha a year	589.17	502.02

The estimated benefit of the long-term actions fluctuates around 464 USD/ha in all the irrigated lands of the Amudarya Basin. Improvement of the existing water resources management system of the Amudarya Basin must be directed towards optimal satisfaction of the

needs of providing high quality water to all consumers. This must consider the situation existing at the present and likely to exist in the future. To achieve this situation, the affected entities need to coordinate their actions for the benefit of the economy of the nations will be required.

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## Measurement of coefficient of convective heat transfer based on silicon oxide nanofluid in the cylindrical channel

**Abstract:** Coefficient of heat transfer is investigated experimentally in nanofluid flow in the cylindrical channel. The nanofluid has been prepared on the basis of distilled water and nanoparticle  $\text{SiO}_2$ . Concentration of nanoparticles was varied ranging from 0.5 to 5% by volume. Significant intensification of heat transfer is established. At particle concentrations above 0.5%, the nanofluid was Non-Newtonian. Consequently, estimates of the rheological parameters of the nanofluid and coefficient of thermal conductivity.

**Keywords:** Thermal conductivity, nanofluid, viscosity, laminar-turbulent transition, coefficient of heat transfer.

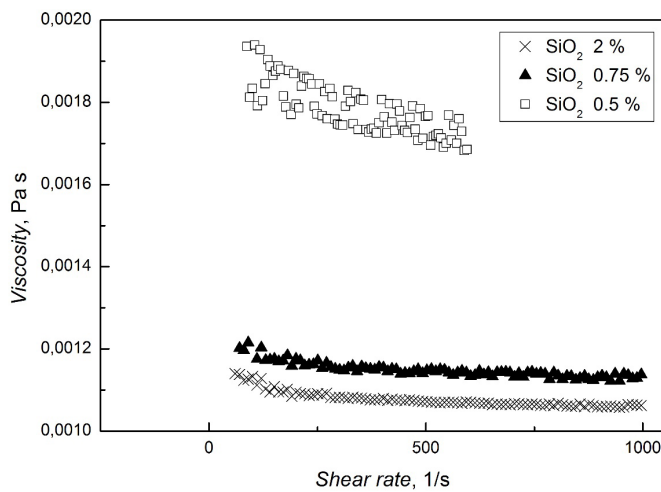
Attempts to use liquid using microparticles for objectives of heat exchange intensification are known since the mid 70 's. On the way to achieve significant effects failed because large particles of sediment quickly enough. The liquid in which the component is dispersed nanoparticles (nanofluid), deprived of this shortcoming. Early experiments have shown that even small additives nanoparticles to fluids can lead to significant growth in its thermal conductivity and heat transfer and critical heat flow can be increased many times (see, for example, [1–4]).

Despite the huge amount of work, in which thermal conductivity of nanofluid and their heat transfer is studied, the results are often contradictory. In most works of increasing heat transfer using nanoparticles. There are, however, and publications, which demonstrates its decrease when you add nanoparticles [5]. There is a need to further study of all specified processes. The key in this issue is not thermal conductivity of nanofluid, that's its heat transfer coefficient. In this work for water based nanofluid and nanoparticle,  $\text{SiO}_2$  is experimentally studied.

Through pump fluid from the tank served in a heated area, after which enters the thermostat. Flow in the circuit is governed by Voltage transformer system. Plot is a heated copper cylindrical pipe with a wall thickness of 1 mm, diameter of 15 mm and a length of 1 m as the heater uses a coiled up on a nichrome channel thread thickness 0.1 mm with an overall resistance 320  $\Omega$ . Channel with the heater is insulated. Heating power regulated power source Lauda Alpha A 24. For measurement of the local temperature channel on its walls at equal distances from each other docked 6 Chromel-Copel thermocouples. As a heat carrier, a nanofluid was used based on distilled water and  $\text{SiO}_2$  nanoparticles with volume concentration  $\varphi$ , equal to 0.5, 0.75, 1.5, 2, 3 and 5%. For preparation of a nano-

fluid applied standard two-step process and used  $\text{SiO}_2$  powder production of “Evonik Industries AG”, (63403 Hanau, Germany). Spherical nanoparticles, the bulk density of the powder equal to 2.2 g/cm<sup>3</sup>. The average size of the nanoparticles was 12 nm. After add the required amount of water tank of nanopowders to destroy conglomerates nanoparticles fit in an ultrasonic mixer UZDN-4. Liquid consumption path changed from 50 to 550 g/min these ranges correspond to a laminar flow for all carriers, except water and nanofluid with concentration of 0.5%. In the last case, laminar-turbulent transition occurs since the flow of about 400 g/min. Thus, three liquids laminar flow regime had taken place, and the fourth is laminar and transition. Conducted measurements showed that adding nanoparticles significantly increase local and convective heat transfer coefficients of the fluid medium. The degree of this extend rises with increasing concentration of nanoparticles. At low flow quantity (up to about 300 g/min), when with certainty we can talk about laminar flow mode as for the nanofluid, and water, the extent of this increase are growing almost proportional to the bulk concentration of nanoparticles. With further increase in consumption observed the rise in the average heat transfer coefficient of water. Starting with 350 g/min flow quantity average heat transfer coefficient of water compared with the corresponding coefficient for nanofluid with small concentrations of nanoparticles, and then begins to exceed them. At the expense of the order of 400 g/min average heat transfer coefficient of water becomes higher than 2 per cent of a nanofluid. Such behaviour is associated with the turbulence of the water flow. This also indirectly indicates, that turbulence of nanofluids at given flow quantity does still not occur. Laminar-turbulent transition is determined by the number of Reynolds. Given the expense of variation values for water and nanofluid can be associated

only with changes in density and coefficient of nanofluid viscosity. But when the volumetric concentrations of nanoparticles change the density of the liquid only leads to slight (no more than a few per cent) Reynolds number change and may not significantly shift the boundary of laminar-turbulent transition. Therefore, it is important to examine the viscosity of a nanofluid. Viscosity of nanofluid experimentally studied in the last decade systematically (see [6–9]



quoted there literature). Reliably determined that adding nanoparticles, firstly, significantly increases the viscosity of the liquid carrier, and secondly, can lead to changes in fluid rheology. Viscosity of nanofluid experiments submitted was measured by means of rotation viscometer Rheostress 600 at a temperature of 20°C. Accuracy was about 1%. First of all, it was found that the rate of investigated nanofluid viscosity significantly depends on the speed of the shift.

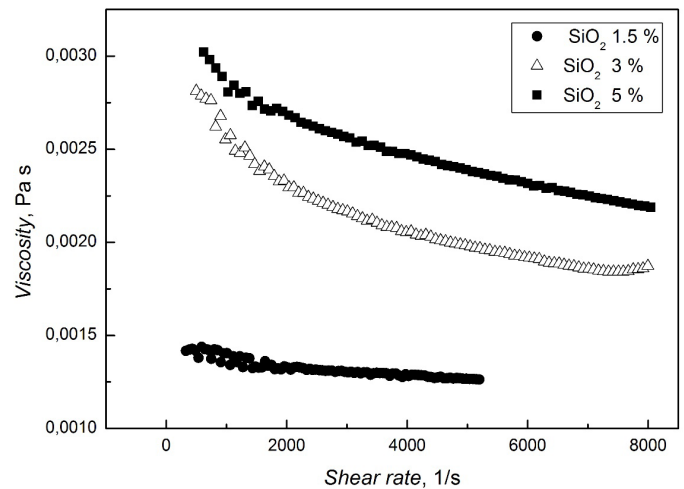


Figure 2. dependence of viscosity of nanofluid from shear

Table 1. – Dependence of rheological parameters of a nanofluid

$\phi, \%$	$n$	$K$
5	0.255	0.03333
3	0.387	0.02511
2	0.502	0.00709
1.5	0.697	0.06433
0.75	0.203	0.01036
0.5	0.173	0.01039

In Figure 2 provided dependence of effective viscosity coefficient  $\mu$  of nanofluid from speed shift  $\gamma$ . Viscosity coefficient of a nanofluid with minimal concentration of nanoparticles (0.25%) does not change with increasing speed shift, i. e. the nanofluid is Newtonian. All the rest nanofluid are non-Newtonian. Found that their rheology is well described by the model power liquid:

$\mu = K \gamma^{n-1}$ . Included in this formula parameters are presented in

Table 1. With increasing concentration of nanoparticles nanofluid index  $n$  decreases, and parameter  $K$  on the contrary, is increasing. Because of researched liquids viscosity significantly different currents of fluid carrier and nanofluid when the specified expense will match different Reynolds numbers, which means and different regimes of flow. For this reason, it is useful to examine the dependence of coefficient of heat transfer from the Reynolds number. Appropriate dependence is shown in Fig. 3, a. Because experimental nanofluid has non-Newtonian properties, the Reynolds number in this case was determined by the standard for power fluid way [7]:

$$Re = \frac{\rho U^{2-n} d^n}{K \cdot 8^{n-1} \left( \frac{3n+1}{4n} \right)^n},$$

where  $U$  – the average speed of the current, which is measured by expenditure,  $d$  – the diameter of the tube. The Figure 3 shows the data for average ratio  $\bar{\alpha} = GC_p (t_o - t_i) S^{-1} (t_w - t_s)^{-1}$ . Here  $G$  – flow,  $S$  – area of the lateral surface of the tube,  $t_o, t_i$  – temperature of the liquid at the outlet and inlet channel,  $t_s$  – the average temperature of the liquid in the tube,  $t_s = (t_i + t_o)/2$ ,  $t_w$  – the arithmetic mean tem-

perature the walls of the tube, according to the average of six received thermocouples,  $C_p$  – the heat carrier  $C_p = \rho^{-1} [(1 - \phi) \rho_f C_{pf} + \phi \rho_p C_{pp}]$ , where  $\rho_f$  – the density of the fluid transport  $\rho_p$  – the density of the material of nanoparticle,  $C_{pf}$  and  $C_{pp}$  – heat carrier liquid and material particles, respectively.

According to Mikheyev's formula, we can dedicate that,  $Nu = 0.021 \cdot Re^{0.8} \cdot Pr^{0.43}$

Table 2. – The dependence of the effective thermal conductivity coefficient from concentration

$\phi, \%$	0.5	0.75	1.5	2	3	5
$\lambda_r$	1.131	1.18	1.33	1.4	1.48	1.41

Intensification of heat transfer when using nanofluid with a fixed number of Reynolds is very significant. So, the heat transfer coefficient for 1% nanofluid more than 40% higher values for water practically at all Re. Obtained for this nanofluid dependence of Reynolds number heat transfer from an extremely cool goes up (fig. 3). Approximate dependence of the coefficient of heat transfer from the Reynolds number for the used nanofluid, you can say with certainty that the excess of heat transfer coefficient turns out twice or more. Naturally, with the decrease concentration of nanoparticles, this effect is monotonically decreasing. When the value of the Reynolds number above 2000 for water takes place laminar-turbulent move that intensifies its heat.

If we assume that Nusselt number  $Nu = (\bar{\alpha} d)/\lambda$  from Reynolds number is universal, according to submitted by experimentation you can evaluate effective values coefficient of thermal conductivity  $\lambda$  reviewed by nanofluid. For this, we should pick up  $\lambda$  so that the dependence of Nusselt number from Reynolds number for these liquids coincided with similar dependent for water. Such a comparison conducted on fig. 3. As you can see, all the good data are consistent if the corresponding coefficients of thermal conductivity values are set, listed in the table 2 (here  $\lambda_r = \lambda_w/\lambda_n$ ,  $\lambda_n$  and  $\lambda_w$  – coefficients of thermal conductivity water and nanofluid accordingly). Received thermal conductivity coefficient on the basis of a nanofluid water and particles of SiO<sub>2</sub> are consistent and direct its dimensions [8].

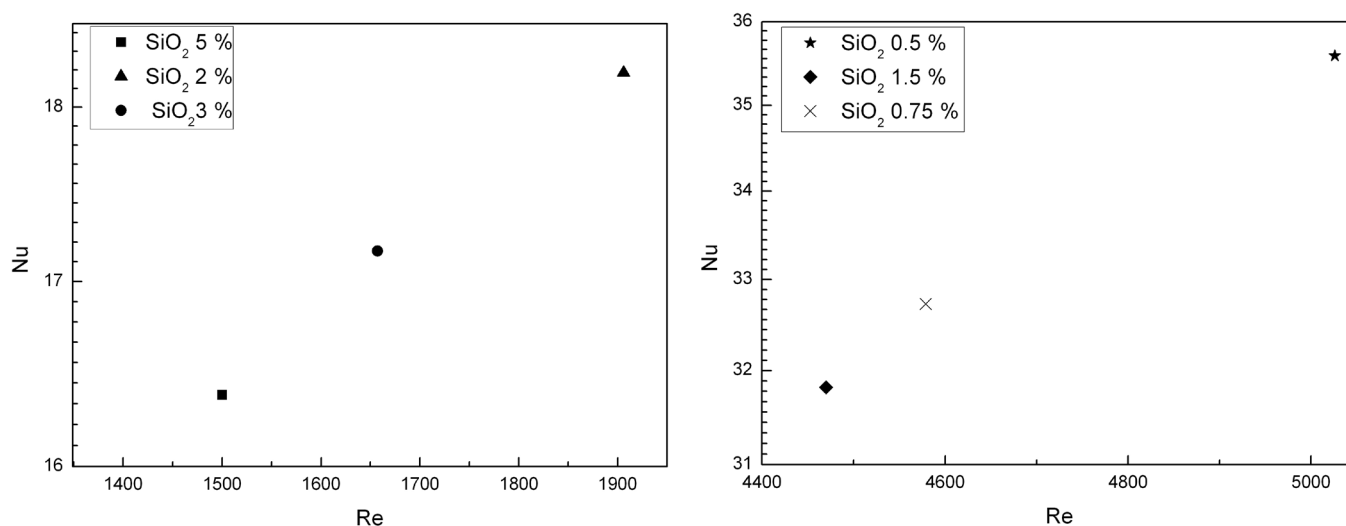


Figure 3. Dependence of Nusselt number from the Reynolds number with various concentration

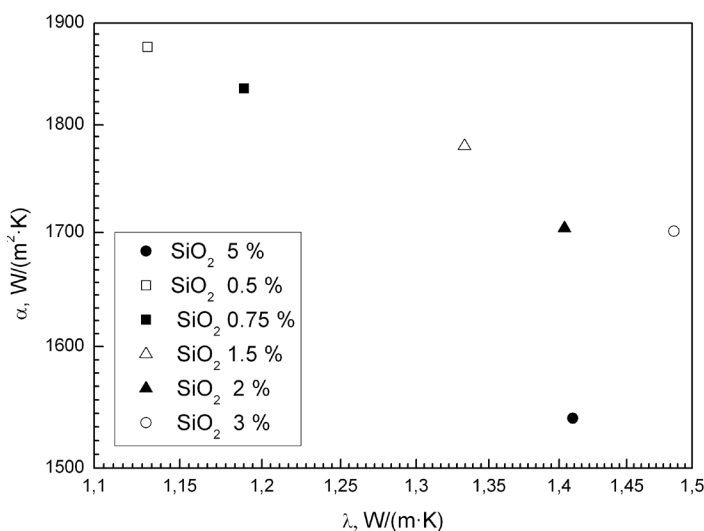


Figure 4. Dependence of coefficient of heat transfer from thermal conductivity with various concentration.

As you can see on fig. 4, with increase concentration of nanoparticles SiO<sub>2</sub>, the thermal conductivity grows. However, with 3% concentration, in our case, it is the highest and at the same time the heat transfer coefficient decreases. It's also registered that with 5% concentration heat transfer coefficient is the lowest [9]. The values obtained for the thermal conductivity exceed the values predicted by Maxwell's theory, and good approximate ratio  $\lambda_r = 1 + 28.2 \varphi - 400 \varphi^2$ .

Thermal conductivity of nanofluid depends on the size and, according to data [10], increases with increasing particle size. Therefore, heat transfer coefficient can be increased, if the use of a nanofluid with larger particles. Energy is also more profitable because larger particles

have lower viscosity [7; 8; 10]. Specifies the ratio for the nanofluid received here at a fixed temperature. However, in [7; 9] it was shown that at not too high concentrations of nanoparticles the dependence of the viscosity of the nanofluid on temperature is determined by the corresponding dependence of the carrier fluid. Therefore, the defining relation obtained here is also sufficient universally.

This work was partially supported by the Grant № FA-A4-F063 "Development of technology for new building materials based on vermiculite with high thermal and sound insulating properties" and "RENAFISA". We would like to thank Professor Sirojiddin Mirzaev for providing valuable feedback on this article.

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## Designing clothing fabrics with defined porous

**Abstract:** The article is dedicated to the design of clothing fabrics with a given porosity and the study of cloth structure parameters.

**Keywords:** yarn, fabric, runner length, weft, warp, armure, density, rapport.

The clothes serve for regulation heat irradiation bodies of the person, creating round an organism the artificial, adjustable temperature environment rather independent of direct influences of environment. Besides the clothes protect an organism from mechanical damages and by that promote health preservation. The clothes is produced mainly from fabrics. Hygienic properties of fabrics depend on properties of an initial material (fibre) and technics of manufacturing of fabrics. Identical results can be received from silk, wool, cotton and flax if to develop them so that they had identical hygienic properties, designing of fabrics on their set properties therefore is expedient. An estimation of properties spend by means of such indicators, as rapport weave on a weft and a warp, number of crossings of threads of one system other system, runner threads, thickness, weight, relative density, porosity and air permeability of fabrics.

For designing cloth fabrics we are set by porosity of fabric  $R_s$ , an weave, a phase of a structure of a fabric, filling factor on a warp or on a weft, linear density of a yarn on a warp and on a weft, factor of a parity of density or diameters of threads, factor of change of the sizes of threads in a fabric [1; 2]. Calculation was spent in the following sequence under following formulas.

Define settlement diameter of a thread before weaving

$$d_{mid} = 0,0316C \sqrt{\frac{T_{warp} + T_{weft}}{2}} \quad (1)$$

Define fabric density on a warp

$$P_{warp} = \frac{100(K_d + 1)K_{Hwarp}}{d_{mid}(K_d \cdot \eta_{warp} + \eta_{weft})\sqrt{4 - K_{Hwarp}^2}} \quad (2)$$

The fabric density on a duck expresses through the greatest possible density on a weft and unknown factor of filling of a fabric a fibrous material

$$P_{weft} = P_{weft\ max} \cdot K_{Hweft} = \frac{100(K_d + 1)K_{Hweft}}{d_{mid}(K_d \cdot \eta_{warp} + \eta_{weft})\sqrt{4 - K_{Hweft}^2}} \quad (3)$$

The coefficient of a fabric on a weft a fibrous material define from a parity of porosity of a fabric

$$R_s = 100 - d_{warp} \cdot P_{warp} - d_{weft} \cdot P_{weft} + 0,01d_{warp} \cdot d_{weft} \cdot P_{warp} \cdot P_{weft} \quad (4)$$

Where:  $d_{warp} = d_{warp} \cdot \eta_{warp}$ ,  $d_{weft} = d_{weft} \cdot \eta_{weft}$

Runnerlength in a fabric on a warp

$$a_{warp} = \frac{L_{warp} - L_{T_{warp}}}{L_{warp}} \cdot 100\% \quad (5)$$

$$L_{warp} = \sqrt{l_{weft}^2 + h_{warp}^2}; L_{T_{warp}} = l_{uf} = 100 / P_{weft};$$

$$h_{warp} = \frac{d_{warp} + d_{weft}}{2} \cdot K_{Hwarp};$$

Runnerlength in a fabric on a weft

$$a_{weft} = \frac{L_{weft} - L_{T_{weft}}}{L_{weft}} \cdot 100\% \quad (6)$$

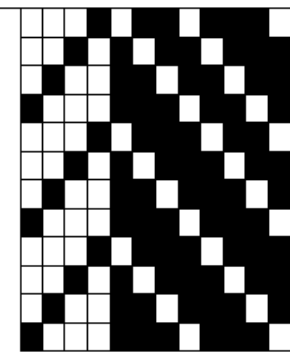
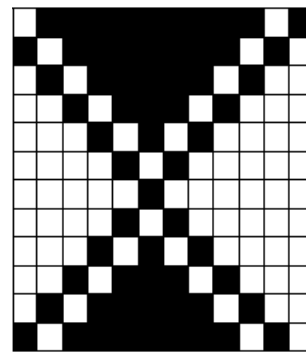
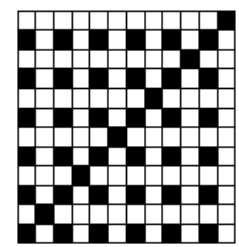
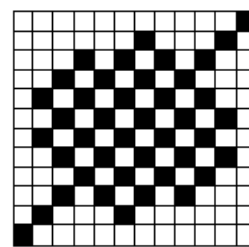
$$L_{weft} = \sqrt{l_{warp}^2 + h_{weft}^2}; L_{T_{weft}} = l_{warp} = 100 / P_{warp};$$

$$h_{weft} = \frac{d_{mid}(\eta_{warp} + \eta_{weft})}{2} \cdot K_{Hweft};$$

The purpose is given, to design a fabric porosity  $R_s = 38 \pm 1$  in linear density on a basis and on a duck  $T_{warp} = 25 \times 2$ ,  $T_{weft} = 45$  tack, factor of yarn  $C = 1,25$ , factor of the relation of diameters of threads of a basis and a duck before weaving  $K_d = 1,1$ , a fabric interlacing on fig. 1, on technical requirements a fabric of VI order of a phase of a structure, i.e. a fabric in the big density on a basis both  $K_{Hwarp} = 1,2$  and  $K_{Hweft} = 0,8$ ;  $K_{Hwarp} = 0,85$ , factor of change of diameters of threads in a fabric  $\eta_{warp} = 1,1$ ,  $\eta_{weft} = 1,1$ ,  $\eta_{warp} = 0,8$ ,  $\eta_{weft} = 0,8$ . Substitution of this data in formulas 1-6 allows to define parametres of a structure of a fabric such, as fabric density on warp  $P_{warp} = 246$  th/dm, fabric density on weft  $P_{weft} = 150$  th/dm, factor of filling of a fabric on weft  $KH_{weft} = 0,73$ , runner length on a warp  $a_{warp} = 6,9\%$ , on a weft  $a_{weft} = 8,1\%$ .

Designed cloth the fabric has been developed on the weaving loom of firm «Comet» with rapport weave on warp  $R_{warp} = 12$  and on weft  $R_{weft} = 12$ , number fine in refuelling 12, number reed  $N = 60$  tooth/dm., number of threads scolded in tooth reed – 4 threads, density on a warp of 250 n/dm. And on a weft of 150 th/dm., linear density of the warp threads  $25 \times 2$  tack, linear density weft threads 45 tack.

On fig. 1 4 variants armure, considering rapport weave on a warp and a weft, number of crossings of threads of one system another  $t_{warpmid}$ ,  $t_{weftmid}$



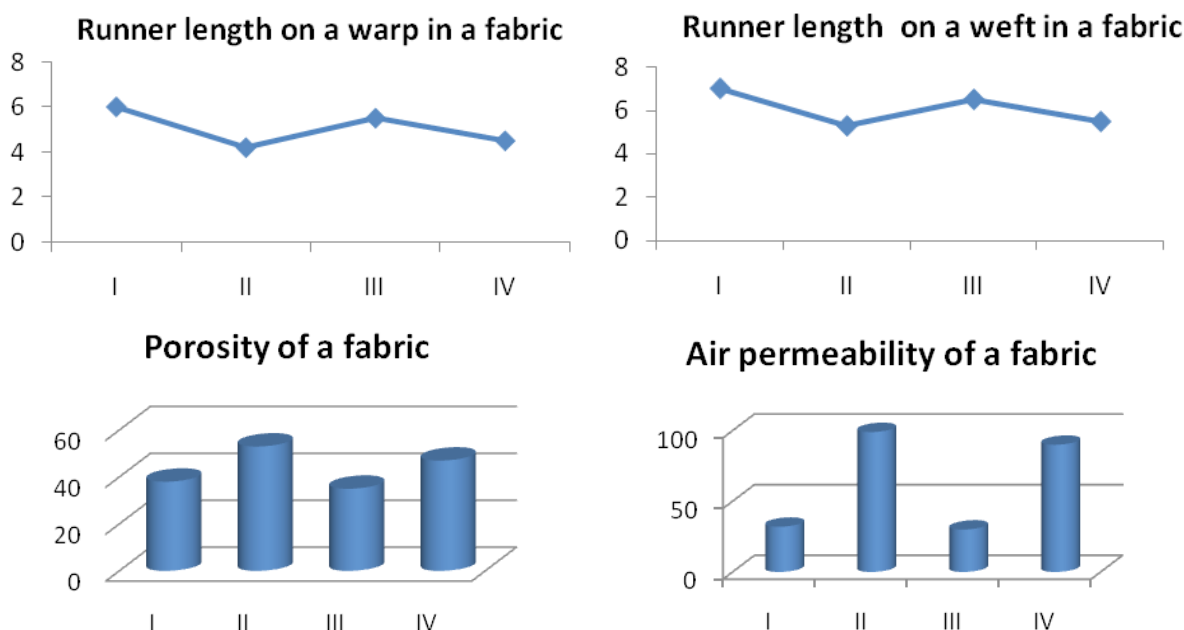
Figures 1.

In the table values runner length are presented, to porosity and air permeability of samples of fabrics which are defined by a known technique. An error of the received values there were in limits of 5 %. The

table analysis (variants of 1 and 2 samples of fabrics) shows that at invariable identical rapport to a fabric and identical crossings of threads (fig. 1 and fig. 2), average runner length threads of a warp and a weft unequal.

Table 1. – Values runner length, porosity and air permeability of samples of fabrics

№	Variant of the developed: Samples-Fabrics	Showings of properties			
		Runner length on a warp in a fabric	Runner length on a weft in a fabric	Porosity of a fabric	Air permeability of a fabric
1	I	6,0	7,0	38	32
2	II	4,2	5,3	53	99
3	III	5,5	6,5	35	30
4	IV	4,5	5,5	47	90



Figures 2.

For a variant 1 (fig. 1) – at  $R_{\text{warp}} = R_{\text{weft}} = 12$ ,  $t_{\text{warp}1} = t_{\text{weft}1} = 2$  at  $n = 2$ ,  $t_{\text{warp}3} = t_{\text{weft}3} = 2$  of  $n = 2$ ,  $t_{\text{warp}6} = t_{\text{weft}6} = 8$  at  $n = 6$ ,  $t_{\text{warp}5} = t_{\text{weft}5} = 10$  at  $n = 2$  average runner length on a warp  $a_{\text{warp}} = 6,0$  %, on a weft  $a_{\text{weft}} = 7,0$  %.

For a variant 2 (fig. 2),  $t_{\text{warp}1} = t_{\text{weft}1} = 2$ , at  $n = 6$  and,  $t_{\text{warp}6} = t_{\text{weft}6} = 12$  at  $n = 6$  average runner length on a warp  $a_{\text{warp}} = 4,2$  %, on a weft  $a_{\text{weft}} = 5,3$  %.

Apparently the number of crossings in rapport is identical, however in the second case of crossing have extreme value  $t_{\text{warp}1} = t_{\text{weft}1}$  and  $t_{\text{warp}6} = t_{\text{weft}6}$ , and in the first case averages value  $t_{\text{warp}4} = t_{\text{weft}4}$  and  $t_{\text{warp}5} = t_{\text{weft}5}$  in the range from  $t1$  to  $t6$  that leads to decrease in values average runner length on a warp on 30 % and on a weft on 24 %. Besides from the table (variants of 1–4 samples of fabrics) that reduction of number of crossings of threads in limits rapport leads to decrease runner length threads of a warp and a weft in a fabric, to increase in porosity of a fabric and as consequence increase of values

of air permeability clothes follows. Therefore use of the second variant of the sample for clothes fabrics is expedient.

### Conclusions

1. The designing technique clothes fabrics on the set porosity where calculations of diameters of threads before weaving, fabric density, factor of filling of a fabric by a fibrous material, geometrical density of a fabric, height of waves of a bend of threads in a fabric, runner length in a fabric are resulted is developed.

2. Researches of samples clothes fabrics are developed and conducted. In all variants reduction of number of crossings in limits rapport leads to decrease runner length of a warp and a weft in a fabric. At identical rapportweave of a fabric and at reduction of number of crossings of threads of one system by other system porosity increases. With increase in porosity of a fabric air permeability clothes fabric raises. Use of the second variant of the sample for clothes fabrics is expedient.

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## Depth of the diluted zone in the humidified loess bases under shaking conditions

**Abstract:** The article is dedicated to results of researches of authors on a problem of studying of a thickness of a diluted zone in loessial humidified soils in the conditions of influence on them of seismic concussions. From a condition of limiting balance of two counteracting forces (seismic and resistance to shift) the formula is received to define the size of a diluted zone at the moment of influence on the bases of seismic fluctuations. According to the recommended formula, seismic stability of any soil besides size of seismic influence depends on strong characteristics of a soil, such as: a corner of an internal friction and cohesive, etc.

**Keywords:** diluted zone; loess soil; concussions; seismic pressure; resistibility to shift; a friction corner; cohesion.

The estimation of stability of the water sated bases of constructions at influence of seismic fluctuations in many respects depends on depth of a diluted zone in the conditions of concussion with value above critical acceleration [4, P. 51].

Thus, initial depth of the diluted zone arising in thickness to fluctuating thickness is defined from a condition:

$$a_s > a_{kr} \quad (1)$$

here  $a_s$  – the maximum seismic acceleration arising in soil thickness;  $a_{kr}$  – critical accelerations of fluctuation of a soil.

The critical acceleration of fluctuation  $a_{kp}$  stands for the maximum quantity which is resistance expressed strength by properties of the fluctuating soil. According to such concept at the seismic accelerations exceeding critical accelerations, particularly taking into account the given soil there is a destruction of structure of the water sated soil with transformation of it into diluted conditions.

Otherwise a soil fluctuations keeps the static condition without any infringement of durability.

For definition of critical acceleration formulais offered by Rasulov [4, P. 72]:

$$a_{kr} = \frac{2\pi g(\sigma \operatorname{tg} \varphi_w + c_w)}{\gamma_w \cdot T \cdot v_k}, \quad (2)$$

where:  $g$  – gravity acceleration;  $\sigma$  – normal pressure from construction weight;  $\varphi_w$  – a corner of an internal friction of a soil at humidity  $w$ ;  $c_w$  – the general cohesion of a soil;  $\gamma_w$  – soil density;  $T$  – the fluctuation period;  $v_k$  – cross speed distributions of seismic waves.

In the course of concussion of the water sated soil special value gets zone definitions dilution when it is observed in following conditions (1).

This zone can be defined from limiting equality:

$$\tau^s = s_{pw} \quad (3)$$

where  $\tau^s$  – the pressure arising in thicknesses of a soil in process distributions of seismic waves (seismic pressure);  $s_{pw}$  – resistibility of a soil to shift (durability of a soil).

Seismic pressure can be defined under formula [2]:

$$\tau^c = \frac{\gamma_w}{2\pi g} T v_c a_c \frac{\gamma_w}{2\pi g} \quad (4)$$

where  $z$  – considered horizon in soil thickness.  $\lambda$  – length of wave.

Resistibility of a soil to shift is defined in following manner:

$$s_{pw} = (\sigma + \gamma_w z) \operatorname{tg} \varphi_w + c_w \quad (5)$$

where  $\sigma$ ,  $\gamma_w$ ,  $\varphi_w$ ,  $c_w$  – have values as in the formula (1).

Equality (3) taking into account (4) and (5) will be copied in a kind:

$$\frac{\gamma_w}{2\pi g} T v_c a_c = \sigma_{din} \operatorname{tg} \varphi_w + c_w \quad (6)$$

For definition of depth of a diluted zone in thickness of a soil we will analysis equalities (6). It is known, that value  $\sigma_{din}$  in it generalized a dynamic condition of two pressure: from the loading operating on a surface of a soil ( $\sigma_z$ ) and from a body weight of the soil ( $\gamma_w z$ ), i.e:

$$\sigma_{din} = \sigma_z + \gamma_w z \quad (7)$$

In case of absence of external loading on a soil surface ( $\sigma_z = 0$ ), the formula (6) can be copied as:

$$\frac{\gamma_w}{2\pi g} T v_c a_c = \gamma_w z \operatorname{tg} \varphi_w + c_w \quad (8)$$

Prof. Medvedev S.V. notes, that the Earthquake period ( $T$ ) is distinguished for different soils and depends, basically, from an addition condition. For a case of homogeneous addition of a soil quantity  $T$  depends on a thickness of fluctuating layer  $H$  and speed of fluctuation of soil particles  $v_c$  in a kind [2, P. 65]:

$$T = \frac{4H}{v_c} \quad (9)$$

Including

$$\frac{a_c}{g} = k_c \quad (10)$$

where  $k_c$  – seismicity factor.

Taking into consideration dependences (9) and (10) formula (8) can be written as follows:

$$0,64 \gamma_w k_c H = \gamma_w z \operatorname{tg} \varphi_w + c_w \quad (11)$$

Parameter  $z$  in this case represents depth of a diluted zone and it is possible to calculate its value as:

$$L = \frac{0,64 k_c \gamma_w H - c_w}{\gamma_w \operatorname{tg} \varphi_w} \quad (12)$$

Formula (12) in each special case allows to define size of a diluted zone in the water sated soil during the moment ( $t = 0$ ) appendices of seismic loading.

As follows from it depth of a diluted zone at concussion of the water sated soil depends from quantity of acceleration of seismic fluctuation ( $a_c$ ), or seismic pressure caused by it ( $\tau^s$ ).

Fig. 1 is illustrated dependence  $L_o = f(\sigma)$  as a result of the spent experimental researches on humidified loessial soils. As fol-

lows from the schedule, any normal pressure from weight of external loading  $\sigma$  promotes reduction of a thickness of diluted zone  $L_o$ . Such conclusion follows and from the formula (12) also. This cir-

cumstance demands the account of weight of a construction at definition of initial value of a dilution zone in the conditions of concussion of the water sated soil.

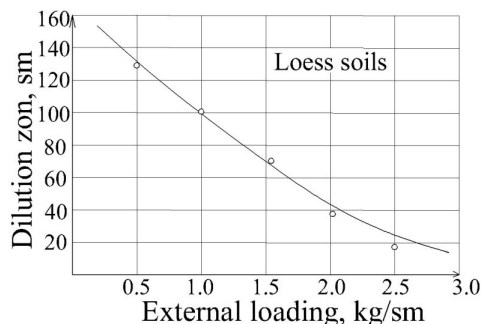


Figure 1. Dependence between dilution zone and external loading

At the same time, it is necessary to underline a positive role of cohesion of a soil in value of a dilution zone. It is known, that any rise cohesion quantity between soil particles promotes to increase in durability and, from here, bearing ability of the basis. If the general cohesion in the formula (12) to spread out to components, i.e. [1, P. 47]:

$$c_v = c_w + c_c \tag{13}$$

where  $c_w$  – the plastic connectivity having water-kolloid character;  $c_c$  – rigid structural cohesion.

Depending on a natural condition the soils can be characterised by various cohesions. From here water sated soils in a plastic condition it is possible to express resistibility of the weakest as:

$$\tau^s = c_w \tag{14}$$

This circumstance testifies the ability to dilute such soils in considerable depth zone. In such condition depth of a diluted zone depends only on plastic cohesion of a soil. And influence of normal pressure from construction weight in considered conditions it is reduced to zero (fig. 2). About extremely instability of water sated soils it is appropriate to note the seismic relation on consequences of last strong Earthquakes [3, P. 174–213]. In small humidified soils above noted phenomenon proceeds a little differently. Presence at them an internal friction and rigid cohesion making positive impact promote shortening a diluted zone.

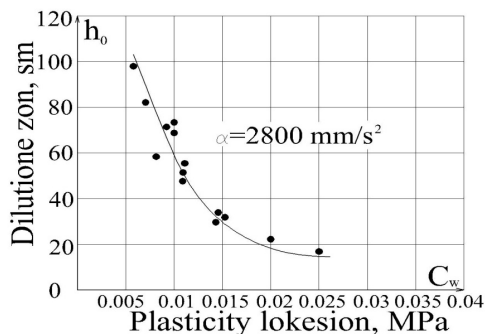


Figure 2. Dependence between dilution zone and plasticity cohesion

In summary it is necessary to notice, that the established depth of a diluted zone under the formula (12) will correspond to the initial moment of the appendix of seismic loading to a soil. At the same

time, the given zone, in certain conditions, can deepens in process of fluctuation of thickness depending on intensity of seismic influence.

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## Change of depth of the diluted zone at concussion of water sated loess

**Abstract:** Article is devoted to questions of research on change of a diluted zone in the water sated loessial thicknesses in conditions of seismic fluctuations. To estimate a process depth of a diluted zone into thicknesses the formula serving a base for the factor of dynamic consolidation of a soil at concussion is proposed. The given factor testifies the speed of consolidation of the particles broken by concussion in each special case is subject to experimental definition. The final size deep a diluted zone depends on time of influence of concussions.

**Keywords:** dilution; concussion; water sated thickness; loessial soils; factor of dynamic consolidation; seismic pressure; dynamic pressure; plastic cohesion, internal friction.

In building practice the cases of subsidence, an inclination, and, sometimes the destructions of buildings and constructions at strong Earthquakes are quite frequent. As one of principal causes of occurrence of such phenomena serves diluted and the subsequent non-uniform a settle water sated soils (loess) lying in their basis.

Despite actions undertaken against diluted soils the analysis of consequences of Earthquakes last for many years and shows all increase in deformations of the constructions erected on water sated soils.

This circumstance testifies that the problem diluted weak soils in the conditions of concussion nevertheless remains actual.

It is known, that under diluted we mean difficult process proceeding in dynamic conditions connected with infringement of structure of a soil, pressure occurrence in pore water and transition in a suspension of particles and soil transition in a fluid condition. The substantiation of such rather difficult process including simultaneously many physical phenomena, is one of a difficult problems of soil mechanics.

Results of researches are more rarely stated in works of authors concerning change of a diluted zone in thickness of a fluctuating soil in the course of fluctuations.

It is known that occurrence diluted in a certain part of soil thickness will happen in cases when seismic pressure within this thickness will exceed the strength indicators of soil [1, P. 66–68]. Within the given part, which have received the names «diluted thickness» forms seismic deformations (seismic subsidence) constructions in the conditions of Earthquake.

The spent experimental researches with water sated loess soils at various fluctuations have shown, that the border of originally formed diluted thickness is not constant size, and changes in the course of concussion. One of principal causes of such phenomenon is served by gradual reduction of force of plastic cohesion between fluctuating particles and simultaneous influence on them of the dynamic pressures arising at consolidation of broken particles of a soil.

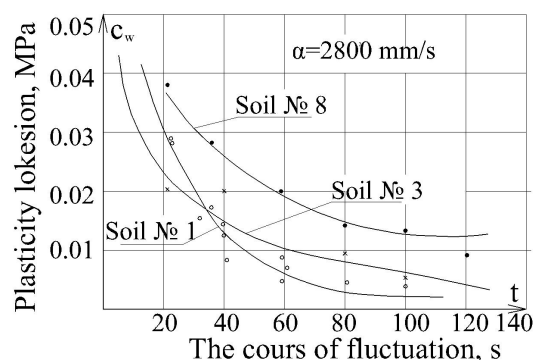


Figure 1. Change plasticity cohesion in the course of fluctuation

In the course of concussion of the water sated soil the change of a condition of a soil is observed, for example, from plastic in a fluid condition. Development of such phenomenon will last to definite time after which expiration there will be already rather longer proceeding return process accompanied by consolidation of particles. During this

process the gradual restoration of the broken plastic connectivity of a soil is also observed. This circumstance is well seen from fig. 1., where dependence of kind  $L_0 = f(c_w)$  for the investigated water sated loessial sandy loam is presented. On the following drawing the reduction of quantity of connectivity of a soil makes in the beginning concussions

4,5 during 80 times in conditions of fluctuation of a soil with acceleration of  $2800 \text{ mm/s}^2$ . The further concussion of a soil leads to attenuation of reduction of connectivity in considered conditions.

Based on results of the spent numerous researches it is possible to notice, that process of reduction of connectivity at concussion comes to the end on the average during 20–30 c. after the appendix of dynamic loading to a soil.

However, decrease in connectivity of a soil in the course of fluctuation in a number a case depends and on quantity of a dynamic pressure in water and filtration ability of a soil.

On fig. 2 the result of one of experiences of measurement of quantity of the dynamic pressures arising in a soil at its consolidation is illustrated. As noted in the schedule, the dynamic pressure

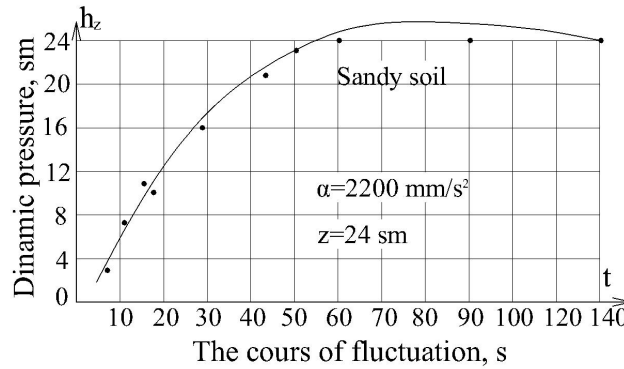


Figure 2. Character of change of a dynamic pressure in time

Reduction of durability of a soil as consequence of the above-named phenomena results entranced, in expansion of a diluted zone within thickness.

Studying thickness a diluted zone in the course of concussion makes a basis of the present research.

It is known, that the diluted zone always promotes reduction of durability and bearing ability of a soil. In cases, when durability of a soil decreases to a minimum (full diluted conditions) a loses soil a condition bearing ability and any loading on its surface will sink deep into thicknesses.

According to H. Z. Rasulov’s theoretical work on “Conditions of dynamic durability water sated loessial soils” the diluted plastic-cohesion of the humidified loess is a consequence of reduction of resistibility to shift of soil  $s_{\sigma,w}$  in result decrease cohesion ( $c_w$ ) and normal pressure from loading ( $\sigma$ ) [2, P. 79–84]. Reduction of normal pressure occurs for the account weighing influence of a dynamic pressure  $h_z$ , arising in considered conditions.

This circumstance is represented in a kind:

a) resistibility of the water sated loess in static conditions:

$$s_{st} = (p_z + \gamma_w z) \text{tg} \varphi_w + c_w \quad (1)$$

b) same in dynamic conditions:

$$s_{din} = [(p_z + \gamma_w z) - \gamma_c h_{z,t}] \text{tg} \varphi_w + c_{w,t} \quad (2)$$

For a case of absence of external loading on thickness of a soil:

$$S_{din} = (\gamma_w z - \gamma_c h_{z,t}) \text{tg} \varphi_w + c_{w,t} \quad (3)$$

where:  $\sigma$  – normal pressure from weight of external loading;  $\gamma_w$  – soil density;  $z$  – considered horizon in soil thickness;  $\varphi_w$  – a corner of an internal friction of a soil;  $c_w$  – plastic cohesion between soil grains.

According to this formula we note the resistibility to shift of the water sated loess at concussion depends on quantity of change of cohesion of a soil and the dynamic pressure arising in a time of a soil at consolidation of particles which promotes decrease in influence of value of normal pressure. Thus the quantity of an operating dynamic pressure  $h_{z,t}$  in any depth  $z$  is defined under the formula:

arising in soil water increases with 0 to certain quantity in the course of concussion. Time of increase of a dynamic pressure, according to comparison of indications, is approximately equaled time of decrease in connectivity of a soil.

Thus, it is possible to note the below-mentioned simultaneous processes proceeding at concussion of water sated loess:

- gradual decrease in quantity of plastic cohesion within thickness of a soil;
- occurrence of dynamic pressures and its increase in time as a result of consolidation of the weakened communications of particles;
- decrease the general durability of a fluctuating soil.

$$h_{z,t} = \frac{v_n}{k_\phi} \left( Hz - \frac{z^2}{2} \right) (e^{-\mu t} - e^{-\lambda t}), \quad (4)$$

where  $v_n$  – factor of the dynamic consolidation, testifying speed of consolidation of a soil;  $k_\phi$  – factor of a filtration of a soil;  $H$  – a thickness of a fluctuating soil;  $z$  – depth of considered horizon;  $\mu, \lambda$  – the dynamic factors defined by practical consideration.

Let’s analyse formulas (4). It shows that the dynamic pressure resulting in a diluted condition of thickness mainly depends on value of factor dynamic consolidation  $v_n$ . This circumstance testifies that the speed of a filtration of superseded water depends on the direct image of the speed of soil particles consolidation. this shows that the more the quantity of factor of dynamic consolidation, the more volume superseded from a time of a soil of water. It in turn raises degrees diluted thicknesses, simultaneously unloading underlying layers of earth that promotes deep diluted zones in these conditions. On the basis told it is possible to notice, that expansion of a diluted zone in thicknesses also depends and on speed of consolidation of the destroyed particles of a soil.

The initial period of influence of concussions depending on dynamic durability of a soil in any part of thickness changes in a diluted condition ( $L_0$ ). The further process of fluctuations, on the basis of the above-stated, promotes deep this zone ( $L_t$ ), that it is possible to track by carrying out of simple dynamic experiences on vibrating installations. Unlike sand, in loessial soils the given process is tightened in time, cohesion of a soil corresponding for infringement.

For the most simple case including this process linear, the differential equation of change of a diluted zone in time it is possible to present in a kind:

$$dL_t = v_n L_0(t) dt \quad (5)$$

where  $v_n$  – on former factor of dynamic consolidation, (1/c).

Integration of the equation (5) leads:

$$L_t = A + C e^{-v_n t} \quad (6)$$

Constants of integration  $A$  and  $C$  are defined on conditions:

$$t = 0 \rightarrow L_t = L_0$$

$$t = \infty \rightarrow L_t = H \quad (7)$$

From here

$$A = H; C = H - L_0 \quad (8)$$

Taking into account (7) and (8) the formula (6) it will be copied in a following definitive kind:

$$L_t = H - (H - L_0) \cdot e^{-v_n \cdot t} \quad (9)$$

Formula (9) once again confirms the conclusion stated earlier about dependence deep diluted thickness in the course of concussion from speed of consolidation ( $v_n$ ) a soil in these conditions.

According to results of our researches it is possible to notice, that the quantity of factor of the dynamic consolidation testifying the speed depends on many factors, most important of which are: conditions of initial density-humidity of a soil, value of plastic cohesion, coarse ground structure, and also intensity of concussion and character (on frequency and amplitude) this influence, etc.

At the same time for a substantiation of the difficult nature of factor  $v_n$  special experimental researches and supervision are required.

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## Substantiating the parameters of operating elements of the enhanced chisel-cultivator

**Abstract:** The research results substantiating the parameters of loosening and arrow-typed claws are specified in the article. It is enhanced in a purpose to reduce the power-capability and increasing the quality of soil crushing by the chisel-cultivator.

**Keywords:** chisel-cultivator, operating elements, loosening claw, arrow-typed claw, chess-typed arrangement, track by track positioning, blocked-type cutting, free cutting, angle of incoming the loosening and arrow-typed claws into the soil, solution angle and seizure width of arrow-typed claw, energy costs, quality of soil crushing.

In conditions of our Republic the chisel-cultivators are the main technical means at pre-sowing soil tillage proceedings. However chisel-cultivators (CHK-3,0, CHKU-4 and others) being applied currently have higher power-capability, and by single running it often doesn't ensure the required quality in soil crushing. Pursuant to above we have developed the enhanced chisel-cultivator. It consists of framework with hang-up, supporting wheels and operating elements installed in three row onto the framework.

Differing from the existing ones the operating elements of the first and second row of developed chisel-cultivator are installed on the frame as rows at staggered sequence, and the operating elements of the second and third rows – trace by trace; in this case the operating elements of the first and third rows are installed (regarding the supporting wheels) to the same stillage depth, i. e. their tabs are mounted in the same horizontal plane; the operating elements of the second row are installed on the less tillage depth (i. e. above) rather than the operating elements of the first and third rows.

In the process of running the enhanced chisel — cultivator the operating elements of the first row interact with soil monolith, i. e. they run in the conditions of blocked-type cutting, and the operating elements of the second and the third rows in the process of work interact with soil layers, zones bordering the loosened operating elements of the first row, i. e. run in conditions of free (debloked-type) cutting.

The main task of operating elements of the first row is to form lateral loosened zones in order for operating elements of the second row to operate in condition of free-typed cutting. Therefore they are made in the form of dual-edged flat wedge, i. e. in a form of narrow loosening claw with a flat working surface. In this case, firstly the soil is deformed to the side of field surface, i. e. in the direction of open surface, secondly volume of being deformed soil is reduced in conditions of blocked-type cutting. As it is well known, [1] both of those two factors lead to reduce energy (power) expenditures for soil tillage.

Operating elements of the second and third rows of the developed chisel — cultivator is made in a form of a three-edged wedge, i. e. in a form of the arrow-type claw, and in this case efforts spent for soil deformation and destruction, they will direct to zones side loosened by the operating elements of the first row and the result is a reduction in energy costs [1; 2].

Arrangement the operating elements of the first and second rows at staggered sequence on the framework, and the second and third rows trace by trace, as well as the installation of the operating elements of the second and third rows stepwise (throughout soil tillage depth), i. e., the installation of the second row operating elements is higher than the third row relatively the operating elements of the third ensures layer by layer soil loosening; and consequently it leads to improvement of the its crushing quality.

The main parameters of the operating elements of developed chisel – cultivator (see figure) are the following:  $\alpha_p$  – crushing angle of the loosening claw;  $\alpha_c$  – crushing angle of the arrow-typed claw;

$b_p$  – width of loosening claw;  $2\gamma_c$  – solution angle of the arrow-typed claw;  $b_c$  – seizure width of the arrow-typed claw.

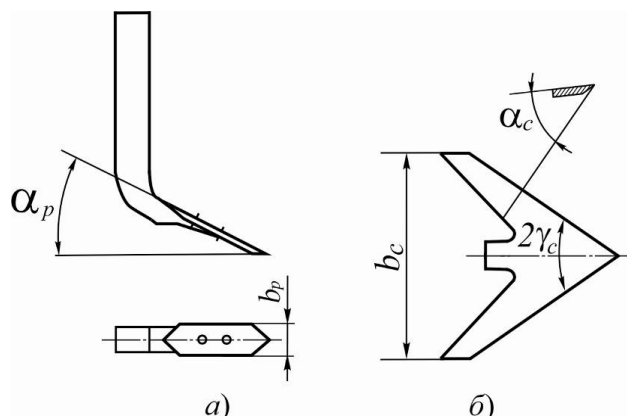


Figure 1. The main parameters of the loosening (a) and arrow-typed; (b) claws of the enhanced chisel-cultivator

**Crushing angle of the loosening and arrow-typed claws** are determined on the next formula obtained from the terms ensured movement and rising the soil formations tillage base on their working surfaces at minimum energy costs

$$\alpha_p = \alpha_c = \arctg \left( \sqrt[3]{-q + \sqrt{q^2 + p^3}} + \sqrt[3]{-q - \sqrt{q^2 + p^3}} - \frac{m}{3n} \right), (1)$$

where  $q = \frac{m^3}{27n^3} - \frac{mc}{6n^2} - \frac{m}{2n}$ ;  $p = \frac{3nc - m^2}{9n^2}$ ;  $m = tg\phi$ ;  $n = 1 + tg^2\phi$ ;  $c = 2tg^2\phi$ ;  $\phi$  – angle of outside soil friction.

**Seizure width of loosening claw** is determined the exception terms of forming at the bottom of the layer cutting grooves with sealed walls being tilled by it, resulting in the deterioration of the physical and mechanical properties of soil and useless energy consumptions [3]. In this case the following dependence will be achieved:

$$b_p \geq \frac{(d + ctg\alpha_p)h}{\left[ 0,1 \frac{T_{cm}}{k_c} (1 + 3ctg\alpha_p + \phi) - k \right]}, (2)$$

where  $h$  – tillage depth;  $T_{cm}$  – specific resistance of soil to crumpling;  $k_c$  – specific resistance of soil to move-off;  $k, d$  – non-dimensional coefficients depending from the physical and mechanical properties of soil.

**Let's determined solution angle of the arrow-type claw** base on formula [4]

$$2\gamma_c = \frac{\pi}{2} - \phi_c (3)$$

$$\text{or } \gamma_c = \frac{\pi}{4} - \frac{\phi_c}{2}, (4)$$

where  $\phi_c$  – weeds friction angle on the arrow-typed claw blade.

When the terms (3) and (4) of wing blades of the arrow-typed claws are ensured in each moment there will be interaction with the minimum number of weeds, and therefore the probability of plugging the operating element by them will be minimal.

**Seizure width of the arrow-typed claw.** In effort to determine this parameter from the conditions when the wing blades of the arrow-typed claws are fully in the conditions of free-typed cutting (as the energy costs for deformation and the soil destruction is reduced [1; 2]), the following dependence is obtained:

$$b_c < 2htg \frac{1}{2}(\alpha_c + \phi + \rho) \cos \gamma_c, (5)$$

where  $\rho$  – angle of soil internal friction.

Calculations by the formulas of (1) – (3) and (5) when  $\phi = 30^\circ$ ;  $d = 4,2$ ;  $h = 0,2$  m;  $T_{cm} = 1,5 \cdot 10^6$  Pa;  $k_c = 2 \cdot 10^4$  Pa;  $k = 2,5$ ;  $\phi_c = 30^\circ$  and  $\rho = 40^\circ$  [3, 5–7] showed that crushing angles of loosening and arrow-typed claws at the developed chisel – cultivator must be  $25^\circ$ ; width of loosening claws – not less than 6,1 cm; solution angle of arrow-typed claw –  $60^\circ$  and seizure width of the arrow-typed claw and not more than 38 cm.

So in effort to ensure the required soil tillage quality with minimum energy costs the crushing angles of loosening and arrow-typed claws at the developed chisel – cultivator must be  $25^\circ$ ; width of loosening claws – not less than 6,1 cm; solution angle and seizure width of the arrow-typed claw – appropriately  $60^\circ$  and not more than 38 cm.

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## Section 10. Transport

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### Maintenance regimes of Mercedes-Benz buses, used in the conditions of Tashkent city

**Abstract:** Buses' reliability operating conditions largely depends on the adopted maintenance regimes. This paper presents the results of research on maintenance regime of buses Mercedes-Benz, used in Tashkent city.

**Keywords:** operating conditions, maintenance, interval, work capacity, list of operations.

On June 4, 1992 by Government of the Republic of Uzbekistan was issued a decree on the establishment of the State Association "Tashgorpasstrans", which identified as key objectives: integration of all types of urban transport in a single system, improve working and living conditions and wages of the passenger transport workers and upgrade transportation. Over the years, bus fleets operated buses of LAZ, PAZ, LIAZ models, as well as the Hungarian "IKARUS" brand production.

It was decided to acquire modern foreign large class buses of Mercedes-Benz to serve a large population of Tashkent city.

Delivery of modern city buses Mercedes-Benz has begun since 1995. Buses were distributed based on population areas in Tashkent in 9 bus parks. In order to maintain the technical condition of buses on a high level of the bus Service Center was established.

In 2015, the number of buses in Tashkent was over 1450 units, while passenger traffic reached – 268,7 million passengers.

Nowadays in Tashkent successfully operated more than 700 units of buses Mercedes-Benz O 405, O 345, Sitaro and Co-necto Low floor.

Buses' operation conditions in Tashkent:

- Climate – extremely continental;
- Temperature – maximum + 44 °C, minimum – 29 °C, the average + 14,8 °C.
- Humidity – during the hottest time of – 21%, cold weather – 55%. The annual precipitation is about 429 mm.
- Barometric pressure – 1 bar.
- Average annual wind speed – 1,4 m/s.
- Solar radiation – 1.52. (Cal/cm<sup>2</sup> min).

Air pollution (number of dust particles in the air 1 sm<sup>3</sup>) is – 137 (in summer) and 77 (in winter).

Tashkent city belongs to the third category of operating conditions: – road surface: cement concrete, asphalt, paving stones, mosaic. Type of relief – plain (altitude is about 200).

Buses of city transport of Tashkent are used very intensively. The average mileage is – 269,3 km per day and annual average – 96.9 thousand km. In two-shift operation, the average duration of a bus operation of Mercedes-Benz is 12,70 hours. Operating speed – 21,10 km/h, the technical readiness coefficient – 0,923, buses graduation rate on the line – 0,919.

The distance between the stops is 800–1000 meters, between traffic lights – 300–500 meters.

Under the scheme of bus routes number of turns is about 10–15 units.

The operating speed varies within 10,8–14,0 km/h in different routes. Solutions of coordination of optimum engine operation regimes with moving conditions of the vehicle are reflected in scientific works [7, 5–213].

Production and technical base provides timely technical maintenance of buses. It consists of three sections which run on the territory of the bus fleet, which are equipped with modern technological equipment in the areas of service and repair.

Reliability of the vehicle is put in the design, obtained in manufacturing and is realized in operation.

Reliability of buses for specific operating conditions largely depends on the accepted regimes of maintenance and repair in the automotive companies.

Development of maintenance regimes of buses performed by the usual method taking into account the specific conditions of operation and features of the bus structure.

Maintenance regime is corrected considering certain operating conditions.

There are resource and operational corrections.

The essence of the resource correction is that the regulations of car operation vary with respect to the reference is corrected using the correction factors for these conditions [2, 139–149].

At resource correcting the maintenance interval is based on regulations, set in “Regulations on maintenance and repair of the vehicles” and “Operation manual of Mercedes-Benz cars O 405” [3; 4; 5].

At operational correcting by considering results of the resource correcting of buses’ maintenance, as well as at the joint analysis of the experience of the service station, of results of chronometry data and expert evaluating the specialists, the maintenance regimes have been developing for specific conditions of buses operation.

The effectiveness of the maintenance and repair system is characterized by a list of operations, interval, species number and the multiplicity of maintenance [6].

Development of maintenance regime is performed in the following sequence:

1. Resource correcting of bus service interval. Choosing regulations for Mercedes-Benz O 405 from operation manual of buses Mercedes-Benz.

The recommended maintenance interval for buses Mercedes-Benz O 405 for Europe conditions is 45000 km [2; 3; 4].

2. For real operating conditions of Tashkent city considering the third category of operating conditions, hot climate region, as well as the quality of fuel (sulphur content) recommended maintenance interval is 15 000 km.

According to results of analysis of maintenance interval based on operation experience of service station for buses Mercedes-Benz O 405, the following intervals and types of services are accepted:  $L_{15} = 15\ 000$  km,  $L_{30} = 30\ 000$  km,  $L_{45} = 45\ 000$  km,  $L_{90} = 90\ 000$  km.

3. Choosing the list of operations from “Manuals for Mercedes-Benz buses”.

Taking into account the operating experience of service station the list of maintenance operations of buses for the specific conditions will be set.

4. Determining the complexity of the maintenance operation for specific conditions of buses operation by experiment (by timing).

5. To organize the technologic process of Mercedes-Benz buses a flow chart (check lists) of maintenance operation develops by intervals  $L_{15} = 15\ 000$  km,  $L_{30} = 30\ 000$  km,  $L_{45} = 45\ 000$  km,  $L_{90} = 90\ 000$  km.

On check lists of maintenance operation a code of operation of maintenance of structural group buses is used.

In carrying out the maintenance  $L_{15} = 15\ 000$  km, a work is done according to routine of maintenance  $L_{15} = 15\ 000$  km.

In carrying out the  $L_{30} = 30\ 000$  km, the works of  $L_{15} = 15\ 000$  km are done and additional works, which are not included to the list of  $L_{15} = 15\ 000$  km are done too;

In carrying out the  $L_{45} = 45\ 000$  km, the works of  $L_{30} = 30\ 000$  km are done and additional works, which are not included to the list of  $L_{30} = 30\ 000$  km are done too;

In carrying out the  $L_{90} = 90\ 000$  km, the works of  $L_{45} = 45\ 000$  km are done and additional works not included to the list of  $L_{45} = 45\ 000$  km are done too.

On the base of conducted researches the following complexity of maintenance of buses are set for buses of Mercedes-Benz O 405:  $t_{15} = 33,0$  person hour,  $t_{30} = 33,0$  person. hour,  $t_{45} = 50,06$  person. hour,  $t_{90} = 68,7$  person. hour.

The results of research on the development of maintenance regimes of Mercedes-Benz O 405 buses in actual operating conditions are applied in motor enterprises and service stations in Tashkent, and in educational process [6, 247–260], in preparation of bachelors on a branch 5521200 – “Maintenance and repair of vehicles” and masters on a specialty 5A521205, “Automobiles and automotive economy”.

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## Section 11. Physics

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### The properties of photon and electron. Part I

**Abstract:** the subject of the present work is devoted to the study of essence and sense of basic physical properties of photon and electron; relativity of perception of properties of these particles is also discussed.

**Keywords:** photon, electron, structure, field generation, interaction, virtuality and relativity of observation.

*Perceiving the essence of things,  
We gain knowledge.  
And understanding the sense of things,  
We create consciousness [1].*

#### Introduction

1. Tendency to non-application of complex mathematics was used in this work. This creates a condition, which let focus major attention on the logic of existence of specific electron properties that characterize it as a fundamental natural phenomenon, and which accordingly promotes a more comprehensive understanding of its real physical essence and sense.

2. Nonlinear effects are not considered in the work, since their influence does not violate the logic of the essence of what is going on.

3. Many physical forecasts, notions and conclusions, which are made in the current work, relate also to other elementary particles.

4. All physical equations, values and constants are used in the CGS measurement system (The centimeter–gram–second system of units).

On the example of electron, we introduce two fundamental constants:

$$m_e r_k = \mathbf{k}, \quad (1)$$

$$\omega_e r_k = c, \quad (2)$$

where:  $m_e$  – rest mass;  $\omega_e$  – frequency of internal energy oscillations;  $r_k$  – Compton radius, which is determined from the ratio  $\lambda_k = 2\pi r_k$ , where  $\lambda_k$  – Compton wave length;  $c$  – light speed in vacuum;

**Definition № 1:** Constants  $\mathbf{k}$  and  $c$  determine the action of mass and frequency of elementary particle within its Compton radius.

The following equations (3, 4, 5) prove the fact that the fundamental constant  $\mathbf{k}$  has a right for universal existence.

Multiplying both sides of the equation (1) by the light speed, we obtain:

$$m_e c r_k = \mathbf{k} c = \mathbf{h}, \quad (3)$$

where:  $\mathbf{h}$  – Planck's constant, which determines the action of impulse of electron internal energy within its Compton radius.

Multiplying both sides of the equation (3) by the light speed, we obtain:

$$E_{el} r_k = m_e c^2 r_k = \mathbf{k} c^2 = \mathbf{h} c = \mathbf{q}^2, \quad (4)$$

where  $\mathbf{q}$  – “blank” electron charge,  $E_{el} = m_e c^2$  – electron internal energy, which acts within its Compton radius.

In the equation (4) we decrease the charge  $\mathbf{q}^2$  by the value  $\beta^2$  and obtain:

$$e^2 \beta^2 = \mathbf{q}^2, \quad (5)$$

where  $\beta$  is determined by the equation:  $\beta^2 \alpha = 1$ ,  $\alpha$  – fine structure constant;

$e$  – electron electric charge, included into Coulomb's law:  $\mathbf{F} = e^2 / r^2$

We write down the equation (4) in the form:

$$m_e c^2 r_k = \mathbf{q}^2. \quad (6)$$

Several fundamental conclusions come from analysis of the equation (6):

1. Full electron internal energy  $m_e c^2$ , which acts within Compton radius  $r_k$ , determines the generation of full electron intrinsic charge  $\mathbf{q}$ .

2. Admission of fullness of electron internal energy  $m_e c^2$  and fullness of its charge  $\mathbf{q}$  in the equation (6) let us conclude, that the real electron radius  $r_e$  concurs with  $r_k$ , i. e.:

$$r_e = r_k = \mathbf{q}^2 / m_e c^2. \quad (7)$$

3. We write down the commonly known equation for classical electron radius:

$$r_{cl} = e^2 / m_e c^2. \quad (8)$$

In a series of scientific works a wrong conclusion was made from the equation (8), that the electron full energy  $m_e c^2$  corresponds to the full energy of electron electrical field  $E_{el} = e^2 / r_{cl}$ . In reality it is not so! As  $e$  is not a full electron charge, but only a small part of it, which is less than  $\mathbf{q}$  in  $\beta$  times, which exactly follows from the equation (5):  $e\beta = \mathbf{q}$ . Essence and sense of classical electron radius  $r_{cl}$  is that it is not real, but virtual, i. e. unobservable. Therefore, there is no possibility to look for explanation to random coincidence of electron radius with the radius of action of nuclear forces.

The essence of the current problem is that full charge  $\mathbf{q}$  and electrical charge  $e$  of the electron are intrinsically not the same.

**Definition № 2:** The relativity of observation over the electron, i. e. from inside or outside, characterizes its different physical perception.

Electron charge  $\mathbf{q}$  determines not only the electron electrostatic field, but also fully determines all kinds of interaction of electron

with the surrounding environment, which includes not only physical vacuum, (in determination of quantum electrodynamics and chromodynamics), but also the fact of existence of dark matter and dark energy. All interactions of electron with the environment occur on the external side of the electron surface, confined by the sphere  $r_k$ , as a result of which the formation of electrical and gravitational fields takes place exactly on this surface, as well as interaction with different virtual particles of the vacuum and probably something else.

In this regard Victor F. Weisskopf [2, 85] made a suggestion in 1972 that formula of electrical field, which encompasses the electron at rest,

$$\mathbf{E}_{el} = \mathbf{e}/r^2, \quad (9)$$

(where  $\mathbf{r}$  – distance from the electron centre) is not correct inside the electron, moreover, in his opinion, it is convenient to assume, that the electron charge  $\mathbf{e}$  is concentrated on the surface of the sphere  $r_{cl}$ , and inside the electron –  $\mathbf{E}_{el} = \mathbf{0}$ .

According to the abovementioned analysis, inside the electron indeed there is an electrical field generated by the electron  $\mathbf{E}_{el} = \mathbf{0}$ , however, the reason of such conjecture needs to be specified. In the equation (9)  $\mathbf{r}$  can not take on values within the range of values  $\mathbf{0}-r_k$ , as the electron generates its own electrical field  $\mathbf{E}_{el}$  on its surface and to the external environment. The electron charge is indeed concentrated on the electron surface, but its full part  $\mathbf{q}$  rather than its small part  $\mathbf{e}$ , besides, within the surface of the electron sphere  $r_k$ . Hence it appears that, if the electron charge  $\mathbf{q}$  is concentrated on the surface of the sphere  $r_k$ , then consequently the electron internal energy  $\mathbf{m}_e c^2$ , which is a carrier of the charge  $\mathbf{q}$ , is in the same place most of the time. Obviousness of this judgment results also from the fact that the amount of time spent by the electron on generation of electrical and gravitational fields, and also on interactions with all representatives of the environment is somewhat more than duration of the half-period of electron internal energy oscillations.

Let us note another equally important conjecture: distribution of the charge density  $\mathbf{q}$  during one half-period of the electron internal energy oscillations occurs with increment in the direction of the propagation gradient of the electron internal energy towards the surface of the sphere  $r_k$ , besides, distribution of the charge density  $\mathbf{q}$  has a linear dimension. This conclusion can be easily confirmed by reduction to absurdity. For this purpose we consider the ratio between Compton radius and classical electron radius. Solving simultaneously the equations (5, 7, 8), we obtain:

$$\mathbf{q}^2/\mathbf{e}^2 = r_k/r_{cl} = \beta^2. \quad (10)$$

From the equation (10) it follows that if we increase the degree of radiuses to 2 D or 3 D dimensionality, then we would have to increase the degree of  $\beta$ , which is not possible.

The conclusion, that inside the electron  $\mathbf{E}_{el} \sim \mathbf{0}$ , is also confirmed by the following circumstances: according to the modern notions of elementary particle physics, the electron is defined as indivisible and structureless particle with the sizes up to less than  $10^{-18}$  cm, moreover, there are recent conjectures that its size is within the range of Planck's values up to  $\mathbf{r} \sim 10^{-33}$  cm. All these circumstances are unlikely, at least because they contradict to the simple reduction to absurdity, from which it follows that in the case of decrease of  $r_k$  in the equation (1) it is impossible to preserve the existing electron energy within the range  $\mathbf{E}_{el} = \mathbf{m}_e c^2$ , remaining always within the fundamental constant  $\mathbf{k}$ . Thus, from the corpuscular viewpoint ( $\mathbf{E}_{el} = \mathbf{m}_e c^2$ ), the electron is really a structureless particle, and, on the contrary, from the wave viewpoint – the electromagnetic field inside the electron is fairly structured.

Thus, it begs the question: if inside the electron is  $\mathbf{E}_{el} \sim \mathbf{0}$ , and charge  $\mathbf{q}$  and energy  $\mathbf{m}_e c^2$  are concentrated on its surface, what is

then inside the electron? In order to find the answer to this question, we consider the result of addition of two equations (1 and 2):

$$\mathbf{m}_e = (\mathbf{k}/c) \omega_e, \quad (11)$$

Then, multiplying both sides of the equation (11) by  $c^2$ , and taking the equation (3) into account, we obtain:

$$\mathbf{m}_e c^2 = \hbar \omega_e. \quad (12)$$

The important conclusion follows from the equation (11), that the existence of mass of the electron at rest is determined by oscillation frequency of some electron internal energy. It is reasonable to assume, that this energy has electromagnetic origin at least due to the fact that electron-positron annihilation results in origination of electromagnetic radiation quanta. And thus, understanding of electron intrinsic properties follow largely from the understanding of photon physical properties. From the equations (11 and 12) it follows that electron internal energy, its mass and frequency are intrinsically the same:

$$\mathbf{E}_{el} = \mathbf{m}_e c^2 = \hbar \omega_e. \quad (13)$$

**Definition № 3:** The mass is intrinsically a closed flow of energy.

The fundamental conclusion about relativity of perception of the electron follows from the equation (13). If we observe the electron from its surrounding environment, then we define the action of its energy as the particle, where  $\mathbf{E}_{el} = \mathbf{m}_e c^2$ , and if we observe it from inside, then the action of its internal energy is presented as photon, i. e. electromagnetic field quantum, where  $\mathbf{E}_{el} = \hbar \omega_e$ . Substantial structural difference between internal energy of photon and electron is that free photon owes its motion to its internal magnetic constituent of electromagnetic field, which twice during one oscillation period shifts lateral oscillations of the electrical field forward along-track direction, and the same occurs inside the electron, except that during one period the electrical field oscillations shift once forwards and once backwards. Figuratively speaking, photon “runs” uninterruptedly forward, and electron “runs” uninterruptedly on the site. This conclusion becomes possible regardless of the modern notions that photon is a stable, structureless elementary particle, and on the other hand, thanks to the recent discovery of photon decay in the external magnetic field with polarization change of newly born photons. Therefore, during the dispersion on crystal lattice at classic speed values, the electron leaves on the screen a diffraction pattern, which is typical for dispersion of electromagnetic wave, which it is actually inside.

Even more important conclusion follows from the equation (11, 13) and definition № 3, that the electron mass  $\mathbf{m}_e$  is not a scalar value, but has vector properties, as exactly  $\omega_e$  is intrinsically a vector value. Scalar properties of the electron mass are important only in the case of averaging out the amount of the internal oscillations of its electromagnetic field for a much longer period of time than the period of one oscillation.

**Definition № 4:** The mass has, intrinsically, vector properties.

The modern standard model of the universe structure defines the photon also as the particle with zero rest mass and zero electrical charge. All current experiments confirm that photon has no charge with accuracy up to  $10^{-33} \mathbf{e}$  and no mass with accuracy up to  $10^{-22} \mathbf{m}_e$ . However, as early as at the beginning of the previous century Eddington proved experimentally that starlight rays are diffracted by the sun; and in Pound and Rebka's experiments it was established that photons, which move in the direction of gravitational field, experience the change of frequency. The apparent paradox follows from these experiments. If we admit that rest mass of photon is zero, then what does attract the sun? And if we admit that in gravitational terms the sun attracts the energy of photons, then we must admit that the description of gravity, which is determined by Newton's universal law of gravitation



$$\mathbf{F}_{gr} = \gamma \mathbf{m}^2 / \mathbf{r}^2, \quad (14)$$

(where  $\gamma$  – gravitational constant,  $\mathbf{m}$  – the mass of interacting objects), needs to be clarified, thus in this case the equation (14) does not fully correspond to the description of the nature of interacting objects. The paradox is eliminated, if we accept the requirement resulting from the Eddington's experiments, related to the extension of the very essence of the concept "gravitational interaction" and hence a respective extension of its description. Extension of the description of gravitational interaction shall be that Newton's equation should include energies of interacting objects, rather than their masses. Although masses are perceived easier and more convenient in earthly sense, despite the fact that the mass is just the proportionality coefficient between force and acceleration, but energy is fundamental in its essence. Introduction of appropriate changes into the equation (14) leads to an equivalent, but expanded in its essence, description of Newton's universal law of gravitation:

$$\mathbf{F}_{gr} = \mathbf{gE}^2 / \mathbf{r}^2, \quad (15)$$

where  $\mathbf{g} = \gamma / \mathbf{c}^4$ ,  $\mathbf{E} = \mathbf{mc}^2 = \hbar \omega$ .

On the other hand, curvature of the photon motion trajectory in the aquatorium of the sun owes its origin to the presence of closed (i. e., lateral towards the photon motion trajectory) oscillations of electric and magnetic component of the photon electromagnetic field, i. e. direction of the vector of these oscillations concurs with the vector of the source gravitational field. Thus, admitting the vector nature of oscillations of fields inside the photon, we must also admit the vector nature of photon mass that corresponds to these oscillations:

$$\mathbf{m} = \hbar \omega / \mathbf{c}^2 \quad (16)$$

Vector nature of the mass is also confirmed by the experiments on study of the photon motion towards the source of gravitational field. In this case, the photon frequency increases as its density increases when it approaches the source of the gravitational field, and, consequently, its elasticity increases, which reacts against lateral oscillations of the photon inner fields. The absence of changes in the photon motion speed towards the source of gravitational field indicates that inside photon there are no lengthwise field oscillations.

**Definition № 5:** Stability of the light speed is determined by the fact that inside the photon there are no oscillations in the direction of its motion trajectory.

Let us write down the equation (6) as follows:

$$\mathbf{m}_e \mathbf{c}^2 = \mathbf{q}^2 / \mathbf{r}_k. \quad (17)$$

From the analysis of the equation (17) it follows that the left part represents the internal energy of one electron, and the right part — interaction energy within the radius  $\mathbf{r}_k$  of quasi two electrons, i. e. in the equation there is no equality in relation to the amount of particles. Logic of formulation of the equations (1–4) presupposed the construction of mathematical expressions for main values that characterize the properties of one electron, but in the equation (4)

quasi second charge appears, but of the virtual electron. What is connected with it? To answer this question, let us consider the conclusion that describes the reason for the photon frequency increase when it moves towards the source of gravitational field. According to this conclusion, internal oscillations of the electron electromagnetic field also have to elastically interact with external fields, which are constantly present in its surrounding environment. As the result of elastic interaction, the electron internal energy  $\mathbf{m}_e \mathbf{c}^2$  produces not only the internal charge  $\mathbf{q}$  of its own electron, but also creates a similar charge  $\mathbf{q}$  of the virtual electron in the external environment, as shown in the equation (17).

**Definition № 6:** the electron exists steadily due to the existence of stable elastic density of respective fields of the environment.

The examples of virtual parameters of the electron are presented below.

1. It is known [2, 45; 3, 50] that the electron charge  $\mathbf{q}$  polarizes around itself the electron-positron pairs  $\mathbf{e}^+ \mathbf{e}^-$ , present in the vacuum, which in their turn screen the primary electron charge  $\mathbf{q}$ , lowering its value in  $\beta$  times up to the value  $\mathbf{e}$ , which is the main source of the electron electric field (9), then the virtual charge and the classical radius of the electron take the following form:

$$\mathbf{e} = \mathbf{q} / \beta, \quad \mathbf{r}_{cl} = \mathbf{e}^2 / \mathbf{m}_e \mathbf{c}^2 = \mathbf{r}_k / \beta^2$$

2. It is known [2, 91–93], that the electron charge  $\mathbf{q}$  is influenced by the electric field of the virtual photons of vacuum, which leads to the fact that the electron moves with a certain mean square displacement, like Brownian particle. In this regard, there is some effective indistinctness of its sizes and, consequently, the shift of electron energy levels, the so-called Lamb shift, as the result of which a virtual Lamb radius and charge emerge:

$$\mathbf{q}_v = \mathbf{q} / \beta^{1/2}, \quad \mathbf{r}_v = \mathbf{r}_k / \beta.$$

3. Despite the fact that the electron gravitational field  $\mathbf{E}_{gr} = \gamma \mathbf{m}_e / \mathbf{r}^2$  is weaker than electrostatic one  $\mathbf{E}_{el} = \mathbf{e} / \mathbf{r}^2$  in about  $10^{25}$  times, however, its generation is obviously connected with the electron internal energy and respectively with only virtual charge  $\mathbf{q}$ , which determines emergence of the electron gravitational field.

Concluding the first part of this work, it is difficult not to recall the optimistic words of the great creator of the classical electron theory Lorentz G. A. [4, 38]: "I speak so boldly about what is going on inside the electron, as if I managed to look inside of these small particles, and afraid that someone would think that it was better not to try to go into all these details. My excuse is that, if we need to have a quite definite equation system, we should not act otherwise; moreover, as we will see further, the experience can really give some indication about size of electrons."

In my defense I will refer to the words of the unknown author: "You can say the right words, but talking nonsense at the same time; and you can say the wrong words, but trying thus to send the important message."

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## Section 12. Chemistry

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### Thermodynamics and mutual distribution of macromolecules in the systems: chlorine-chlorocontaining polymers

**Abstract:** It is shown that the values of the parameter of solubility method and OGH and TDT can be used for predicting solubility parameter for polymers.

**Keywords:** polymer-polymer mixtures, chlorinated polyethylenes (CPE), polymethylmethacrylate (PMMA), polyethylene of low density (PELD), chlorocarboxylated polyethylene of low density (CCPE) chlorinated PELD (CPE), polyvinyl chloride (PVC), criteria of compatibility, chlorination, upper and lower critical temperature, specific holding of volume, Gibbs mixing energy, parameter of solubility, distribution of macromolecules, chlorine-chlorocontaining polymers, polar groups, thermodynamical compatibility, sorbate, gas-carrier.

Need of industry in new polymer materials, possessing by necessary properties for work in extremal conditions continuously increase. It may be achieved by synthesis of the new types of polymers and creation of polymer compositions where properties of the separate components additively are the complement of one another.

Therefore development of different polymer compositions by simplification of technology its production and processing, shortening expenditures on production of materials with necessary complexes of properties is extremely actual.

For production of the new types of polymer materials by use of polymer-polymer mixtures determination of its thermodynamical stability as one of the factors, determining a structure and properties of the final product acquire essential interest.

Use of chlorocontaining polymers in industry, stipulated by complex of enough good properties determine the desire to improvement of series them indices. From this point of view research of thermodynamical conduct of chloropolymers mixtures with another chloropolymers, having in their composition the polar groups of chloropolymers present a special interest.

In the work the thermodynamical compatibility of chlorinated polyethylenes (CPE) with different chlorination degree, shown that by dominant of dispersion forces compatibility is possible by proximity parameters of solubility and interaction. Analysis of compatible and incompatible pairs shown that:

- by difference in chlorine content, reaching;
- 18 mas%  $\Delta H_m$  is relatively high (+0.519 Joule/g).

Owing to big difference in thermal coefficients expansion –  $T \Delta S_m$  is positive (+ 0.276 Joule/g). The total energy  $\Delta G_m$  is positive (+ 0.795 Joule/g). From this it is concluded that a mixture must be immixing (incompatible);

– by approximately near content of chlorine (27 and 35 mas%) the dispersion forces between molecule, owing to similarity lead to little interaction degree. By calculation, a big difference in thermal coefficients expansion gives a little negative value  $\Delta H_m$  (– 0.108 Joule/g). But this difference causes a big positive –  $T \Delta S_m$  (+ 0.761 Joule/g) and in result  $\Delta G_m$  (+0.653 Joule/g) doesn't favourable to mixing.

It have been determined, that uniting criteria of compatibility  $\Delta G_m < 0$  in total case is carried out, although a structural compatibility is possible also by little positive values of  $\Delta G_m$ . In all cases the surplus energy  $\Delta S_m$  doesn't favourable to mixing, but by proximity of per cent content of chlorine and coefficient of thermal expansion the compatibility is possible.

In the work the system (CPE – PMMA) have been studied. It was shown that polymethylmethacrylate (PMMA) is compatible with chlorinated polyethylene by appointed chlorination degree of the last and only by appointed temperatures. It have been determined that a mixtures have an upper and lower critical temperatures of solubility.

The present work devotes to study of thermodynamic interaction between components mixture of chlorocontaining polymers, one of which in its composition have a polar carboxylic groupings. By that the method of turned gas chromatography have been used, which at the last time is widely applied for study of polymers compatibility.

As initial raw materials the industrial samples of polymers: chlorocarboxylated polyethylene of low density PELD (CCPE) with content of chlorine equal 27 mas% and carboxylic groups 1.2 mas.% correspondingly, chlorinated PELD (XPE) with chlorine content 35 mas.% and polyvinylchloride (PVC) by brand C-70 have been used, the characteristics of which are presented in the table.

Table 1. – Characteristic of investigated polymers

polymer	content of chlorine mas. %	content of carboxylic groups, mas. %	alcohol ethyl propyl alcohol	D: B:0	M·10 <sup>-4</sup>	M·10 <sup>-3</sup>	M/M	by 298 K, g/sm <sup>2</sup>	k·1·10 <sup>-4</sup>	T <sub>c</sub> K
CCPE	2.7	1.2	–	–	3.5	5.7	6.11	1.0713	8.64	239
CPE	35	–	–	–	3.5	5.8	6.08	1.0713	5.80	263
PVC	57	–	–	–	15.0	47.0	3.19	1.3446	3.09	349
packing products	–	–	–	4:3:1	3.0	10.2	2.95	1.2284	4.63	238
SKEP	–	–	1.0	–	9.0	30.2	2.98	0.8723	8.59	2.11

*D: B:0\** – 4.4 – diphenylmethanediisocyanate;

*1.4* – butadiol: oligoethylenebutyleneglycol adipinate

For research the chromatographic columns with individual polymers and its mixtures by correlation of components 30:40, 50:50, 70:20 have been prepared/In the work the chromatograph “Tsvet-100” with flame ionization detector have been used. As a

gas-carrier the nitrogen and as sorbate ten solvents, relating to different classes (alcohols, ketons and chloroderivatives of aliphatic hydrocarbons) have been used.

## Section 13. Economics and management

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### Ways of sustainable development of Ukraine in the conditions of current instability

**Abstract:** The article examines the factors that threaten macroeconomic stability of Ukraine. Analyses challenges in budgetary sector that affect fiscal policy of the country, as well as determines the directions to overcome the crisis and defines priorities for the forthcoming development of Ukraine within the period until 2020.

**Keywords:** strategy of sustainable development, motion vectors, reforms, investment climate, macroeconomic indicators.

Tax system plays an important role in the process of strengthening the financial security of the country. In regards to the complexity of the system of economic relations in the country and the world, it requires constant development and improvement. During the years of independence of Ukraine the process of tax system reforming obtained certain permanent features. However, it did not become the defining driver of sustainable long-term socio-economic growth.

Analysis of the economy of Ukraine indicates that there is a number of weak points in the fiscal sector that cause serious challenges.

According to the World Bank estimates the growing needs of public infrastructure (including its repair due to depreciation) in 2006–2015 amounted to 100 bln. dollars USA [1]. Given the type of necessary basic infrastructure there is a need to increase the current level of spending in public infrastructure by at least three times.

Due to the limited competition in all sectors that slows down the implementation and further upgrading of technology, the country failed over the last decade to upgrade its technology base and it got stuck on the way to extensive, product oriented growth which is also enhanced by increasing instability and limited productivity growth. This vicious circle prevents country from restructuring of its economy and restrains the achievement of higher levels of per capita income as well as living standards of citizens of Ukraine.

Unreformed pension system and aging population of Ukraine (over 14 millions retired people) threaten the short-term fiscal sustainability (to finance them becomes more difficult) and long-term stability (up to 2020 there will be one retiree per each pension tax payer and eventually this ratio will change for worse). Life expectancy in the country is 71 years old, this is 10 years less than the average EU level.

The education system is facing a reduction in the ranks of students. Economy requires improving of the quality of education, but without spending additional resources on it.

All mentioned above requirements should be met with gradual and parallel decrease of state intervention in the economy and creation of the conditions for wider involvement of private sector.

For now Ukraine, it seems, fell into the trap of a long-term stagnation caused by factors listed in Figure 1. Distrust related to bad governance and corruption is the main obstacle on the way to attract foreign direct investments.

Entrepreneurs face a lot of rules and regulations, complex procedures of obtaining permits and licenses, outdated regulations and certification requirements, as well as insufficient legislation in the sphere of real estate ownership (including land), contractual rights and intellectual property rights.

Barriers to entry associate with the high cost for transportation and logistics services. While competition law is generally consistent with international practice, its application in some cases is under political pressure.

On the way of capital inflow there are macroeconomic imbalances and fears associated also with fiscal policy. Marginal rates for direct taxes are high. While the average tax burden is not significantly higher than in other European countries, it is high enough compared to countries with the same level of income, and other countries in transition phase. High costs are also associated with tax compliance (including frequent and aggravating audits).

An important step in overcoming the crisis was the signing of the Decree “Strategy of Sustainable Development “Ukraine – 2020” by the President of Ukraine in January 12<sup>th</sup>, 2015.

With regards to the European aspirations of Ukraine, the main document to determine the direction and priorities of Ukraine for the period until 2020 was the Strategy of Sustainable Development of the European Union developed by European countries in June 2001 and confirmed in adopted in 2010 Communication from the European Commission “Europe 2020” in which EU member states have identified five ambitious goals by 2020 in the areas such as labor employment, innovation development, education, social integration, climate/energy [2]. However, each member state has developed its own national targets in each of these areas, and concrete measures on the national level to be taken with a view to their implementation.

Strategy of Sustainable Development “Ukraine – 2020” identified four vectors of directions: sustainable development; security, business and citizens; responsibility and social justice; pride for Ukraine in Europe and worldwide, — including 62 reforms with the following priorities: reform of national defense and security system, renewal of authorities and anti-corruption reform, judicial reform, law enforcement reform, decentralization and public administration reform, deregulation and enterprise development, reform of health care system, tax reform.



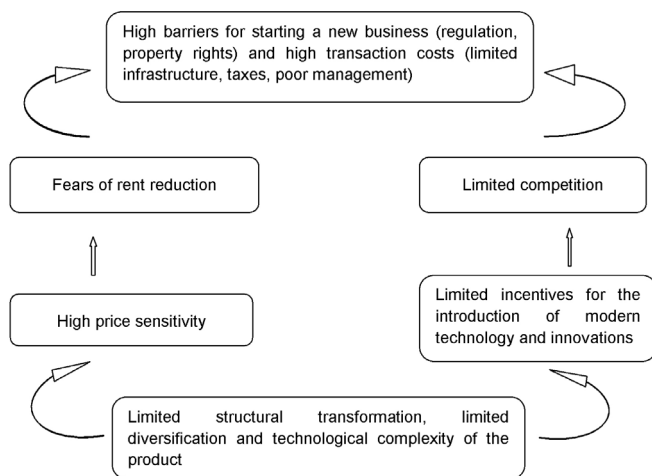


Figure 1. Factors that hinder investments, competition development and structural adjustment in Ukraine

Realization of defined strategy suggests accomplishment of 25 key indicators that evaluate the implementation process of reforms and programs, including: achieving a place among the first 30 positions in the World Bank “Doing Business”; net FDI inflow for the period of 2015–2020 in the amount of more than 40 bln. dollars USA, according to the World Bank; maximum ratio of budget deficit to gross domestic product (GDP) estimated by the IMF less than 3%; spending on national security and defense should be not less than 3% of GDP; based on the corruption perception index calculated by Transparency International, Ukraine should be among the top 50 countries in the world; the World Bank estimated increase in human life expectancy by 3 years for Ukraine; based on the results of the international study of education quality PISA, Ukraine should be among the top 50 countries [3].

The research results of “Doing Business” in Ukraine conducted by the World Bank Group from 2014 to 2017 indicate that country is approaching the best practices, however, at the same time not all reforms are conducted in the efficient way (see Table 1).

Table 1. – Rating for Ukraine reforms implemented in 2014–2017

Year	Rating, %%							
	Company registration	Obtaining building permits	Property registration	Getting credit	Taxation	International trade	Enforcement of contracts (quality of justice)	General
2014	47	41	97	13	164	148	45	112
2015	70	139	64	17	106	109	98	87
2016	24	137	62	19	83	110	93	81
2017	20	140	63	20	84	115	81	80

Note. Table compiled from data [4; 5].

Yet, drastic reforms undertaken in 2014 and 2015 helped to stabilize the economy and improved the investment climate. According to macroeconomic indicators presented in Table 2 GDP growth in 2016 was 2.3% compared to 16% decline accumulated during the period of two previous years.

Growth of gross fixed capital formation in 2016 exceeded 20% due to increased investment in production machinery and equipment [6], indicating improved investment environment.

The poverty rate after a significant increase from 15% in 2014 to 22% in 2015 because of a deep economic recession and high inflation began to decline in 2016 and was 11%.

Inflation decreased from 43.3% at the end of 2015 to 12.4% in 2016. However, the labor market situation remains difficult, the

unemployment rate increased from 9.1% in 2015 to 9.3% in 2016, while spending on pensions in 2016 amounted to 10.8% of GDP, leading to the formation of the pension fund deficit at around 5% of GDP [6] and is currently a major fiscal risks.

However, due to increased economic activity in 2016 some tax revenues exceeded expectations from value added tax, tax on personal income and corporate income tax revenues increased by 7.6%, 13.1% and 25.7% respectively [7].

State direct and guaranteed debt of Ukraine in 2016 increased to 81.2% of GDP (mainly through Privat recapitalization in December 2016), but the growth of foreign direct investment, which mainly associated with an increase in banks’ capital was sufficient and international reserves increased to 15,5 bln. dollars USA [6].

Table 2. – Major macroeconomic indicators of Ukraine

	2014	2015	2016	2017*	2018*	2019*
Nominal GDP, bln. UAH	1,587	1,980	2,383	2,735	3,085	3,450
Real GDP,% change	- 6.6	- 9.8	2.3	2.0	3.5	4.0
Consumption,% change	- 6.2	-15.9	1.4	3.1	2.8	3.3
Exports,% change	- 14.2	- 13.2	- 1.6	1.6	3.0	5.0
Imports,% change	- 22.1	- 17.9	8.4	1.7	1.6	6.7
External debt,% of GDP	97.6	131.5	129.6	131.6	125.4	107.5
Budget revenues% of GDP	40.3	42.1	38.4	38.8	38.9	39.0
Budget expenditure% of GDP	44.8	43.2	40.6	41.9	41.5	41.4
Balance of the budget expanded government,% of GDP	- 4.5	- 1.2	- 2.2	- 3.1	- 2.6	- 2.4
State and guarantor. debt% of GDP	70.3	79.4	81.2	88.8	83.5	75.9

\* – World Bank forecast

Note. Table compiled from data [6].

World Bank forecast economic growth in Ukraine remains moderate: in 2017–2% in 2018–3.5% and in 2019–4% [8] in the slow process of reform in a complex political environment. In addition, from January 2017 exacerbated the conflict in eastern Ukraine, there is a negative impact of the termination of trade with not by controlled territories of Donetsk region for two such important sectors as metallurgy and electricity (short steel exports and increasing imports of coal may lead to increase in 2017 the deficit of the current deficit to 4.1% of GDP).

Challenges in the public sector are also significant in 2017 is expected to increase the government deficit expanded to up to 3.1%

of GDP by increasing minimum wages and a large pension fund deficit, bringing public and publicly guaranteed debt will rise to almost 89% of GDP.

To maintain macroeconomic stability and ensure a gradual reduction of the debt burden (net repayment of foreign loans is estimated at 7 bln. dollars USA per year for 2017–2019) fiscal policy Ukraine should ensure deficit reduction in 2020 to a level that does not exceed 2% of GDP. Achieving this level of deficit requires a system of fiscal consolidation, supported by thorough structural reforms in tax administration, broadening the tax base, reform of the pension and social security.

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## Improving the regulatory framework of financial accounting and reporting the tourist organizations of Uzbekistan

**Abstract:** The article deals with questions of normative and legal basis of the organization of the financial accounting and reporting in the tourist organizations of the Republic of Uzbekistan.

**Keywords:** regulatory-legal framework, law, financial accounting, reporting, travel agency.

In my opinion, the topic of “State of the tourism management” is one of the most interesting submitted for consideration.

The urgency of this problem lies in the fact that tourism is an integral part of the lives of people on the planet. This is a complex, high-yield interdisciplinary complex represents one of the major sectors of the world economy, promotes a high level of employment, as well as development, economic cohesion and cultural diversity of the world.

The experience of different countries shows that the success of tourism development depends on how at the state level, this industry is perceived as it enjoys government support. Any civilized state to receive income from the tourism industry in the budget, should invest in the research of their territories to assess the tourism potential, the preparation of tourism business development programs, projects, infrastructure and resort areas and tourist centers and in advertising [1].

Of private sector will never be able to cover the large investment needs for the development of the resort, hotel, tourism enterprises. All travel powers have such organizations, subordinates, as a rule, the ministries that are engaged in the development of national programs for the development of tourism: in Veliko Britain — BTA (British Tourist Authority), in Spain — Turespana, Norway — NOR-TRA. They contain a representation of tourism in other countries, they develop into tourist attractions of the program and ensure the flow of tourist information.

The specifics of tourism associated with the international character and the wide range of relations, which have to engage those involved in the organization of leisure and travel. This increases the complexity of the legal regulation.

In any state relations “tourist — travel agency”, “tourist-state”, “travel agency-state”, is regulated by the relevant legislation. Depending on the state of civilization, its degree of approximation to the

concept of the rule of law, legislation to become more detailed and complete.

Tourism, the activities of persons traveling to and staying in places outside their usual environment for a period not exceeding one year in a row, in order to rest and other business interests [2].

According to the Law "About bases of tourist activity in the Republic of Uzbekistan" Tourism — temporary visits of citizens of the Republic of Uzbekistan, foreign citizens and stateless persons with permanent residence in the medical and sanitary, recreational, educational, professional, business and other purposes not engage in activities related to the receipt of income from sources in the country (place) of temporary stay.

According to the report agency Tourism of the Republic of Uzbekistan, the main factors hindering the development of outbound and inbound tourism in the Republic of Uzbekistan, is: [3].

The image of the Republic of Uzbekistan as a country hostile to tourism, to create a separate means of foreign media; the current procedure for issuing visas to citizens of Uzbek foreign countries; underdeveloped tourist infrastructure, a small number of hotel accommodation facilities (2–3 "stars") with a modern level of comfort, the discrepancy of price, quality hotels and others.

While maintaining the current situation in the Republic of Uzbekistan in the sphere of tourism in the coming years would be a reduction of inbound tourism and outbound tourism increase of Uzbek citizens abroad, which, respectively, will result in: an increase in prices for tourist services and reduce tourism to the public; an outflow of young and promising personnel abroad, a decrease of employment, to reduce receipts from tourism in the budgets of all levels.

Thus, in the field of tourism policy should be aimed at the formation of the Republic of Uzbekistan in the modern tourist complex, providing ample opportunities to meet the needs of Russian and foreign citizens in tourism services, ensuring the conditions for sustainable tourism development.

The state should ensure the formation of a competitive Russian tourist market, improving the quality of tourist services, the advertising image promotion of the Republic of Uzbekistan as a country favorable for tourism, development of priority tourist centers.

In the Republic of Uzbekistan carries out the management of tourist activity Tourism Agency. And also have an effect on tourism: The Ministry of Foreign Affairs of the Republic of Uzbekistan, the Ministry of Internal Affairs of the Republic of Uzbekistan, the Migration Service, Security Service and Customs Service of the Republic of Uzbekistan.

Agency on Tourism is a body of executive authority responsible for the provision of state services and managing state property, as well as law enforcement functions in the sphere of tourism.

Guide tourism activities by the Ministry of Sport, Tourism and Youth Policy of Uzbekistan.

The main functions of the agency for tourism:

The implementation of the priority directions of state regulation of tourist activity in the Republic of Uzbekistan, the exercise of creating and maintaining a single register of tour operators;

Implementation of the promotion of tourist products in the domestic and international markets;

Informing the established order of tour operators, travel agents and tourists on the tourist security risk in the country of temporary residence;

Create offices outside the Republic of Uzbekistan in the sphere of tourism;

The organization of reception of citizens, to ensure the consideration of oral and written applications.

The Ministry of Foreign Affairs of the Republic of Uzbekistan. Ministry of Foreign Affairs of the Republic of Uzbekistan is the executive authority responsible for drafting and implementation of the state policy and normative legal regulation in the sphere of international relations.

Ministry of Foreign Affairs of the Republic of Uzbekistan carries out its activities directly and through diplomatic missions and consular offices of the Republic of Uzbekistan, Mission of the Republic of Uzbekistan in international organizations [4].

The main tasks of the Ministry of Foreign Affairs of the Republic of Uzbekistan in the field of tourism are:

Protection of diplomatic and international legal means of rights, freedoms and interests of citizens and legal entities of the Republic of Uzbekistan abroad;

Promotion of relations and contacts with compatriots living abroad;

Organization in the territory of the Republic of Uzbekistan and abroad consular work;

Registration of the passport and visa documentation.

The Ministry of Internal Affairs of the Republic of Uzbekistan Ministry of Internal Affairs of the Republic of Uzbekistan is the executive authority responsible for drafting and implementation of the state policy and normative legal regulation in the sphere of internal affairs, including in the field of migration.

In tourism, the Ministry of Interior of the Republic of Uzbekistan shall:

– providing, within its powers to protect the rights and freedoms of man and citizen;

– a warning; suppression of administrative offenses; ensuring the protection of public order.

Migration Service (MS Republic of Uzbekistan) — executive authority, carrying out law enforcement functions, the monitoring and supervision in the field of migration.

MS Republic of Uzbekistan carries out its activities directly and through its territorial bodies.

The main objectives of the MS of the Republic of Uzbekistan in the field of tourism are:

Processing and issuing of foreigners and persons without citizenship documents for entry into the Republic of Uzbekistan;

Control over the observance of foreign citizens and stateless persons of the rules of residence of temporary stay in the Republic of Uzbekistan.

The same article referred to state regulation methods of tourist activities, such as:

The definition of priority directions of development of tourism;

Laws and regulations in the field of tourism;

Assistance in promotion of tourist products in the domestic and international markets;

Protecting the rights and interests of tourists, protection of their safety;

Promotion of staffing in the tourism sector;

The development of scientific research in the field of tourism;

Standardization and classification of objects of tourist industry;

The formation and maintenance of a single register of tour operators;

Cooperation with foreign states and international organizations in the sphere of tourism [5].

State regulation of tourist activity in the Republic of Uzbekistan carries out executive authority, with responsibilities for the state policy, legal regulation, the provision of public services — Agency for Tourism, ie Uzbektourism.



One of the ways of state regulation of tourist activity in the Republic of Uzbekistan — keeping the Unified Register of tour operators. Register shall be maintained Tourism Agency.

In order to protect the rights and interests of tourists in the territory of the Republic of Uzbekistan Article 4 of the Law of the Republic of Uzbekistan “On the bases of tourist activity in the Republic of Uzbekistan” requires tour operators to obtain financial security in the form of a contract of insurance of civil liability for failure or improper fulfillment of obligations under the contract of sale of the tourist or banking performance guarantees under the contract on the implementation of the tourism product. Details about the tour operator which has received such security shall be entered in the register.

Summing up the experience of the existing strategic development of tourism regions of Uzbekistan, which, as a rule, implemented within the framework of various kinds programs and concepts, according to the author, it is possible to offer a standard approach to the formation of regional strategic programs for the development of tourism with a systematic approach. In general, the sequence should be the following algorithm interrelated activities:

1. Identify the existing problems in the management of regional tourism.
2. Identify the problem on the basis of the main goals to achieve the desired result in the management of regional tourism.

3. Building a tree of objectives.
4. Determination of the main elements of the regional tourism management system.
5. The development of regional tourism management options.
6. Evaluation and selection of effective options.
7. Development of regional tourism management project in the framework of a regulatory document (for example, the target program).
8. Monitoring of the regional tourism management and control.
9. The adjustment in the event of deviations.

The proposed system allows the first stage to assess and identify the main goal. The proposed method of constructing the tree can be replaced by targets, for example, matrix method or a method of constructing the network models. In the second stage, this approach will highlight the essential elements which have major influence on the development and management of regional tourism. The third stage aims to develop options for the development of regional tourism, as well as the subsequent choice of the optimal variant. The fourth stage of developing and implementing project management, expressed in legal and regulatory documents of regional significance. The fifth step is necessary from the point of view of monitoring the implementation of the monitoring and adjustment purposes in the case of tourism development deviation from the set parameters. On a table-1 we can see key financial indicators for 2014–2015, enterprises.

Table 1. – Key financial indicators for 2014–2015, enterprises

OKONH	Name industry	Net revenue from sales of products (goods and services)	Cost of sales (goods and services)	Spending period	Other costs	Other income	Profit (Loss (-)) before income tax	Net income (loss (-))
90220	Hotel industry	137818629,6	67780112,9	54955817,0	4007332,4	7530424,5	18605791,8	11987305,1
91517	Sanatory institutions	107251968,5	80953367,0	23903880,2	977576,0	2516121,0	3933266,3	2743314,8
91610	Health institutions and recreational establishments	23633184,0	13749669,0	9218224,0	1241333,0	4668776,0	4092734,0	2987944,9
91620	Tourism	134898981,7	77279242,2	43827129,2	3927461,4	4731476,4	14596625,3	8391373,3

As we saw on this table-1 hotel industry were equal to 137818629,6, cost of sales (goods and services) were equal to 67780112,9, Health institutions and recreational establishments net income were equal to 2987944,9. Tourism net income were equal to 8391373,3.

Identification of the problem. In modern conditions of the Uzbekistan economy, which at the beginning of the XXI century is included in the post-industrial stage of development, and acquires the features of the so-called “service economy”, the need for development of the service sectors of the economy has a real need for both nationwide and at the regional level. Therefore, on a regional level of tourism development is necessary not only in the development of services and the transfer of raw materials orientation of the region’s economy, but also in the qualitative development of tourism, which has a significant multiplier effect, whereby it is possible to achieve significant results in improving the profitability of the region, as well as meet the needs of people in the town.

Setting goals. Based on the given problem can be identified following a global goal of strategic tourism management at the regional level: the development of regional tourism in accordance with modern requirements, as a mechanism to improve the efficiency of the regional economy, creation of favorable conditions for the region’s

population in terms of rest and recuperation, as well as development of international tourism.

Building a “tree of objectives”. Defining goals is long-term, goal-setting as an option so it is advisable to use “objectives tree” method for detecting the concentration of the main areas of management of development of regional tourism. Structuring objectives, according to the author, will clearly distinguish between existing sub-regional tourism management strategy.

Determination of the main elements of (sub) regional tourism. Tourism at the regional level may be considered as a set of subsystems, which directly affect the process of tourism development and management strategy should accordingly be in the process of management of development of these subsystems. Among the major sub-systems, which must be considered as affecting the strategic process of regional tourism development are the following: subsystem “tourism marketing at the regional level” subsystem “of natural and recreational potential,” subsystem “cultural-historical potential,” subsystem “tourism infrastructure” subsystem “scientific-educational and human resources”, subsystem “tourism enterprise”, the financial subsystem, “legal framework”, “security” subsystem, the subsystem “monitoring and statistics.”



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## Technology absorption capability evaluation of small and medium enterprises in Vietnam: Conditions from the State and Enterprises

**Abstract:** In the context of the world and the region, in the face of rapid integration and economic globalization, Vietnam must implement international commitments in free trade agreements. This will have a very positive impact to enterprises in the context of Vietnam is a developing country at low level, the enterprise is mostly absorbed in technology and most of it is transferred from abroad. According to economic experts, Vietnam currently has about 500,000 enterprises with over 90% of small and medium enterprises. It is forecasted that in the time to come, businesses will be more and more difficult when Vietnam officially joins bilateral and multilateral agreements with other countries. Therefore, how to measure and assess the technology absorption capability of enterprises in order to improve the technology capacity of enterprises in general and technology absorption capacity in particular is one sentence ask for both the S&T management agencies and for the enterprise itself in the context of deepening international integration.

**Keywords:** Technology absorption, Technology absorption capability evaluation, Small and medium enterprises.

### Current status of technology absorption capability of Vietnamese enterprises

*First, the limitations of the production link channel*

For the developing country, production linkage is an important channel for the spillover effect and absorption of technology from FDI enterprises to domestic firms. According to the experience of some countries, the most positive impact and absorption of technology is through contracts for the production of components and auxiliary accessories ordered by FDI enterprises for domestic enterprises.

According to a study conducted by the Central Institute for Economic Management (CIEM), the supply of raw materials (both raw and intermediate) to FDI enterprises and Vietnamese enterprises comes mainly from Asia where China is the largest supplier, accounting for 26.4%. This result is not surprising as China is a cheap source of input. However, this also demonstrates the loose production linkage between FDI enterprises and local firms in the supply of raw materials and this will also limit the spillover effects and absorption of technology from FDI enterprises to domestic enterprises.

The duration of the contract with the supplier also correlates with the existence of a production link. According to CIEM research, all contracts have an average term of less than 12 months. In the FDI sector alone, the contracts of FDI enterprises with foreign suppliers are higher than those of domestic suppliers. Such short contracts will limit the benefits that domestic firms can derive from spillover effects, not enough time to establish good working relationships and this is also a constraint of production linkage between FDI enterprises and domestic enterprises.

According to CIEM survey data, the supply of raw materials to FDI enterprises by domestic enterprises only accounts for about 1/3 of the total supply. In terms of product distribution channels, the proportion of products that FDI firms distribute through domestic firms is relatively low. This also demonstrates the limitation of the technology spillover channel from FDI enterprises as well as the limitation of technology absorption capacity of Vietnamese enterprises through FDI.

*Second, the limitations of technical work channels*

Up to now, one of the indicators used to measure technology absorption capability is the educational level or expertise of employees in enterprises and the indicators for technological innovation of enterprises through R&D activities.

Another limitation is that the channel of labor migration, skilled workers moving from FDI to domestic enterprises is considered as an important channel that can generate positive technological spillover effects. There are two ways to create a spillover effect and to absorb technology in this channel: workers leave the FDI enterprises to set up their own companies or transfer them to domestic enterprises, especially enterprises in the same industry. However, according to CIEM survey data, more than 30% of FDI enterprises surveyed said that migrant labor was mainly transferred to other FDI enterprises.

*Third, the limitations of the enterprise's R&D capability*

According to a survey by CIEM in 2013, the cost of R&D activities of enterprises in Vietnam comes from the owners of more than 86%, mobilized from credit sources of about 10%, from the state budget only about 3%. FDI enterprises spend about three times more on R&D than domestic ones. While domestic firms are mostly

small and medium enterprises limited financial power compared to FDI enterprises. This demonstrates the limited ability to invest in R&D and technology research and development capacity of Vietnamese enterprises compared to FDI enterprises.

Therefore, the conditions for the spillover effect will be more difficult due to the technology gap. Therefore, in order to absorb technology from FDI enterprises, the domestic enterprises themselves must strive to narrow the technology gap with FDI enterprises through their R&D capability.

Fourth, limitations in the assessment of technology absorption capability of enterprises

Businesses are not aware of the meaning of evaluation as a kind of work that is not enthusiastic work. Even evade and make it difficult to process the work, get information and evaluation.

Some of the information for the evaluation process is within the scope of business secrets, which are protected by law, so businesses do not want to provide information to outsiders, or provide inaccurate information that result in incorrect results when conducting analysis and evaluation.

Businesses passive in the assessment process so some methodological points are not discussed and feedback, leading to slow adjustment and improvement of assessment methods.

#### **Conditions for enhancing technology absorption capability of Vietnamese enterprises**

##### *First, on the State side*

The assessment of technology capacity in general and assessment of technology absorption capability in particular is complex and highly specialized, so often the enterprises do not have sufficient capacity and often hire consultants. It is often the case that the parties place a commission on trusting and coordinating. Therefore, the main consultant is the evaluator. Counseling agencies are usually universities, research institutes, or related institutions. At present, the number of consultancy units as well as skills and experience in the assessment field is limited.

Therefore, it is necessary to clearly define the requirements, tasks and interests of the subjects involved in the assessment. For businesses that are the most beneficiaries of the assessment process. Therefore, they must take an active role in the assessment. For groups of agencies such as ministries, branches, and scientific bodies..., there should be coordination and full information from the

enterprises to accurately assess technological absorption capability of enterprises. This group should also have the power to decide on the technology innovation of the business, so the evaluation results should be considered as an important source and should be used for policy making or policy making of state management agencies involved in technology renovation activities of enterprises.

For the units conducting the assessment, it is necessary to invest in intensive training to improve the capacity of officials and experts to conduct the assessment. There should be provision for sharing of information among evaluating bodies. In addition, it is necessary to build a system of expert knowledge for unified evaluation on a national scale. The Ministry of Science and Technology needs to put the content of technology assessment into operation regularly every year so that the evaluation results are continually updated regularly and form a unified database across the country. Furthermore, it is also necessary to define a system of uniform criteria for evaluation and to develop a rating system that quantifies the criteria for assessing the technology absorption capability of enterprises, especially small and medium enterprises by sector.

It is necessary to add specific conditions to organizations that perform advisory and evaluation tasks, especially those on organization and personnel, and must have a database of specialists who can serve the evaluation tasks.

Second, the conditions on the side of the enterprises

For an enterprise directly owning the technology to produce products and goods or services, the assessment will help the business know the current state of its technology competency relative to its competitors in the same field. Therefore, the enterprise is the subject of the evaluation process and has full discretion in making decisions about its technology. Businesses are also the most beneficiaries of the assessment process, and they must take an active role in the assessment.

Today, businesses, especially small and medium enterprises, are often not paying enough attention to evaluating. Therefore, enterprises need to be empowered to see that they are the most beneficiaries of the assessment and should take an active role in this activity. In addition, evaluations should be considered as an important source of information that is used for the decision-making process or policy formulation of relevant government agencies.

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